IMMobilization and Catheter Guidance for
BREast BRACHytherapy
USIng PATient-Specific Templates

by

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Abstract

Brachytherapy is an important method of breast cancer treatment; however, improvements in both treatment planning and delivery are needed. The procedure involves insertion of catheters in the tumor site, which, in current practice, is prone to clinically significant error. In order to improve on contemporary catheter placement accuracy, integration of pre-operative imaging, supplemented by computerized surgical planning and mathematical optimization were used to develop and test an intra-operative immobilization and catheter guidance system.

A custom-template specific to each patient with optimally-placed guide-holes for catheter insertion was designed and fabricated for use on phantom studies. Template creation is based on a virtual reality reconstruction of the patient’s anatomy from computed tomography imaging. The template fits on the patient’s breast, immobilizing the soft tissue, to provide pre-planned catheter insertion holes for guidance to the tumor site.

Agar-based phantom and target models were used for quantitative validation of the template using computed tomography imaging for template planning and validation. Planned catheter tracks were compared to post-insertion image data and distance measurements from target location were used to create an error measure. Using the latest template design spanning multiple experiments resulted in a mean of 2.6mm,
$95\% \text{ CI} = 3.1 - 2.2$, which is within the clinically acceptable range of $3 \text{mm}$, as validated with our clinical collaborators.

Validation of the brachytherapy template on phantom tissue produced clinically acceptable results. Use of a patient-specific template for breast brachytherapy is feasible and may improve the procedure accuracy and outcome. This work has been a proof-of-concept, providing evidence to support moving forward with the next phase of patient-specific breast template trials for use in brachytherapy.
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Statement of Originality

I hereby declare that this submission is my own work and to the best of my knowledge it contains no materials previously published or written by another person, except where due acknowledgement is made in the thesis. Any contribution made to the research by others is explicitly acknowledged in the thesis. The thesis expands on work perviously published with myself as the first author in the International Journal of Computer Assisted Radiology and Surgery [29].
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Chapter 1

Introduction

1.1 Motivation

Breast cancer is the most prevalent form of cancer in women, with one in nine Americans developing the disease during their lifetime [38]. Radiation therapy has become a routine component in the breast cancer treatment regimen. However, local control of the disease using radiation therapy depends on achieving adequate full-tumor dose coverage [39]. Brachytherapy is a form of radiation therapy that involves inserting sealed radioactive sources into the tissue via catheters. The success of brachytherapy relies on accurate insertion of the radioactive seeds in which the immobilization of the breast and guidance of the catheters are of key importance. The goal of this project is to integrate image-based computerized planning with effective intra-operative catheter guidance and breast immobilization.

1.2 Proposed Method

We propose to create a custom-made template, specific to each patient, with optimally placed guide holes for catheter insertion. Creation of the template is based on a virtual
1.3. THESIS OBJECTIVES

reality reconstruction of the anatomy from computed tomography (CT) imaging. The concept of patient-specific templates has been previously investigated in orthopedic surgery [15, 9, 27] and neurosurgery [31]. We propose to adapt this concept for breast tissue by implementing a patient-specific template that fits over the breast, immobilizing the soft tissue and providing insertion holes for guidance of the catheters to the tumor sites.

In order to test the technical feasibility of this idea, we used standard biopsy breast phantoms as well as produced agar-based phantoms with target sites in clinically representative locations. The phantom breast tissue was imaged using computed tomography (CT). The breast and embedded targets were reconstructed in three dimensions and a cast that would serve as the guide template was designed over the breast surface. Catheter trajectories were planned to intersect embedded targets to determine guide holes and short guide sleeves locations on the virtual enclosure model, resulting in a patient-specific template for breast immobilization and catheter guidance. The virtual template model was printed using a 3D rapid prototype printer. The printed template was placed over the breast and catheters were inserted through the guide holes into the target lesions (Fig. 1.1). The breast, template, and catheters were again imaged using CT and the accuracy of needle placement was assessed using the distance from the target as the measure of error.

1.3 Thesis Objectives

The purpose of this work is to contribute to the breast brachytherapy protocol by simplifying the catheter placement and improving patient comfort. Through the use of a patient-specific template in which pre-planned catheter insertion site have been
made, we hope to improve patient care. This work seeks to demonstrate that the use of patient-specific templates in breast brachytherapy is a feasible alternative to current practices.

1.4 Thesis Contributions

A summary of the contributions of this thesis are as follows:

- Designed a patient-specific template suitable for brachytherapy catheter insertion. The template includes long guide tracts for better catheter accuracy, integrated markers for proper template placement, and a breakaway design for
simple removal post-catheter insertion.

- Developed and implemented a template creation workflow. Created an easy to follow workflow using available medical imaging software from Materialise (Leuven, Belgium).

- Validated the use of a patient-specific template for breast brachytherapy catheter insertions. Using the phantom tissue, we were able to produce an accuracy of 2.9\text{mm} for catheter placement.

1.5 Thesis Outline

This thesis presents breast brachytherapy patient templates, describes the experimental setup and validation method, and discusses the collected results. The thesis is divided into six chapters as follows:

- **Chapter 2 Background**: contains background information on breast cancer and its treatment as well as discusses prior work on immobilization and guidance systems used for breast radiotherapy. Prior work with regards to patient-specific templates will also be highlighted.

- **Chapter 3 Methodology**: details the materials, software, techniques, and workflows utilized for validation of patient-specific template in brachytherapy.

- **Chapter 4 Data Collection and Experimental Design**: describes the set of tests used for validation of the proposed patient-specific template. Data acquisition is detailed along with an explanation of error calculations.
• **Chapter 5 Results:** delivers the collected data on catheter insertion errors for the patient-specific template.

• **Chapter 6 Conclusions and Future Work:** summarizes the findings and conclusions drawn from template testing and discusses possible areas of future work that can aid in preparing this work for clinical use.
Chapter 2

Background

Breast cancer is currently the most prevalent form of cancer in women. One in nine American women will develop breast cancer during her life time [38]. Current treatments for breast cancer include surgery, chemotherapy, and radiation therapy. This thesis will not discuss any of the pharmaceutical aspects of treatment and will instead focus specifically on radiation therapy.

Breast cancer treatment currently consists of surgical tumor removal followed by radiation therapy. Standard whole breast irradiation, however, requires six to seven weeks. The long treatment causes many candidate patients to rely on other quicker methods of treatment instead, such as radical breast removal surgery [7]. Time, distance and monetary constraints caused by work or distance to clinic can restrict patients willing to undergo radiation treatment. Brachytherapy, a radiation therapy which requires only one week, has the potential to become the standard adjunct to surgery. Brachytherapy relies on accurate catheter insertion and dose coverage; thus, immobilization and guidance are key factors in brachytherapy treatments.

This section will review current immobilization and guidance systems developed for radiation therapy with an emphasis on radiotherapy for breast cancer.
2.1 Management of Breast Cancer

Breast cancer management has evolved from radical surgery to breast-conserving techniques. The original standard for breast cancer treatment consisted of a full mastectomy - the complete removal of one or both breasts. Mastectomies are a very effective treatment method, but radical surgery is also very traumatic for the patient. Lumpectomy evolved as a more conservational surgical approach, which spares the breast by removing only the tumor and a region of surrounding tissue. The new standard of care consists of a lumpectomy followed by whole breast irradiation. The conservation of the breast during cancer treatment has become subject of great interest recently due to morbidity associated with mastectomies.

Radiotherapy, a widely practiced breast-conserving treatment used for breast cancer, uses ionizing radiation to damage tumor cell DNA \[16\]. Radiation therapy works on the principle that cancerous cells are apt at reproduction yet do not repair effectively, unlike non-cancerous cells. Thus, using ionizing radiation to damage cancerous cells that are unable to repair can allow for tumor death while allowing healthy cells to repair.

Currently, there are two main types of breast radiation treatments - external beam radiotherapy (EBRT) and brachytherapy. EBRT delivers radiation externally making it dangerous when used to treat breast cancer as both the skin and vital organs are situated near the chest wall. However, EBRT is the current standard of treatment (along with a lumpectomy) for breast conservation \[46\]. In breast cancer, an external beam delivers a dose of radiation to the whole breast and is performed over a period of 5 to 7 weeks \[43\]. The treatment produces high local control rates that are greater than ninety percent and provides strong cosmetic results \[6\]. Brachytherapy,
conversely, is an internal procedure which reduces damage to the skin and allows for the localization of the radiation dose around the tumor as opposed to the whole breast; minimizing the radiation dose given to vital organs [6]. Radioactive sources, commonly referred to as “seeds”, are either implanted or temporarily placed in the targeted tissue. These seeds emit radiation outward, localizing the radiation to specific areas. Brachytherapy also has the advantage of reducing patient hospital time as the treatment can be completed over the course of a week rather than several.

Breast brachytherapy is usually performed using a high-dose rate (HDR) technique. The technique is performed using a remote afterloader that pushes radiation sources through inserted catheters leaving them in specific positions for pre-calculated amounts of time and then removing them. The HDR afterloader is controlled from a separate room from which the technician can view the dose plan being carried out, thus reducing exposure to the clinical staff. The HDR remote afterloader follows a dose plan that is pre-defined by the medical physicist and confirmed by the oncologist. Radiation source dwell times and locations are determined as part of the dosimetric design. The dosimetry plan is created in order to cover an optimal amount of the tumor cavity while reducing dose to healthy and vital organs.

There are other considerations when analyzing the differences between brachytherapy and external beam radiation. Due to the physics of the treatment, using brachytherapy produces an inherently non-uniform dosimetry. Dosimetry is the calculated absorbed dose in tissue caused from the exposure to ionizing radiation. Strengths and weaknesses arise from this lack of dose homogeneity. Brachytherapy procedures can be planned such that the highest dose is delivered to a central target, ideally where the highest concentration of tumor cells should be. However, the localization of this
high dose can also cause fat necrosis, excess fibrosis, and poor wound healing due to increased radiation[16]. The localization of the tumor will also play a larger role in brachytherapy as misplaced seeds will radiate more healthy tissues than target tissues. Compared to the errors introduced by external beam, errors in the brachytherapy are less forgiving.

A correctly planned brachytherapy procedure has the potential to perform better than EBRT because of reduced treatment time and costs. In 2008, the California Technology Assessment Forum performed a comprehensive review on the safety and efficacy of brachytherapy. They concluded that while this treatment could potentially outperform external beam radiation, there are currently not enough long-term studies to support this conclusion [38]. While there are clear strengths and advantages in using brachytherapy for breast cancer treatment, the development of improved brachytherapy techniques could potentially aid in increasing the effectiveness and the applicability of this therapy.

2.1.1 Dosimetry Guidelines

Dosimetry guidelines have evolved over time, with current techniques utilizing 3D planning software to assign dose coverage plans. Using 3D brachytherapy treatment planning software the target volume is first defined and then seed dwell times are determined so as to achieve optimal dose coverage. Current dosimetric coverage protocol requires that ninety percent of planning treatment volume (PTV) receives at least ninety percent of the prescription dose[44]. The PTV is defined as the lumpectomy cavity plus a 1.5 − 2.0cm margin, but constrained by size of the breast[45]. Ideally the dose should be limited to the PTV while excluding chest wall structures
and reducing dose exposure to within 5\text{mm} of the skin\cite{44}.

\subsection*{LDR vs HDR}

Low dose-rate (LDR) brachytherapy involves using low dose radiation sources that emit radiation at a rate of up to 2 Grays per hour\cite{37}. High dose-rate (HDR) brachytherapy is characterized by using high dose radioactive seeds that emit radiation at a rate that exceeds 12 Grays per hour. The use of LDR in breast brachytherapy has been mostly abandoned in favor of high dose-rate (HDR) brachytherapy. HDR provides improved control of dosimetry, better radiation safety, and shorter treatment times making it a stronger brachytherapy method\cite{44}.

\subsection*{2.1.2 Evolution of Brachytherapy}

The first published cases of brachytherapy breast conservation treatments were in the 1920s by Geoffrey Keynes \cite{13}. The treatment consisted of placing radium needles throughout the entire breast. Keynes reported high control rates, acceptable cosmetic outcomes and survival rates comparable to the radical mastectomy. After working with this treatment for thirteen years, Keynes regarded radium needle treatments as being preferable to surgery as it provided equivalent results without the required breast removal. The onset of World War II forced the removal of radium needles from hospitals to secret locations, halting research on brachytherapy for breast cancer \cite{16}. For the following 30 years, mastectomies were the primary form of breast cancer treatment.

The evolution from radical surgery to lumpectomy came in the 1970s with treatments consisting of gross tumor removal followed by whole breast radiation treatments
The theory behind this treatment method is that by removing the primary tumor through surgery, and then radiating the whole breast, one could disinfect the entire breast and control the disease. Breast brachytherapy was not re-implemented until 1991 when a woman at the Conference and Clinic at the Ochsner Clinic in New Orleans requested an alternative to external beam radiation therapy [45]. The woman required a treatment that did not extend over several weeks since the closest linear accelerator was 8 hours from her home.

Breast conservation treatments using external beam radiation as its radiotherapy solution is safe and effective. Although it is a proven technique, only thirty to fifty percent of candidate patients opt for breast conservation treatments [7]. The extensive time-requirements for this treatment make it difficult for most women to receive it. The short time requirements associated with brachytherapy and the initial results of the technique are very promising making it a highly desirable treatment option.

2.1.3 Current Trends

There is no current consensus on which accelerated partial breast irradiation (APBI) treatment works best. The techniques that seem to outperform others are techniques which incorporate image guidance for treatment [6]. Image-guided procedures allow for the localization of the tumor and help to optimize the dosimetry. There are two main implementations of brachytherapy for breast cancer: multi-catheter implants and a single catheter insertion [28].

Multi-catheter interstitial brachytherapy was the first APBI technique developed. The technique involves the placement of multiple catheters through and around the lumpectomy site for optimal dose coverage. In order to simplify the procedure, a
single intracavity balloon-catheter was developed called the mammosite (Fig. 2.1). The hope was that this device would shorten the required learning curve for catheter insertion as well as increase the reproducibility of placement. Early results show that the mammosite is both technically easier for the clinician and more comfortable for the patient [6]. The SAVI product tries to combine the strengths of both of the other widely used techniques. The SAVI applicator (Fig. 2.2) is a new device that combines both a multi-catheter insertion delivery with the placement of only one catheter like the mammosite [32]. Both methods are still in their infancy and require further research and development.
2.2 Immobilization and Guidance

Controlling local disease using radiation therapy depends on delivering adequate full-tumor coverage, as has been made clear by many retrospective studies which show the correlation between local recurrence and inadequate coverage [39]. The ability to consistently localize the tumor site for eventual full irradiation is very important in radiation therapy. Immobilization and guidance play a key role in proper patient treatment by providing reproducible target localization setups. New immobilization techniques have allowed clinicians to immobilize almost any area of the body to approximately $3 \text{ mm}$ [39]. The importance of immobilization and guidance is connected to the large dose-response curve. Many studies have shown that dose reductions of around three to five percent to a tumor site can have significant effects on local recurrence rates [8, 3, 21].

Patient immobilization can be used to limit patient motion while aiding in tumor localization for treatment, thus reducing treatment error. Immobilization devices not only perform the task of fixating the patient, but can also reduce daily patient set-up and increase patient security in their treatment choice.

Immobilization techniques and devices have changed significantly over the years for many of the radiotherapy procedures. Initial methods included the use of simple tools like: tape, support cushions, and breath regulation [39]. For the purposes of this review, we will limit the scope of immobilization devices to those applicable for breast tissue.

Immobilizing breast tissue relative to other internal structures is a difficult task,
due to the deformability of breast tissue. Many of the external beam breast radiotherapy devices examined in this section are involved in immobilizing of the breast. External beam radiation treatment has had significantly more time to mature compared to brachytherapy, thus more devices and techniques are available for immobilization. When working with brachytherapy, the literature suggests that a higher priority is placed on the guidance tools and techniques employed leaving immobilization at a lower concern. Tumor localization is the main objective of both immobilization and guidance so both are reviewed below.

Patient immobilization is relevant to many different fields, from patient positioning to specific tissue immobilization devices. Positioning of the patient during radiotherapy is a much debated topic. The patient’s arm is usually extended overhead to expose the axilla during external beam radiation. Positioning the patient in a supine position, lying on their back, is the common method for treatment but a current push for prone position delivery [25, 22, 14] is emerging. Immobilization devices include: thermoplastics (Fig. 2.4), the Kuske breast applicator (Fig. 2.3), custom-casts, evacuated bead bags, brassieres (Fig. 2.5), and vacuum-sealed devices. Most of the immobilization devices are used for external beam treatment. The Kuske breast applicator is currently the only known widely-used brachytherapy immobilization device.

2.3 Radiotherapy Immobilization and Guidance Systems

A literature review of the current immobilization devices and guidance techniques used in breast cancer radiation treatments will follow. Although the use of guidance and immobilization both aim at better localization and treatment of the tumor site, the two topics will be discussed separately. The first section of this review will discuss
2.3. RADIOTHERAPY IMMOBILIZATION AND GUIDANCE SYSTEMS

Figure 2.3: The Kuske applicator which consists of an adjustable template with integrated guiding template that ensures an exact placement of needles for brachytherapy.

Figure 2.4: Thermoplastic breast positioning is primarily intended to hold the breast up and away from the chest wall, reducing both skin folds and unwanted radiation dose into the patient’s lung and heart.

Figure 2.5: The Treatment Brassiere positions the breast into a reproducible shape while moving the contralateral breast away from the beam. [4]
2.3. RADIOTHERAPY IMMobilIZATION AND GUIDANCE SYSTEMS

breast immobilization devices while the second section will deal with imaged guided intervention techniques.

2.3.1 Breast Immobilization

The breast consists of soft tissue, blood vessels, lymph vessels, and the underlying pectoral muscle. Due to the malleable nature of the tissue, it is very hard to easily immobilize for treatment. Fixating the tissue is not the only challenge, since the device must be compatible with the equipment used during the procedure. This means that for brachytherapy techniques, the device should work with multiple imaging devices, such as CT and ultrasound. For external beam treatments, the devices should allow for unobstructed imaging of the target area and should be unaffected by the radiation passing through the device.

Immobilizing the breast for radiotherapy is an important aspect of treatment. Providing a stable target ensures the correct dose is delivered to the target tissue. External beam radiation has the potential to substantially damage important, healthy tissues since the breast is situated near the heart, lung and other important organs. Tissue sparing can be incorporated by immobilizing the breast using a method that moves the breast farther from the chest wall. Fixation of the breast for brachytherapy helps to compress the tissue for easy cavity localization.

Some of the devices commonly used in breast cancer radiotherapy treatments will be reviewed below.
2.3. RADIOTHERAPY IMMOBILIZATION AND GUIDANCE SYSTEMS

Vac-Fix Immobilization

The Vac-Fix system is an air-tight bead-filled bag. The bag is malleable in its natural state but becomes firm when the air is removed. The device is placed on the patient and the air is removed to create firm support contoured to individual patients. Once used, the device can be put back to its flexible state or left rigid for the duration of the treatment. The ability to preserve the device’s shape also allows for the re-use of it as a patient-specific support system to maintain uniform treatment over several weeks. Although Nalder et al. looked at the use of a vac-fix immobilization device and compared it to their regular technique [26], more research into the vac-fix system for breast immobilization must be performed before a conclusion on its effectiveness for radiotherapy can be made.

Thermoplastic Immobilization System

Thermoplastics have been extensively used in head and neck radiotherapy treatments. A thermoplastic is a polymer that turns liquid when heated and hardens when cooled. An advantage of the device is that it can be reset and remolded for multiple uses. Thermoplastics can be activated when placed in hot water and, once malleable, have a certain amount of time before they set into a specified shape. The use of thermoplastics for breast immobilization is a relatively new concept with little literature available. The inaugural studies on the use of thermoplastics for breast immobilization in conjunction with radiation therapy are being done by the Strydhorst group [36]. The thermoplastic is first dipped in a hot water bath then placed on the patient’s breast and formed into a patient-specific template that helps move the breast away from the chest wall.
2.3. RADIOTHERAPY IMMOBILIZATION AND GUIDANCE SYSTEMS

Strydhorst’s group performed a study to evaluate the effectiveness of thermoplastic as a breast immobilization technique. Using 4D-CT images of the breast with the thermoplastic shell, infraction motion caused by breathing was captured and analyzed. Initial results suggest that the thermoplastic does aid in immobilization of the patient for radiation therapy. Further research into this method is required before a conclusion on its effectiveness can be formed.

**Kuske Applicator**

The Kuske applicator is the current gold standard for template-guided brachytherapy catheter insertion. The Kuske applicator consists of an adjustable template with integrated guiding template that aids in placement of needles for brachytherapy. The rigid template should be placed such that the lumpectomy cavity is at the center of the template coordinate system. The device serves as both an immobilization device and a guide tool. Once the immobilization template is placed, a guide template is slid into the device to help create parallel catheter insertions. This device, although a guide, is not discussed in the guidance section since it does not perform the task of true guidance - its only task is to create parallel catheter tracts and not to optimally place catheters for full tumor dose coverage. The template applicator is most commonly used in conjunction with imaging guidance. Although the template has been effective for brachytherapy delivery, it can be quite uncomfortable for patients based on feedback to our clinicians. The template also cannot be employed universally such as when dealing with very small breast or very large breasts. Currently, there are no other options readily available for brachytherapy templates.
2.3. RADIOTHERAPY IMMOBILIZATION AND GUIDANCE SYSTEMS

2.3.2 Image-Guided Breast Brachytherapy

Whole-breast irradiation is a treatment that most researchers are veering away from due to the large time commitments required to implement the method. Researchers are instead considering the advantages of brachytherapy, if the target can be properly localized to optimize the dose provided to the target tissue. In general, brachytherapy procedures that incorporate image-guidance systems have historically performed better than those without guidance [28]. Recent advances made in imaging technology have increased the potential for better guidance during catheter insertions. In conjunction with imaging systems, stronger computer simulation programs, and the development of improved image processing techniques, guidance has been greatly improved. Using both imaging and pre-planning dosimetry software together produces well-placed catheters and an effective dose distribution.

CT-Guided Brachytherapy

CT-guided brachytherapy, a method where CT scans are used to plan and guide catheter placement, although now the gold standard, was not originally the preferred method of guidance. In 2005, Cuttino’s group looked at the use of CT guidance compared to other conventional methods used at the time [5]. Catheter guidance was originally performed under fluoroscopy. Orthogonal films were used for dosimetric planning with surgical clips delineating the cavity site, while dummy seeds were used to distinguish the catheters. The original method was compared to the CT-guided and planned method. The group found that CT-guided and CT-based dosimetry was able to increase the percentage of patients satisfying all dosimetric goals from 42% to 93% as well as increase the mean dose coverage from 89% to 95%. A statistically
significant increase in patient dose coverage was found, making CT guidance a strong technique for catheter insertion.

The now common method of brachytherapy planning is the use of two CT-scans to properly align the catheters and plan dose distributions. The first imaging step, performed prior to catheter insertions, locates the tumor site in order to pre-plan the dose distribution to give the clinician a plan for the insertions. This step is performed prior to catheter insertions and gives the clinician a plan for the insertions. The second imaging step is used to locate the inserted catheters and update the planned dosimetry according to the true catheter locations.

**Hands-Free 3D Ultrasound Guidance System**

Although CT-guidance performs very well, the requirement of two CT-imaging steps is logistically difficult. CT-imaging a patient involves having to move the patient from the brachytherapy suite to a CT-ready room, consuming time and manpower and therefore increasing procedural costs. De Jean’s group at the Robarts Institute at the University of Western Ontario created a hands-free 3D ultrasound (3D-US) probe (Fig. 2.6) for brachytherapy catheter insertion to replace CT imaging requirements [12].

The goal of the project was to replace all steps requiring CT with the newly developed 3D-US while leaving the rest of the procedure intact. The 3D-US scanner was designed to fit the Kuske breast applicator set as seen in Figure 2.6. A comparative study was performed to assess the efficacy of the 3D-US probe versus CT images. A proof-of-concept experiment using phantoms was performed showing the 3D-US’s ability to accurately image and measure tumor volumes. Localization of the
2.4. PATIENT-SPECIFIC TEMPLATES

Figure 2.6: Schematic illustration of the 3DUS translation scanner mounted on top of the Kuske breast applicator set [12].

catheters was also possible in US and performed similarly to those in CT. The US system’s ability to produce comparable imaging data to the CT while removing the need to transport the patient is promising. Transportation of the patient requires time, money, and could cause problems with tissue-shifting. Clinical trials to test this device are currently underway [12].

2.4 Patient-Specific Templates

Personalized guide templates are designed using pre-operative images, usually CT, so as to fit uniquely to the patient’s anatomy. Guides are designed and embedded into the template using computer visualized, pre-planned trajectories to aid in surgery. The concept of patient-specific guides has been developed in polycarbonate using milling machines [30] as well as new rapid prototyping technologies, which work via the printing of plastic in thin layers to build an object up layer by layer. The advent of widely available rapid prototyping equipment that can deliver more complex designs, has overshadowed milling, which is infrequently used for the production of patient-specific templates [2].
Patient-specific templates were designed to fill a need in orthopedic surgeries. The goal of this novel technique is to remove the need for intraoperative image navigation systems that can be cumbersome, slow, and difficult to learn [18]. Conversely, both guidance or navigation in orthopedic surgeries has been shown to improve patient outcomes [2]. The patient-specific template provides the needed guidance while removing bulky equipment from the operating room and simplifies the procedure. Many studies have shown the efficacy of personalized templates for orthopedic surgeries [18, 2, 15, 9, 27].

2.5 Summary

Radiation therapy is a prominent technique employed in breast cancer treatment. Radical surgeries are being performed less frequently in favour of breast-conserving treatments. In these breast conserving treatments, accurate tumor localization and guidance can greatly improve treatment outcomes by ensuring optimum dose coverage. The inherent issues with the soft tissue of the breast and its location near vital organs make immobilization and guidance important procedural requirements for proper dose distribution.

Currently a lumpectomy followed by whole breast external beam radiation is the de facto treatment for breast cancer. However, due to the lengthy time commitments required for whole breast radiotherapy, many candidate patients do not opt to receive this treatment. Promising brachytherapy research may allow this one week treatment option to become standard practice. With better localization and guidance techniques this treatment can also reduce radiation to healthy tissue.
2.5. SUMMARY

Multiple immobilization devices exist for external beam treatment, but the standard of care for brachytherapy consists of using the Kuske applicator in conjunction with an imaging modality. Guidance systems are improving, but the option for better stabilization in brachytherapy is still available. Patient-specific templates have effectively been used in the orthopedic realm, yet there have been no studies on its applicability to soft tissue. Validation of the feasibility of patient-specific templates for soft tissue applications such as breast brachytherapy catheter insertion is needed. Before brachytherapy can become the gold standard of care, longer treatment studies are required along with improved fixation and guidance systems.
Chapter 3

Methodology

The goal of this project is to integrate pre-surgical computer plans and create a method of immobilization and guidance. The resulting protocol, which can be seen in Fig. 3.1, was established to eliminate one pre-operative patient visit and improve the comfort of the patients during the procedure. The central idea uses patient-specific custom-made immobilization casts with embedded guidance holes for the brachytherapy catheters. The surface of the breast can be segmented using pre-operative computed tomography (CT) images and the reconstructed surface used for template creation. The pre-operative CT also allows for the localization of the tumor site. A patient-specific cast encompassing the breast is then printed in three dimensions using a rapid prototype printer. The printed cast also contains pre-planned catheter insertion holes. The concept of patient-specific templates has been investigated in orthopedic surgery [9, 15, 19, 30, 2, 18] and neurosurgery [31]. To our best knowledge, there has been no research into adapting this concept for a soft tissue, such as the breast. We propose to extend this concept for breast tissue by implementing a patient-specific template that fits over the breast, immobilizes the soft tissues, and provides insertion holes for guiding the catheters to the tumor sites.
3.1 Clinical Workflow

The workflow designed for catheter insertion with patient-specific breast brachytherapy template is highlighted in Fig. 3.1. Clinically, the workflow would be similar to current brachytherapy treatment procedures (Fig. 3.2). However, we hope to remove the need for multiple imaging sessions and to improve patient comfort. In current brachytherapy practice, the patient is first imaged in CT to discern the tumor site, and then a catheter insertion plan and a dosimetry plan is created. The patient then undergoes catheter insertion using the Kuske applicator, usually performed under some form of image guidance. Following catheter insertion, the patient undergoes a second CT imaging session to confirm catheter locations and to update the dosimetry plan. The proposed clinical workflow (Fig. 3.1) would commence in a similar fashion with
CT imaging, catheter planning, and dosimetry. In our proposed method, however, the catheter insertion plan would be incorporated into designing the patient-specific template. The template would act as an immobilization device for the soft tissue as well as a guidance device for catheter insertion. This would eliminate the need for the Kuske applicator and possibly the need for intra-operative and post-insertion imaging. Thus, irradiation may commence immediately following catheter insertion.

Figure 3.2: Current brachytherapy workflow used in a clinical setting

3.2 Overview of Experimental Workflow

Both standard breast biopsy phantoms from CIRS (Norfolk, Virginia, USA) and agar-based phantoms produced in-lab were used for validation of the patient-specific
templates. All the phantoms contained embedded objects, in clinically representative locations, that represent tumor sites targeted in brachytherapy. The phantom breast tissue was imaged with CT and visualized using modeling software. The breast and embedded targets were reconstructed in three dimensions and an enclosure to serve as the template was designed over the breast surface. The catheter trajectories were planned to target the tumor sites (Fig. 3.4(a)) and their intersections with the breast surface were identified (Fig. 3.4(b)). Guide holes and short guide sleeves were added to the virtual enclosure model (Fig. 3.4(c)), resulting in a patient-specific template for breast immobilization and catheter guidance. The virtual template model was printed using a 3D rapid prototype printer. The printed template was placed over the breast and catheters were inserted through the guide holes into the target lesions (Fig. 3.4(d)). The tissue, template, and catheters were then all imaged using a CT machine and registration techniques were implemented in order to assess the quality of catheter placement.

3.3 Software

Creation of a 3D template and post-surgical validation of inserted catheters requires various visualization and modeling tools. In order to create the patient-specific template, two software tools created by Materialise (Leuven, Belgium) are used. Mimics 13.0 and Magics 14.01 were used for 3D modeling of the tissue, template creation, and post-operative validation.

Mimics was designed for medical image processing. The processing and editing of image data (CT, \( \mu \)CT, MRI, etc.) is easily and accurately done using Mimics. The construction of 3D models, powerful segmentation tools and measurements tools
Figure 3.3: Experimental workflow with phantoms for validation of patient-specific templates

make this a strong platform for medical image analysis. *Mimics* can also easily export your 3D data to a wide range of output formats.

*Magics* is a rapid prototyping software that allows for the importing of various modeling formats as well as easy exporting for rapid prototype printing. *Magics* contains a variety of modeling tools for 3D model creation, optimization, parts analysis, and repair. We choose these tools because they have been used extensively in the field of patient-specific guide design [9, 15, 27, 19, 18].
3.4 Catheter Analogue

To evaluate the validity of a patient-specific template on soft tissue, multiple experiments are needed to show significance. As clinical-grade supplies are rather expensive, a suitable analogue of 18-gauge catheters and needles were created and verified with clinicians to be suitable. Twelve precision miniature stainless steel-welded and drawn
3.5. BREAST TISSUE ANALOGUE

(a) Catheter on bottom and needle anologue on top  (b) Close up image of catheter anologue

Figure 3.5: Catheter Analogue

tubing sized at 18 GA, which have an outer diameter of 1.27mm and an inner diameter of 0.838, were purchased to simulate the brachytherapy catheters (Fig. 3.5(b)). Miniature stainless steel drive shafts with a length of 12” or 304.8mm and an outer diameter of 0.794mm were purchased to represent the needle (Fig. 3.5(a)) that usually runs through the catheter.

3.5 Breast Tissue Analogue

In order to validate the feasibility of patient-specific templates, artificial breast tissue models, also known as phantoms, were needed. In order to properly simulate breast tissue in consistency and imaging potential, two standard breast biopsy phantoms were purchased (Fig. 3.6) from CIRS (Norfolk, Virginia, USA).

Using the purchased breast biopsy phantoms as models, a large quantity of agar-based phantoms were produced in-house. Three differently sized molds were created using the originally purchased biopsy phantom for overall shape (Fig. 3.7). The three molds were designed to include diversity in breast sizes. All of the molds were created
3.5. BREAST TISSUE ANALOGUE

(a) Triple modality biopsy phantom made by CIRS. Phantom has physical density and attenuation characteristics of a breast under x-ray, ultrasound and MRI

(b) Agar-gelatin phantom produced in-house to simulate breast.

Figure 3.6: Two types of phantom models on which patient-specific templates were tested

by segmenting the breast contour from a CT image of the purchased breast phantom. The segmented contour was then easily rescaled to produce a larger and smaller mold for printing.

The small mold was created as close to a 32A cup size as possible. The mid-sized mold was an unscaled a reproduction of the purchased breast biopsy phantom for further phantom creation. The plus size mold was created to simulate a cup size of 38DD. A large spectrum of breast sizes was needed, because according to our clinical collaborators, the biggest incidence of issues with current treatment involved breasts of irregular size and shape.

The in-house phantoms were produced using agar and gelatin. Combining 80 parts water, 2 parts agar, 4 parts gelatin, and 1 part glycerol over a hot plate makes a suitable tissue substitute that can be imaged easily with CT and, if necessary, with
3.5. BREAST TISSUE ANALOGUE

Figure 3.7: Phantom production molds created using shape of originally purchased biopsy phantoms and created size differentials using quantitative volume data on small and plus sized breasts.

ultrasound. Once the water is heated to 75° C, the agar and gelatin are slowly added to avoid clumping. The glycerol is added after all the agar and gelatin have dissolved fully. The mixture is then stirred to ensure proper incorporation of the glycerol and then left to cool to 50°C. The mixture is then poured into the fabricated breast molds and left to set in refrigerator for at least 12 hours.

To simulate a tumor site, the tips of agar filled latex gloves were placed into the breast phantoms prior to cooling at random locations to mimic reality. The embedded target design was updated after the first two experiments to strengthen the error calculation. Experimental rounds 3 through 6 received small CT compatible spheres as surrogate tumor site markers. The targets varied in diameter from around 1.2mm to 2.0mm. The tumor sites were selected over the whole breast, both close to
the insertion site and far from the insertion site.

Figure 3.8: CT-compatable marker used as localization points in breast tissue

3.6 Template

From pre-operative CT imaging, the patient’s anatomy including the breast surface, tumor, and surrounding structures are graphically reconstructed in three dimensions on a computer. The optimal position of the catheters is computed to provide optimal dose coverage of the tumor. In a virtual reality computer interface, a template mask is designed to cover the breast surface with guide holes for the catheters. Finally, the template is printed using three-dimensional rapid prototyping technology. Upon sterilization, the template is placed on the patient’s breast and catheters can be inserted through the guide holes.

The key to the proposed technique is using the patient’s anatomy to create a comfortable immobilization device that incorporates catheter guidance. The initial analysis of CT image data is first rendered with the Mimics software. The design of the patient-specific template is achieved with using the Magics software tool, the output of which is then exported for 3D printing.
3.6. TEMPLATE

The template is created during the pre-operative stage of our workflow and requires 3D imaging of the tissue. The CT images of the agar phantom is loaded into Mimics (Fig. 3.9(a)). Mimics segmentation tools are used to discern the tissues contour, vital organs, and tumor site (Fig. 3.9(b)). Using the software, a 3D model of the segmented areas (Fig. 3.9(c)) can be created and exported in a modeling format for processing and template creation in Magics. The model of the tissue and tumor site is then loaded into Magics. Creation of catheter models in Magics is done so as to visualize how treatment should be given to the tissue (Fig. 3.4(a), 3.4(b)). The modeled catheters are then placed at clinically feasible trajectories to cover the tumor sites (Fig. 3.4(a)). A template is then created using the tissue contour as a guide so that the template will fit snugly over the imaged tissue (Fig. 3.4(c)). The catheter insertion sites are then subtracted from the template so as to create guides for the catheters. Initial tests used a simple hole in the template as guides as seen in Fig. 3.10(a). Improvements in the design led to using longer guide tubes for the needles (Fig. 3.10(b)), in order to reduce catheter insertion errors. The template is then exported for rapid 3D prototype printing.

3.6.1 Steps for Template Creation Using Materialise Software

Mimics 13.0

1. Segment breast skin contour (breast)
2. Segment tumor (tumor)
3. Segment skin markers (marker)
4. Created 3D molds of all segmented regions
(a) Shows the layout of Mimics right after importing CT images of the breast tissue. Mimics has three screens showing different views of the tissue and one screen incorporating all views into a 3D visualization.

(b) Segmented breast tissue (yellow) and 3D (c) 3D rendered model of segmented rendered model of breast tumor sites (green)

Figure 3.9: Screenshots from Mimics
3.6. TEMPLATE

(a) First template designed and printed for catheter guidance
(b) Template printed during second round of experimentation with improvements to template made

Figure 3.10: Templates created using 3D rapid prototype printer

Magics 14.01

1. Import 3D molds of all segmented regions \((breast, tumor, marker)\)
2. Duplicate breast model \((breast_{copy})\)
3. Shrink wrap \(breast_{copy} 2.0\text{mm}\)
4. Shrink wrap \(breast 3.0\text{mm}\)
5. Rescale \(breast_{copy}\) by 1.06
6. Translate \(breast_{copy} -4\) in \(dY\) plan
7. Create three new objects. Spheres with a radius of 2mm
8. Align sphere to point on fiducial (each sphere should be aligned to a different fiducial)
9. Using back-view move each sphere outwards with \(breast_{copy}\) in wire view
10. Merge spheres with \(breast_{copy}\)
11. Place 3D models of needles where you would like
12. Merge box around needle with $breast_{copy}$

13. Bool remove breast

14. Duplicate needles ($needle_{copy}$)

15. Merge cone with cylinder

16. Bool remove $needle_{copy}$
Chapter 4

Data Collection and Experimental Design

In order to validate patient-specific templates for brachytherapy, the post-operative catheter tracts should be sufficiently accurate, in that they closely resemble or replicate the pre-planned catheter tracts. The template planning and implementation process were carried out as discussed in Chapter 3, for six sets of experiments as described next. The phantom, template, and catheters were imaged with CT following catheter insertion. The images were loaded into Mimics and processed to produce 3D renderings of the phantom, template and needles. Integrated Mimics tools allowed for simple registrations and quantitative measurements that were needed for determining the catheter placement error.

Six sets of phantom-based tests were performed, with improvements incorporated into each subsequent setup. In this chapter, we describe how the results were gathered and error measurements performed. A breakdown of each experimental setup and a description of the changes made with reasoning for improvements are detailed.
4.1  Error Measurement

It is essential that the patient-specific templates accurately and precisely guide catheters through soft tissue to desired locations. The accuracy of needle guidance was determined by how close the post-insertion needles lay from the original needle placement plan. Needle precision was determined by measuring the repeatability of template guidance under constant conditions. The methodology used to determine accuracy was updated after the first two experimental rounds to simplify error calculations. The embedded targets used in the first two experimental rounds consisted of agar-encased latex masses. After the first two rounds, experiments received CT-compatible spherical markers rather than large tumorous masses. Substituting the large masses with small markers simplified error measurement calculations. An explanation of the different calculations for determining error is detailed below.

4.1.1  Targeting Tumors

Calculating error when targeting larger simulated tumor objects requires a registration step, followed by needle distance measurements. Registration and then measurements were done after segmenting all important objects from the post insertion CT image.

A Mimics registration tool that minimizes the least squares distance was used to register the pre-operative breast tissue to post-operative breast tissue. Once the pre-operative and post-operative breast tissues were registered, the transformation matrix used for the initial alignment was applied to the post-operative needles and template. These registration steps were required for proper comparison of the pre-operative and post-operative needle. Once these registration steps were completed, a
visual inspection of the needles was made first, and a quantitative measure was taken from the data using a Mimics distance measurement tool.

Due to the needle bending in the tissue, it was difficult to measure the displacement from planned to actual needle. Since the tumorous mass was a volume rather than a point in space, the distance of the actual needle tract from the planned needle tract from the centroid of the tumor object was used. It was reasoned that as the tumors were targeted, the distance of the actual needle to the planned needle from the most central point in the tumor would provide the best error measure.

4.1.2 Targeting CT Compatible Markers

The motivation of catheter placement is the targeting of specific sites. A paradigm shift in what targets should be used occurred to better suit site-specific guidance. After the second experiment, the embedded targets changed from large masses to small ball bearing markers with a diameter ranging from 1.15\text{mm} to 1.90\text{mm}. Changing the materials, shape, and size of the targets required an update of the error calculations. Rather than requiring a registration step and needle distance measurements, error calculation was streamlined into a single measurement.

After segmentation of the post-insertion CT images for objects of interest, error calculation was simply a measure of distance. Error was determined by measuring the distance of the needle from the CT-compatible marker. As seen in Figure 4.1, measurements were taken from the centroid of the needle to the centroid of the marker in three fields of view (axial, lateral, sagittal) and the largest distance was used as the final error.
4.2. EXPERIMENTAL TESTING ROUNDS

For the purposes of this thesis, an experimental setup or testing round signifies a batch of phantoms receiving the same experimental treatment. In order to test the template workflow and design, multiple phantoms were tested in each setup and data was collected over six different testing rounds. The number of phantoms for each set of tests, as well as the quantity of needles placed per phantom, varied. Details of each experimental setup are discussed below.

4.2.1 Round 1

The first test contained two of the purchased phantoms of average size with pre-defined tumorous masses. Each phantom in the first experiment had five needles planned and inserted. Each of the five needles were planned so as to intercept the
centroids of five different tumors. In the first breast phantom, one of the five needles inserted exited the pre-planned exit-hole, leaving four needles pressed against the edge of the template. In the second breast phantom, two of the five needles passed through the breast tissue and exited through the corresponding hole.

4.2.2 Round 2

To reduce positioning problems, the second experiments template design and workflow were modified. The addition of three fiducial markers to the breast tissue was incorporated to the workflow to improve template placement. The template itself was improved by incorporating a longer needle guide as seen in Figure 4.2 to reduce the needle’s rotational freedom. Guides were also placed along the bottom of the template for aligning with the skin fiducials placed on the tissue.

Two phantoms of differing sizes were used in this round of experimentation: a plus size and a small. Both of the phantoms contained one tumor created from an agar-filled latex glove. The large phantom received a four needle insertion plan that targeted one tumor, while the small phantom received a two needle insertion plan that targeted one tumor.

4.2.3 Round 3

Following the first two rounds of testing, an integral aspect of the validation procedure was changed to improve results. Simplification and improvement in error measurement was accomplished by updating the embedded target to a small object. The change in reasoning streamlined the workflow removing the need for a registration step. The new design required each needle to target a point in space delineated by a
CT-compatible marker.

Three phantoms consisting of two plus sized models and one small model were tested during the third round of experimentation. Both plus sized phantoms contained three markers - all of which were targeted by needle insertion plans. Only one marker was placed centrally in the smaller phantom and then targeted by a needle.

4.2.4 Round 4

The experimental setup stabilized and no changes to the workflow or template design were made. Five large phantoms were tested, with the same setup used in Round 3 in order to collect enough data to show significance.
Three of the phantoms received three markers, while the remaining two received two due restrictions in amount of material available. Of the two phantoms receiving two markers, one of the phantoms was inserted with just one of the two planned needles due to a broken guide tract caused by a post-print cleaning.

4.2.5 Round 5

A precision measure or reproducibility quantification is needed for proper validation of an immobilization and guidance system. To determine such a measure, two of the phantoms from experimental Round 4 were retested. Phantoms 4\textsuperscript{d} and 4\textsuperscript{e} from test Round 4 were reused as were their templates. The phantoms were allowed to sit without inserted needles for two days in a sealed container in the refrigerator to remove some distortion previous tracts might cause. The same templates used in Round 4 where then placed over the previously tested phantoms. New needles were then inserted through the guide sleeves targeting embedded markers. Although the experiment contained two large phantoms each harboring three markers, one test only received two needles due to cracking of one of the guide sleeves.

4.2.6 Round 6

The final round of experiments contained three large phantoms: two inserted with two needles and one inserted with three needles. The phantoms 4\textsuperscript{a}, 4\textsuperscript{b}, 4\textsuperscript{c} from experimental Round 4 were used in this test in order to test precision. Round 6 of testing was also used to validate the use of a breakaway template design. The phantoms and corresponding template designs from Round 4 were used, however, one aspect of the template was updated in order to provide a template design more suitable for clinical
4.2. EXPERIMENTAL TESTING ROUNDS

use. A simple jig-saw break was incorporated to the template that split the template into two pieces that fit together. The breakaway design allows the template to be easily removed, post-insertion, but leaves the basic design of the template unchanged (Fig. 4.3). The need for a template that can be easily removed from the catheters post-insertion is paramount when dealing with a clinical case as the catheters must remain in the patient over the course of a six day treatment without the template.

Figure 4.3: 3D Printed template with breakaway design
Chapter 5

Results

Correct catheter placement in a brachytherapy procedure, as discussed in Chapter 1, is paramount to adequate dose coverage of the tumor cavity. No standard exists currently in the literature for an acceptable catheter placement for breast brachytherapy. The clinicians we worked with provided us with $3\text{mm}$ as an acceptable error for breast brachytherapy catheter insertions. For the purposes of this thesis, the clinically acceptable placement error of catheters will be $3\text{mm}$, which is consistent with literature on clinically acceptable prostate brachytherapy procedures.

Results in catheter placement over all tests yielded a mean error of $3.2\text{mm}$ (SD 1.9), but once the initial tests using the older templates were removed from the data set, a mean error of $2.6\text{mm}$ (SD 1.1) was achieved. All needle placement results can be viewed in Table 5.1.

The first round of tests was performed on templates with neither long enough needle guides nor a marker system for correct template alignment on the tissue. Initial results of template testing yielded high error values for catheter placement. As the template design and experimental workflow evolved, the errors were reduced substantially. Rounds 2,3 and 4 consisted of tests performed with a marker integrated system
for template placement and long guide tracts. The template design remained relatively stable over the course of these rounds, thus providing a strong indication of the templates’ accuracy. The mean error over rounds two through four was 2.6 mm (SD 1.1). Testing Rounds 5 and 6 were performed to test re-application of the template and yielded precision results of 0.8 mm as seen in Table 5.2. Round 6 of testing also examined the efficacy of a breakaway template which in conjunction with precision results showed the validity of the breakaway design.

5.1 Accuracy

The average needle trajectory placement error (shown in Table 5.1) in the first experiment was 4.8 mm and 4.2 mm for the two phantoms. Large variations in targeting error were observed with the largest error being 10.1 mm and the smallest error being 1.9 mm. It was observed that positioning of the template, post-printing, caused potentially large errors. The template was placed over the tissue, but rotation and slight tilting of the template during placement as seen in Fig. 5.3 was causing large errors in catheter placement. The inability of all the needles to pass through the tissue and exit appropriately out of the template indicated an error in needle placement through the template, most likely caused by a slight rotation during needle insertion. The mean error for all tests in experimental round 1 was found to be 4.5 mm (SD 2.8). A histogram of the data collected from the original template which was done during round one of testing can be seen in Fig 5.1.
Table 5.1: Needle Insertion Errors

<table>
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<th>Distance from Target - Error Measure (mm)</th>
<th>Needle¹</th>
<th>Needle²</th>
<th>Needle³</th>
<th>Needle⁴</th>
<th>Needle⁵</th>
<th>Avg Error</th>
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<td>4.9</td>
<td>8.2</td>
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<td>4.8</td>
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<td>10.1</td>
<td>1.9</td>
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<td>4.2</td>
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<tr>
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<td>2.3</td>
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<td>-</td>
<td>-</td>
<td>-</td>
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<td>3.2</td>
<td>1.8</td>
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<td>-</td>
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</tr>
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<td>2.5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2.6</td>
</tr>
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</table>

¹ CIRS triple modality biopsy phantoms used
² Phantoms contained agar encased in latex to serve as targeted tumors
³ All phantoms contained ball-bearing like CT-compatible markers to serve as targeted tumors unless specified
A marked improvement between the first and second experiment can be seen. The average error for each phantom in the second experiment was almost half that of the first two phantoms. The variation in error measures were also greatly improved, with most of the errors lying within a relatively narrow range in the second experiment, while the first experiment produced variations of up to $8.3\text{mm}$. The small changes made in template design and workflow greatly improved the overall outcome of the results producing a mean of $2.7\text{mm}$ (SD 1.2). A histogram of the results can be viewed in Fig 5.2.

![Needle Insertion Errors: Experimental Round 1](image)

**Figure 5.1:** Histogram for experiment results of round 1 in testing needle placement error.

The introduction of a more reliable error measure was incorporated into the third round of testing by using smaller embedded targets. Experiment three’s results showed a decrease in mean error to $2.3\text{mm}$ (SD 0.8) as well as a decrease in the variation.

Test group four contained the largest number of phantoms tested at one time. Five large phantoms were tested with mean results of $2.8\text{mm}$ (SD 1.3). Of the twelve needles inserted into the five phantoms, all but two were within a clinically acceptable
5.1. ACCURACY

Figure 5.2: Histogram for experiment results of round 2 in testing needle placement error.

(a) Post-operative 3D rendering of tumors (blue), (b) Post-operative 3D rendering (yellow) with template (yellow) and needles (yellow) created for pre-operative template and needles (red) overlaid after transformation was applied. Shows the error incurred from inaccurate placement of the template (yellow)

Figure 5.3: Screenshots from Mimics
range. Both Needle$^2$ of breasts 4d and Needle$^3$ of breast 4b were above the clinically acceptable threshold with errors of 4.9mm and 6.2mm respectively. Both of the needle guides that performed poorly were retested during the precision experiments to see if the error was repeatable, which was confirmed. As both experimental round three and four used the same protocol the data from each was combined in Fig 5.4.

![Needle Insertion Errors: Experimental Rounds 3 & 4](image)

**Figure 5.4:** Histogram for experiment results of round 3 and 4 in testing needle placement error.

The template designs and phantoms used in round four were re-tested in rounds five and six to determine precision of the templates. Precision results can be viewed in Table 5.2. Rounds five and six are re-testing of existing templates, therefore they were not included in accuracy results. The histograms shows that most of the data lies within a clinically acceptable range. The mean of the data from rounds two through four which uses the latest template design was 2.6mm with a 95% confidence interval of 2.2 – 3.1, indicating that a majority of the data was below the clinical cutoff.
5.2 Precision

Precision was measured through the re-testing of all the phantoms used in Round 4 of testing. Error measures were related by using corresponding needles. As seen in Table 5.2, most of the needles were within 1 mm difference between tests — very precise. Two of the tests returned higher than 1 mm precision: \textit{phantom}_b(needle^2) and \textit{phantom}_d(needle^3). Results from \textit{phantom}_b(needle^2) showed the highest error in needle placements. That needle was also the source of the highest needle insertion error in all tests. Since the error was so far above all others, it is likely that there were issues with the initial design of the template. If the poorly planned needle tract’s results were omitted from the precision results, the average difference between needle placements tests would be brought down from 0.8 mm to 0.5 mm. Overall reproducibility tests show high precision.
### Table 5.2: Needle Precision Calculations

<table>
<thead>
<tr>
<th>Name</th>
<th>Needle(^1)</th>
<th>Needle(^2)</th>
<th>Needle(^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phantom(_a)</td>
<td>2.8(^b)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>3.5(^b)</td>
<td>1.9(^a)</td>
<td>-</td>
</tr>
<tr>
<td>difference</td>
<td>.7</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Phantom(_b)</td>
<td>2.4(^a)</td>
<td>6.2(^b)</td>
<td>2.2(^b)</td>
</tr>
<tr>
<td></td>
<td>2.7(^a)</td>
<td>10.2(^b)</td>
<td>2.0(^b)</td>
</tr>
<tr>
<td>difference</td>
<td>.3</td>
<td>4</td>
<td>.2</td>
</tr>
<tr>
<td>Phantom(_c)</td>
<td>2.5(^a)</td>
<td>1.9(^c)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2.7(^a)</td>
<td>2.5(^c)</td>
<td>-</td>
</tr>
<tr>
<td>difference</td>
<td>.2</td>
<td>.6</td>
<td>-</td>
</tr>
<tr>
<td>Phantom(_d)</td>
<td>1.6(^a)</td>
<td>2.1(^b)</td>
<td>4.9(^b)</td>
</tr>
<tr>
<td></td>
<td>2.9(^a)</td>
<td>2.6(^b)</td>
<td>4.4(^b)</td>
</tr>
<tr>
<td>difference</td>
<td>1.3</td>
<td>.5</td>
<td>.5</td>
</tr>
<tr>
<td>Phantom(_e)</td>
<td>2.6(^a)</td>
<td>2.0(^b)</td>
<td>2.9(^c)</td>
</tr>
<tr>
<td></td>
<td>2.5(^a)</td>
<td>1.9(^b)</td>
<td>-</td>
</tr>
<tr>
<td>difference</td>
<td>.1</td>
<td>.1</td>
<td>-</td>
</tr>
</tbody>
</table>

Average Needle Reapplication Error | .8

\(^a\) Target located near insertion site, defined as within first third of the tissue measured from insertion site.

\(^b\) Target located far from insertion site, defined as within last third of the tissue measured from insertion site.

\(^c\) Target located centrally in the tissue, defined as within middle third of the tissue measured from insertion site.
Chapter 6

Conclusions and Future Work

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

6.1 Summary of Contributions

In this work, a novel patient-specific breast brachytherapy device was developed. The device is intended for intraoperative immobilization of the breast tissue and guidance of catheters to the tumor cavity. In order to have a clinically viable immobilization and guidance system, the device was designed with the following features:

1. The template accurately and precisely guides brachytherapy catheters to the target areas within the breast tissue.

2. The device can be easily removed from the tissue at anytime during the procedure without disturbing the already inserted catheters due to the breakaway design.

3. The template can be easily sterilized for clinical use.
The phantom studies have shown the patient-specific template to be both accurate and precise. The template is designed with a rigid shell to immobilize the tissue and breakaway design that makes it easy to disassemble and remove the template without disturbing the inserted catheters. The use of tissue markers in conjunction with markers integrated into the template allow for the correct alignment of the template with the required tissue. In addition, long needle tracts on the template guide the catheters accurately to the required target locations.

For the breast-based phantoms, the patient-specific templates accurately guided the catheters within 2.6\text{mm} (SD 1.1) of the target locations, a distance that is clinically acceptable. The templates were also able to re-guide catheters within a mean distance of 0.8\text{mm}, a measure which shows the precision of the template. Although most tests guided catheters within a clinically acceptable range, there were a few catheters that were poorly guided. However, it should be noted that the catheter guides that performed poorly and were re-tested were still fairly precise; that is, when re-tested, they closely mirrored their placement in the original results. Thus, the poor placement of these catheters stemmed from the placement of these template guides and not from an issue inherent in template design.

In conclusion, we introduced an alternative immobilization and guidance device for breast brachytherapy catheter placement and demonstrated the concept of patient-specific using templates integrated with image-based computer-assisted planning. Small changes applied to template and workflow designs yielded major improvements with current results yielding clinically acceptable accuracies.
6.2 Future Work

While the patient-specific template has shown promise in the tests, it still requires further improvements in its implementation in order to be ready for a clinical application. Ongoing work is aimed at improving the workflow and template design while generating more experimental data involving a variety of breast phantoms and, eventually, human subjects. The focus of future developments will be to improve the accuracy of needle guidance and streamline the process for cadaver studies. The following are my suggestions for future work:

- The breakaway template requires more tests to properly assess its accuracy.
- The data collected on tumor location should be elaborated on and analyzed. A relationship between locations of tumors and needle placement error should be explored.
- In order to move the template to clinical trials the template needs to be studied on true breast tissue. Cadaver studies are needed to create a workflow that governs patient imaging and template alignment. The breast tissue of cadavers will allow us to address the following issues:

  **Tissue imaging** As our phantoms cannot fully simulate the malleability of actual breast tissue, studies that investigate the best way to image real breast tissue prior to template design are required. Two possible methods of imaging are placing the patient in a prone position or using thermoplastics to constrain the breast. The use of a prone positioned patient with blocks supporting the chest away from the CT table would allow for the breasts to be in their most natural free form. The use of a thermoplastic
could also be useful to partially constrain the breast while lifting the breast tissue farther away from the chest wall.

**Template placement** Using phantoms makes placement of fiducial markers around the tissue simple and stable. In contrast, a patient will require the stitching of markers or the placement of CT-compatible stickers on the tissue as a marker system. Testing of the marker system on actual tissue is required to confirm that a marker system is all that is required for the accurate placement of the template on the tissue.
Bibliography


[38] Jeffrey A. Tice. Brachytherapy as primary radiation following breast-conserving surgery for stage i or ii breast cancer. Technical report, California Technology Assessment Forum, 2008. 1, 6, 9


