EVALUATION OF THE CLINICAL IMPLEMENTATION OF A DEEP INSPIRATION BREATH HOLD LEFT BREAST TANGENTIAL BEAM RADIOTHERAPY TREATMENT

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Evaluation of the Clinical Implementation of a Deep Inspiration Breath Hold Left Breast Tangential Beam Radiotherapy Treatment

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DEDICATION

This document along with the efforts behind it are here in dedicated to the human race, whose eternal struggle for knowledge has led to unbelievable explanations for the way nature behaves and methods to manipulate it for the best interests of life. Without the questions and mistakes of past conscience beings, we would still be just a bunch of particles floating around in a gravitational field. From the first creature that realized it could control its environment to the last living thing to inhabit the known universe, I thank thee for simply being. To know that there are other conscience entities is truly magical. To be alive is simply wonderful. To understand and solve a problem is utterly divine.
ABSTRACT OF THE THESIS

Evaluation of the Clinical Implementation of a Deep Inspiration Breath Hold Left Breast Tangential Beam Radiotherapy Treatment
by
Taylor Dylan Harry
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Radiation to the heart during left breast cancer radiotherapy has proven to lead to late cardiac complications. It has been shown that treatment at deep inspiration breath hold (DIBH) reduces radiation to the heart in these treatments. We have implemented a workflow for DIBH treatment of left breast patients using surface imaging and visual feedback for patient simulation, setup, and treatment delivery. The dosimetric impacts to the heart and to the left anterior descending coronary artery (LAD) have been evaluated. Prior to treatment, patients are set up at DIBH based on surface information in order to reproduce the setup of the simulation day, without guaranteeing that the same lung inspiration level will be achieved every day. To study the effect of lung inspiration level variability, we have recreated several inspiration levels using deformable registration between computed tomography (CT) scans at DIBH and free breathing (FB), and compared doses at those inspiration levels.

The successful implementation of left breast cancer treatment at DIBH using surface imaging for set up and monitoring purposes is shown in this thesis. Four patients have undergone treatment so far. Treatment takes 16.7 minutes on average for the first four patients, and has continually decreased in time as all have become more familiar with the procedure. Patient compliance to perform a DIBH was excellent and thus far every patient has been able to produce a reproducible and stable DIBH using the visual feedback. An analysis of the CT scans shows that on average the heart was displaced 0.8 cm from the chest wall and 1.5 cm inferiorly in the abdomen from FB to DIBH. A demons algorithm running on the Graphics Processing Unit (GPU) was used to obtain the deformable registration field from the FB and DIBH scans. The vector field was interpolated and extrapolated to recreate scans at 75%, 90%, and 110% inspiration levels, considering FB as 0% and DIBH as 100%. For these scans, the mean dose to the heart was decreased on average by 52%, 59%, 59% and 63% respectively compared to FB, while the volume of the heart receiving 50% of the prescribed dose decreased by 82%, 86%, 88% and 90% for the 75, 90, 100, and 110 percent inspiration levels. On average the mean dose to the LAD was decreased by 48%, 61%, 63%, and 69% for the 75, 90, 100, 110 percent inspiration levels compared to FB. The volume of the LAD receiving 50% of the perspired dose was decreased by 55%, 72%, 74%, and 81% for the 75, 90, 100, 110 percent inspiration levels compared to FB.

The successful implementation of a DIBH has already provided a reduction in dose received to the cardiac structures by several patients. It is clear that all will benefit from a DIBH treatment, but the exact extent is patient dependent. Surface imaging has shown to be an effective tool for setup and delivery. Its accuracy for set up and delivery have proven to
be superior to previous tattoos and SSD alignment as well as to have exposed previously unknown setup errors in six degrees of freedom.
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CHAPTER 1

INTRODUCTION OF DIBH

This chapter provides a brief introduction as to the reasons why existing tangential beam therapy needs to be altered in order to spare organs at risk and a possible method in doing so.

1.1 A BRIEF HISTORY OF BREAST CANCER

Breast cancer is currently the most commonly diagnosed cancer in women and the second leading cause of cancer mortality among women.\(^1\) The advancement of medical technology has led to earlier diagnoses, better, more precise and accurate ways to eradicate this disease. Increasing telecommunications have enabled more women to be properly informed of the disease and their chances with it. Extensive databases of knowledge and amazing organization have pushed this disease into headlines of the media, governing bodies and lives of first world females. Still 1 in 8 women will develop some form of breast cancer in their life and 1 in 35 will die.\(^1\) As the average life expectancy continues to increase in the first world, statistically speaking, more cases will arise, inducing more treatments to be conducted. Survivors from breast cancer will increase their chances for reoccurrence, or other possible complications induced from treatment. Because of this, new techniques are required to perfect existing treatments to cure the disease and prevent further diseases and complications related to the method of treatment from developing.

USA Today reported that in 2007 nearly 1 billion dollars has been spent on breast cancer research and 16.5 billion was spent on breast cancer medical care alone in the US in 2010.\(^2,3\) This accounts for 13% of all funds spent on breast cancer, making it the most costly form of cancer in Americas dwindling economic status.\(^3\) It is clear that the developed world is putting time, money and resources into dealing with this disease. That is just the estimated amount spent alone on dealing with the cancer, there is still a financial number to be placed on the cost to society for the hours that a patient is made unable to perform normal
daily duties while dealing with the disease. It is important then to develop methods to make treatments more efficient and effective to minimize treatment times and overall costs.

Early diagnosis is a key issue today. The gold standard early diagnoses tool for breast cancer is the mammogram. Recent debate questions arose on whether or not a significant number of cancers themselves are generated due to the biological radiation effects from the mammogram. Catching breast cancer while it is still small and has not metastasized to other parts of the body allows fewer procedures to be conducted during the course of treatment. For instance a smaller tumor means less tissue needs not be removed, less area to irradiate, and less drugs or hormones required to eradicate the disease. Discovering the disease early greatly reduces the risk or mortality in women. This results in a cheaper cost and less time for initial treatment. From here, prevention of reoccurrence and other anatomical complications will minimize future costs and procedures.

1.2 TREATMENT HISTORY

Over the years many methods have been implemented to cure and treat breast cancer. One of the oldest and more common methods in some form or another is mastectomy. Mastectomy is a surgical procedure removing one or both of the breasts, underarm lymph nodes and connective tissues lining the anterior chest wall. As knowledge and experience of the disease progressed, breast conservation methods began developing for smaller and less severe diseases. Removal of smaller portions of diseased tissues is known as lumpectomy. This is generally done for lower stage diseases and benign tumors not posing a metastasis threat. These represent the two surgical methods used for breast cancer treatments. Both rely on the same principle of removing diseased tissue so that it cannot continue to grow or spread in any form.

Surgery alone, however, does not guarantee that reoccurrence will be prevented. To make these surgical methods more beneficial, accompanying treatments help kill rogue cancer cells as well as prevent further growth. Chemotherapy uses antineoplastic drugs to target and kill rapidly dividing cells. These chemicals target DNA strands and the metabolic centers of less differentiated cells discouraging growth, development and reproduction. Hormonal therapy, mainly Tamoxifen, blocks the production of estrogen in Estrogen Receptor positive cancer types which is the main chemical initiating growth. Radiation is a
noninvasive method which when properly used, kills less differentiated or diseased cells faster than more differentiated or healthy cells. Radiation can either be used to reduce tumor size, killing the majority of diseased tissue, or can be used to kill any remaining cells that may have drifted from the original tumor site to other parts of the body. Depending on the severity of the cancer, one or many of these methods may be used to treat a patient to kill the tumor and prevent further mutated growths from developing. Radiation will be the main focus of this paper.

Radiation can either be naturally occurring or mechanically induced creating photons or electrons of high energies to bombard molecular strands. They are produce in a field that is overlaid on the diseased anatomy. These particles deposit their energy in the living tissues most notably causing strand breaks in the cancers DNA chain. This is the mechanism which stops growth, development and reproduction. Radiation therapy is of particular interest because of its noninvasive technique to accomplish the same goals as chemicals and surgery. Radiation is generally an outpatient procedure that can accompany all other forms of treatment. In the past two decades the amount of patients receiving radiation has substantially increased. Breast conservation techniques are being implemented more readily because of earlier detection of tumors and desire to maintain a normal female anatomy.

For breasts there are two primary methods used to irradiate carcinogenic tissue. They are partial breast radiotherapy (PBRT) and whole breast radiotherapy (WBRT). Both aim to kill any additional cancer cells that could not be removed during surgery or killed from chemotherapy. WBRT is usually done in five to six weeks, generally corresponding around 25 treatments at 2 Gray each. PBRT has come into play more recently and the long term effects are still under study. PBRT developed from efforts for breast conservation treatments as they became more of an option for women receiving treatment. The idea is the same as WBRT except that treatment is accelerated and a higher dose is delivered to a smaller area over a shorter period of time.

The simplest form of breast radiotherapy is tangential beam radiotherapy (TBRT). Tangential field therapy uses two rectangular fields that are ideally tangent to the anterior surface of the chest wall. Gantry rotation angles used are generally 110 and 290 degrees with 0 degrees being the anterior to posterior beam perpendicular to the patient lying supine. The field size depends on the size of the patient breast tissue. These two fields can cover the
breast tissue while minimizing exposure to the rest of the body. For more difficult cases additional fields can be added to give proper dose distribution to all diseased sites while sparing healthy tissues.

1.3 RADIATION INDUCED COMPLICATIONS

Standard tangential field radiotherapy of the breast is an effective treatment, but bears a risk of late complications to adjacent normal tissue. Specifically doses to the cardiac tissue have shown to be a significant factor in causing ischemic heart disease (IHD) in left breast patients. 6-11 This is due to the apex of the heart extending laterally to the left and its proximal location to the anterior chest wall. The borders of the tangential field in left breast cancer patients can thus include the anterior portions of the heart located within the thoracic cavity. This can lead to cardiac morbidity and mortality in patients who receive TBRT.6-11 By simply viewing the patients scan the proximity of the heart muscle in relation to the anterior chest wall can be seen. Not all patients display a significantly close proximity, but a substantial number of individuals do making, heart sparing techniques an issue to be addressed during treatment consideration. As the issue has become more prevalent in literature and practice, new ideas to combat it are being developed to increase the overall effectiveness of treatment.

Patients with left-sided breast cancer receiving radiotherapy are at an elevated risk for complications of the heart developing 10 to 15 years later in life due to its location to the anterior chest wall. 6-11 Several studies showed that breast cancer is slightly more common to occur in left vs. right tissue. 12, 13 Anterior portions of the heart can fall into the field absorbing a considerable amount of dose as the diseased breast is irradiated. Damage to the heart can prevent proper physiological functions from occurring impeding the regulation and flow of blood to the rest of the body. The left anterior descending coronary artery (LAD), which provides the majority of the left ventricles blood flow, sits in the anterior sulcus of the heart. Damage to this vessel can cause the propulsion of oxygenated blood to the left ventricle leading to heart attack and failure. 14, 15 Cardiac complications are related to the volume of the heart irradiated, with a greater risk for a greater volume. 7, 8, 16 Designing treatment plans which minimize the volume of cardiac tissue in the treatment field can thus prevent IHD and other complications occurring later in life.
1.4 DIBH vs. FB

Motion induced complications have become less of a problem in current day practice as advancement in radiotherapy treatments provide more accurate and precise dose delivery. Many techniques have been employed to limit this problem. A simple and effective way to move the hearts location in relation to the anterior chest wall is by taking a deep breath. Deep Inspiration Breath Holds (DIBH) offer several potential improvements compared to the standard free breathing (FB) breast radiotherapy. The motion from FB to DIBH can cause superior and inferior displacement of the diaphragm up to 20 mm while causing an anterior posterior displacement of the chest wall by 8 mm. Deep Inspiration increases the distance between the tumor and organs at risk (OAR) deep to the target by pulling the diaphragm and heart inferiorly while expanding the anterior chest wall. The act of a breath hold ceases thoracic respiratory motion and immobilizes the target tumor as well as the surrounding OARs. This can be seen in Figure 1.1.

DIBH is a relatively cheap and easy way to solve the problem of cardiac toxicities. The dosimetric effects of DIBH relative to FB have been evaluated by several studies, showing reductions in the volume of the heart and LAD that can be present in the treatment field. Applying this knowledge can help further increase the overall effectiveness of eliminating diseased tissue and sparing healthy tissues within the patient. Since cardiac complications tend to arise years later, this type of procedure is much more beneficial for patients of a young age and healthier individuals who are projected to live extended periods of time after they receive treatment. Since the overall goal of treatment is to save patients’ lives, causing another disease from treatment is something that should be avoided at all cost. The next question is how to implement a DIBH procedure with precision and accuracy to ensure that dose to the target is not compromised while dose to the surrounding OAR is reduced. A DIBH treatment planned reference position must be established and reproduced fairly accurately for all treatment fractions.
Figure 1.1. The hearts position between FB (left) and DIBH (right). The cardiac tissue is moved posteriorly and inferiorly in relation to the chest wall and diseased breast tissue. This is shown from an axial (top), coronal (middle) and sagittal (bottom) view.
CHAPTER 2

SURFACE IMAGING

This chapter provides an explanation to the science behind surface imaging and how it can be incorporated into existing radiotherapy treatments.

2.1 WHAT IS A SURFACE IMAGE?

Surface imaging is an imaging modality for generating 3D digital models of an object’s external features. The gradient and curvature of an object’s geometry provides a very unique form of identification, which has become incorporated in many applications across the world. Until recently in the history of the human race, images were only able to be accurately acquired in 2D. This would leave out valuable information concerning depth and orientation of an object’s location in 3D space. With the development of sophisticated technologies, 3D surface imaging can now be quickly and easily performed. From facial recognition software, to geological surveys and medical applications, surface imaging information continues to help mimic and describe the world that surrounds us in greater detail than ever seen before. For the remainder of this paper, surface imaging in medical applications will be our primary focus.

Image-guided radiation therapy (IGRT) continues to develop as sophisticated methods for complicated treatments become more practical in everyday clinical use. The use of external markers and tattoos are no longer needed if an image can be generated of superficial patient anatomy to a linear accelerators isocenter. We plan to incorporate surface imaging for setup and monitoring of the patient through the course of treatment. Surface imaging is a means of acquiring surface information via a non-ionizing technique. We hope to minimize portal image films taken to ensure proper patient set up. In order to do this we must understand exactly what surface images represent and how they are generated. For a patient, a surface image is essentially their body contour or most superficial anatomical structure. The gradient and curvature of patients’ superficial surface is unique to each
individual and therefore can be used to identify, monitor, locate and replicate their surface structures.

2.2 ACQUIRING A SURFACE IMAGE

In order to generate a surface image many different devices must work together to develop a uniqueness of points located on the gradient of an objects surface. The main components used to generate surface images are a speckle pattern projector and two stereovision cameras. The surface imaging system (SIS) unit we used consists of a speckle projector, a speckle or strobe light flash, two stereovision cameras, and a texture camera located in a convenient housing unit for installation and protection (see Figure 2.1).

![Figure 2.1. Align RT surface imaging camera pod.](image)

First the speckle projector produces a pseudo randomized pattern of points projected onto a surface. This is nothing more than a sheet of light projected over an object. The light pattern can either be a continuous projection, for real time applications, or static flash for non-dynamic applications. This sheet of light forms a mesh grid pattern displaying points or vertices that are unique to the current surface that it is produced upon. Once these points are established on a surface, they must be localized in space to define where they are in relation to each other, as well as their relationship to the cameras frame of reference. These points will come to represent infinitesimal 3D coordinates for a vector array mathematically describing the surface in computer algorithm.

Defining points in the camera’s reference frame is accomplished through triangulation and the two stereoscopic cameras arranged at opposite sides of the camera housing unit. Triangulation is a method for deciphering the location of an unknown point by
means of other known point distances and the angles these points make to the known points through the use of trigonometry. Surveying, navigation, model rocketry, astronomy and human vision are examples of triangulation in action. The two stereoscopic cameras work together just as two human eyes do to decipher the depth and orientation of an object, or to relate that object into 3D space for the observer. Figure 2.2 demonstrates this method visually.

![Triangulation shown visually from the camera pods stereoscopic camera’s perspective.](image)

Each stereoscopic camera visualizes all individual points produced by the speckle pattern spread across an objects surface. The distance between the two stereoscopic cameras is known and set by the manufacturer. The angle at which this individual point is in relation to each camera can be easily measured. A perpendicular line to the stereoscopic cameras axis extends to the individual points location. The length of this line is in fact the distance to the individual point and central axis of the camera pod. This creates two right triangles whose base lengths added together equal the known distance between the two stereoscopic cameras. Since these two triangles share the same height or side d, the trigonometric
functions of their angles can be equated leading to a simple solution that will give the
distance to the corresponding point. A schematic for this derivation is shown in Figure 2.3.

![Figure 2.3. Geometric diagram for triangulation derivation.](image)

The information provided through these projection angles, intersection with the
cameras axis and object distance allows the orientation and position of the 3D coordinate for
the point under inspection to be registered in the cameras 3D reference frame using the
following equation:

\[
d = \frac{l \cdot \sin \alpha \cdot \sin \beta}{\sin (\alpha + \beta)}
\]  

(2.1)

Through the use of an integrated computer algorithm, this can be done rather quickly
for tens of thousands of points produced by the speckle projector over an objects surface. As
each point becomes registered in the cameras reference frame, a mesh contour is generated
mimicking the observed surfaces gradient and curvature in a 3D vector array. The 3D image
information is hence created for either online or offline analysis. Depending on how smooth
or rough the surface is, a texture camera is attached and can be incorporated into the SIS to
produce a higher quality surface image. This camera adjusts and produces speckle light
patterns that are optimized for deciphering points of different surface textures and types. The
default texture, intended for use with human skin, has been adequate for all our needs during
this project producing acceptable images of volunteers as well as various quality assurance
(QA) objects used for analysis.
2.3 Align RT

Align RT is the high speed reconstruction algorithm software that accompanies the SIS camera pods. Both are produced by Vision RT Inc. London. Align RT provides a user friendly graphical user interface allowing one to view static and dynamic surface images that are either recently acquired or imported from other imaging modalities (mainly computed tomography [CT]). The high speed algorithms are optimized for matching two surfaces and calculating their differences in six degrees of freedom, three for each translational and rotational displacement (the vertical, longitudinal and lateral directions). Align RT provides a unique, robust and quick method to generate 3D surface data for immediate or later use making it a very useful piece of equipment for clinical and research applications. The three major components include defining reference surfaces, verifying currents surface, and monitoring these surfaces with real time displacement delta information.

Align RT’s capability of performing both static and dynamic surface images make it a very versatile tool. This can aid in patient set up and monitoring of patient position and motion during treatment. The time it takes to generate a static 3D surface image is 5-7 seconds depending on the surface. The speckle camera flashes the speckle pattern onto the surface establishing a uniqueness of the surfaces points based off of the surfaces individual gradient and curvature. This surface can be saved to either verify a position or used itself as reference position for a particular patient position or surface orientation. The algorithm can then compare two surfaces, the reference and current surfaces, and calculates to a high degree of accuracy the differences between the two positions for the six degrees of freedom. A reference surface and a surface being verified to that reference surface are shown in Figure 2.4.

The displacements are known as deltas and are displayed in two ways. The first is a visual display overlapping both surfaces (as seen in Figure 2.4). The reference surface is displayed in purple, while the current surface is displayed in green. This allows the user to see where exactly on the body a difference in surface position occur aiding in adjustment and knowledge of the patient's surface orientation. The second is a quantitative manner in which the numerical displacements are displayed for each degree of freedom (see Figure 2.5). Quantitative values of deltas allow the user to manually shift the couch or rotate the patient by the calculated deltas to align the current image to the reference image. Both are
Figure 2.4. A: A static Reference surface acquired with the SIS cameras. B: A current surface being compared to the reference surface. The green indicates the current surfaces location showing exactly where the two surfaces vary.

Figure 2.5. Deltas displaying the differences in position between a reference surface and current surface of a patient. In this case the patient is 3 cm below their reference position.
extremely helpful for locating where on the surface there is an alignment error, and what exactly the alignment error is. In this case they are static deltas corresponding to the type of surfaces being analyzed and compared (static surfaces). This application is better suited but not restrained to setup or verification of more rigid surfaces and structures.

The dynamic surface imaging mode varies some but is very similar to the static image option. An established reference surface is still needed for baseline comparison. Once again this can be an acquired reference surface, or one imported from another imaging modality such as CT. The reference surface is always a static surface. The speckle pattern is then projected onto the surface for an extended amount of time, the length of which is how long one wishes to monitor the surface. Align RT then displays the displacement deltas in real time as shown in Figure 2.6.

![Real-Time Deltas](image)

**Figure 2.6.** Real Time Deltas for the differences between a reference and current surface.

The deltas are now called real time deltas since they are update and displayed as time and motion continue forth in the arrow of time. This allows a user to watch a surface and see how it moves over the course of monitoring.

Preventing latency in the real time delta display vs. the actual delta information is crucial for clinical applications. In order to ensure optimal real time delta displays and exclude extraneous anatomy that may not be necessary for treatment monitoring, a region of interest (ROI) can be selected. The size of the ROI may vary depending on what anatomical
part needs to be monitored and the procedure being performed. The larger the size, the more delay there will be between the real time delta displays and the actual patient position. Applications that involve gating or small beam tolerances for treatments require minimal delay. A compromise must be made then for the ROI size allowing the frame rate to be adequately updated on the graphical user interface for implementation purposes. The geometry of the ROI is important for maintaining knowledge of position and orientation of the surface. Take for a example the orientation of a sphere and a flat surface. For a flat surface, translational errors within a plane will be hard to calculate as all points in the ROI plane can easily be represented by others points in that same plane. For a sphere, rotational errors will be hard to calculate as spherical symmetry depends on a points distance to the origin only, allowing any point on the sphere to represent every other point. Thus ROI selection should include a proper sized geometrical shape which demonstrates the unique gradient and curvature of that surface. A sample ROI used for monitoring breast patients is shown in Figure 2.7.

If the Align RT SIS is calibrated to the linac isocenter, information from various imaging modalities can be imported and registered to provide easy verification and use for clinical procedures. For instance the body contour and isocenter information for a patient are imported and displayed, registering the surface to the linacs isocenter and Align RT coordinate system. This is very useful for incorporating the SIS use to the treatment simulation through the actual treatment of a patient. Treatment planning and simulation can continue to proceed as normal, then the necessary information can be exported to aid and assist during treatment via Align RT. For superficial diseases, this could eliminate the need for daily films to align patient anatomy to the treatment planned position lowering the overall dose received by the patient through the whole course of treatment. Monitoring patient motion is becoming an important part of modern radiotherapy as treatments are becoming more involved, complicated and sophisticated to deliver the necessary dose properly while sparing healthy tissues. To quote Align RT, “knowing where your patient is makes all the difference”, and this is definitely the case for Radiotherapy treatments.
2.4 APPLYING SURFACE IMAGE INFORMATION

In order for a surface image acquired with this SIS to be usable in radiation oncology, it must be installed and calibrated to the linac isocenter. The system at University of California San Diego Department of Radiation Oncology consists of three ceiling mounted camera pods and a central processing unit (CPU). One pod is placed at the foot of the couch while the other two pods are situated laterally to the couch (see Figure 2.8).

This distribution ensures that, as the gantry rotates around the rooms’ isocenter, two cameras will always have a clear view of the surface that is to be monitored. This enables that there will be accurate monitoring information for all treatment positions should any camera become occluded during use. The cameras are placed to ensure that their viewing angles are centered on the linac isocenter.

The surfacing imaging cameras reference frame must be the same as the linac reference frame for proper registration alignment and use. Before use in the clinic, commissioning and QA must be performed to establish the actual limits of the commercial product. Upon commission in our department it was determined that the SIS was
accurate to within 1 mm translational error and 1 degree rotational error. QA for our SIS is done daily as well as monthly with a calibration board supplied by the manufacturer. The calibration board consists of numerous points fixed on a grid pattern with four points larger than the rest arranged in a square symmetrically around the crosshair center (see Figure 2.9).

Figure 2.8. Three camera pods encircling the Linacs Isocenter to ensure the isocenter can be viewed at all times as the gantry and therapists may occluded certain angles at given treatment times.

Figure 2.9. Align RT calibration board.
The board’s center cross heir is aligned to the lasers indicating the linac isocenter and raised to 100 cm source to surface distance (SSD). For the monthly calibration, all three cameras take reference images of the board. The four larger points are then manually selected to establish rotational and translational base points. These cameras reference images are then saved. Daily QA is done a similar way. Images are taken, and then compared to the stored reference images acquired and calibrated during monthly QA. Calibration is successful when all points are within less than a millimeter of the reference images calibration points. Monthly QA takes roughly 7 minutes while the daily QA take about 4 minutes to complete. Now that our cameras frames of reference are calibrated and in fact the same as the linac frame of reference, one can localize its images with respect to the treatment room isocenter.
CHAPTER 3

DIBH REPRODUCIBILITY

This chapter explores the use of computer programming to aid in the dose analysis of various reproducibility levels a patient produces.

3.1 PATIENT REPRODUCIBILITY AND STABILITY

It is clear from many studies that cardiac dose is reduced greatly between FB and DIBH. Figure 3.1 shows the amount of cardiac tissue that can be removed and distanced from the field during a DIBH.

![Figure 3.1. Patient FB (left) compared to DIBH (right) displaying the distance that the heart is moved from the treatment field.](image)

The challenge in providing DIBH treatments lie in the patient producing a DIBH that is reproducible and stable. Reproducibility means that the patient inhales the same volume of air in all DIBH while expanding to a predetermined thoracic shape. Stability means that the patient is able to hold and maintain this volume of air and thoracic shape for the duration of the DIBH. The average distance of anterior chest wall displacement for patients in this study was 7.8 mm, with an inferior diaphragm drop of 1.5 cm. If the patient is only capable of producing a DIBH that is 75% of their treatment planned DIHB, their organ displacements will be less causing greater portions of the heart and LAD to be in into the treatment field.
Patients with smaller than average displacements will need more precise reproducibility while patients with larger than average displacements can have more variability in their daily breath holds compared to their treatment planned breath hold. Patient ability to produce a Reproducible and Stable DIBH are crucial for maintaining high levels of accuracy in providing adequate treatment. Without this, set up and delivery of the treatment plan cannot be properly executed.

An important factor for a DIBH treatment is the reproducibility of the patients DIBH. By obtaining the patients breathing signal, the rigid anterior posterior (AP) displacement of the chest wall during respiration can be monitored. The patient’s 3D thoracic expansion is directly proportional to the vertical amplitude of their chest wall displacement during respiration. When the patient’s chest wall is at a certain position then their thoracic anatomy is roughly in the same for that position. We define our CT DIBH reference position as zero. As the patient FB and then produces a DIBH, their breathing signal’s amplitude will rise from their FB amplitude to zero. When the breathing signal reaches this zero line, or target line, then the patient’s position matches their DIBH reference position. An example of the breathing signal between FB and DIBH is shown in Figure 3.2.

![Figure 3.2. Patient breathing signal represented as amplitude vs. time of chest wall displacement with the DIBH reference position set at zero.](image)

There are many ways to monitor a patients breathing cycle. For simplicities sake, we would like to choose a method that incorporates the least amount of excess work in comparison to normal TBRT treatments while still maintaining a high level of delivered beam accuracy and providing patient comfort. Several methods and techniques have been developed to implement DIBH treatments with Reproducibility and Stability in the clinic.
All of them essentially measure the patient’s respiratory cycle to localize the patient’s position for setup, monitoring and treatment purposes. An active breathing control (ABC), real time position monitoring (RPM), linear position transducer (LPT), and 3D SIS are all examples of devices incorporated to help the patient achieve their treatment planned DIBH. 22-25 ABC uses a pneumonic device that allows a predetermined volume of air to flow through a tube into the patient’s lungs enabling the patient to inhale the same volume of air with every deep breath. 22 The Varian RPM system places an infrared block on the patient’s chest to monitor the vertical amplitude of their respiratory motion24. LPT relays on a pressure sensitive belt to signal when a patient’s thorax has expanded to a predetermined volume. 24 SIS use 3D Cameras coupled with a computer Algorithm configuration to image the patient’s superior surface, or patient body contour, and match that to the treatment planned body contour. 25

All breathing monitoring devices discussed above incorporate a computer system to process the respiratory information to be used for treatment. They also require purchase/order and/or insulation/storage. The LPT, ABC, and RPM all require an additional object to be placed on the patient or mouth piece inserted. The LPT and ABC set ups take longer than the RPM and SIS due to the excess equipment involved. The RPM light weight block can be placed on the patient’s chest in less than 10 seconds when the patient is set up. Once the patient is placed on the table a surface image can be generated by the SIS in less than 10 seconds. The LPT, ABC and RPM do not account for any rotational errors that can be present during the breath hold process. The SIS is the only method that accounts for all six translational and rotational degrees of freedom. Thus patients breathing signal can be acquired faster with higher accuracy with the SIS.

Despite these techniques and precautions, patients will still produce various levels of inspiration through the course of treatment. One study showed that 35% of healthy volunteers vertical amplitude between breath holds varied by more than 2 mm. 26 This was just between breath holds of the same session, not even accounting for day to day variation in patient position. Visual aid can be given to the patient to help them produce more consistent stable and reproducible DIBH.

Visual Aid has shown to increase the overall reproducibility and stability of patient breathing techniques.26 The idea begins with the fact that the patient is the one who has
control over their respiratory function. As much as therapists and physicians can make adjustments to compensate for misalignments, in the end that patient still physically takes the breath. The anatomical mechanics of breathing are quite complex and involve many deformable structures molding to each other as well as the rigid skeleton of the thorax. Intercostal muscles, diaphragm, ribs, contents of the stomach, fatigue, vertebra position, and time of day are some of the factors that must be considered in thoracic anatomy changes with the respiratory cycle. Reproducing all of these functions exactly is an impossible task. Reproducing enough of these functions to achieve repositioning accuracies within several millimeters is an attainable aspiration. If the patient is able to see and understand where they are in their breathing cycle, they can then inhale or exhale to adjust as needed to reach the specific point in their respiratory cycle that has been designated for treatment. Visual aid is a means of displaying a patients breathing signal to them allowing them to control their respiratory cycle more accurately.

For this study visual aid is supplied in the form of a set of video goggles as seen in Figure 3.3.

![Vuzix Iwear goggles used for visual aid.](image)

Vuzix Iwear goggles were originally designed as an entertainment product to work with the Ipod for 3D movie enjoyment. This allows high compatibility with computer hardware. The goggles are connected in series with a RCA cable to a scan converter to the
computer that houses the SIS software. The scan converter splits the signal that is sent to SIS computer monitor and also directs it to the video goggles. A rough schematic is shown in Figure 3.4.

**Figure 3.4. Workflow of visual aid goggles connecting to the Align RT computer.**

The screen that is displayed on the monitor is now displayed within the goggles. The scan converter allows the user to zoom in and view select parts of the screen. The portion where the patients breathing signal is displayed is focused upon. The patient can now visualize their location within their breathing signal. The patient view of the software displaying the breathing signal is displayed below in Figure 3.5.

**Figure 3.5. Patient view of their breathing signal. They begin at FB then inhale increasing their vertical amplitude.**

Once the patient can view their breathing signal they can inhale or exhale to reach a predetermined position in their respiratory cycle. This predetermined position will be their treatment planned position, or their DIBH position acquired and defined in their CT
simulation scan. The CT simulation scan is imported into Align RT and saved as the reference surface. This reference surface defines the zero line on the Y axis of their breathing signal. While the patients FB their signal will be below their treatment planned position. The zero line on the Y axis appears as a standard black line for a Cartesian coordinate system. This is the target line that the patient must reach with their breathing signal while inhaling. A patient performed FB and then performing a DIBH can be seen in Figure 3.5 (p. 22). Once the patient reaches the target line, they are within tolerance of their treatment planned position.

Our goal is to have the patient reach this line during treatments, but reaching it exactly is again affected by varying inspiration levels they can perform at that time. If the patients DIBH is less than their treatment planned DIBH, setup will be compensated for by aligning our patients to their anterior surface. The breast tissue is the area to be treated so this is the anatomy that we always want to be in the treatment planned position or within the treatment field. If their breath is not as deep, the couch will be shifted upward until their anterior surface matches the reference DIBH surface. Anatomy deep to the chest wall will then be closer to the treatment field, but still further away than during FB resulting in lower absorbed dose. The anterior surface however will always be in the same position in accordance to the plan so the target dose will not be affected. Volumes of the OAR can move into the treatment field when the patient is unable to produce a full DIBH. The dosimetric impact to OAR’s is still less than that at FB, but the actual absorbed dose remains unknown. We would like to evaluate the actual dose that OAR can receive at these varying inspiration levels to make sure that they do not receive a significant dose that could cause complications.

The variability in dose from different inspiration levels remains a difficult task to estimate. Even if the patient is within tolerance, they could still be producing a DIBH that is 25% off of their treatment planned position since we align to the patients anterior external surface. Acquiring sufficient varying inspiration level scans would be difficult and time consuming. Obtaining enough CT scans of patients’ variable inspiration levels necessary for a dose risk estimate study would in itself supply an even greater risk for radiation induced disease than TBRT performed at FB. Port films of a patients’ inspiration level would have to be taken daily, or a large number of patients’ would have to be treated to reach a significantly
sound statistical model to evaluate. Once again the excess dose to patients as well as the time to accumulate an adequate dataset is counterproductive to our overall goals. Respiratory gated MRI studies are an option, but time and resources are demotivating factors as well as finding machines and persons who are capable of performing 4D MRIs. Image processing is the next tool that comes to mind for a possible analysis of patients varying reproducibility levels impact on dose to OAR.

### 3.2 Deformable Image Registration (DEMONS)

Image Registration has become an important tool in the medical practice. It is a specific type of geometrical transformation (GT) in image processing. By modifying the spatial relationships between voxels, an image can be shifted, rotated, stretched, shrunk, and manipulated to align similar scenes or objects. To accomplish any of these, each voxel of an input spatial coordinate, \((x, y, z)\), must relocate to a voxel of an output spatial coordinate, \((t, u, v)\). The transform is a function which relates these voxels two spatial coordinates,

\[
(x, y, z) = T((t, u, v))
\]

(3.1)

describing the differentiable gradient map that modifies their spatial relations in a manner that the user desires. The path from output to input coordinate would be described by the inverse transform:

\[
(t, u, v) = T^{-1}((x, y, z))
\]

(3.2)

A simple example would be rotating an image of a square 45 degrees to form a diamond and mapping how vertices change in a coordinate system. Knowing this path enables any image to be normalized to a set coordinate system and manipulated to form the desired orientation. This coordinate system is a 3D representation of actual space built into a computers frame of reference. This is necessary when comparing images from different modalities, or different images of the same patient.

Solving for this transform has traditionally been done using a change of variable to simplify an integral for a known function describing the geometry mathematically. In these cases the object, or mathematical function, was known from prior information. For image processing however this prior information is not readily available. The first step to image registration then is defining the objects of interest that a user wishes to focus on. Through
either manual or automatic segmentation, the boundaries of rigid structures can be outlined. Image segmentation is a technique which depicts points, lines and edges in an image by detecting where within the image voxels intensity discontinuities exist. Generally a convolution mask or gradient computation between neighboring voxels identifies these intensity discontinuities.27 Many built-in segmentation tools exist in Matlab, and choosing the best one fitted for the users procedure is all that needs to be done. Once outlines are established, their voxels become our coordinates to be mapped from input space to output space. As rigid structures move, their geometry does not change making translational or rotational shifts the only transformations between two time sequences. These structures are easily identifiable and hence can be easily matched. In medical imaging the skeletal system is the best representation of rigid objects that do not deform over time.

Rigid registration is thus detecting and matching user defined features to infer the geometric transformations existing between multiple images. Because the human anatomy is comprised of much more than rigid skeletal structures, our registration methods must evolve to compensate for the organs and structures whose geometry varies over the course of time. Once the skeletal system has been identified and registered, the deformable anatomy is localized to the corresponding skeletal foundations of the human anatomy. For example, the lungs are always located within the thoracic cavity enclosed by the ribs and vertebra. Thus as they deform due to physiological functions, their geometry will be confined to this space and the boundaries defined by the cavity they are located in. With this, one can more accurately model the deformations that take place from physiological processes in deformable organs. Knowing the constraints narrows the actual realistic transformations that can occur as a deformable objects geometry changes over time. Once a deformable organ is localized to the space it can move in, the transformations between two images in time can then be calculated. The new challenge then comes in mapping the coordinates of an object from input to output space whose geometry varies. This will be done in the form of deformable registration in which a model must be selected to accurately represent the transformation of an objects’ whose geometry has changed.

Recent advances in deformable image registration (DIR) allow elastic geometrical transformations to be generated and applied between two images fast and accurately. These are particularly useful for these cases when rigid registration is not applicable for anatomical
structures that do not simply translate or rotate with patient motion and physiological functions. Examples include respiratory motion, gastrointestinal motion, cardiac motion, and peristalsis. These transformations can be used to mimic a wide variety of anatomical positions and structures correlating to the images from which they arose. There are two types of DIR models, attractors and demons. The latter has emerged as the dominating model for research and clinical uses. The primary focus for discussion of DIR will detail the demons method which originates from a thermodynamic optical flow diffusion process known as Maxwell’s Demons.

The demons algorithm was first introduced in 1995 by Thirion for DIR. Its basis is a theoretical thermodynamic paradox in which a “demon”, or entity capable of distinguishing between two states, decides and allows two types of particles to pass between a semi permeable interface until the two types of particles are distributed evenly on each side of the interface. Basically all particles of the same type end up on one side of the semi permeable interface. Its conjunction with medical imaging comes in an algorithm in which a demon distinguishes how a deformable model of voxels, a 3D moving image data set, deforms to a static model, or a 3D static image data set. For this study the data sets were CT patient scans to be described later. The intensity values of each voxel correspond to the different densities of materials comprising the human anatomy. This occurs from the attenuation of x-rays that transverse the patient’s anatomy during a CT scan. Iso-intensities represent the various tissues, organs and structures of that patients’ anatomy. A “demon” moves the deformable models voxels until their intensities accurately represent the static model voxels intensities. The forces that the demon must use to push or pull those voxels can help describe the way deformable human anatomy deforms over time as well as how deformable structures interact with one another and with rigid structures.

Using an optical flow model, Thirion proposed to represent the velocity of these particles, or voxels, as they travel in time between two spatial frames mathematically as:

\[ \vec{v} \cdot \nabla s = (m - s) \]  

Here \( m \) and \( s \) represent the CT intensities from each image; \( \nabla s \) represent the gradient of the static image intensities (when it is held constant) and \( \vec{v} \) represents the displacement vectors between the two images intensities. Equation 2 states that the difference between
the intensity \((m - s)\) for the same object in different time frames with which a deformable substance moves from one position to another should be equal to the rate at which it travels, \(\dot{v}\), multiplied by the gradient of the path it follows \((\nabla s)\). In order to avoid computation and constraint errors when values of \(\nabla s\) are small one can algebraically manipulate this equation to provide a more stable form as seen below.

\[
\dot{v} = \frac{(m - s)\nabla s}{(\nabla s)^2 + (m - s)^2}
\]  

(3.4)

We now have a mathematical model to represent the diffusion process as similar intensity values flow from one voxel in input space to a voxel in output space. The two images will represent the same observable patient features in 3D space (tissues, organs, bones) described at two independent time coordinates, for instance, two images of a patient at different points in their respiratory cycle. The image we wish to match to another will be defined as our moving or model image \(M\), while the image we are matching to will be defined as our static or scene image \(S\). We consider \(M\) to be a deformable 3D object whose voxels will relocate to the corresponding voxels of \(S\). Each voxel will be considered as an iteration point \(P\). The intensity values will remain constant as the \(M(P)\) voxel are either moved or drawn into the \(S(P)\) voxels position to match the deformable model contour since the density of tissues, organs and structures remains static. Essentially we have a function vector array \(M(P)\) that we wish to deform to \(S(P')\), \(P'\) being each iteration in the contour of the static image \(S\) called a demon.

The demons will be placed along our \(S\) iso-intensity contour voxels representing the various patient anatomical structures. From here they will decide whether the iteration intensities of \(M\) are in or outside of \(S\). When a voxel is labeled as inside, our demon pushes this voxel towards the inner surface of our \(S\) image contour. When a voxel is outside, then it is pushed towards the outer surface of our \(S\) image contour. The voxels could also be pulled into place by the demon resulting in two possible types of acting forces. A passive force pulls the voxels to displace them while active forces pushes voxels to displace them. A passive forces is derived from the static image alone and, like gravity, pulls the voxel \(M(P)\) to its \(S(P)\) 3D position. For image processing it is simpler to consider the velocity to actually be a translational displacement, or the distance a voxel moves to match its coordinated
position in another image. Applying this to Thirion’s original equation the displacement vectors can be described as

\[ d\vec{r} = \frac{(I_m - I_s)\vec{V}I_s}{(\vec{V}I_s)^2 + (I_m - I_s)^2} \]  

(3.5)

where \( I_m, I_s \) represent the CT intensities; \( \vec{V}I_s \) represent the gradient of the static image and \( d\vec{r} \) represents the displacement vectors between the two images intensities. Here the displacement vectors are normalized to the static image. An Active force is the force that drives the M (P) voxel into S (P’)s 3D position. This instead normalizes the displacement vectors to the moving image before each iteration and is represented similarly as:

\[ d\vec{r} = \frac{(I_m - I_s)\vec{V}I_m}{(\vec{V}I_m)^2 + (I_m - I_s)^2} \]  

(3.6)

Wang et al. developed a method where the active and passive forces in the demons algorithm combine to move the M (P) voxel to the S (P’) location. In this double force method they also introduced a normalization factor \( \alpha \) that was supposed to adjust the length of the displacement vector at each iteration. However, for implementation, \( \alpha \) is usually fixed at \( \alpha = 0.4 \) based on their findings while working with CT images.  

Our final formula for describing the displacement of voxels between two images is thus:

\[ d\vec{r} = \frac{(I_m - I_s)\vec{V}I_s}{(\vec{V}I_s)^2 + \alpha^2 (I_m - I_s)^2} + \frac{(I_m - I_s)\vec{V}I_m}{(\vec{V}I_m)^2 + \alpha^2 (I_m - I_s)^2} \]  

(3.7)

From here one can generate a computer program to calculate the displacement vector at each iteration between the two images. Speed and accuracy are the next issues to be dealt with.

### 3.3 DEMONS GPU IMPLEMENTATION

We wish to calculate the deformation vectors in a relatively fast and accurate manner as to apply them as needed. Modern CPU computation can take hours to perform such calculations, making it not applicable in the clinic, and a hassle for performing research involving multiple image arrays. With recent developments using graphics processing units (GPU) for parallel computing, complex DIR Algorithms now allow fast and accurate generation of the 3D displacement vectors that arise between two different images of a patient. One such algorithm developed by X. Gu et al, which we used in this study, allows
256x256x100 array data sets at 2.5mm slice thickness to produce 3D vectors with an average 3D spatial error, ranging from 1.5mm to 1.8mm for each demons variant, in 11 seconds. Other groups have developed algorithms with similar results.

When a graphics card is used for computations other than visualization, the process is referred to as general purpose graphics processing units (GPGPU). GPGPU are displaying tremendous capabilities for scientific research in which mass of amounts of data must be processed through similar mathematical functions repeatedly. GPGPU programming is essentially an extension of the C language platform and is organized much in the same way. The extension language library developed by NVIDIA for their manufactured GPUs is known as Compute Unified Device Architecture (CUDA). They have developed many GPU cards available for purchase with higher priced cards capable of more powerful computations. For the purpose of this paper we will discuss implementation on a Tesla C1060, which is the GPU we used for this project. The Tesla C1060 unit consists of 240 processor cores grouped into 30 multiprocessors with 8 cores each. Each core has a clock speed of 1.3 GHz. Basically it is like connecting 240 CPU’s with 1.3 GHz in a network for computational purposes. The physical graphics card is shown in Figure 3.6.

![NVIDIA Tesla C1060 graphics card](image)

**Figure 3.6. NVIDIA Tesla C1060 graphics card.**

The speed up of computation in GPU programming comes from parallel computing. Parallel computing is a process in which many computations can be calculated concurrently over large data sets. This enables a function to simultaneously work on the elements data of an array. The GPU has evolved over the years to allow floating point performance memory in the range of teraflops. The GPU operates off of a host computer, or a CPU. The CPU
runs the sequential applications while the computationally intensive applications are passed on to the GPU due to its high performance.

For implementation on a GPU, the iterations used are important for parallel computing to allow various kernels to work on an iterative data set. We hold our static image intensity and gradient constant then step through our moving image sample by sample. The next step involved is optimization in computational processing of the displacement vectors. A multi scale, or multi resolution, solution can increase the 3D displacement vector accuracy and speed up over all computational time. Images are down sampled to a lower resolution. The iterations for the displacement vectors are calculated first for the lowest resolution images (for our case 64x64xZ), Z being the number of slice for the corresponding patient CT scan. These displacement vectors are then up sampled, along with the images by a factor of 2. The displacement vectors serve as the initial displacement vectors at a higher resolution for an initial estimate. The vectors are then recalculated at the higher resolution and reoptimized.

Previous Steps are continually done until the displacement vectors reach a stopping criterion. The criterion is set to stop calculations when there is “no” force displacing the voxels anymore. A criterion related to spatial accuracy is chosen as opposed to image similarity to find more accurate deformed vector fields related to the contours between the two CT images. Once this is complete the vectors are saved and exported as individual files from the algorithm. We now have vectors describing the amount of voxel displacement that exists between the iso-intensity values of the two images.

3.4 Fictional CT Patient Scans

We can now use the Demons DIR to produce the 3D displacement vectors between two images of a patient at different times. The resulting 3D vectors can be manipulated and applied to their corresponding images to generate a wide range of fictional anatomical scans between the two time frames mimicking the respiratory cycle. Using FB scan as one image and DIBH scan as the other, various levels of inspiration can be created by applying different percentages of the deformation vectors to the FB scan. Thus the FB scans represent and are defined as the baseline for the change of volume of the patient’s thorax, or their zero percent inspiration level and the DIBH scan represents full inspiration, or their one hundred percent
inspiration level. These new inspiration level scans can be saved and then be imported into a treatment planning system, or imported into a dose calculation algorithm to estimate the dosimetric impact that varying levels of inspiration can have. For this study patient scans were created at 75, 90, 100 and 110 percent inspiration levels to evaluate the dosimetric impact from varying reproducibility.

After IRB approval, 13 Patients who were to undergo TBRT for left breast cancer were asked to have two CT scans at our institution. The patients first completed a CT scan while FB, then completed a CT scan at DIBH. Scan time for each scan was roughly 35 seconds depending on patient size. Patients were placed laying on the couch supine with both arms above their head. Each patient was immobilized on a breast board to support their head, back, elbows, arms and shoulders. A 4 slice with 4 detectors GE lightspeed scanner was used with a 2.5mm slice width. The technique for acquiring the scans used was a chest protocol of 120 KvP with 20 mA tube current. The FB and DIBH scans were exported for offline analysis on a GPU and Matlab. Both scans were down sampled in Matlab from 512x512xZ to 256x256xZ arrays. The scans were then rigidly registered to each other, and then deformably registered to each other. Both registrations were done on a GPGPU using algorithms developed at UCSD by X. Gu et al. The displacement vectors were extracted, saved and exported for offline analysis on CPU. Using a tri-linear interpolation function in Matlab, interpt3, the vectors were applied to the FB scan at 75, 90, 100 and 110 percent magnitude. Each newly created image array represents a fictional anatomical data set of the patient at that percentage of their inspiration level. Each virtual image was then up sampled back to 512x512xZ. Each plane in the Z direction represents a CT slice. The fictional anatomical scans are shown in Figure 3.7:

Each newly created slice must come to represent a scan acquired from a CT machine. In order to import these fictional CT slices into a treatment planning system for a dosimetric evaluation, they must be saved and written in the DICOM standard format. These images where then written and saved as individual DICOM slices with the DICOM metadata from the original DIBH DICOM slice files. First the metadata between the FB and DIBH scan were compared. Since they were two separate scans, metadata specific to an individual scan will be different between the two. The rest of the metadata corresponds to machine, institution and other patient identification information. Various DICOM metadata,
Figure 3.7. Original scans plus created scans. 75, 90, 100, 110 percent of inspiration levels.

specifically Unique Identifier DICOM IDs (UID), were altered to mimic the creation of an actual CT scan taken of the patients allowing easy and organized importation into treatment planning systems. The UID’s contain the registration information which must be altered in order to apply geometric transformations allowing these fictional scans to be registered into the proper coordinate system for comparison. In order to maintain consistency when evaluating these scans for dose estimation, all inspiration levels where created using the methods mentioned earlier to account for errors occurring in the demons algorithm 3D Displacement Vectors. The new patient DICOM files were saved to be used for further analysis.

The fictional percentage inspiration level CT images were imported into Eclipse (Varian System Inc.) treatment planning system as separate CT scan simulations. Each new scan was rigidly registered to the surface anatomy of the original DIBH scan. All scans were registered to the anterior surface due to the fact that the breast tissue was our main concern and this must always be in the field. The Body, Heart, and LAD were all contoured by our
Resident Radiation Oncologist. The heart contour started at the most inferior portions of the vena cava, aorta, and pulmonary valves continuing to the superior portion of the diaphragm. This portion includes only the majority if not all of the cardiac muscle. The LAD contour sits between the right and left ventricles in the inter-ventricular sulcus that runs inferiorly along the anterior portion of the cardiac muscle. It originates behind the left pulmonary value and travels anteriorly until it begins to descend down the inter-ventricular sulcus. The lungs were initially contoured as well, however several of the patient scans did not included the entire lung volume so analysis was unable to be performed accurately. The original DIBH plan was copied and applied to the variable inspiration levels for dose analysis. The contours and plans were verified and saved. Cumulative dose analysis was then performed and compared on the two original scans (FB and DIBH) as well as in the four virtual scans. The dose volume histograms (DVH’s) for the OAR’s of each patients inspiration levels where exported for comparison and analysis.

The main results of this study are shown in Tables 3.1 through 3.4. The pair sampled T-test was used to determine statistical significance between various inspiration level doses estimated to the heart and LAD.

**Table 3.1. Average Heart Mean Dose with Corresponding P Value Comparisons**

<table>
<thead>
<tr>
<th>Breath hold level</th>
<th>Heart Mean Dose (Gy)</th>
<th>P value vs. FB</th>
<th>P value vs. DIBH</th>
</tr>
</thead>
<tbody>
<tr>
<td>FB</td>
<td>2.7</td>
<td>N/A</td>
<td>.02</td>
</tr>
<tr>
<td>75</td>
<td>1.3</td>
<td>.02</td>
<td>.012</td>
</tr>
<tr>
<td>90</td>
<td>1.1</td>
<td>.02</td>
<td>.004</td>
</tr>
<tr>
<td>DIBH</td>
<td>1.1</td>
<td>.02</td>
<td>N/A</td>
</tr>
<tr>
<td>110</td>
<td>1.0</td>
<td>.02</td>
<td>.016</td>
</tr>
</tbody>
</table>
Table 3.2. Average Heart Volume Receiving 50% of Prescribed Dose with Corresponding P Value Comparisons

<table>
<thead>
<tr>
<th>Breath hold level</th>
<th>Heart V(50) (%)</th>
<th>P value vs. FB</th>
<th>P value vs. DIBH</th>
</tr>
</thead>
<tbody>
<tr>
<td>FB</td>
<td>5.0</td>
<td>N/A</td>
<td>.039</td>
</tr>
<tr>
<td>75</td>
<td>0.9</td>
<td>.031</td>
<td>.016</td>
</tr>
<tr>
<td>90</td>
<td>0.7</td>
<td>.039</td>
<td>.031</td>
</tr>
<tr>
<td>DIBH</td>
<td>0.6</td>
<td>.039</td>
<td>N/A</td>
</tr>
<tr>
<td>110</td>
<td>0.5</td>
<td>.039</td>
<td>.016</td>
</tr>
</tbody>
</table>

Table 3.3. Average LAD Mean Dose with Corresponding P Value Comparisons

<table>
<thead>
<tr>
<th>Breath hold level</th>
<th>LAD Mean Dose (Gy)</th>
<th>P value vs. FB</th>
<th>P value vs. DIBH</th>
</tr>
</thead>
<tbody>
<tr>
<td>FB</td>
<td>22.4</td>
<td>N/A</td>
<td>.007</td>
</tr>
<tr>
<td>75</td>
<td>11.6</td>
<td>.001</td>
<td>.032</td>
</tr>
<tr>
<td>90</td>
<td>8.8</td>
<td>.007</td>
<td>.365</td>
</tr>
<tr>
<td>DIBH</td>
<td>8.3</td>
<td>.007</td>
<td>N/A</td>
</tr>
<tr>
<td>110</td>
<td>6.9</td>
<td>.006</td>
<td>.145</td>
</tr>
</tbody>
</table>
Table 3.4. Average LAD Volume Receiving 50% of Prescribed Dose with Corresponding P Values Comparisons

<table>
<thead>
<tr>
<th>Breath hold level</th>
<th>LAD V(50) (%)</th>
<th>P value vs. FB</th>
<th>P value vs. DIBH</th>
</tr>
</thead>
<tbody>
<tr>
<td>FB</td>
<td>39.7</td>
<td>N/A</td>
<td>.014</td>
</tr>
<tr>
<td>75</td>
<td>18.0</td>
<td>.008</td>
<td>.031</td>
</tr>
<tr>
<td>90</td>
<td>11.0</td>
<td>.015</td>
<td>.100</td>
</tr>
<tr>
<td>DIBH</td>
<td>10.4</td>
<td>.014</td>
<td>N/A</td>
</tr>
<tr>
<td>110</td>
<td>7.5</td>
<td>.008</td>
<td>.313</td>
</tr>
</tbody>
</table>

Initial results show that all patients will benefit from a DIBH procedure. The exact extent of benefit is patient dependent, and some patients should have a DIBH procedure whereas in others it is as not as much of a concern as the cardiac tissue is not significantly located within the tangential fields. In order to determine whether or not a patient will benefit from a DIBH treatment to spare the cardiac tissue, an initial FB scan is needed for visual inspection. There is no way to know unless one can physically look to see where the heart is or will be in relation to the treatment fields. At this point no way around an FB scan has become available.

The mean dose to the heart was decreased on average by 52%, 59%, 59% and 63% respectively compared to FB, while the volume of the heart receiving 50% of the prescribed dose decreased by 82%, 86%, 88% and 90% for the 75, 90, 100, and 110 percent inspiration levels. On average the mean dose to the LAD was decreased by 48%, 61%, 63%, and 69% for the 75, 90, 100, 110 percent inspiration levels compared to FB. On average the Volume of the LAD receiving 50% of the prescribed dose was decreased by 55%, 72%, 74%, and 81% for the 75, 90, 100, 110 percent inspiration levels compared to FB.
A greater volume of the heart is always removed from the field when compared to the LAD. This of course is due to the LAD anterior location in the hearts inter-ventricular sulcus and will always remain that way. The mean dose reduction to both organs is quite similar as the inspiration level increases. From this data it is clear that the amount of dose the LAD receives is always much greater than the heart. 10% of the LAD volume absorbs 8.3 Gy at DIBH while the 0.6% of the heart receives 1.1 Gy.

This study shows that the overall dose and volume of the heart and LADCA receiving that dose varies little between greater inspiration levels (from 75% to 110%). The LAD dose and volume receiving that dose however has a larger difference between inspiration levels, but the differences are not statistically significant. We believe that, although the larger the DIBH level the better the treatment, dose variations within different DIBH levels are acceptable for treatment. Using visual aid, our target DIBH level should be reached regularly causing small dose differences in varying inspiration levels to have less of an effect on the corresponding OARs compared to constant treatment at any single percent inspiration level. From here we plan to implement a procedure for this treatment using surface imaging and visual aid to align the anterior surface of the patient at DIBH to spare the heart and LAD.
CHAPTER 4

CLINICAL IMPLEMENTATION

This chapter discusses the results of the initial implementation of the Deep Inspiration Breath Hold procedure.

4.1 PATIENT SELECTION

For implementing new procedures patient selection is important to minimize variable errors that may occur. This procedure was approved by the UCSD IRB. Choosing patients that are highly competent and compliant with the procedure helps to solidify the work flow into a routine for the employees involved. All patients for this study would come from candidates that were receiving adjuvant TBRT of the whole breast. Patients who showed a considerable amount of cardiac tissue in the treatment field from their initial CT scan at free breathing were chosen. Younger, more healthier (with the exception of their cancer) individuals were targeted to avoid complications due to age and endurance while producing DIBH as well as the fact that their possible life expectancies could far exceed the 15 years in which cardiac complications could occur. Willing patients would also be chosen for the understanding that this was a new procedure that had not been implemented before so it would not be flawless. Patients meeting these criteria were asked to undergo in this treatment by their treating physician. Upon agreement the patient was given a brief information sheet providing tips and ideas for replicating breath holds. It was made clear and evident that they would be required to hold their breath for 40 seconds in order for this procedure to work. Patients were then brought back in for a second treatment simulation scan this time acquired while the patient performed a DIBH.

4.2 TREATMENT SIMULATION

The first step for a radiation therapy treatment is proper simulation. During simulation, the reference surface and patient position at DIBH will be established from the CT scan. It is essential that the patient understands that this position is the position they must match during treatment. Therefore during simulation they must achieve a comfortable
position to lay in through the course of treatment. Before the actual scan, a 15-30 minute training session was held explaining to the patient their role in achieving a reproducible and stable DIBH. During these training sessions, it was explained that the patient must concentrate on inhaling air into their chest as opposed to their abdomen. This ensures that the lung’s volume expansion affects the upper thoracic cavity more than the abdomen by pushing the anterior chest wall away from the heart. In some patients the heart will also move inferiorly to the sternum’s location from the lungs expansion. The patient then performed a few practice breaths to become familiar with chest breathing, and to verify that they were capable of a 40 second breath hold. Patient immobilization was addressed. They were informed they must remain as still as possible once set up for their treatment with the exception of the breath hold movement. The SIS was discussed explaining the projection pattern of non-ionizing light that would be displayed over them to produce their surface image in the computer’s reference frame. They were then introduced to the Visual Aid Goggles and Align RT software. The breathing signal was described thoroughly from the sinusoidal FB pattern to the vertical amplitude rise from producing a DIBH. A black target line would appear above their FB breathing signal and when asked they would inhale until their breathing signal reached the target line. The patient then performed a DIBH and a reference image was acquired. They then practiced inhaling to reach the target line and their reference position. This was done until the patient felt comfortable with the procedure. From here treatment simulation proceeded as normal with a DIBH scan instead of a FB scan.

Patients were placed laying on the couch supine with both arms above their head. Each patient was immobilized on a breast board to support their head, back, elbows, arms and shoulders. A knee cushion was provided for comfort. The Radiation Oncologist was then paged to apply radiopaque markers and tattoos for alignment and treatment planning aids. The tattoos were placed on the sternum and lateral rib and defined the patient isocenter plane. The radiopaque markers defined the field borders to be used for planning and treatment. These markers were placed while the patient was FB. Proper adjustments would be made during treatment planning accounting for the change in position of these markers due to their displacement during DIBH for set up purposes. It had been discuss to place these markers on while the patient produced a DIBH when the therapist had become more familiar with the procedure. The patients then completed a CT scan at DIBH.
Treatment planning was done to the discretion of our Radiation Oncologist. 50Gy were delivered over 25 Fractions in 5 weeks. In some cases an additional electron boost was given to areas of concern. Depending on the amount of tissue to be penetrated by the beam, either 6 or 15 MV photons were used with corresponding monitor units. Generally if there is a 24 cm gap between the medial and lateral tattoos 15 MV photons are used. A medial and lateral tangential field would deliver the dose. The medial field gantry angle was generally around 290 degrees while the lateral field gantry was around 110 degrees. The collimator generally was held at 0 degrees. Field sizes were within 9x16 cm margins. MLC heart blocks were drawn into the plan for extra precaution for patients that still had a close cardiac proximity to the field at DIBH. Treatment planning was done with the Eclipse treatment planning system designed by Varian Inc. Patients would return for treatment the following week. For set up notes, SSD on the FB and DIBH were provided. The lateral tattoos position in reference to the breast board the patient was immobilized on was given for both FB and DIBH in the set up as well. For the simulation or pretreatment process, the following work flow chart was developed to assist those involved. It can be seen in Figure 4.1.

4.3 Treatment Procedure

The procedure was discussed with Radiation Therapists prior to inform them of the details and trouble shoot for possible problems. The first 3 days of treatment, portal films were taken to ensure correct alignment and verify that the patient position was the same as simulation. Films were taken weekly from then till the end of treatment. Setup and monitoring would be done using the SIS system, but the portal films would remain as the ground truth for positioning and accuracy. This was done to verify and build confidence in the overall accuracy of Align RT. The treatment tolerances were set to be no greater the 3 mm translational error and 3 degrees rotational error.

The patient’s reference position in Align RT was loaded prior to the patient entering the treatment room. The patient was brought into the treatment room and positioned and immobilized on the breast board as during simulation. The visual aid goggles were prepared and given to the patient at this time. The therapist then aligned the patient tattoos to the room’s lasers indicating the isocenter. The vertical position was adjusted until the patient FB SSD match that of the set up notes. The gantry was then moved to the medial field’s position.
Figure 4.1. Work flow for pretreatment simulation process for DIBH.
and the patient was shifted to isocenter. The patient was then asked to perform a DIBH. The DIBH SSD was checked as well as the field borders to ensure they matched the borders placed on by the physician. The patient would always be aligned to their anterior surface. Thus the couch would be adjusted until the DIBH SSD matched that of the plan. The FB SSD was used only for initial set up to place the patient in the general area so as to not have any drastic vertical shifts that would be made. The gantry was then moved to the lateral field position and the patient produce a DIBH once again. SSD and field border alignments were verified again.

The SIS was then turned on to monitor the patient’s position during respiration. The patient was then asked to produce another DIBH inhaling to the target line. The couch and patient were then adjusted until the translation and rotational errors inAlign RT were within tolerance. The patient FB and then was asked to perform a DIBH one more time to verify their position was that of the treatment position. Films at DIBH were then taken to compare to the treatment planned position. If they were considerably off, the patient was shifted and new films were acquired until they were approved by the treating physician. At this point a new reference image was acquired to correct for any inconsistencies between the SIS CT reference image and the films. As therapist became more familiar with the treatment the Align RT and SSD set up verification were done simultaneously. Once verified the room was cleared to begin treatment.

The patient was asked to perform a DIBH via the Linac safety intercom from outside of the treatment room. Upon reaching their treatment DIBH and all displacements errors within tolerance, the beam was turned on. If for some reason they were outside of tolerance they were asked to FB and then perform another DIBH. If this occurred a second time, or their displacements were significantly outside of tolerance, the therapists reentered the room to shift the patient back within tolerance. For the first patients the beam hold function in Align RT was disabled and performed manually if the patient exceeded tolerance. The following work flow chart was developed to aid throughout the treatment process as seen in Figure 4.2.
4.4 Initial Experience

Our initial experience was gained from four patients that we were able to treat in an approximate two month span. Like any new procedure, proper preparation can still not detect all problems and errors that may occur when beginning implementation. Upon multiple discussions finalizing our new procedure we were prepared to begin implementation expecting unforeseen errors to occur. We thus included in our development of DIBH treatment a flexible workflow that would allow us to adjust as needed to deal with new issues.
that arouse and as we became aware of more efficient methods of accomplishing our goals. We ideally intended for our procedure length to fit into a 15 minute time slot in the daily treatment routine. We over estimated the number of breath holds required for setup to ensure our methods were accurate and evaluate which BH were necessary and most efficient overall for set up. Three therapists would initially be trained, and then new members would be rotated in to be trained. Prior to the first treatment a brief meeting was held to describe why we were performing this treatment and the methods we would go about to accomplish this treatment. All involved were consulted for ideas and concerns to make our procedure more robust. We eventually came to the conclusion that we had to just go ahead and begin treatment to see how reality would work out in comparison to theory.

We began knowing that most were unfamiliar with the SIS. The few that had used the SIS had done so with Frameless Maskless brain SRS treatments in which sub millimeter position was critical. For breast treatments our parameters were much loser and we constantly had to remind ourselves that sub millimeter accuracy was an unreasonable goal. However, this still loomed in the back of everyone’s mind, which I believe helped implement this with very high positioning accuracy compared to all other forms of breast treatments. Even though our tolerances were set at 3 mm, it always seemed that we were trying to reduce our translational errors to less than 1 mm, which did occur for many patient fractions and are displayed in the results of Table 4.1.

Surface alignment was a new concept to most. It took several fractions before therapists really understood why we were doing surface alignment and the benefit it played in our procedure. They had always relied on tattoo placement and assumed that if the tattoos were on with the lasers the rest of the anatomy was to. There were several instances however where the tattoos were very close but Align RT considerably off. Upon seeing errors in Align RT with set up, therapist were quick to jump to the conclusion that something was malfunctioning with our SIS. This was proven not true when the portal imaging films were viewed. When an error was shown with the SIS, the films displayed a set up misalignment. This helped them gain confidence in Align RT as well as expose other minimal errors in normal breast treatments.
Table 4.1. Initial Clinical Experience Data for the First Three Patients Treated at DIBH at UCSD

<table>
<thead>
<tr>
<th>Initial Data</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td># of breath holds</td>
<td>7.4</td>
<td>6.2</td>
<td>4.6</td>
<td>6.1</td>
</tr>
<tr>
<td>Setup time (min)</td>
<td>18.3</td>
<td>14.0</td>
<td>11.7</td>
<td>14.7</td>
</tr>
<tr>
<td>Total time (min)</td>
<td>21.7</td>
<td>16.3</td>
<td>14.4</td>
<td>17.5</td>
</tr>
<tr>
<td>VRT (mm)</td>
<td>-0.1</td>
<td>-0.2</td>
<td>-0.1</td>
<td>-0.1</td>
</tr>
<tr>
<td>LNG (mm)</td>
<td>-0.2</td>
<td>0.3</td>
<td>-0.8</td>
<td>-0.2</td>
</tr>
<tr>
<td>LAT (mm)</td>
<td>0.4</td>
<td>0.3</td>
<td>-0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>Rotational VRT (°)</td>
<td>1.8</td>
<td>2.4</td>
<td>-0.5</td>
<td>1.2</td>
</tr>
<tr>
<td>Rotational LNG (°)</td>
<td>-1.2</td>
<td>0.8</td>
<td>-0.3</td>
<td>-0.2</td>
</tr>
<tr>
<td>Rotational LAT(°)</td>
<td>1.7</td>
<td>1.2</td>
<td>2.6</td>
<td>1.8</td>
</tr>
</tbody>
</table>

Minimizing the rotational errors was our major issue. Translational displacements were easy to correct for as they were a direct couch shift. The rotational errors however were more counter intuitive as to how to adjust the patient to minimize them. The vertical and lateral varied the most with setup and treatment. The vertical was discovered to be caused by the patient’s shoulders not being properly aligned when placed on the table. Instead of having their vertebra in parallel with the center length of the table, they would have a slight angle. Shifting their shoulders laterally corrected for this error. The lateral angle was directly affected by the act of a BH. Upon inhaling patients were seen to arch their back while attempting to chest breath. We believe one reason this was occurring was because patients were too compliant. They were simply over compensating for chest breathing by exaggerating the vertical rise in their chest due to respiration. The knee cushion also had a
large effect on the lateral rotational error. Depending on how their legs laid on the cushion, their torso could be elongated or arched causing the error.

These rotational errors did not occur for every fraction or consistently in any manner. They happened randomly and caused some confusion at first as to what was happening with our setup method. They were a little discouraging as they caused a couple treatment fractions to take a considerable amount of time. After one particularly poor fraction, we called in an extra physicist and the planning dosimetrist to assist in the next fraction. The next fraction was errorless and continued through smoothly. By our third patient however, these errors were not a problem. We learned how to adjust them quickly and knew what to look for while setting up the patient to minimize these errors before they occurred. They also reinstated how important communication with the patient was during setup. We found patients knew when they were arching their back or out of place for the most part.

Despite these errors and troubles that we had, our initial treatments went very well. We were able to reduce the overall treatment time and setup by 7 minutes from the first to third patient. We also decreased the number of breath holds for setup by 3. For our third patient we averaged 14.4 minutes for overall treatment time with an 11.7 minute required for setup with 4.6 breath holds for set up. We were very happy to see these types of reductions from our first to fourth patient. This showed that the feasibility of making this a fast and accurate heart sparing treatment was very high. The average times, breath holds and displacements in six degrees of freedom are shown in Table 4.1 (p. 44) for our first three patients.

All involved were quite impressed with the overall success of our implementation. For the most part it was believed that setup, treatment times, and errors would vary much more than they actually did. Being able to use this procedure in the 15 minute slot that we originally wished to have it in was proven to be a highly valuable option. Physicians and therapists were all quiet pleased with the results of the treatment. The accuracy in which these breast patients were treated was highly superior compared to those treated normally.

4.5 **Overall Summary**

This document has been provided to show the applicability of implementing a DIBH treatment using surface imaging with visual aid in clinic practice. We have seen the effects
and costs that breast cancer has on society and the female population. Recent evidence has shown the need for refined treatment methods in order to account for radiation induced complications that can arise while treating diseased tissue. DIBH procedures deal with these concerns and are added to the total arsenal of methods used to treat this epidemic. The quantitative effects of the dosimetric impact variable reproducibility plays in DIBH have also been outlined for the first time to the best of our knowledge. Image processing has shown to be an effective tool for providing alternate methods to understand how absorbed dose can vary with patient and philological motion.

Surface imaging, while still new to the medical world, provides valuable information that can be used to aid patient treatments in a quick and efficient manner. Its non-ionizing technique help incorporate it into existing forms of treatment to reduce the overall patient dose delivered from alignment films. Surface imaging provides a fast and accurate method to set up and monitor patients based on their anterior features. Alignment to the patients’ anterior surface at DIBH allows the prescribed tumor dose not to be compromised while effectively sparing the cardiac tissues preventing radiation induced complications when a patient is unable to perform a DIBH of full magnitude. Visual aid has proven to be effective in helping patients achieve reproducible and stable DIBH. Patients were able to produce DIBH with high reproducibility and stability with the use of visual aid and proper coaching.

Image processing applications continue to provide increased knowledge in the medical field which would otherwise be unattainable. Through the use of DIR we have provide a method in which fictional patient scans can be created to further understand how radiation affects the human anatomy. This can continue to aid in designing and evaluating new and old procedures to assess their feasibility as well as possible outcomes. Image processing once again is proven to be valuable tool in medicine to help understand, diagnose and treat various diseases.

Our implementation of this DIBH procedure has been a valuable experience through the entire process from diagnoses to post treatment. Sparing of critical OAR has become more important as life expectancies continue to rise. A procedure that is easy, quick and effective is also necessary as institutions continue to treat more patients on a daily basis. As we continue to refine and perfect our treatment methods, better care can be given to a wider variety of humans. I would like to say that one day the world may be disease free, but this is
of course impossible. However, with the continuing work of many individuals, living in a world in which there are no longer terminal diseases is an evident possibility.
REFERENCES


5 E. J. Hall, Radiobiology for the Radiologist, 6th ed. (Lippincott Williams & Wilkins, Philadelphia, PA, 2006).


