THE USE OF ELECTRONIC TISSUE COMPENSATORS
IN PRONE BREAST IRRADIATION

A Research Project Report Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Science in Medical Dosimetry

Jackson Lau

College of Science & Health
Medical Dosimetry Program

May 2013
THE USE OF ELECTRONIC TISSUE COMPENSATORS
IN PRONE BREAST IRRADIATION

By Jackson Lau

We recommend acceptance of this project report in partial fulfillment of the candidate's requirements for the degree of Master of Science in Medical Dosimetry

The candidate has met all of the project completion requirements.

Nishele Lenards, M.S.
Graduate Program Director

April 19, 2013
Date
Abstract

Women with early stage breast carcinoma are commonly treated with radiation therapy following lumpectomy. The worldwide standard for radiation therapy treatments for this cohort include the use of two opposed wedged tangential photon beams and segmented fields with the patient in the supine position. However, this technique has shown to produce suboptimal dose homogeneity and increase heart and lung volume irradiation particularly in women with pendulous breasts. This can lead to radiation induced cardiopulmonary toxicity and secondary malignancies decades after the initial treatment. Alternatives such as treating the patient prone or the use of compensators have independently been proposed in literature. This study examines the potential improvements in dose homogeneity and irradiation reductions to the heart and lungs through the use of electronic tissue compensators in the prone setup.
A special thanks to the Radiation Oncology Teams at the University of Illinois Hospital and Health Sciences System and the University of Chicago Medicine for their guidance and support in this endeavor.
# Table of Contents

<table>
<thead>
<tr>
<th>Chapter I: Introduction</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statement of the Problem</td>
<td>10</td>
</tr>
<tr>
<td>Purpose of the Study</td>
<td>10</td>
</tr>
<tr>
<td>Assumptions of the Study</td>
<td>10</td>
</tr>
<tr>
<td>Definition of Terms</td>
<td>11</td>
</tr>
<tr>
<td>Limitations of the Study</td>
<td>13</td>
</tr>
<tr>
<td>Methodology</td>
<td>13</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chapter II: Literature Review</th>
<th>Page</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Chapter III: Methodology</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Selection and Description</td>
<td>27</td>
</tr>
<tr>
<td>Instrumentation</td>
<td>27</td>
</tr>
<tr>
<td>Data Collection Procedures</td>
<td>28</td>
</tr>
<tr>
<td>Data Analysis</td>
<td>30</td>
</tr>
<tr>
<td>Limitations</td>
<td>30</td>
</tr>
<tr>
<td>Summary</td>
<td>30</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chapter IV: Results</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Item Analysis</td>
<td>31</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chapter V: Discussion</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limitations</td>
<td>34</td>
</tr>
<tr>
<td>Conclusions</td>
<td>34</td>
</tr>
<tr>
<td>Recommendations</td>
<td>36</td>
</tr>
</tbody>
</table>

References ................................................................. 50
List of Tables

Table 1: Dosimetric Parameters Mean Values.................................................................37
**List of Figures**

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Prone Breast Board</td>
<td>38</td>
</tr>
<tr>
<td>2</td>
<td>Homogeneity Index Comparisons</td>
<td>39</td>
</tr>
<tr>
<td>3</td>
<td>Conformity Index Comparisons</td>
<td>39</td>
</tr>
<tr>
<td>4a</td>
<td>Patient #5 Axial Central Slices</td>
<td>40</td>
</tr>
<tr>
<td>4b</td>
<td>Patient #5 Axial Global Maximum Dose Slices</td>
<td>40</td>
</tr>
<tr>
<td>5a</td>
<td>Patient #12 Axial Central Slices</td>
<td>41</td>
</tr>
<tr>
<td>5b</td>
<td>Patient #12 Axial Global Maximum Dose Slices</td>
<td>41</td>
</tr>
<tr>
<td>6</td>
<td>PTV V_{105} Comparisons</td>
<td>42</td>
</tr>
<tr>
<td>7</td>
<td>PTV V_{110} Comparisons</td>
<td>42</td>
</tr>
<tr>
<td>8</td>
<td>Boxplot of 3D Maximum Dose</td>
<td>43</td>
</tr>
<tr>
<td>9</td>
<td>3D Maximum Dose Improvement with ISC vs Separation</td>
<td>43</td>
</tr>
<tr>
<td>10</td>
<td>Average Cumulative PTV Dose Volume Histogram Comparisons</td>
<td>44</td>
</tr>
<tr>
<td>11</td>
<td>Heart Mean Dose Comparisons</td>
<td>45</td>
</tr>
<tr>
<td>12</td>
<td>Heart V₅ Comparisons</td>
<td>45</td>
</tr>
<tr>
<td>13</td>
<td>Ipsilateral Lung Mean Dose Comparisons</td>
<td>46</td>
</tr>
<tr>
<td>14</td>
<td>Ipsilateral Lung V₅ Comparisons</td>
<td>46</td>
</tr>
<tr>
<td>15</td>
<td>Average Heart Cumulative Dose Volume Histogram</td>
<td>47</td>
</tr>
<tr>
<td>16</td>
<td>Average Ipsilateral Lung Cumulative Dose Volume Histogram</td>
<td>47</td>
</tr>
<tr>
<td>17</td>
<td>Homogeneity Index Isocenter Shift Comparisons</td>
<td>48</td>
</tr>
<tr>
<td>18</td>
<td>Conformity Index Isocenter Shift Comparisons</td>
<td>48</td>
</tr>
<tr>
<td>19</td>
<td>Heart Mean Dose Isocenter Shift Comparisons</td>
<td>49</td>
</tr>
<tr>
<td>20</td>
<td>Ipsilateral Lung Mean Dose Isocenter Shift Comparisons</td>
<td>49</td>
</tr>
</tbody>
</table>
Chapter I: Introduction

Breast cancer is one of the most common fatal cancers in women and ranks first in cancer death within the 20-59 year age group.\(^1\) Surgical treatment for carcinoma of the breast has traditionally been radical mastectomy. Over the past decade, the decrease in death rates from breast cancer is largely attributed to the improvements in early detection and treatment. Women presented with early stage breast carcinoma (stage I and II) have the option of electing breast conservation therapy following lumpectomy in lieu of radical mastectomy. This preferred treatment option employs external beam irradiation to the breast tissue while preserving the breast. The breast conservation therapy technique is now an established treatment alternative to mastectomy.\(^2\) Several studies have shown comparable results from breast conservation therapy and those of mastectomy in the management of early stage breast carcinoma.\(^2-6\) Additionally, Margolis and Goodman\(^7\) have reported that 96% of women chose breast conservation therapy over mastectomy based on self image. Much research over the past decade has focused on clinical improvements in radiation therapy delivery techniques in the prevention of local recurrence and the reduction of secondary malignancies following breast conservation therapy.

The standard for radiation therapy treatments for stage I and II breast carcinoma include the use of two opposed wedged tangential photon beams and segmented fields with the patient in the supine position. In this setup, patients are placed supine on a breast board with arms above their head. This method provides ease with patient immobilization and reproducibility and offers desirable local control and cosmetic outcome.\(^8\) However, in some patients, particularly those with pendulous breasts, the standard supine treatment position may not be particularly advantageous. Mitchell et al\(^9\) have reported that while the use of external beam radiation therapy helps to improve local control and increase survival, it is oftentimes at the expense of increased radiation induced cardiopulmonary toxicity and secondary malignancies. Patients with pendulous breasts treated in the supine position, require the tangential beams to be placed more posteriorly to include the entire breast, increasing heart and lung volume irradiation. These patients also exhibit greater changes in external contour and compromised setup reproducibility when compared with smaller sized breast patients.\(^10\) Furthermore, the wider field separations result in greater dose inhomogeneity with some cases in excess of 20%, increasing the probability of poor cosmetic outcomes.\(^11\)
An alternative method used to minimize irradiation of the heart and lungs and to improve dose uniformity is to position the patient in the prone position. Patients treated in this position lie prone on a dedicated mattress or prone breast board with the treated breast hanging through a cutout in the mattress or board. In this setup, the breast tissue is displaced anteriorly, away from the heart and ipsilateral lung. The importance of dose reduction to the heart and lungs is evident from various studies evaluating the long-term mortality rates from heart disease and lung cancer after radiotherapy for early stage breast cancer. Studies conducted by Darby et al,\textsuperscript{12} using data from the US Surveillance Epidemiology and End Results (SEER) cancer registries, showed a strong correlation between radiotherapy and an increase in mortality from heart disease and lung cancer 10-20 years after treatment. Other studies reached similar conclusions regarding the increased risks and hazards from radiotherapy.\textsuperscript{13-16}

Despite the potential future complications and side effects aforementioned, in treating large breasted patients supine, there are currently few studies published evaluating the prone position technique as an alternative treatment modality. These techniques have yet to gain widespread acceptance in clinic.\textsuperscript{9,17} Based on the studies comparing the supine and prone position, there is convincing evidence that the prone setup is more beneficial in treating patients with pendulous breasts. Griem et al\textsuperscript{8} demonstrated a reduction in ipsilateral and contralateral lung volumes in patients treated in the prone position. Additionally, a reduction in irradiated heart volume and a significant decrease in maximum doses was observed in most patients.\textsuperscript{17} A reduction in respiratory associated movements of the breast was also reported with acceptable setup variability by DeWyngaert et al\textsuperscript{18} and Mitchell et al.\textsuperscript{9} Small breasted patients can also be afforded similar benefits of being treated in the prone position. Studies by Griem et al\textsuperscript{8} demonstrated a reduction in the dose to the ipsilateral and contralateral lung with improved dose homogeneity regardless of breast size.

Dose inhomogeneity is a common concern for large breasted patients undergoing breast conservation therapy due to larger field separations. Complications from excessive dose inhomogeneity include side effects such as ischaemic heart disease, and non-fatal complications such as arm lymphedema, brachial plexopathy, breast pain, poor cosmesis and pneumonitis.\textsuperscript{19} Studies have shown differences in maximum and minimum doses as high as 25%, in excess of the normally considered acceptable value of 10%.\textsuperscript{20} The use of electronic tissue compensators has been prescribed to significantly reduce the dose inhomogeneity primarily with the patient in
the supine position. These compensators can improve the three-dimensional (3D) dose distribution by accounting for lung heterogeneities as well as changes in breast contour through the use of dynamic multileaf collimators to modulate the radiation beam. Likewise, published literature suggests improved dose homogeneity in patients treated in the prone position. Grann et al\textsuperscript{21} demonstrated improvements in dose homogeneity both at the apex of the breast and at the periphery in pendulous breast plans by placing the patient in the prone position. However, the potential added benefit with the inclusion of electronic tissue compensators for patients in the prone position have yet to be studied.

**Statement of the Problem**

It is well documented that a correlation exists between the use of radiotherapy to treat patients with early stage breast carcinoma and the increased incidences of complications decades later, specifically among patients with pendulous breasts. These incidences include cardiopulmonary secondary malignancies, radiation induced cancer to the contralateral breast, and inferior cosmetic results due to dose inhomogeneity. Electronic tissue compensators have traditionally been used to improve the later, namely dose homogeneity, but have also been shown to substantially reduce doses to the heart, lung and contralateral breast.\textsuperscript{22} Several studies also show improvements in these areas when patients with pendulous breasts are treated in the prone position. However, to the knowledge of the researcher, published literature examining the benefits of prone treatment in conjunction with the use electronic tissue compensators is limited. The potential improvements in combining electronic tissue compensators in prone patients with pendulous breasts were discussed in this study.

**Purpose of the Study**

The purpose of this study was to assess the combined effect of utilizing electronic tissue compensators in prone breast plans on dose inhomogeneity and other dose distribution metrics. Retrospective prone breast plans from the University of Illinois Hospital and Health Sciences System and University of Chicago Medicine were planned with an electronic tissue compensator using the Eclipse v8.6 treatment planning system. Data was collected and evaluated using statistical analysis and presented for discussion.

**Assumptions of the Study**

Literature has shown that the severity of late side effects from radiotherapy in the treatment of early stage breast cancer is directly proportional to the irradiated volume, total dose
and technique used. In this study, the researcher evaluated the potential added benefit of using electronic tissue compensators with prone patient positioning in terms of improvements in dose homogeneity and reductions in heart and lung dose. It is assumed that these enhancements in dose distributions will correspond to further reductions in long-term complications and improve mortality.

**Definition of Terms**

**Beam’s Eye View (BEV)** – Display of the target and normal structures in a plane perpendicular to the central axis of the beam, as if being viewed from the vantage point of the radiation source.

**Breast Conservation Therapy** – A treatment technique in which the breast tumor is surgically removed while preserving the breast followed by radiation.

**Clinical Target Volume (CTV)** – Consists of the demonstrated tumor and any other tissue with presumed disease.

**Cobolt 60** – A radioactive isotope used as a source for external beam radiation therapy.

**Computed Tomography (CT)** – An imaging procedure utilizing an x-ray source system to acquire projection views. From these projections, image reconstruction algorithms generate an image matrix in which each pixel is an accurate measure of the electron density.

**Conformity Index** – A parameter used to evaluate dose conformation during treatment planning and was defined as the ratio of the 95% isodose volume to the PTV.

**Contralateral** – Pertaining to the opposite side of the body.

**Dose Inhomogeneity** – Variations in dose as a result of changes in patient thickness or differences in tissue density.

**Dose Volume Histogram (DVH)** – Plot of target or normal structure volume as a function of dose.

**Electronic Tissue Compensator** – A beam modifier, using a multileaf collimator, that changes radiation output relative to loss of attenuation over a changing patient contour.

**Homogeneity Index** – Describes the uniformity of dose within a treated target volume as described by the ratio of the maximum dose deviation (maximum-minimum) to the mean dose within the planning target volume.

**Immobilization** – Process of ensuring that a patient does not move out of treatment position, thus allowing for reproducibility and accuracy in treatment.
Intensity Modulated Radiation Therapy (IMRT) – The use of computer controlled multileaf collimators to modulate the intensity of the radiation beam to create highly conformal dose distributions for the treatment of the planning target volume.\(^{25}\)

**Ipsilateral** – Pertaining to the same side of the body.

**Isocenter** – The point of intersection of the three axes of rotation on the treatment unit.\(^{24}\)

**Lumpectomy** – The surgical removal of a discrete lump from the affected breast while preserving the breast.

**Mastectomy** – The surgical removal of one or both breasts, partially or completely to treat breast cancer.

**Megavoltage Linear Accelerator** – A radiation therapy treatment unit that accelerates electrons and produces x-rays or electrons for treatment.\(^{24}\)

**Monitor Units (MUs)** – A unit of output measure used for linear accelerators.\(^{24}\)

**Multileaf Collimator (MLC)** – A part of the linear accelerator that allows treatment field shaping and blocking through the use of motorized leaves in the head of the machine.\(^{24}\)

**Orthovoltage Therapy** – Treatments using x-rays produced at potentials ranging from 150 to 500 kV.\(^{24}\)

**Pendulous Breasts** – Large breasts that hang loosely.

**Planning Target Volume (PTV)** – A volume that indicates the clinical target volume (CTV) plus margins for geometric uncertainties, such as patient motion, beam penumbra, and treatment setup differences.\(^{24}\)

**SEER** – The Surveillance, Epidemiology and End Results Program initiated in 1973 to collect data in an effort to determine the epidemiology and etiology of cancer.\(^{24}\)

**Simulation** – A mockup procedure of a patient treatment with radiographic documentation of the treatment portals carried out by the radiation therapist under the supervision of the radiation oncologist.\(^{24}\)

**Tomotherapy** – An IMRT technique in which the patient is treated slice by slice by intensity modulated beams.\(^{25}\)

**Transmission Penetration Depth (TPD)** – A user specified parameter for demarcating the compensation surface; defined as a percentage of the geometric path length of the beamlet through the patient.\(^{26}\)
**Wedged Tangential Photon Beams** – A conventional irradiation treatment technique for breast cancer in which the photon beams are positioned tangential to the breast or chest wall, along with a wedge to account for the sloping surface of the breast to improve dose distributions. May be used along with segmented fields to improve homogeneity.

**Limitations of the Study**

A possible limitation of this study was the relatively small sample size of available patient data. A larger cohort with a wider range of breast sizes from multiple institutions, using a variety of different prone breast boards, and treatment plans generated by a variety of planners, would potentially yield more representative results. Additionally, the isocenter shifts used in this study to assess dosimetric changes as a result of setup errors were crude estimates and did not include various factors such as accounting for the summation of the combined directional shifts or changes in actual patient anatomy.

**Methodology**

This study examined 12 retrospective patients treated at the University of Illinois Hospital and Health Sciences System and University of Chicago Medicine for early stage breast carcinoma after breast conservation surgery during 2010 - 2012. These patients were simulated and treated in the prone position using a prone breast board. Treatment plans were recreated using the Eclipse v8.6 treatment planning software. Various dosimetric parameters obtained from the treatment plans, were compared for statistical significance. Finally, a conclusion was drawn based on the analysis and an evaluation of the study was provided for discussion.
Chapter II: Literature Review

Breast carcinoma is one of the most commonly diagnosed cancers and is expected to account for 26% of all new cancers among women. The method of surgically removing the entire breast through radical mastectomy for treating women with early stage breast carcinoma has largely been replaced by more modern radiation therapy techniques conserving most of the breast tissue. The use of radiation therapy in breast conservation therapy is now an established modality in the treatment of early stage breast carcinoma, with comparable results in local tumor control and survival to radical mastectomy. Numerous trials have been conducted to study the differences in rates of survival for patients treated with lumpectomy and radiation to those with mastectomy. Jacobson et al concluded that the overall survival at 10 years yielded a 2% difference favoring lumpectomy with radiation. Other studies confirmed similar rates of survival. Given the comparable clinical outcomes, a majority of patients elect breast conservation therapy as their primary treatment based on psychological and quality of life issues.

The standard technique employed for whole breast radiotherapy is the two opposed wedged tangential photon beams and segmented fields with the patient in the supine position. Radiation fields are positioned tangential to the chest wall from the lateral to medial markers encompassing the entire PTV. The use of half blocked beams or over rotated tangents minimizes the beam divergence into the lung. Physical or electronic wedges are customarily used in this technique to account for the changes in breast contour and to improve dose homogeneity. Although the standard wedged tangents technique is used in most centers worldwide, numerous studies have reported suboptimal clinical outcomes and dose variations as high as 20%-25% as a function of breast size. Factors such as changes in surface contours of the breast, variations in separation supra-inferiorly or medio-laterally, and tissue heterogeneities contribute to the high dose distributions. As a consequence, despite the reduction in breast cancer mortality from radiotherapy, both short and long term side effects and clinical complications have increased for larger breast patients.

Cosmesis

Moody et al studied the changes in breast appearance of 559 patients after receiving radiotherapy for early stage breast cancer over a period of 5 years after treatment. The patients were treated in the supine position with randomized fractionation schedules of 39 Gy in 13 fractions, 42.9 Gy in 13 fractions or 50 Gy in 25 fractions. Field widths ranged from 65 mm to
115 mm and field lengths ranged from 150 mm to 195 mm. Within one year after treatment, a strong connection between breast size and change in breast appearance was noticed. The probability of breast change increased significantly after 5 years. In the study, 6% of patients with small breasts developed moderate or severe late changes as compared to 22% and 39% for medium and large breasts, respectively. The data suggests that when treated in the supine position, patients with larger breasts experience poorer cosmetic results correlating with an increase in dose inhomogeneity due to increased breast thickness.

Taylor et al. demonstrated the relationship between breast size and cosmetic result ratings for 458 patients with stage I or II breast carcinoma, who underwent breast conservation therapy between January 1969 and December 1990. The pathologic stage for this cohort consisted of 62% T1N0, 14% T1N1, 15% T2N0 and 42% T2N1. Dose prescription varied between 45.0 Gy and 50.4 Gy at 1.8 Gy to 2.0 Gy fractions. Field setup consisted of opposed tangential fields with 4-6 megavoltage (MV) photon beams and the inclusion of compensating filters and/or bolus. Four hundred fifty eight patients and their physicians independently rated their cosmetic outcome from multiple follow up visits. A high percentage of the scores were rated excellent or good. However, it was observed that patients with larger breasts with greater separations had lower “excellent/good” cosmetic ratings. The study showed that separations of 22 cm or less compared with those greater than 22 cm had “excellent/good” ratings of 85% vs. 69%, respectively. The results of the study confirmed a few points. First, the data stressed the importance of compensating filters or similar techniques to improve dose homogeneity and long term cosmesis (p= 0.002). Second, patients with larger separations had higher doses and greater inhomogeneity resulting in lower cosmetic ratings. Lastly, data from the study also confirmed that cosmetic results continue to decline beyond 5 years and additional studies are needed to evaluate long-term cosmetic consequences.

Johansen et al. investigated the cosmetic and functional outcome of 266 breast cancer patients from the Danish Breast Cancer Cooperative Group’s (DBCG) trial after receiving breast conservation radiation therapy. The patients were prescribed a dose of 50 Gy delivered in 25 fractions using conventional tangential fields to the entire breast treated with 6-10 MV. Additionally, a boost was delivered to the surgical scar and primary tumor bed using either photons or electrons. After a mean follow up time of 6.6 years, 73% of the cohort reported having “excellent/good” cosmetic outcomes. Patients with inferior cosmetic outcomes had more...
physical changes including breast retraction. The patient assessments from this study correlated well with the degree of breast retraction to increasing breast sizes ($p = 0.0009$) due to the larger dose inhomogeneities found in larger breast patients.

Early side effects, such as cosmetic outcomes from breast conservation therapy using the standard supine wedge tangent technique are more notable though less detrimental, than the long-term risks and late effects associated with this treatment modality. Poor cosmetic outcomes generally associated with larger breasted patients, usually present themselves within five years and in some cases as early as one year after treatment. However, the long-term risks and complications, including heart disease and lung cancer, often go unheeded until decades later.

**Heart Disease and Lung Cancer**

Darby et al$^{12}$ analyzed data from about 300,000 women treated for early stage breast cancer in the 1970s and 1980s to assess the hazards of irradiation, namely heart disease and lung cancer. This cohort study was obtained from the SEER cancer registries. The data suggested that women irradiated during the period from 1973-1983, had higher mortality from heart disease for those with left sided breast tumors compared to those with right sided breast tumors. Likewise, the cancer mortality rates for lung cancer was higher for the ipsilateral lung as compared to the contralateral lung.$^{12}$ It was also observed that the mortality rates for heart disease and lung cancer were larger during the second decade after irradiation than during the first decade. One can surmise that such mortality rates will follow similar trends after the second decade, though it remains inconclusive due to lack of long term data.

Fortunately, technological advancements in radiotherapy since the 1970s have changed dramatically, resulting in lower doses to the heart and lungs. Women irradiated in the 1990s compared to those irradiated in the 1970s experienced a reduction in early cardiac hazards.$^{12}$ Improvements in treatment planning such as new algorithms in 3D planning, dose delivery and quality assurance have helped to manage the amount of radiation delivered to the heart and lungs during breast conservation therapy.$^{23}$ Harris et al$^{30}$ studied the long term cardiac mortality of early stage breast cancer patients using contemporary irradiation techniques. Medical records were reviewed for women with stage I or II breast carcinoma between 1977-1994 treated with breast conservation therapy. Treatment included radiation to the whole breast using tangential coplanar fields using 6 MV and 15 MV photon beams, a boost with a median cumulative tumor bed dose of 64 Gy, and a supraclavicular photon field when the regional nodes required
treatment. The data presented show that although there was an increase in coronary artery
disease and myocardial infarction, there was no increased risk of cardiac death within 20 years
after treatment. The result of this study confirmed two points. First, the current treatment
standards of megavoltage linear accelerators and the use of tangential fields as compared to the
antiquated standards of cobalt 60 or orthovoltage therapy has led to a reduction in heart volume
exposure to radiation. Although the result of modern methods concludes that there is no increase
in cardiac mortality, contrary to those previously reported by Darby et al,12 there is still a
significant increase in post treatment development of ischemic cardiac disease in patients with
left sided tumors, which highlights the second point.30 There still remains much to be done to
improve our radiation techniques and treatment methods for early stage breast cancer to reduce
radiation to normal tissues.

Marks et al31 conducted a prospective clinical trail at Duke University Medical Center, to
study the cardiac function of women with left sided breast carcinoma after receiving radiation
therapy treatments. Between the years of 1998 to 2001, 114 patients treated with conventional
radiation therapy techniques such as with tangential photon beams in the supine position, were
enrolled in this study. A total dose of 46 Gy to 50 Gy at 1.8 Gy to 2 Gy fractions was prescribed
with the addition of a boost of 16 Gy to 18 Gy in 2 Gy fractions with enface electrons. Nuclear
medical cardiac imaging and 3D treatment planning tools were used to assess the changes in
cardiac function. To quantitatively measure the cardiac function, single-photon emission
computed tomography (SPECT) cardiac perfusions scans were acquired. The SPECT images
were then registered to the CT images in the treatment planning system. Pre and post radiation
therapy images were compared and evaluated. It was demonstrated that new perfusion defects
develop over time and approximately 27%, 29%, 38% and 40% of the patients suffer from new
regional cardiac perfusion defects after 6, 12, 18 and 24 months, respectively, of receiving
radiation therapy.31 The data suggests that the degree of cardiac defects developed after radiation
therapy is related to the amount of heart volume irradiated, dose delivered and elapsed time.31
The long term cardiac complications beyond the 24 month follow up period is likely to increase
and new techniques for reducing cardiac irradiation is clearly warranted.

Supine vs. Prone

Over the past decade, researchers have examined various alternative methods in breast
irradiation to minimize doses delivered to normal tissues. One method that has recently emerged
in literature is the technique of positioning the patient prone rather than the conventional supine setup. In the conventional setup, patients are positioned supine on a breast board with both arms placed above the head. Adjustments using isocenter shifts are then performed to align the setup position to the isocenter. In the prone setup, patients are positioned prone and elevated from the couch using a prone breast board. One or both arms are placed above the patient’s head using the adjustable handlebars on the board. The treated breast hangs away from the chest wall through an aperture in the prone breast board, while the contralateral breast rests on the board and is displaced away from the treatment fields.

Patients positioned in the prone position minimize both breast separation and irradiated heart and lung volume by displacing the breast volume away from the chest wall, which allows the tangential fields to be placed more anteriorly. Various researchers have studied this method for treatment, though not exhaustive, showing the reduction in radiation to the heart and ipsilateral lung volume, as well as improved dose homogeneity particularly for patients with pendulous breasts. One of the earlier studies conducted in the 1990s by Merchant and McCormick demonstrated the benefits of treating patients with pendulous breasts in the prone setup. Reduction in high dose regions at the base of the breast from 116-118% to 102-103% in the supine and prone positions, respectively, was observed. In addition, the heart, lungs, chest wall and contralateral breast all received lower dose. The study concluded that prone breast irradiation is a simple and effective alternative to the conventional supine position for cases where dose homogeneity may be compromised.

Similarly, Grann et al presented data supporting those of Merchant and McCormick. In her study, Grann designed a prototype prone breast board and treated 56 early stage breast cancer patients with pendulous breasts in the prone position using wedged tangential fields at Memorial Sloan Kettering Cancer Center. Pendulous breasts were classified as having a medial to lateral separation exceeding 23 cm. An aperture in the prone breast board allowed the breast to fall anteriorly from the chest wall. Treatments were delivered using 6 MV tangential photon beams with typical gantry angles of 275° and 75° for the medial and lateral beams respectively. The median prescribed dose was 46.8 Gy in 1.8 Gy fractions, treated 5 days a week. A boost was also delivered with a median dose of 14 Gy via enface electrons. Comparisons in isodose distributions for supine and prone positions revealed significantly lower maximum doses and improved dose homogeneity in the prone position due to the decrease in separation. Hot spots at
the apex and periphery of the breast was observed to be as high as 20% for pendulous breast patients in the supine setup. Additionally, irradiated heart and lung volumes were minimized and all of the patients had an overall score of good or excellent on their cosmetic outcomes. The investigators indicated that based on the study, the prone breast treatment offered a good alternative for pendulous breast patients with early stage breast carcinoma.

Larger heart and lung volumes are usually irradiated in patients in the supine position to obtain adequate coverage of breast tissue. Griem et al compared the dose homogeneity and volume of normal tissue irradiated in both the supine and prone positions. Fifteen patients ranging from 39 to 73 years of age with stage I and II carcinoma were recruited for this study. Medial and lateral borders were determined and marked by wires. These patients were scanned in both the supine and prone positions for comparison but were ultimately treated in the traditional supine position with two field tangential photon beams using a half beam technique with asymmetric jaws. A dose of 50 Gy was prescribed to a point located one third the distance from the isocenter to the apex of the ipsilateral breast. The same point was used for both supine and prone positions. The research demonstrated that patients positioned in the prone position experienced a reduction in heart and ipsilateral lung volumes of 2.81±5.37% and 0.81±11.51%, respectively. The volume of breast that received 52.5 Gy or more was significantly less in the prone position. Improvements in dose homogeneity and reduction in the doses to the lungs were demonstrated in all fifteen patients regardless of breast size. The study suggested that although the standard supine techniques currently produce acceptable results, further improvements in irradiation reductions to normal tissues can be realized particularly for the ipsilateral lung and potentially for the heart, when the patient is treated prone.

Furthermore, Bieri et al demonstrated in a Rando-Alderson phantom, that prone breast tangents resulted in three to four times lower ipsilateral lung doses than in the supine position and cardiac irradiation was completely avoided in the prone position. Peripheral doses in surrounding normal tissues were significantly lower for prone positions than for supine positions including the upper abdomen, pelvic organs, bone marrow and ipsilateral lung. The study suggested that by treating patients prone using tangential beams, peripheral doses to these organs and tissues can be reduced by 40 to 70%. More recent studies by Buijsen et al reached similar conclusions in reduced dose to normal tissues and improved dose homogeneity in patients treated in the prone position.
Significant reductions in ipsilateral lung dose have also been recorded in more recent studies. Varga et al\textsuperscript{35} reported a mean lung dose of 7.45±2.6 Gy in the supine position versus 2.02±1.2 Gy for prone position in a sample of 61 patients. The $V_{20}$ of 14.3±5.4% and 3.3±2.5%, respectively, was also noted. In this study, treatment planning was performed for both supine and prone positions. Patients were randomly selected to receive either the supine or prone treatment. In the supine setup, patients were positioned on a 15° thorax wedge cushion with the arms above the head. A thermoplastic mask covering the chin to the abdomen was applied to immobilize the patient. In the prone setup, the patients were placed on a prone breast platform with the ipsilateral breast positioned through the aperture in the platform. The patient’s arms were placed superolaterally. Positioning landmarks were marked on the patient using the lateral and overhead lasers. The treatment plans were developed using 6 MV tangential photon fields as well as 6 MV or 15 MV segmented fields using MLCs. A mean dose of 50 Gy was prescribed encompassing 95% of the PTV. It was demonstrated that when patients were treated prone, particularly those with pendulous breasts, they experienced significant reductions in lung dose. These benefits were also observed in smaller breast patients. Kirby et al\textsuperscript{36} observed drastic reductions (4.4 to 0.8 Gy) in ipsilateral mean lung dose for all 65 cases in their study regardless of breast size. These results can translate to potentially drastic reductions in radiation induced pulmonary disease and complications for all patients.

The dosimetric advantages for the ipsilateral lung in prone breast treatment are indisputable. However, the benefits for the heart have been less convincing due to the lack of consensus in reported literature. Chino and Marks\textsuperscript{37} quantified the displacement of the heart in patients treated with tangential photons in the prone position and discussed the potential implications associated with such movements. For each case, patient CT and MRI scans were studied by measuring the distance between the anterior pericardium and the anterior chest wall at various locations. Comparisons of 16 patient scans in the supine and prone positions showed that the lateral and superior aspect of the heart has a systematic mean anterior displacement towards the chest wall of 19 mm. Several studies have shown reduced irradiated heart volume and lower dose in prone breast treatments while others have reported otherwise.\textsuperscript{21,32,35,36,38} Chino and Marks\textsuperscript{37} suggested that the location of the target tissues and tumor bed differs among patients and some may require the tangential radiation fields to be placed more posterior to obtain
adequate coverage, increasing the amount of irradiated heart volume. Such considerations should be accounted for when recommending the prone breast treatment modality for patients.

Finally, the long-term clinical outcomes for tumor recurrence and survival rates for the prone breast technique have also been investigated. In the study conducted by Stegman et al\textsuperscript{39} 245 retrospective patients treated in the prone position at the Memorial Sloan Kettering Cancer Center were compared to the data from conventional supine techniques from existing literature. The cohort from this study was treated with 6 MV photons with a median dose of 46.8 Gy delivered in fractions of 1.8 to 2 Gy. The local tumor recurrence rate at 5 years was 4.8% with an overall survival rate of 93%, yielding similar results reported in the literature for supine treatments.\textsuperscript{39} Excellent dose homogeneity (104-108\%) and low rates of Grade 2 to 3 skin toxicity (4.4\%) were also achieved.\textsuperscript{39}

\textit{Setup Variability}

The dosimetric benefits for patients with pendulous breasts treated in the prone position have been supported by existing literature. However, facilities have been slow to adopt this technique as a standard due to the perceived difficulty in patient immobilization and setup variability.\textsuperscript{9} In a study conducted by Varga et al,\textsuperscript{35} a total of 41 patients were randomly selected for treatment in the supine or prone position and analyzed for repositioning accuracy. Supine patients were placed on a thorax wedge cushion, arms elevated on an arm support and immobilized from the chin down to the abdomen. Prone patients were positioned on a platform, head resting on a pillow facing the contralateral side, and the ipsilateral breast placed in the aperture in the platform. Prior to the start of treatment, the isocenter position was confirmed with the CT simulator. Treatment was delivered 5 times a week and positioning accuracy was checked 3 times a week using the electronic portal imaging device with the aid of radio-opaque reference markers on the patient. Analysis of each image included measuring the distance between the reference markers, the central lung distance, the lung area in the field, the central flash distance, and the inferior central margin. Systematic and random errors were then calculated using the measured displacements. The data showed that the displacement in the prone position was significantly higher as compared to the supine position with an average displacement of 8.06±4.66 mm and 6.60±3.05 mm, respectively. After successive treatments, the repositioning accuracy gradually improved, which suggests that with more training and expertise, the setup variability can be minimized.\textsuperscript{35}
Kirby et al\textsuperscript{40} also demonstrated larger setup errors when treating patients with pendulous breasts in the prone setup. A total of 26 patients were scanned in both the supine and prone positions. In the supine setup, patients were placed on a supine breast board with the arms above the head. Superior, inferior, lateral and medial borders were delineated using radio-opaque wires. Midline and bilateral reference markers were also placed on the patient. In the prone setup, patients were positioned on a foam mattress resting on a custom made prone platform with the arms above the head. The conventional opposed tangential fields were used with a prescribed dose of 40 Gy in 15 fractions. In the first half of the treatment, each patient was randomized for treatment in either the prone or supine positions. The position was switched for the remaining half of the treatment. Both the supine and prone positions were reproduced by aligning tattoos to the lasers and performing visual checks of the position of field edges. Setup errors were then measured using iView electronic portal imaging and shifts were applied if the measured error was greater than 5 mm. Based on the study, the overall displacement for supine and prone positions was 3.8 mm and 4.6 mm, respectively. The authors indicated that the larger setup errors observed in the prone position is likely due to the experience level of the team. Although a correlation study between experience level and prone setup variability is lacking, there seems to be an inherent relationship based on literature. When performed by an experienced team, Goodman et al\textsuperscript{41} witnessed no difference in the number of shifts based on weekly port films between supine and prone setups during a 6 week treatment course. An increase in staff expertise has been suggested to reduce prone setup errors.\textsuperscript{9,40}

The tendency for larger setup errors in prone breast treatment necessitates adequate margin around the target volume to ensure sufficient coverage is achieved. Mitchell et al\textsuperscript{9} studied the interfraction and intrafraction setup variations in 10 patients using the New York University (NYU) prone breast technique. The age of the patients ranged from 46 - 70 years. These patients were treated with tangent fields with a prescribed dose of 40.5 Gy in 15 fractions while positioned prone. Three fiducial markers were placed on the patient’s back and sides for daily setup and a fourth fiducial marker on the lateral side of the breast to indicate the displacement and setup errors in three directions.\textsuperscript{9} The study demonstrated the mean interfraction setup variability was 0.08 cm in the anterior to posterior (AP) direction and 0.04 cm in the superior to inferior (SI) direction.\textsuperscript{9} The mean intrafraction displacement was 0.13 cm.\textsuperscript{9} The authors concluded that the setup variability in prone breast treatment was acceptable and recommended
the clinical target volume (CTV) to planning target volume (PTV) margin of 1.4 cm to be adequate. A margin of 2.2 cm around the contour of the breast for flash was deemed appropriate to account for the displacement and setup errors of the breast when positioned prone.

Morrow et al demonstrated similar findings regarding the presence of large setup errors between daily treatment fractions for 15 prone patients with early stage breast cancer. The patients were prescribed a dose of 50 Gy delivered in 25 fractions, while positioned prone with the arms and head immobilized with an alpha cradle. The daily setup errors ranged from 0.0 cm to 1.65 cm and determined a CTV to PTV margin of up to 2 cm to be adequate. The study also verified that when positioned prone, patients had less chest wall motion due to respiration when compared to the free motion of the chest when positioned supine. The respiratory motion was reduced from 2.3±0.9 mm to 0.1±0.4 mm in the supine and prone setup, respectively. Although the daily setup variations for prone patients are significant enough to be wary, studies suggest that the use of image guided radiotherapy, improvements in the design of prone breast boards and immobilization devices, and the increase in experience and expertise of the staff delivering the treatment, can allow patients with pendulous breasts to benefit from the dosimetric advantages associated with prone breast treatments.

Challenges for Prone Setup

The use of the prone setup for breast radiotherapy can pose a number of challenges for institutions adopting this technique. First, a high level of expertise is needed to achieve optimal patient setup and repositioning accuracy. Setup methods such as turning the patient’s head away from the treated breast to minimize heart irradiation or following procedures that achieve high setup accuracy and reproducibility in a reasonable amount of time, as delineated by the NYU prone technique, can only be achieved with extensive experience with prone breast radiotherapy. Secondly, the prone setup is generally deemed inadequate to provide sufficient axillary nodal coverage. The mean dose to levels I-III axillary nodes was 50% less in the prone as compared to the supine position. For patients requiring axillary nodal irradiation, the supine setup may be more suitable. Lastly, treating in the prone setup may be difficult for the elderly or obese patients with limited mobility when positioning themselves on the prone breast board. Patients have reported neck and spine pain from maintaining the prone position for extended periods of time, possibly contributing to the setup errors. Physicians and their team need to account for these limitations when considering the use of the prone technique.
Electronic Tissue Compensators

The use of tangential photon beams in the treatment of whole breast irradiation has traditionally employed wedges to improve the dose distribution by correcting for dose inhomogeneity. However, this worldwide technique often results in uneven dose distributions and worsens with increasing breast sizes. One method that has been studied and utilized in some cancer centers, though not as mainstream as the standard wedge technique, is the use of electronic tissue compensators. Compensators improve the uniformity of dose by modifying the radiation beam to accommodate the irregular contour of the patient. The construction of compensators, particularly for 3D physical compensators, was considered laborious and time consuming. Electronic tissue compensators eliminate the need for special mechanical devices and personnel resources once required of physical compensators. Electronic tissue compensators modulate the fluence using dynamic MLCs instead of a physical compensator and adjust the dose inhomogeneity resulting from a changing patient contour.

Goyal et al demonstrated the improvement in dose homogeneity with electronic tissue compensation with whole brain patients. Although the study focused on a different anatomical site, the results showed the benefits of incorporating electronic tissue compensators in treatment. The compensated plans significantly reduced the mean maximum dose and the intracranial volume receiving greater than 103% of the prescribed dose. It was shown to be a more time efficient process over the IMRT plans. The study suggested that electronic tissue compensators can effectively improve the dose homogeneity and can be used in lieu of conventional wedges.

Researchers have also studied the electronic compensator technique for whole breast irradiation. Caudell et al compared three whole breast irradiation techniques including electronic tissue compensation, inverse planned IMRT and tomotherapy. A sample of 10 patients with early stage (T1N0) left sided breast cancer was selected for planning. The patients were positioned supine on a breast board, left arm positioned above the head and the head turned to the contralateral side. Radio-opaque wires were used to delineate field borders. A total of 45 Gy in 25 fractions were prescribed to the whole breast. The electronic tissue compensated plans were designed using the electronic compensator tool available in the Eclipse treatment planning software. Using the beam’s eye view (BEV) of the medial field, the field was adjusted to include the target volume while minimizing the amount of heart and lung in the field. This field was then opposed to create the lateral tangent field and the gantry angle adjusted to eliminate field
It was demonstrated that the electronic tissue compensated plans showed much lower doses to the heart, lungs and contralateral breast when compared with the IMRT and tomotherapy plans. Additionally, these plans resulted in the lowest mean dose, lowest number of monitor units (MUs) and were generated in the shortest amount of time. The results of this study also demonstrated that the electronic compensated plans yield similar target coverage and better dose homogeneity when compared to inverse planned IMRT and tomotherapy.

Su et al\textsuperscript{44} examined the dosimetric benefits between the electronic tissue compensator technique and the conventional physical wedge technique for a whole breast tangential field irradiation treatment. A total of 17 patients with chest wall separations ranging from 16 to 26 cm were studied in the supine position. Treatment plans were generated using the Eclipse treatment planning system. Both the compensated and wedge plans for each case had the same beam setup, beam weighting, normalization point and energy. A mix of 6 MV and 18 MV photon energies were used. Compared with the physical wedge plans, the electronic tissue compensated plans had a lower minimum dose and reduced dose inhomogeneity. Hotspots decreased by about 3\%, and the total MUs decreased by approximately 9\%. Based on the results of the study, the authors concluded that the use of electronic tissue compensators clearly showed a dosimetric benefit in whole breast tangential field irradiation.\textsuperscript{44}

Emmens et al\textsuperscript{26} demonstrated the use of irregular surface compensation for radiotherapy of the breast for 60 patients treated in their department. An irregular surface compensator is a specific type of electronic tissue compensator available within the Eclipse treatment planning software, compensating to a curved surface. The study examined the correlation between modifying the position of the compensation surface as specified by the transmission penetration depth (TPD) and the changes in dose distribution. Standard tangential fields with nondiverging borders were utilized with either 6 MV alone or a combination of 6 MV and 18 MV energies. The user defined TPD was shown to be effective in modifying dose profiles and reducing the size and magnitude of hot spots. Data from the study showed that as the TPD was decreased from 50\%, the size and magnitude of the hotspots in the medial and lateral regions on the posterior side were reduced while shifting the dose anteriorly. The average dose inhomogeneity using wedges and compensators was found to be 12\% and 8\%, respectively. The study demonstrated that by adjusting the TPD for irregular surface compensators, substantial improvements in dose homogeneity in 3D throughout the breast could be obtained.\textsuperscript{26} Others have
also reached similar conclusions regarding improvements in dose distribution and homogeneity with electronic tissue compensators over standard wedges.\textsuperscript{20,45}

Conclusion

Patients with pendulous breasts have often been associated with inferior cosmetic outcomes and a higher incidence of complications including heart disease and lung cancer decades after their initial treatment. Much of the research presented in literature has focused on reducing the doses to these organs using techniques such as positioning the patient in the prone position. Independently, electronic tissue compensators have also shown to improve patient cosmesis with improved dose homogeneity. However, there is a limited amount of literature on the combined effect of treating patients in the prone position using electronic tissue compensators in lieu of conventional techniques. This study aimed to quantify the potential added benefits in reducing irradiated heart and lung volumes, as well as improvements in dose homogeneity by combining the use of electronic tissue compensators in prone breast patients.
Chapter III: Methodology

It has been well documented that early stage breast carcinoma patients with pendulous breasts treated with radiation therapy in the supine position have inferior dose homogeneity and increased radiation to the heart and ipsilateral lung due to larger separations.\(^8,21,32,35\) As a result, these patients have been shown to exhibit poor cosmetic results and are at a higher risk of developing severe cardiopulmonary complications decades later when compared to smaller breasted patients. Treatment in the prone position has been investigated to reduce short and long term complications including cosmisis outcomes and risks of secondary malignancies. The University of Illinois Hospital and Health Sciences System and the University of Chicago Medicine currently utilize the prone setup technique for a select number of early stage breast carcinoma patients in lieu of the standard supine position. Twelve patients treated in the prone position were selected from these two institutions and retrospectively replanned using an irregular surface compensator, a type of electronic tissue compensator, instead of the traditional use of electronic dynamic wedges and segmented fields to assess the potential improvements in various dosimetric parameters. The methodology used to conduct these studies is discussed.

Sample Selection and Description

Twelve patients treated for stage I and II breast carcinoma in the prone position at the University of Illinois Hospital and Health Sciences System and the University of Chicago Medicine were selected for this study. This cohort, undergoing breast conservation therapy during 2010-2012 for carcinoma of the breast, consisted of 4 patients treated for the left breast and 8 for the right breast. Literature suggests that most patients regardless of breast size benefit from the prone technique.\(^35\) Therefore, patients included in this study included a variety of separations and PTV volumes. Separations ranged from 12.85 cm to 25.09 cm and PTV volumes from 529 cm\(^3\) to 3079 cm\(^3\). The patient ages ranged from 29-87 years with a mean of 61. The patients either received 5040 cGy in 28 fractions, 4680 cGy in 26 fractions or 4256 cGy in 16 fractions.

Instrumentation

Patients were positioned prone on a prone breast board\(^46\) and scanned using a Philips Brilliance Computed Tomography (CT) simulator. The prone breast board at the University of Illinois Hospital and Health Sciences Center consisted of a carbon fiber insert sandwiched between a 6 cm dual density memory foam to enhance patient comfort. A support 22 cm in
height was indexed to the treatment couch (Figure 1). A similar board by the same manufacturer was used at the University of Chicago Medicine with the exception that a thin mattress enclosed within a vinyl cover was used instead of the memory foam. The ipsilateral breast was positioned over the prone board aperture and was allowed to hang freely away from the chest wall. The contralateral breast was moved away from the aperture while resting on the contralateral breast pad. The patient’s arms were placed superiolaterally while holding on to an adjustable handle fixed to the board. The patient’s head was turned away from the treated breast.

The superior, inferior, lateral and medial borders of the treated breast tissue were determined by the physician and were marked using radio-opaque wires. The CT simulator had an 85 cm aperture bore and the CT images were taken at 0.3 cm slices. The acquired CT data sets were then transferred to the Eclipse v8.6 (Pinnacle v9.0 at University of Chicago) for treatment planning. The patients were then treated with a Varian Clinac 21EX linear accelerator.

**Data Collection Procedures**

All treatment plans were created by the same medical dosimetrist to maintain consistency. A total of 60 prone breast treatment plans were generated for this study. Five plans were created for each of the 12 patients. The initial plan was retrospectively replanned using the same patient scans, field sizes, isocenter, and contoured structures as approved by the radiation oncologist for actual treatment. These plans utilized opposed tangential fields, an electronic dynamic wedge when needed, a mix of 6 MV and 18 MV beam energies and segmented fields with MLCs to reduce hot spots when required. This technique will be denoted as the ‘standard’ technique. The field weights for the 6 MV and 18 MV fields were typically around 0.4 and 0.1, respectively. Monitor units for the 18 MV fields remained less than 20% of the total number of monitor units to avoid the use of bolus. Plans with segmented fields commonly were assigned a weight of 0.04-0.05, with monitor units equal to or greater than 10 MU to ensure adequate delivery. The plans were normalized to provide sufficient dosimetric coverage. The PTV structures were created with the 80-95% isodose lines and were used to evaluate adequacy of coverage.

The second plan used a similar field setup with the addition of an irregular surface compensator (ISC) in lieu of the electronic dynamic wedge and/or segmented fields. The ISC technique was used to compensate for uneven body surfaces to give homogeneous dose distributions. In Eclipse v8.9, an ISC was created for the medial and lateral tangential fields. A
transmission penetration depth (TPD) between 40-50% was typically selected. The TPD is the distance between the entry and exit points of each fan line of the beam traversing the breast. A TPD of 50% is a point located between the entry and exit points while a lower TPD such as 40% would be closer to the entry point. By connecting all the points on each fan line, an irregular surface is created, for which dose can be optimized using the Dose Volume Optimizer (DVO). To begin dose calculation, ‘fixed jaws’ are selected and the dynamic multileaf collimator (DMLC) sequences are calculated. The dose distributions are subsequently displayed for evaluation and can be modified by using the fluence editing tools.

In this study, the TPD for the ISC plans was set at 50% for separations 24 cm or less and 40% for separations greater than 24 cm as recommended by Emmens et al. The 6 MV and 18 MV fields were weighted at 0.4 and 0.1, respectively. An ISC was added to each of the medial and lateral 6 MV fields using the DVO v8.9.08. The plan was then calculated using the Anisotropic Analytical Algorithm (AAA) v8.9.08. Using the fluence editor tool in Eclipse, the fluence values were sampled and manually modified to decrease hotspots. The same tool was used to smooth out the fluence. Lastly, a 2 cm flash was added around the surface contour of the breast to account for intrafraction movements and setup errors. This was accomplished using the skin flash tool, which aids in visualizing the fluence of the selected field in the beam’s eye view (BEV). This tool was used to sample points inside the fluence to allow the dose variation to be reproduced out into the flash.

The setup variability in prone breast treatments has been studied and reported in literature. The tendency for larger systematic and random setup errors for patients treated in the prone position when compared to their supine counterparts have been partially attributed to the level of expertise and experience of the oncology staff. In this study the sensitivity of various shift positions in the x, y and z directions were examined and the changes for various dosimetric parameters were evaluated. Mitchell et al reported maximum AP setup errors as 9.6 mm. As such, in this current study, 1 cm shifts in the x, y and z directions were applied to the isocenter thereby shifting the treatment fields for the 12 ISC plans in their respective directions. The isocenter was shifted towards the centerline of the breast (±x direction), posteriorly towards the heart and lungs (-y direction) and inferiorly (-z direction) and were evaluated independently. Three additional plans for each patient were created for each directional shift while maintaining the same delivery parameters (i.e. MUs) as the original ISC plan where no shift was applied.
Various dose distribution parameters from each plan were collected, tabulated, and analyzed for statistical significance.

**Data Analysis**

Treatment plans using the conventional standard and ISC techniques for 12 early stage breast carcinoma patients positioned in the prone position were assessed. The following dose distributions were collected from these plans and analyzed: PTV maximum, mean and minimum dose, 3D maximum dose, PTV $V_{105}$, PTV $V_{110}$, PTV coverage, homogeneity and conformity indices, mean heart and ipsilateral lung dose, and the volume of heart and lung irradiated at 5 Gy ($V_5$). The homogeneity index was computed by taking the ratio of the maximum dose deviation (maximum minus minimum) to the mean dose within the PTV. The conformity index was the ratio of the 95% isodose volume to the PTV. These indices are consistent with the evaluation criteria as recommended in ICRU Report 62. The statistical software, Minitab 15, was used for the data analysis. A two-sided paired t-test was performed to determine statistical significance with a significance threshold level of 0.05. The mean, standard deviation and p values were calculated for the two treatment techniques and are provided for comparison and discussion.

**Limitations**

A possible limitation of this study was the relatively small sample size of available patient data. A larger cohort with a wider range of breast sizes from multiple institutions, using a variety of different prone breast boards, and treatment plans generated by a variety of planners, would potentially yield more representative results. Additionally, the isocenter shifts used in this study to assess dosimetric changes as a result of setup errors were crude estimates and did not include various factors such as accounting for the summation of the combined directional shifts or changes in actual patient anatomy.

**Summary**

The methodology discussed in this chapter provided the basis from which the results presented in the following chapter were generated. The sample selection criteria, instrumentation used, data collection and analysis methods were representative of those used at the University of Illinois Hospital and Health Sciences System and at the University of Chicago Medicine. The intention of this preliminary comparison study was to provide statistical data in order to assess the potential benefits that may be realized when treating patients with pendulous breasts in the prone position using irregular surface compensators.
Chapter IV: Results

Patients treated for early stage breast cancer with radiation therapy commonly employ the standard technique of two opposed wedged tangential photon beams in the supine position. However, patients with pendulous breasts have a tendency to experience greater dose inhomogeneity and an increase in heart and ipsilateral lung irradiation due to larger field separations. Treating these patients prone has been suggested in literature to improve dosimetric outcomes. This study demonstrated that when the prone position was used with irregular electronic compensators, additional improvements could be realized for all patients regardless of breast size (Table 1).

Item Analysis

Dose Homogeneity

The homogeneity index was calculated for both the standard and the ISC plans. The standard method resulted in a mean homogeneity index of 0.25 (range: 0.21-0.45) and 0.23 (range 0.18-0.40), respectively (p = 0.068). Irregular surface compensated plans experienced an average reduction of 7.5% in dose heterogeneity over plans using the standard technique (Figure 2). Plans with ISC improved the homogeneity index in 83% of the patients (except Patient 8 and 11). The mean conformity index for standard and ISC was 1.24 (range: 0.77-1.56) and 1.19 (range: 0.79-1.49), respectively (p = 0.002). Of the 12 patients included in this study, 83% experienced improvements in target conformity with ISC plans, while 17% had equal or slightly worse conformity (Figure 3).

In addition to the homogeneity and conformity indices, dose distributions within the breast volume were evaluated. Two patients (Patient 5 and 12) representing different breast contours were selected to illustrate dose distribution comparisons. Axial central slices and global maximums for Patients 5 and 12 are shown in Figures 4-5. The ISC plans resulted in better PTV coverage with the 100% isodose line and experienced lower 3D maximum doses. The location of the maximum dose for most patients planned with the standard technique was positioned more proximal to the chest wall, potentially increasing the heart and ipsilateral lung dose, while those planned with ISC were located more anterior.

The PTV volume for the 12 patients ranged from 581 cm$^3$ to 3079 cm$^3$. The PTV coverage was first evaluated at 100% of the prescribed dose covering 95% of the PTV. Two of the 12 patients (17%) met the criteria with the standard technique, while 7 of 12 patients (58%)
with ISC. The PTV coverage was then evaluated at 95% of the prescribed dose covering 99% of the PTV. Ten patients (83%) met the criteria for both techniques. The average \( V_{105} \) of the PTV increased by 9.0% but was reduced to 0% for \( V_{110} \) in the ISC plans (Figures 6 and 7). The 3D maximum dose reduced an average of 170 cGy (range: 112 cGy-229 cGy) or 3.2% for plans with ISC \((p = 0.000)\) (Figure 8). Patient 5 demonstrated the largest reduction (4.3%) of 229 cGy with a separation of 14.54 cm and breast volume of 639 cm\(^3\). Additionally, the 3D maximum dose also improved (range 2.3-4.9%) for ISC plans regardless of separation as shown in Figure 9. Overall, ISC plans produced better PTV coverage with lower 3D maximum dose as illustrated in Figure 10.

*Heart and Lung Dose*

Significant reductions in heart and ipsilateral lung dose were observed with ISC compared with the standard technique \((p < 0.001\) for both). The heart mean dose was reduced by an average of 33\% (range: 17\%-48\%). Greater reductions were observed for left sided patients compared to their right sided counterparts with an average reduction of 50.5 cGy and 24.5 cGy, respectively. For patients with \( V_5 \) for the heart, the ISC plans reduced the volume receiving \( V_5 \) in all cases, with a maximum reduction of 1.7\% (Patient 5) (Figures 11 and 12). The ipsilateral lung mean dose also experienced similar magnitudes in dose reductions for plans with ISC. The average reduction was 25\% (range: 11\%-52\%). The \( V_5 \) for the ipsilateral lung had a maximum improvement of 1\% (Patient 4). The ipsilateral lung dose for the 12 patients using each technique is shown in Figures 13 and 14. The average cumulative DVH showing lower irradiated volumes at low doses with ISC for the heart and the ipsilateral lung are illustrated in Figures 15 and 16.

*Setup Variability*

Isocenter shifts of 1 cm in the x, y and z directions with the ISC plans were used as a crude means to simulate the potential setup variability that may be encountered during patient treatment. The homogeneity index was influenced most by the \( z \) shift towards the inferior direction, resulting in a 3-fold increase in the average homogeneity index when compared to ISC plans with no shift. Shifts in the x and y directions also demonstrated increased average homogeneity to a lesser degree with an average increase of 0.16 and 0.01, respectively. The average conformity index increased mostly in the y direction (0.18) while the x and z directions remained relatively constant for most patients (Figures 17 and 18).
The heart mean dose experienced a substantial increase in Patients 2, 5 and 11, in which the isocenter of the treatment fields were shifted posteriorly in the y direction, irradiating a larger volume of the heart. The impact of the shift is dependent on the proximity of the heart to the treatment fields. The average mean heart dose for the 12 patients doubled from 83.6 cGy to 162.7 cGy with the y shift. The mean dose for the heart was essentially unaffected by the x and z shifts. Similar trends were also observed for the mean dose in the ipsilateral lung. The posterior shift in the y direction increased the average ipsilateral lung mean dose by 83.3 cGy, while shifts in the x and y directions decreased an average of 7.5 cGy and increased 6.5 cGy, respectively (Figures 19 and 20).

The results obtained from this study demonstrate the potential in using irregular surface compensators in prone breast treatment to improve the dose homogeneity and PTV coverage. Most patients from the study experienced lower maximum doses and homogeneity indices as well as better PTV coverage. The use of these compensators also reduced the heart and ipsilateral lung mean doses for all 12 patients, potentially translating to a reduction of secondary malignancies and improved clinical outcomes. The increase in setup variations has often been associated with the prone technique. Shifting the treatment fields 1 cm posteriorly demonstrated a greater impact in the increase of heart and ipsilateral lung dose than in the superior/inferior or left/right directions, as expected. Further studies to evaluate the effect of these setup variations are suggested.
Chapter V: Discussion

Patients with pendulous breasts treated for early stage breast cancer using standard supine radiotherapy techniques often exhibit inferior cosmetic outcomes and a higher incidence of heart disease and lung cancer compared to their smaller breasted counterparts. Larger dose inhomogeneities are typically found in larger breasted patients and have correlated to poorer cosmetic results. The larger field separations from pendulous breast patients encompassing greater heart and lung volume from conventional radiotherapy methods have been associated with cardiac and lung complications post treatment. Treatment in the prone position has shown to improve dose inhomogeneities and reduce cardiac and lung irradiation as reported in literature. The results from this study demonstrated that further benefits can be realized with the utilization of irregular surface compensators in prone breast plans. The 3D maximum dose and homogeneity indices improved with ISC plans while slightly sacrificing the conformity indices. The volume of the PTV receiving 105% of the prescription dose ($V_{105}$) increased for 7 out of 12 patients, though not statistically significant, while never exceeding 110% ($V_{110}$) for all patients. More notable were the average reductions in heart and ipsilateral lung mean doses of 33% and 25%, respectively. Such improvements with ISC in prone breast treatment plans have the potential to minimize normal tissue complications decades after irradiation.

Limitations

A possible limitation of this study was the relatively small sample size of available patient data. A larger cohort with a wider range of breast sizes from multiple institutions, using a variety of different prone breast boards, and treatment plans generated by a variety of planners, would potentially yield more representative results. Additionally, the isocenter shifts used in this study to assess dosimetric changes as a result of setup errors were crude estimates and did not include various factors such as accounting for the summation of the combined directional shifts or changes in actual patient anatomy.

Conclusions

In this study, 10 of the 12 prone patients had more narrow ranges of doses ($D_{\text{max}}-D_{\text{min}}$) while all patients experienced improved PTV coverage at 100% of the dose when planned with ISC versus the standard method. The reduction in dose range and better coverage is consistent with the results reported by Carruthers et al.\textsuperscript{45} Additionally, the 3D maximum dose improved in ISC plans, with reductions ranging from 2.3% to 4.9%. Similar magnitudes were also
demonstrated in the study conducted by Carruthers et al\textsuperscript{45} using compensators. High dose regions in the ISC plans typically occurred at the medial aspects of the breast near the chest wall. The use of the fluence editor in the Eclipse treatment planning system (TPS) successfully reduced these high dose regions thereby contributing to the reductions in the maximum dose and improvements in homogeneity throughout the breast tissue.

Substantial reductions in cardiac dose with ISC were also demonstrated in this study. It has been reported by Kirby et al\textsuperscript{36} that the prone position may not improve cardiac dose for all patients particularly those with smaller breasts due to the smaller anterior displacement of the breast tissue relative to the cardiac tissue. However, based on this current study, patients treated prone had significant reductions in cardiac irradiation when ISC was incorporated in their treatment plans. All 12 patients planned with ISC demonstrated reductions in the mean dose delivered to the heart, with reductions up to 50\%. These improvements occurred predominantly with low doses under 5 Gy. Caudell et al\textsuperscript{22} showed even larger improvements with reduced doses delivered to the heart up to 75\% on compensated plans when compared to the standard plans in supine patients. Low dose radiation as low as 1 Gy has been hypothesized in contributing to increases in the risk of cardiovascular disease.\textsuperscript{36,47} Consequently, the use of ISC in prone breast treatment plans and the potential reductions in cardiac irradiation at low doses may have significant implications.

Likewise, ipsilateral lung dose was substantially lowered in treatment plans with ISC. All patients experienced reductions in ipsilateral lung mean dose with the greatest improvement for volumes receiving low doses (< 5 Gy) regardless of breast size. Kirby et al\textsuperscript{36} reported all patients treated in the prone instead of the supine position had significant reductions in lung dose for all breast sizes. This indicates that the lungs do not exhibit the tendency to shift anteriorly to the same degree, as does the heart. The concern for low dose stochastic effects as reported by Kirby et al\textsuperscript{36} raises the importance of the reported findings with ISC in prone treatment plans. A reduction in median lung dose from 4.4 to 0.8 Gy with the prone position was estimated to prevent approximately 3 secondary primary lung cancers per year per 10,000 women in 10 year post radiotherapy.\textsuperscript{36} Further reductions with ISC may translate to significant long term clinical outcomes.

Furthermore, larger setup variability in prone patients has been reported in literature. This can be improved by developing better prone breast boards, carefully placing tattoos and
increasing the experience level of the staff. In this current study, the isocenter was individually shifted in the x, y and z directions to simulate patient shifts and setup variability. Shifting posteriorly (-y direction) can potentially increase the heart and lung dose beyond baseline levels irradiating more heart and ipsilateral lung tissue than warranted. Such a scenario can result from the patient feeling more relaxed during successive treatments causing anterior displacement of the treated breast and chest wall. The combined effects of the shifts, the impact and consequences of such combinations have not been evaluated but are indicated for future studies.

**Recommendations**

Further research as extensions from this study can be undertaken to examine the sensitivity of inter and intra-fractional setup variations and patient shifts to provide more conclusive results regarding these differences when using modulated beams with ISC as compared to the standard technique. It is also suggested that the inclusion of a larger sample size and the use of different models of prone breast boards may provide more representative results. Additionally, dose reductions to the contralateral breast in ISC plans were not included in this study but certainly may prove to be significant. Lastly, the results from this study can be extrapolated to assess clinical outcomes and potential reductions in long-term normal tissue complications and mortality rates in a more comprehensive study.
Table 1. Dosimetric Parameters Mean Value ± Standard Deviation Between Standard versus Irregular Surface Compensator (ISC) Techniques

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Standard</th>
<th>ISC</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>$D_{\text{max}}$ (cGy)</td>
<td>5238 ± 326</td>
<td>5068 ± 323</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>$D_{\text{mean}}$ (cGy)</td>
<td>4918 ± 300</td>
<td>4910 ± 314</td>
<td>0.641</td>
</tr>
<tr>
<td>$D_{\text{min}}$ (cGy)</td>
<td>3995 ± 375</td>
<td>3924 ± 448</td>
<td>0.125</td>
</tr>
<tr>
<td>Homogeneity Index</td>
<td>0.3 ± 0.1</td>
<td>0.2 ± 0.1</td>
<td>0.068</td>
</tr>
<tr>
<td>Conformity Index</td>
<td>1.2 ± 0.2</td>
<td>1.2 ± 0.2</td>
<td>0.002</td>
</tr>
<tr>
<td>PTV $V_{105}$ (%)</td>
<td>60.8 ± 15.5</td>
<td>66.3 ± 17.2</td>
<td>0.350</td>
</tr>
<tr>
<td>PTV $V_{110}$ (%)</td>
<td>5.1 ± 4.3</td>
<td>0.0</td>
<td>0.002</td>
</tr>
<tr>
<td>PTV $100%$ (%)</td>
<td>92.4 ± 5.1</td>
<td>95.0 ± 2.3</td>
<td>0.028</td>
</tr>
<tr>
<td>PTV $95%$ (%)</td>
<td>99.4 ± 0.4</td>
<td>99.3 ± 0.8</td>
<td>0.555</td>
</tr>
<tr>
<td>3D Dose Max (%)</td>
<td>112.3 ± 1.0</td>
<td>108.7 ± 1.0</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Heart Mean (cGy)</td>
<td>116.8 ± 80.1</td>
<td>83.6 ± 67.1</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Heart $V_5$ (%)</td>
<td>1.4 ± 2.7</td>
<td>1.0 ± 2.2</td>
<td>0.086</td>
</tr>
<tr>
<td>Ipsilateral Lung Mean (cGy)</td>
<td>118.6 ± 102.1</td>
<td>95.0 ± 92.7</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Ipsilateral Lung $V_5$ (%)</td>
<td>2.4 ± 3.8</td>
<td>2.0 ± 3.5</td>
<td>0.006</td>
</tr>
</tbody>
</table>

* Significance tested using Paired-T test. (N=12)
Figure 1. Prone Breast Board. Courtesy of CDR Systems.\textsuperscript{46}
Figure 2. Homogeneity Index Comparisons Between Standard and ISC Techniques

Figure 3. Conformity Index Comparisons Between Standard and ISC Techniques
Figure 4a. Patient 5 Axial Central Slices using Standard (left) and ISC (right) Techniques

Figure 4b. Patient 5 Axial Global Maximum Dose Slices using Standard (left) and ISC (right) Techniques
Figure 5a. Patient 12 Axial Central Slices using Standard (left) and ISC (right) Techniques

Figure 5b. Patient 12 Axial Global Maximum Dose Slices using Standard (left) and ISC (right) Techniques
**Figure 6.** PTV $V_{105}$ Comparisons Between Standard and ISC Techniques

**Figure 7.** PTV $V_{110}$ Comparisons Between Standard and ISC Techniques
Figure 8. Plot of 3D Maximum Dose Variations Between Standard and ISC Techniques.

Figure 9. 3D Maximum Dose Improvement with ISC over Standard Techniques versus Separation
Figure 10. Average Cumulative PTV Dose Volume Histogram (DVH) Comparisons Between Standard and ISC Techniques For Patients 1-12
Figure 11. Heart Mean Dose Comparisons Between Standard and ISC Techniques

Figure 12. Heart V5 Comparisons Between Standard and ISC Techniques
**Figure 13.** Ipsilateral Lung Mean Dose Comparisons Between Standard and ISC Techniques

**Figure 14.** Ipsilateral Lung V5 Comparisons Between Standard and ISC Techniques
**Figure 15.** Average Heart Cumulative Dose Volume Histogram (DVH) Comparison Between Standard and ISC Techniques

**Figure 16.** Average Ipsilateral Lung Cumulative Dose Volume Histogram (DVH) Comparison Between Standard and ISC Techniques
Figure 17. Homogeneity Index Isocenter Shift Comparisons

Figure 18. Conformity Index Isocenter Shift Comparisons
Figure 19. Heart Mean Dose Isocenter Shift Comparisons

Figure 20. Ipsilateral Lung Mean Dose Isocenter Shift Comparisons
References


