DEVELOPMENT OF A STANDARD LINEAR ACCELERATOR BASED BACK-UP PLAN FOR TOTAL MARROW IRRADIATION WITH HELICAL TOMOTHERAPY

By

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CERTIFICATE OF APPROVAL

This is to certify that the Master's thesis of

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has been approved

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Mentor/Advisor

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Abstract

Purpose: To identify a field match line for TMI treatment interruption, and to develop a total body irradiation (TBI) completion plan to be used in the case of a treatment interruption during a total marrow irradiation (TMI) treatment with helical tomotherapy.

Methods: TMI has been determined to be feasible on TomoTherapy, but requires a backup plan in the event that TomoTherapy breaks down during a patient's treatment. A TomoTherapy helical treatment plan was created with a 10 cm x 15 cm x 110 cm phantom in order to simulate a TMI patient treatment. Film dosimetry measurements were taken to capture a treatment interruption, and these films were analyzed to find the distance from the interrupt table position to the 50% isodose line. Four pitches were investigated to determine if pitch would have any effect on the position of the 50% isodose line with respect to the treatment interrupt position. Composite film measurements were taken with an Elekta linear accelerator in a TBI setup in order to find an ideal match line for a completion treatment. The match lines investigated in this study included overlap distances of 0 cm, 0.5 cm, 1 cm, 1.5 cm, and 2 cm between the TMI table interrupt position and the field edge of the TBI completion treatment.

Results: It was determined that the average distance from the TMI table interrupt position to the 50% isodose line was 4.23 ± 0.10 mm ($1\ \sigma$). This result was determined to match closely to the expected value from TomoTherapy's Planned Adaptive module. The distance from the interrupt position to the 50% isodose line was determined to be independent of pitch. Several match lines were investigated, and it was found that the higher the overlap between the two treatments, the higher the hot spot produced, and the lower the cold spot. The 0 cm and 0.5 cm match lines produced the most homogenous dose distributions across the junction.

Conclusion: Finding a match line from a TMI treatment interruption using film dosimetry was determined to be feasible. A completion procedure using a standard TBI setup is feasible, although further investigation into field size feathering is required in order to achieve adequate dose homogeneity in the junction region.

1. Introduction

In 2019, an estimated 176,200 patients will be diagnosed with lymphoma, myeloma, or leukemia.[1] Many patients with diseases that fall under these categories will be candidates for hematopoietic stem cell transplant (HSCT). HSCT involves implanting a graft of bone marrow, peripheral stem cells, or umbilical cord blood, and the graft can be obtained either from the patient themselves, or a matched donor. HSCT is a routine treatment for patients with diseases such as multiple myeloma, non-Hodgkin lymphoma, acute myelogenous leukemia, myelodysplastic syndrome, Hodgkin disease, and acute lymphoid leukemia.[2] To condition the patient's body before undergoing HSCT, the patient will typically receive chemotherapy, total body irradiation, or a combination of the two.

Total body irradiation, or TBI, is a radiotherapy treatment that delivers a uniform dose of radiation to a patient's entire body, with the purpose of destroying any residual malignant cells and hematopoietic stem cells. This treatment also causes the immunosuppression of the patient, which aids in avoiding graft rejection.[2] There are many benefits to using TBI to supplement chemotherapy, including the capability of treating sanctuary sites such as the testes and the central nervous system, and the fact that treatment delivery does not depend on the functionality of the blood supply to the body. TBI also allows for the manipulation of dose distribution through the introduction of organ blocks and compensators.

Despite the many benefits of TBI and the ability to a certain extent to control the dose distribution, many TBI patients experience side effects. These side effects include nausea, vomiting, diarrhea, headache, and fatigue.[3] Because TBI is such an integral part of treating these

patients, it would be advantageous to find an alternative option that accomplishes the same treatment goals while minimizing the side effects that patients will experience. Total marrow irradiation, or TMI, functions as one such alternative treatment. TMI serves the same purpose as TBI in that the patient receives the same myeloablative dose to bone and marrow, but it allows for lower doses to organs at risk by conforming dose only to target regions. Because of this benefit, TMI has a higher therapeutic ratio than TBI.

Another option is intensity modulated radiation therapy (IMRT) based TBI, which is similar to TMI in that it uses intensity modulation to limit dose to organs at risk, but the target region essentially remains the whole body.[4] In this case, the resulting side effects and their severity depend on which structures are designated as organs at risk and removed from the target area during planning.

IMRT-based TBI or TMI can be delivered on a standard linear accelerator or with helical tomotherapy. Helical tomotherapy is advantageous in this situation as it allows for continuous translation of the couch, which means that a patient's entire body may be treated with one or two separate plans and set-ups, whereas IMRT-based TBI on a standard linear accelerator would take several plans junctioned together to treat the patient's entire body.

While TMI on helical tomotherapy has be proven to be clinically feasible,[56] it is important to consider practical issues that may come up during patient treatment. In particular, it is a possibility that TomoTherapy could break down during a patient's treatment, in which case only a fraction of their body will have been treated with TMI. Due to an intense fractionation scheme required for TBI and TMI, the fraction will need to be completed as soon as possible. One way to complete this treatment is with a basic TBI treatment on a standard linear accelerator. For this

type of completion treatment, a match line would be required to find the junction point at which the TBI treatment would start on the patient in order to achieve a homogenous dose for that fraction. The purpose of this thesis is to determine the appropriate match line that will achieve a homogenous dose when delivering a completion TBI procedure after a treatment interrupt during a TMI treatment on helical tomotherapy.

2. Background and Materials

2.1. Total Body Irradiation

TBI continues to be an important procedure in the treatment of lymphoma, myeloma, and leukemia. The goal of TBI is to deliver a homogenous dose to the patient's entire body, and this is typically achieved by positioning the patient at an extended source to surface distance (SSD) so that the patient's body fits within the radiation beam (Figure 1). The accepted treatment regimen for TBI consists of a whole body dose of 12 to 15 Gy delivered in 6 to 12 fractions over 3 to 5 days.[2] Dose is prescribed to the patient's midline at the level of the umbilicus, and TBI is typically delivered with 18 MV photon beams. The standard adult full TBI protocol at Oregon Health and Science University (OHSU) is a dose of 12 Gy delivered in 8 fractions, with two fractions a day given 6 hours apart.

TBI treatments can be performed in a standing AP/PA position, in which the beam is delivered anteriorly and posteriorly (Figure 2), or in a lateral position with the patient seated on a treatment couch.

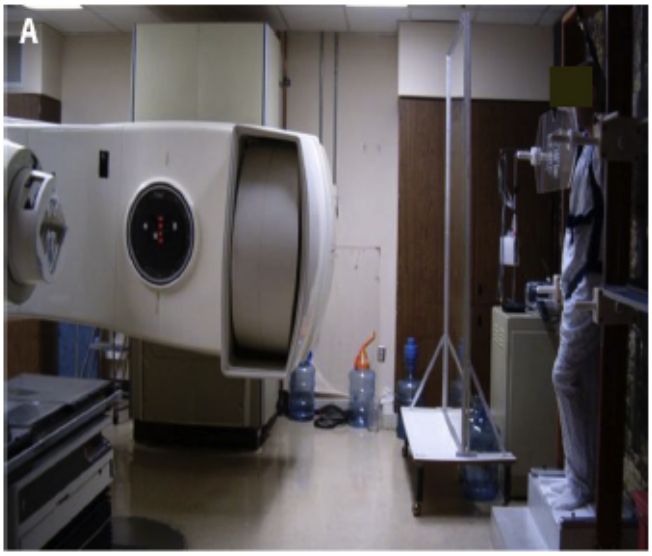

Figure 1. Total Body Irradiation Patient Setup.[7]

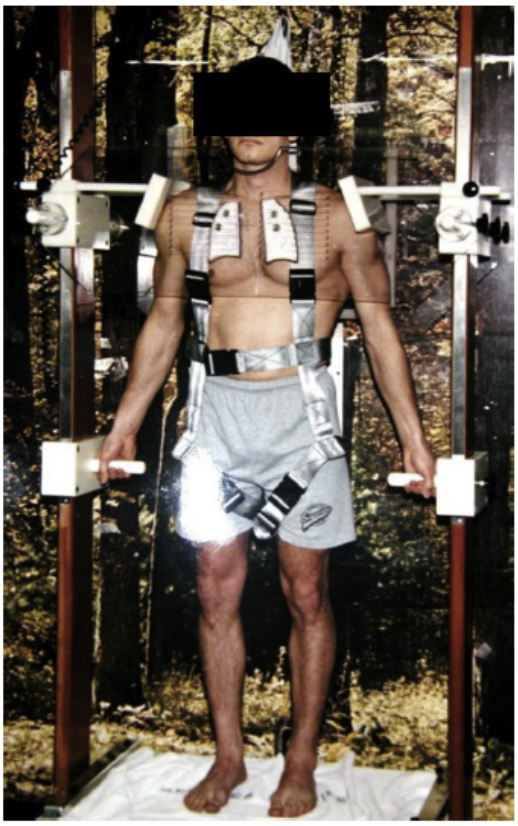

Figure 2. Total Body Irradiation AP/PA Patient Setup.[7]

Dose inhomogeneity is expected to be within ±10% of the prescription dose.[2] Brass compensators are used to account for differences in patient thickness along the body, in order to prevent thinner parts of the body, such as the head, neck, and other extremities, from receiving too high of a dose. Lung blocks are used to reduce the dose to the lungs, as lung toxicity is a concern when treating the whole body. At OHSU, lung blocks with 25% transmission are used during the first four fractions, and then removed for the remaining four fractions. This helps to keep risk of lung toxicity low while still delivering enough dose to the surrounding tissues to hopefully avoid recurrence of disease.

2.2. Helical Tomotherapy

2.2.1. TomoTherapy HD Device Description

Helical tomotherapy is a specially designed linear accelerator capable of continuous rotation around the longitudinal axis of the treatment couch. The patient is translated through the machine's aperture in a manner similar to a helical CT scan.[8] Due to this unique treatment style, helical tomotherapy can easily perform long and complex treatments that otherwise can be difficult to achieve on a traditional linear accelerator. TomoTherapy HD is a linear accelerator model that uses helical tomotherapy, and this was the machine used for all tomotherapy measurements in this study (Figure 3).

Figure 3. TomoTherapy HD

TomoTherapy HD has a single nominal photon energy of 6 MV, so all treatments are performed at this energy. The maximum longitudinal couch translation is 160 cm, which is achieved when the couch is at the height of the isocenter plane. The maximum treatment length is dependent on the height of the couch, however, and with a typical patient set-up, the treatment length is closer to 135 cm.[9] Accordingly, TMI patients with a height longer than about 135 cm would need their treatment split into two in order to cover their whole body.

TomoTherapy HD delivers IMRT with a multi-leaf collimator (MLC) that utilizes binary leaf collimation. The fan beam of radiation delivered has a width of 40 cm at isocenter. The field widths available for treatment include 1 cm, 2.5 cm, and 5 cm, and both fixed and dynamic jaw options are available. Fixed jaw treatments maintain the same field width from start to finish throughout the treatment. In dynamic jaw treatments, the field size starts at 1 cm, gradually opens to the selected field width as the beam approaches the target, treats the entire target with the selected field width, and closes back down to 1 cm as the beam reaches the end of the target. This leaves a sharper dose fall-off at the edges of the target.

An important factor in TomoTherapy treatment planning is the pitch. Pitch is defined as the ratio of the longitudinal couch travel per gantry rotation to the field width.[10] Changing the pitch of a treatment will change the speed of the couch travel, and will thus change the duration of a patient's treatment.

2.3.2. Tomotherapy-Based TBI & TMI

There have been several studies investigating the feasibility of TMI (Figure 4) or TBI (Figure 5) treatments using helical tomotherapy.[4,5,6,11] The benefits of using this modality include the intensity modulation allowed by multi-leaf collimation, as well as the fact that patients will lay down on the treatment couch for treatment, which is a better tolerated position for patients who have difficulty standing for the duration of a TBI treatment.

Because the treatment planning process for TMI allows for the avoidance of organs at risk, it has been shown that TMI on helical tomotherapy results in reduced organ doses, and therefore reduced side effects from treatment. TMI also introduces the possibility of dose escalation to the target. It has been shown that a dose of 20 Gy can be delivered to target areas with TMI while keeping organ doses lower than in a 12 Gy TBI treatment.[6]

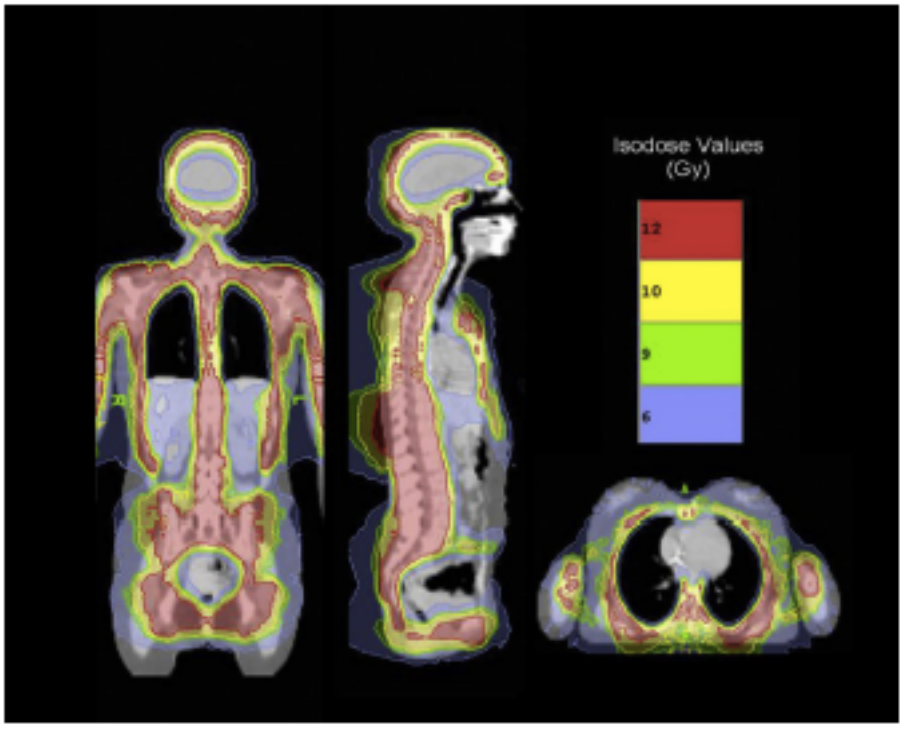

Figure 4. TMI Patient Treatment on TomoTherapy.[6]

 https://doi.org/10.1016/j.bbmt.2005.10.026

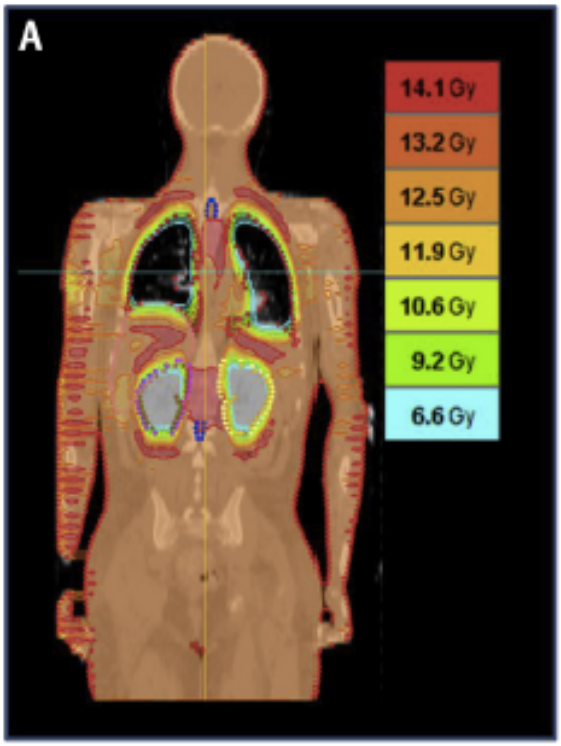

Figure 5. TBI Patient Treatment on TomoTherapy.[6]

 https://doi.org/10.1016/j.bbmt.2005.10.026

2.3.3. Thread Effect

A feature of helical tomotherapy is a dosimetric ripple that results from helical beam junctioning.[12] This ripple is known as the thread effect, and it is caused by several factors that are unique to the helical beam delivery provided with tomotherapy.[13] It has been determined that there are specific pitches that result in a minimal thread effect, and these pitches occur at values 0.86/n.[12] Several pitches, including 0.215, 0.287, and 0.43 which correspond to a minimal thread effect, are investigated in this study to determine the effect of pitch in determining a match line after a TMI treatment interruption on TomoTherapy.

2.5. Measurements with GAFchromic film

2.5.1. GAFchromic Film

GAFchromic EBT3 film is a self-developing radiochromic film that is used for dosimetry at radiotherapy energy ranges. The optimal dose range for this film is from 0.1 to 10 Gy, making it suitable for measurements in radiotherapy dose ranges. The structure of this film consists of a 28 μm thick active layer between two 125 μm thick layers of matte-polyester substrates.[14] When exposed to radiation, the active element in this film reacts to form a blue polymer, and the darkness of this color increases with increasing absorbed dose.

GAFchromic EBT3 film has little energy dependency, and the net optical density will be within 5% when exposed at between 100 keV and 18 MeV. EBT3 film also has little dose fractionation response and little dose rate response, and the net optical density should be within 5% due to changes in these factors.[14]

One of the recommended scanners for this film is the EPSON Expression 10000XL Photo scanner, which is the scanner that was used for all film scanning in this study. The software used to scan in these films was EPSON Scan. It is important that the orientation of the film is kept constant during scanning, as changes in orientation from landscape to portrait style can result in up to 4.5% difference in net optical density.[15]

Studies have shown that scanning the film between 24 and 72 hours post-irradiation results in a very small difference in net optical density, and the stabilization time recommended is two hours.[15] For this study, all films were left to develop for at least 24 hours before scanning in order to ensure full stabilization.

2.5.2. DoseLab (Varian Medical Systems)

DoseLab is a software that is used for quality assurance for linear accelerators as well as for film dosimetry.[16] The film dosimetry portion of DoseLab offers analysis features including region of interest dose measurements, dose profiles, isodose line maps, and more. DoseLab version 6.80 was used for this study to analyze all of the film measurements taken in this study.

2.6. Virtual Water Phantom

Virtual Water is a water-equivalent material supplied by Standard Imaging.[17] The amount of scatter and photon attenuation that this material creates is within 0.5% of the response of water. Virtual Water was chosen as the material for the phantom in this study, because a uniform and homogenous material was desirable, and the water equivalence of this phantom material approximates the response to radiation that a patient would have.

The phantom used for this study was comprised of six slabs of Virtual Water (Figure 6). Three of these slabs had a dimension of 55 cm × 15 cm × 5 cm, while the remaining three slabs were combined together to form an equivalent of one of the first three slabs. These slabs were combined to form a total phantom size of 110 cm × 15 cm × 10 cm. Some of the slabs used to create the phantom included holes for ion chambers, and were used to hold the Exradin A1SL ionization chamber for some measurements in this study. This phantom configuration was

Figure 6. Virtual Water Phantom.

chosen in order to approximate the shape and size of a small child, who would be the ideal candidate for a TBI treatment on TomoTherapy due to a height less than 135 cm.

2.7. Ionization Chambers

The Wellhofer FC65-G Farmer chamber (Scanditronix) (Figure 7) is an ionization chamber that is used for photon, electron, and proton beam dosimetry in radiotherapy. The cavity volume

of this ion chamber is 0.65 cm^3, the cavity length is 23.1 mm, and the cavity radius is 3.1 mm.[19] This chamber is used for monthly quality assurance at OHSU, and was chosen due to its known performance on the Elekta linear accelerator used for this study.

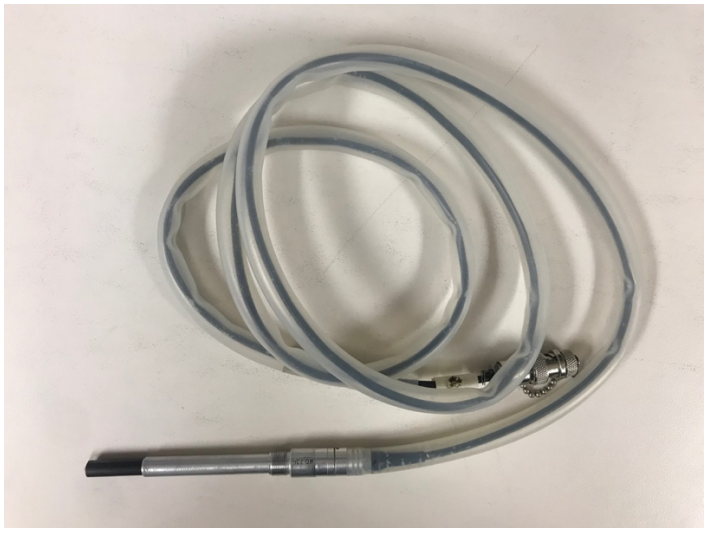

Figure 7. Wellhofer Ion Chamber.

The Exradin A1SL chamber (Standard Imaging) (Figure 8) is an ionization chamber with a small collecting volume of 0.057 cm^3 and a collector diameter of 1.0 mm.[20] This chamber was used because it fit inside holes inherent within the phantom's structure, and because it is the standard chamber of practice for TomoTherapy.

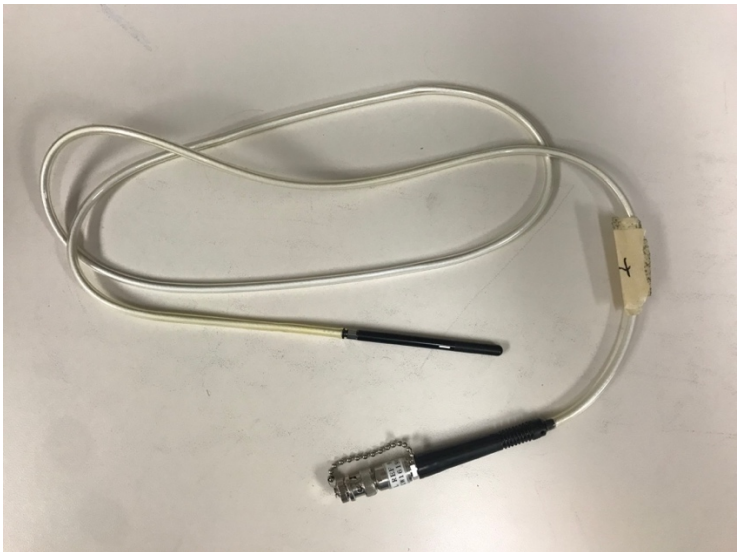

Figure 8. Exradin Ion Chamber.

3. Methods

3.1. CT Simulation of the Phantom

The CT simulation of the phantom was performed on a Philips CT Big Bore. A tomotherapy TBI pediatric protocol was used to perform the CT, and this protocol utilized a photon energy of 120 kV and 150 mAs per slice. Several markers were placed on the phantom for localization. The type of marker used in this study was the CT-Spot 120 4 mm pellets created by Beekley Medical.[21] CT-Spot skin markers appear as bright spots in a CT, while avoiding streak artifacts due to being non-metallic.[22] These markers were placed in sets of three in order to mark locations close to the center of the phantom. These locations were chosen slightly anteriorly to the physical center of the phantom, in order to avoid the junction of two separate slabs of Virtual Water.

3.2. Treatment Planning

3.2.1. Contouring

Structure contouring was performed in Eclipse Version 13.6 (Varian Medical Systems). A cylindrical target volume was contoured along the superior-inferior axis of the phantom with a radius of 2 cm. This target structure can be seen in green in Figures 9 and 10. A hollow cylinder was contoured around this target volume with an inner radius of 2.15 cm and an outer radius of 2.65 cm. This hollow cylinder functioned as a dose suppression structure, to help achieve a desirable dose distribution. This structure can be seen in pink in Figures 9 and 10.

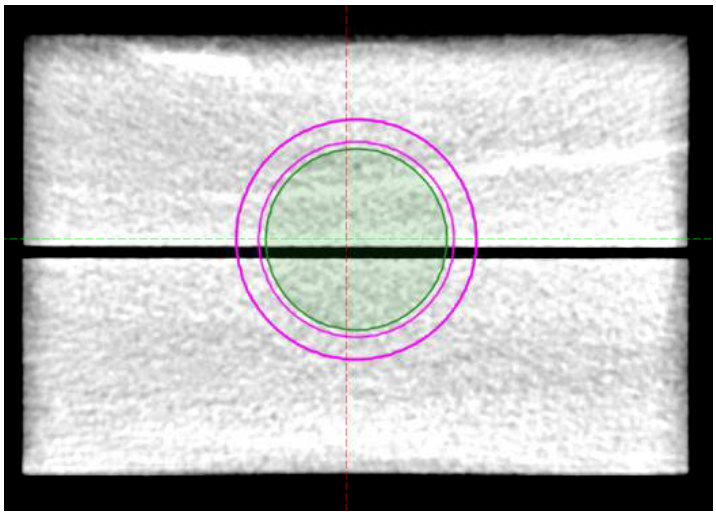

Figure 9. Axial slice of phantom with contours.

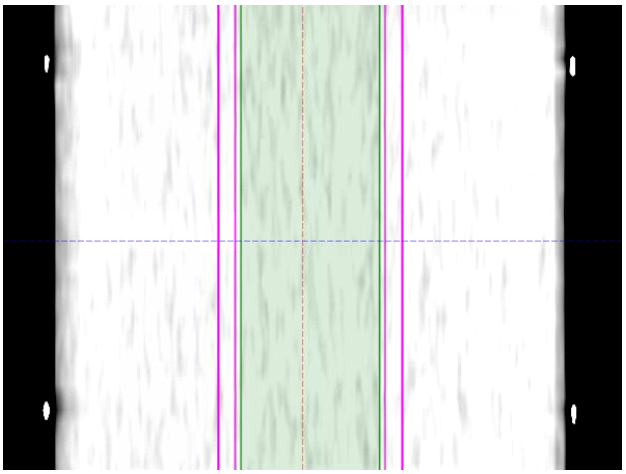

Figure 10. Coronal slice of phantom with contours.

3.2.2. Treatment Planning with TomoTherapy

Treatment planning was performed in the TomoTherapy treatment planning system. Several treatment plans were created throughout the course of this study. A pitch study was conducted in which four plans were created to deliver 300 cGy to the target; these plans were identical in every aspect other than the pitch selected. The four pitches chosen were 0.215, 0.287, 0.43, and 0.3. These plans were all selected to have a 5 cm dynamic jaw field width.

A new plan was created after this initial pitch study, in order to correct some issues that arose during this first stage. The main error in the initial plans was that the location of the films

was set to measure a slice of the target that was far from the center. The new plan ensured that the film would capture a slice of the target at the very center, so that the film would measure the maximum dose to the target. This plan also prescribed 300 cGy to the target, and the pitch chosen for the final plan was 0.43, which was determined to be the most likely pitch chosen for clinical use. The plan implemented a fixed jaw and a 5 cm field width. 5 cm is the largest option for field width, and this choice shortens the treatment time, which is of concern with large treatment fields, as is the case with TMI.

The target coverage is defined as the ratio of the volume of the target receiving the prescription dose to the total volume of the target. The ideal plan has a target coverage of 1, and the plan created for TMI treatment interruption measurements had a target coverage of $TC = \frac{V_{T,presc}}{V_T} = 0.981$. The homogeneity index is defined as the difference in the dose to 2% of the target volume and the dose to 98% of the target volume, divided by the median dose to the target volume. The ideal plan has a homogeneity index of 0, and the plan created for TMI treatment interruption measurements had a homogeneity index of $HI = \frac{D_{2\%} - D_{98\%}}{D_{median}} = \frac{32.14 - 30.13}{31.20} = 0.064$.

3.3. Film Calibration

Calibration films were acquired on an Elekta Versa HD linear accelerator. Small strips of GAFchromic film, from the same batch as all other measurements, were placed within a 30 cm x 30 cm Solid Water phantom, at a depth of 1.5 cm and with 10 cm of Solid Water providing backscatter. The calibration films were irradiated with 6 MV photon beams at an SSD of 100 cm,

with a 10 cm × 10 cm field size. Ten calibration films were created, respectively receiving 0 cGy, 50 cGy, 100 cGy, 150 cGy, 200 cGy, 250 cGy, 300 cGy, 350 cGy, 400 cGy, and 450 cGy (Figure 11).

DoseLab Pro software was used to create a calibration curve from the ten calibration films acquired. A region of interest was selected within each of the calibration films, and the average optical density within that region was set to correspond with the known dose delivered to that film. Using these values, a calibration curve was created using a 3rd order polynomial fit (Figure 12). This curve has an equation of $y = (4 \times 10^{-10})x^3 + (2 \times 10^{-6})x^2 + (0.0438)x + 4.79$, and the R^2 value for this fit is 0.9985. The same calibration curve was used to analyze all films included in this study.

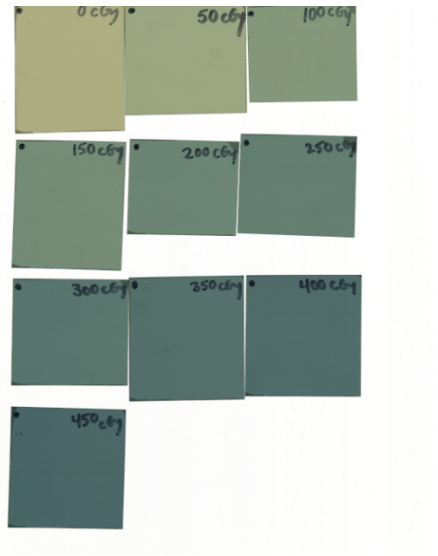

Figure 11. Calibration Films.

The film calibration created was validated by taking region of interest dose measurements both for films used to create the calibration, as well as independent strips of films that had a known dose delivered to them. This validation showed that the dose measurements were all within approximately 3% of the expected dose.

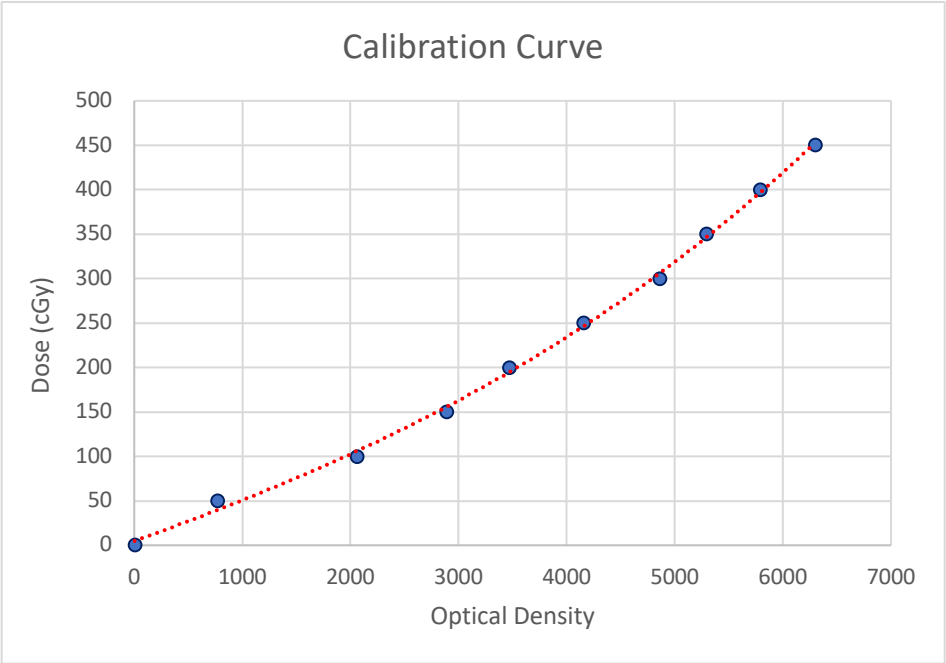

*Figure 12. Film Calibration Curve.**

*DoseLab multiplies the true optical density by a factor of 17,500.[23]

3.4. Film Measurements on TomoTherapy

Film measurements on TomoTherapy were taken with GAFchromic film placed between two 5-cm-thick slabs of Virtual Water. The film was marked with permanent marker at the location of the CT-Spot markers on the phantom, for the purpose of localization (Figure 13). The treatment plan was delivered to the phantom, but interrupted after a time had elapsed so that the area of treatment interruption would be captured on the film. During the acquisition of these film measurements, several table positions were noted for later analysis. These table positions included the table position at the start of treatment as well as at the time of treatment interruption. The third table position, which gave the location of the CT-spot marker used for localization, was acquired using an MVCT. The slice acquisition was set to "Fine" so that the determination of the marker's table position would be the most accurate. The slices of the MVCT

were chosen so that the very first slice contained the marker. When the table was moved into position to begin the MVCT acquisition, this starting position was noted and served as the marker's table position.

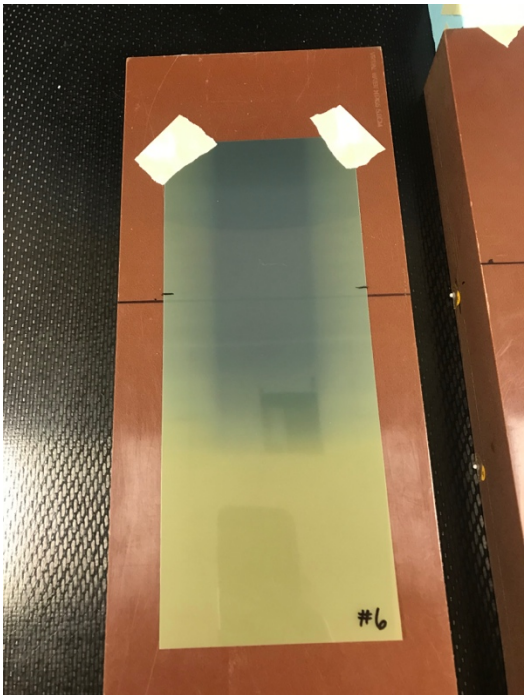

Figure 13. TomoTherapy TMI Treatment Interruption Film Measurements.

These interruption films were scanned using the EPSON Expression 10000XL Photo scanner, and these scans were then analyzed using DoseLab. The isodose tool in DoseLab was used to create isodose lines around the target.

The isodose lines were normalized so that the largest dose that homogenously covered the target was set as the 100% isodose line. Due to some variation of the film, not all films displayed an even coverage of the target with the 300 cGy isodose line, so each film was individualized in this way. The 50% isodose line was then determined based on this normalization. A screenshot of each set of isodose lines was analyzed using Excel (Figure 14). A distance scale was created by drawing a line along the x-axis of the graph, and converting Excel's distance units

into centimeters. Using this distance scale, a line that matched the known distance from the marker position to the interrupt position was drawn on the graph. This gave the spatial position of the interrupt table position. From this location, a line was drawn to the 50% isodose line, and the distance was found using the scale. In this manner, the distance from the interrupt table position to the 50% isodose line was found for each TMI treatment interruption film.

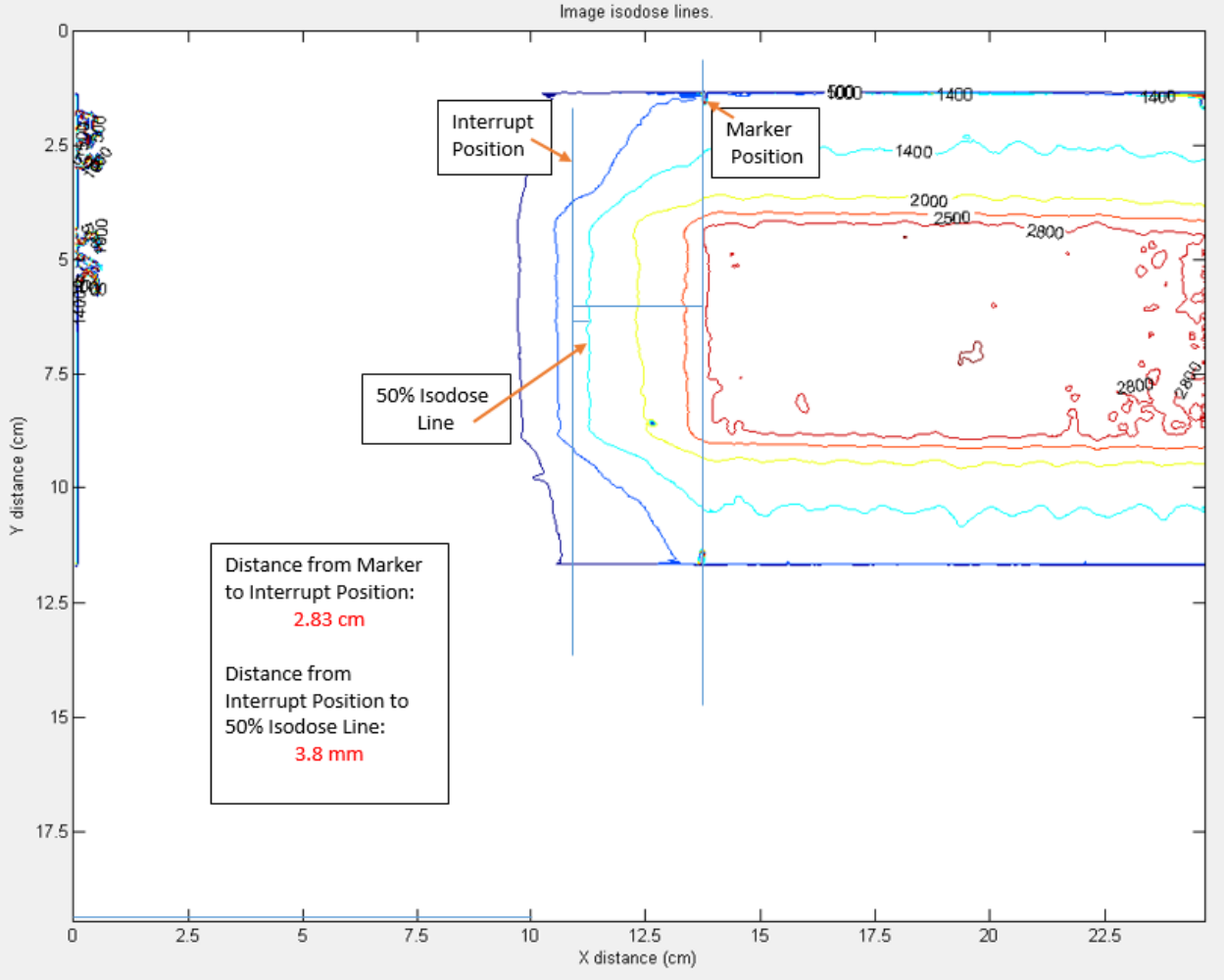

Figure 14. Finding the Distance from the Interrupt Position to the 50% Isodose Line.

3.4.1. Dose Verification on TomoTherapy

Throughout the TMI treatment interruption film measurements, there was a noticeable variation in dose measured by each of the films. To verify that the film measurements were

providing an accurate representation of the dose delivered by TomoTherapy, a dose verification was performed using an ionization chamber. The chamber used for this dose verification was the Exradin A1SL ionization chamber, and it was chosen because it fit inside the holes within the 10 cm x 15 cm x 110 cm phantom used for TMI treatment measurements. Because the chamber fit within holes that were inherent to the phantom, it was possible to acquire the ionization chamber measurement simultaneously with a film measurement. It is important to note that the film and ion chamber measurements were taken at slightly different depths within the phantom, and this may contribute to any differences in dose found.

For the dose verification measurements, the entire TMI treatment was delivered without any treatment interruption. This was to avoid any dose fall-off in the regions of measurement and to achieve a true measurement of the dose to the target.

3.5. Film Measurements for the TBI Completion Procedure

To simulate a TBI treatment, a 10 cm x 15 cm x 55 cm phantom was placed in a TBI setup (Figure 15). This phantom setup consisted of only half of the Virtual Water blocks used for the TMI treatment on TomoTherapy, because it would have been difficult to use the entire phantom in the TBI setup, and the full length of the phantom was not necessary for measurements. Styrofoam blocks were used to raise the phantom to the height of the central beam axis, with the gantry at 270°. Strips of film were placed between the two 5-cm-thick slabs of Virtual Water, so that the film was at the center of a 10-cm-thick phantom. For the therapy vault used in this study, the TBI source to midline distance was 381 cm, so the distance from the source to the film was 381 cm. A 1.5 cm-thick beam spoiler was used to increase the dose in the buildup region.

Figure 15. TBI Film Measurement Setup.

3.5.1. Penumbra Measurements

To measure the penumbra, films were placed on the phantom so that they would capture the field edge, as well as regions on both sides of the field edge. Two field sizes were used for these measurements, including the 0 cm x 20 cm field size and the 15 cm x 20 cm field size, because these were the two field sizes deemed most likely to be used clinically. To measure the penumbra, 1000 monitor units were delivered.

3.5.2. Dose Measurements

It was determined that 4100 monitor units would deliver 300 cGy to the center of a phantom with a 10 cm separation. Several films were irradiated in the TBI setup in order to measure the dose on both sides of the field edge after a TBI completion treatment. Both 0 cm x 20 cm and 15 cm x 20 cm field sizes were used for these measurements. These films were

acquired in order to determine the contribution of the TBI completion treatment to the composite films taken later in this study (Section 3.5.4).

3.5.3. Dose Verification for TBI Measurements

Due to some variation and uncertainty in film measurements, a dose verification was performed on the Elekta linear accelerator. Two ion chambers were used for this purpose, including the Wellhofer ionization chamber as well as the Exradin A1SL ionization chamber. For both of these chambers, a dose calibration was performed at 100 cm SSD.

The machine output was verified by delivering 100 monitor units to the Wellhofer chamber while it was at a depth in Solid Water of 10 cm, with an SSD of 100 cm and a field size of 10 cm x 10 cm. The Solid Water blocks used were 30 cm x 30 cm in dimension. Next, the Wellhofer chamber was moved to 3.3 cm depth, which is the depth of maximum dose for 18 MV photons. 100 monitor units were delivered, which should correspond to 100 cGy, because the machine was calibrated for this conversion. Using the charge reading acquired during this measurement, a dose calibration was acquired for the Wellhofer ionization chamber.

A similar dose calibration process was followed for the Exradin A1SL chamber. However, the phantom size required to hold this chamber was 15 cm x 55 cm. The shorter width of 15 cm of this phantom means that less side scatter would have entered the chamber, which would lead to the ion chamber reading a smaller dose. In order to avoid this issue, additional blocks of Solid Water were stacked around the phantom (Figure 16).

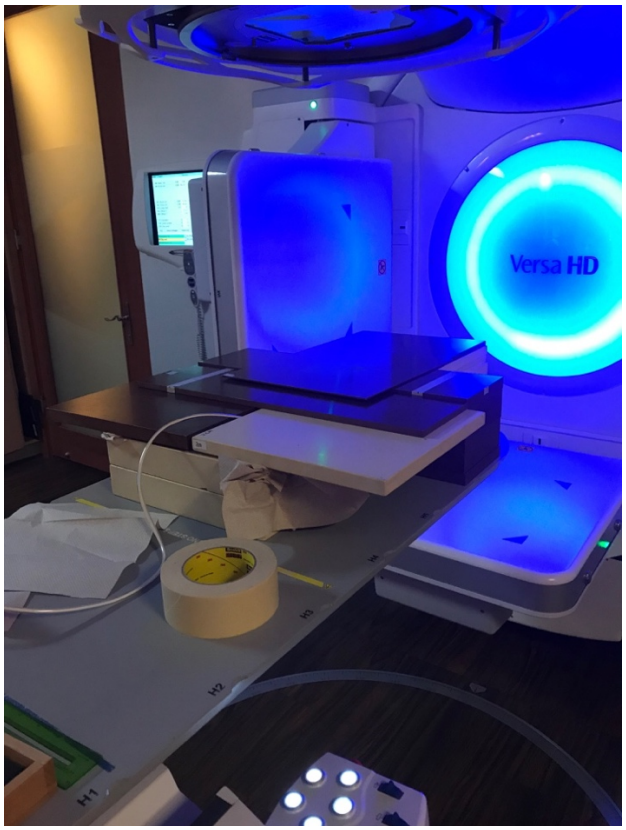

Figure 16. Dose Calibration Acquisition for Exradin Ion Chamber.

Once dose calibrations were acquired for both of the ion chambers, each ion chamber was used to measure the dose received by the target during a TBI completion treatment. In each case, the ion chamber was positioned to be 10 cm away from the field edge. The two ion chambers required slightly different setups, due to the limitations imposed by using holes built into Solid Water slabs. There was no hole large enough to fit the Wellhofer ion chamber in a 15 cm x 55 cm slab, so a 2-cm-thick 30 cm x 30 cm slab was inserted into the middle of a phantom made of 15 cm x 55 cm slabs, so that the total thickness of the phantom was 10 cm (Figure 17). The Exradin ion chamber required no additional Solid Water, as it fit directly into the 10 cm x15 cm x 55 cm phantom.

Figure 17. TBI Dose Measurement with Wellhofer Ion Chamber.

3.5.4. Composite Film Measurements

Five films that were previously irradiated with TMI treatment interruptions on TomoTherapy were irradiated with a TBI completion treatment on the Elekta linear accelerator. Various match lines were studied in order to determine the ideal match line for a completion treatment. The match line was achieved by setting the field edge of the TBI treatment to the known TMI treatment interrupt position, and then introducing a set amount of overlap between the two treatments. The amounts of overlap investigated in this study included 0 cm, 0.5 cm, 1 cm, 1.5 cm, and 2 cm.

4. Results

4.1 TomoTherapy Treatment Interruption Measurements

Eleven different films were used to determine the location of the 50% isodose line that results from treatment interruption on TomoTherapy. The pitch used for all of these

measurements was 0.43, and the field width was 5 cm with a fixed jaw. The 50% isodose line was found with respect to the treatment interrupt table position, and thus is represented as a distance from this interrupt position. After analyzing each film separately, the average distance from the interrupt table position to the 50% isodose line was determined to be 4.23 ± 0.1 mm (1 σ).

Film	1	2	3	4	5	6	7	8	9	10	11
Marker Position (cm)	104.54	104.53	104.54	104.5	104.5	104.53	108.78	108.65	108.67	108.74	108.72
Interrupt Position (cm)	107.02	108.04	112.39	109.04	110.03	111.04	111.28	112.32	113.26	110.21	109.24
Interrupt Position - Marker Position (cm)	2.48	3.51	7.85	4.54	5.53	6.51	2.5	3.67	4.59	1.47	0.52
Distance from Interrupt Position to 50% Isodose Line (cm)	0.54	0.5	0.47	0.53	0.47	0.28	0.22	0.38	0.47	0.38	0.41
Average Distance (mm) ± 1 σ	4.23 ± 0.1										

Table 1. Distance from Interrupt Position to 50% Isodose Line.

One of the TMI treatment interruption films was for a dose measurement in DoseLab. Dose measurements were taken both in the target region, as well as about 3 cm past the treatment interruption (Table 2). These measurements were used to quantify the contribution

of the TMI treatment dose to the composite film measurements after a TBI completion procedure had taken place.

TMI Treatment Interruption Dose	
In field Dose (cGy) ± 1 σ	306 ± 4.8
Out of Field Dose (cGy) ± 1 σ	6.6 ± 1.9

Table 2. In-Field and Out-of-Field Doses for TomoTherapy Treatment.

4.2 TomoTherapy's Planned Adaptive Module

One film measurement was used to compare the methods of this study with TomoTherapy's Planned Adaptive module. Using the same methods, the 50% isodose line was determined to be 2.45 cm away from the marker's position, or 3.8 mm away from the interrupt position. The Planned Adaptive module allows the user to see the isodose lines as calculated after a treatment interruption. Using this module, the distance between the marker position and the 50% isodose line was determined to be 2.25 cm. This matches closely with the film measurement of 2.45 cm, and thus validates the methods used for this study.

4.3 Pitch Study

A study was conducted to determine whether or not the chosen pitch for the TomoTherapy treatment would play a role in the distance from the interrupt position to the 50% isodose line. Four treatment plans were created, each with a different pitch. The pitches included in this study were 0.215, 0.287, 0.43, and 0.3. The first three of these pitches correspond to the formula of 0.86/n that lead to a minimal thread effect. The fourth pitch does not come from this

formula, and was included to determine if this would be an important factor. The film with a pitch of 0.3 resulted in the longest distance from the interrupt position to the 50% isodose line. However, it is of little clinical significance, because this pitch would not be used to treat patients. For each of the given pitches, a film was used to determine the distance from the treatment interrupt table position to the 50% isodose line (Table 2). The distances found from these films were not significantly different from each other, and it was determined that the pitch does not play an important role in this case.

Film	1	2	3	4
Pitch	0.215	0.287	0.43	0.3
Marker Position (cm)	102.76	103.61	103.64	103.55
Interrupt Position (cm)	107.85	115.58	115.24	119.31
Interrupt Position - Marker Position (cm)	5.09	11.97	11.6	15.76
Distance from Interrupt Position to 50% Isodose Line (cm)	0.76	0.79	0.88	1.07
Average Distance (cm) ± 1 σ	0.88 ± 0.12			

Table 3. Pitch Study - Distance from Interrupt Position to 50% Isodose Line.

4.4 Dose Verification on TomoTherapy

The dose received by these films was varied, so a dose verification was performed with an ion chamber measurement, using an Exradin A1SL ionization chamber. It was determined that after delivering the full planned treatment, the dose received by the film matched well with the ion chamber reading. A slight difference in dose between the two measurements is to be

expected due to the slight difference in depth within the phantom. Both measurements, however, showed a lower dose than was planned; however, this difference is less than 4%.

15 cm x 110 cm Phantom	
Measurement Device	Dose Measured (cGy) $\pm 1\ \sigma$
Film	302 ± 6.9
Ion Chamber	307
Planned	314

Table 4. TomoTherapy Treatment Dose Verification.

4.5 Linear Accelerator Penumbra Measurements

The penumbra width for the 18 MV energy beam was studied for the two treatment field sizes. For this study, the penumbra is defined to be the width between 80% and 20% of the average dose delivered inside the field. The two field sizes included in this study were 0 cm x 20 cm and 15 cm x 20 cm, because these were the two field sizes determined to be the most likely to be used clinically. The composite film measurements showing the result of field matching for a completion treatment were created using a field size of 15 cm x 20 cm. Therefore, more film measurements were performed for this field size in an attempt to more accurately determine the penumbra.

	0 cm x 20 cm			15 cm x 20 cm	
	TBI Distance		100 cm SAD	TBI Distance	
	4100 MU	1000 MU	100 MU	4100 MU	1000 MU
Penumbra Width (cm)	1.23	1.27	0.78	1.38	1.45
				1.2	
				1.13	

Table 5. Penumbra Widths for 0 cm x 20 cm and 15 cm x 20 cm Field Sizes.

The dose was measured both in and out of the field for the 15 cm x 20 cm field size. The dose was measured at 10 cm from the field edge in both directions. For this measurement, 1000 monitor units were delivered to the film. It was calculated that 4100 monitor units were required to deliver 300 cGy to the film with a TBI set-up, so the dose measurements were scaled by a factor of 4.1 in order to determine the dose that would be received at 4100 monitor units.

Elekta Penumbra Film Measurement	
5 cm depth, 1000 MU	
Scaled up to 4100 MU	
In field Dose (cGy) ± 1 σ	302.5 ± 5.8
Out of Field Dose (cGy) ± 1 σ	44.9 ± 4.1

Table 6. In-Field and Out-of-Field Doses for TBI Treatment.

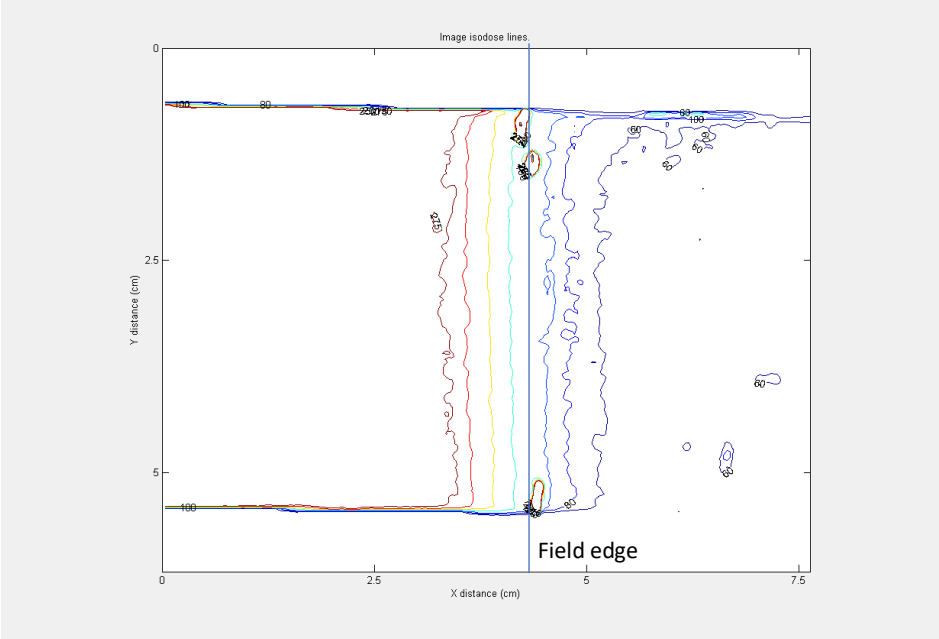

Figure 18. Linear Accelerator Penumbra Isodose Lines.

4.6 Dose Verification for Linear Accelerator Measurements

The dose received by film measurements was verified by two different ion chamber measurements. The first ion chamber was the Exradin A1SL chamber, the same ion chamber used to verify the film dose for the TomoTherapy treatment. The second ion chamber was the Wellhofer ion chamber. The set-up for these two measurements were slightly different, due to limitations in using Solid Water slabs with built in holes for specific ion chambers. A 30 cm x 30 cm, 2 cm thick slab of Solid Water was added to the center of the phantom to hold the Wellhofer ion chamber, whereas a 15 cm x 55 cm slab was used to hold the Exradin ion chamber. The differing set-ups for each ion chamber mean that a different amount of scatter was introduced in each of these measurements. Therefore, the dose received by each ion chamber should not be compared to each other, but rather to the respective film measured in each case.

Each ion chamber dose measurement matches very closely with the dose measured by film for the same setup. This confirms that the film measurements are accurately representing the true dose received, although there may be some variation from film to film.

Field Size = 15 cm x 20 cm, 4100MU, TBI Distance	
Measurement Device	Dose (cGy) $\pm 1\ \sigma$
Film	279 ± 3.5
	284 ± 4.2
Exradin Ion Chamber	287

Table 7. Dose Verification of TBI Treatment with Exradin Ion Chamber.

Field Size = 15 cm x 20 cm, 4100MU, TBI Distance	
Measurement Device	Dose (cGy) ± 1 σ
Film	300 ± 3.6
Wellhofer Ion Chamber	298

Table 8. Dose Verification of TBI Treatment with Wellhofer Ion Chamber.

4.7 Composite Film Measurements

Six films that had been previously irradiated with a treatment interruption on TomoTherapy were irradiated with a completion TBI procedure. Each film was placed at a slightly different position with respect to the field edge during the completion TBI procedure. The first film was positioned so that the treatment interrupt position from the TomoTherapy TMI treatment was aligned with the field edge for the TBI completion. This is labeled as the 0 cm match line. The rest of the films are all moved in toward the TomoTherapy treatment area, so that each consecutive film has more overlap in dose from the TMI and TBI treatments. These different match lines were investigated in order to determine the ideal match line for one of these treatments.

Calculations showed that 4100 monitor units in a TBI set-up would give these films 300 cGy. However, due to previous film measurements showing a lower film response compared to ion chamber measurements, the monitor units were scaled up by 10% in an attempt to have the films display a dose of 300 cGy. Therefore, 4510 monitor units were delivered to all of the composite films in the TBI region. Unfortunately, the film measurements that this decision was

based on were inaccurate, and thus the dose in the TBI region of these films are consistently about 10% higher than 300 cGy.

The dose was measured in several regions of each of these composite films (Table 9). The dose in each area was measured with a region of interest measurement in DoseLab, and the location of these regions of interest were held relatively constant from film to film (Figure 19). The first region measured was the TBI region, where the treatment had been completed using the standard linear accelerator. The second region was the TomoTherapy region, which included the dose delivered from the TMI treatment on TomoTherapy, as well as any scatter included from the TBI completion treatment. The third region measured was a hot spot located within the TBI region. This hot spot was created from the gradual dose fall-off from the TomoTherapy treatment, and the dose at this spot increases as the match line value increases. The final region measured was a cold spot, and this occurs between the hot spot and the full-dose TomoTherapy region. The cold spot decreases as the overlap of the two treatments increases.

Film		1	2	3	4	5
Match Line		0 cm	0.5 cm	1 cm	1.5 cm	2 cm
TBI Region	Dose (cGy) ± 1 σ	340.6 ± 6.4	336.0 ± 4.7	346.5 ± 5.8	329.2 ± 6.9	329.4 ± 4.9
	% Difference from Prescription Dose	103%	102%	105%	100%	100%
TomoTherapy Region	Dose (cGy) ± 1 σ	361.4 ±5.7	347.7 ± 5.8	363.6 ± 3.9	343.7 ± 8.1	343.3 ± 5.9
	% Difference from Prescription Dose	110%	105%	110%	104%	104%
Hot Spot	Dose (cGy) ± 1 σ	374.3 ± 8.0	395.1 ± 7.5	432.5 ± 37.0	433.0 ± 18.7	450+
	% Difference from Prescription Dose	113%	120%	131%	131%	136% +
Cold Spot	Dose (cGy) ± 1 σ	265.5 ± 6.2	271.6 ± 4.8	312.1 ± 5.8	326.0 ± 6.5	334.6 ± 5.2
	% Difference from Prescription Dose	80%	82%	95%	99%	101%

Table 9. Composite Film Dose Measurements. The prescription Dose is defined as 330 cGy.

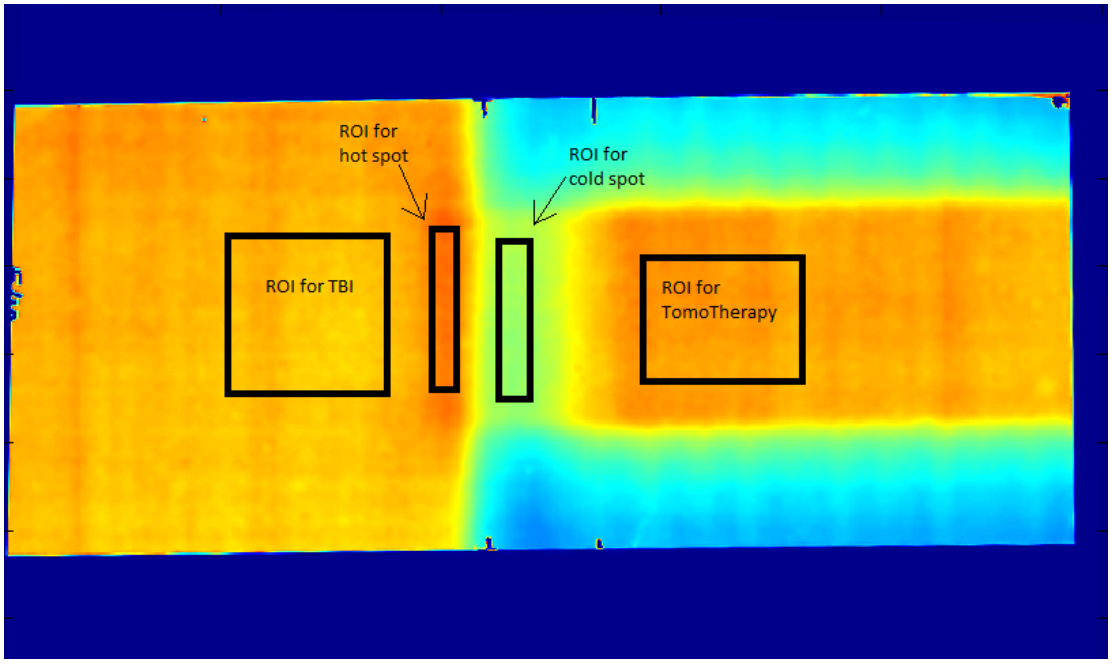

Figure 19. Dose Regions of Interest for Composite Films.

Dose profiles were taken through the center of the films, in order to quantify how the dose distribution of the composite films changes with changing match lines. These profiles are displayed together in Figure 20. This figure shows that as the two treatments are pushed closer together, the hot spot increases, and the cold spot decreases. Because the goal of a TBI or TMI treatment is a homogenous dose distribution, an optimal completion treatment would show as flat a profile as possible. Therefore, intermediate values for the hot spot and cold spot are desirable.

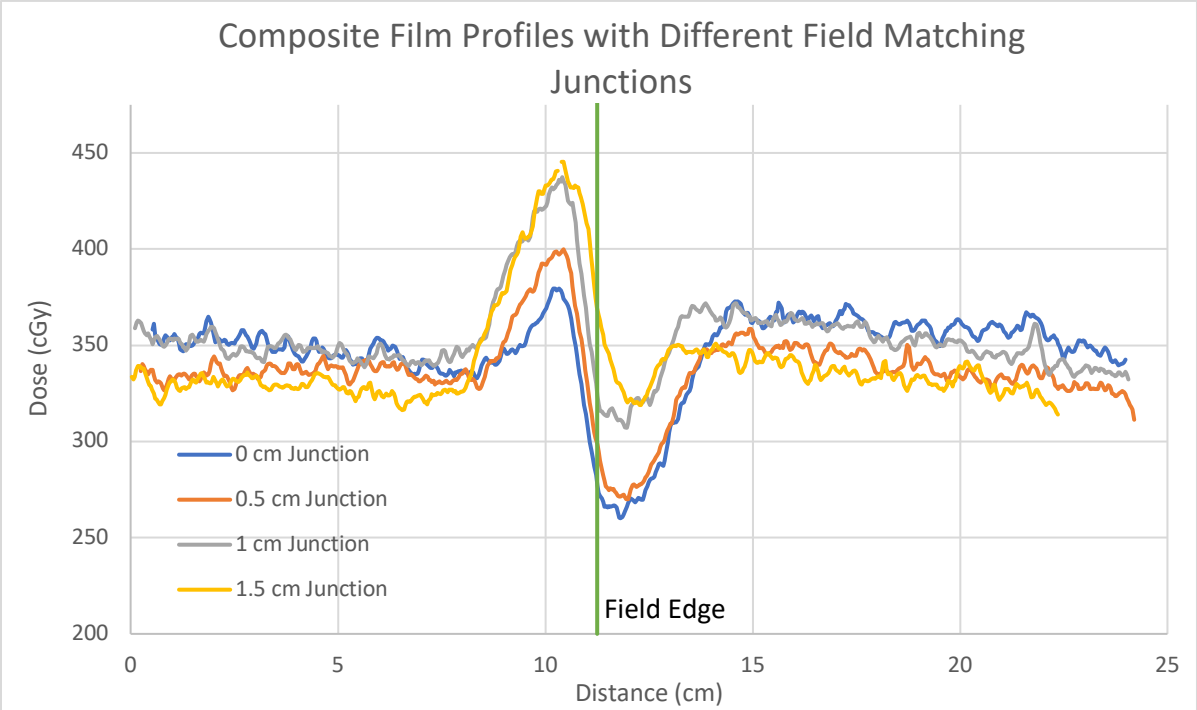

Figure 20. Composite Film Profiles, with 0 cm, 0.5 cm, 1 cm, 1.5 cm, and 2 cm Field Matching Junctions.

4.7.1. Hot Spot Origin

The hot spot displayed in each of the composite films is a result of the gradual dose fall-off from the TMI treatment interruption (Figure 21). Because the interruption is unplanned, the dose does not fall conformally around the edge of the target like it would if the treatment

proceeded according to plan. Instead, the dose falls off gradually and provides significant dose to the film for several centimeters beyond the 100% isodose line (Figure 22). This residual dose remains significant past the interruption point, and thus past the match lines chosen for this study. When the composite films were irradiated with the TBI completion procedure, a hot spot is thus created in the TBI treatment region from this residual dose left over from the TMI treatment.

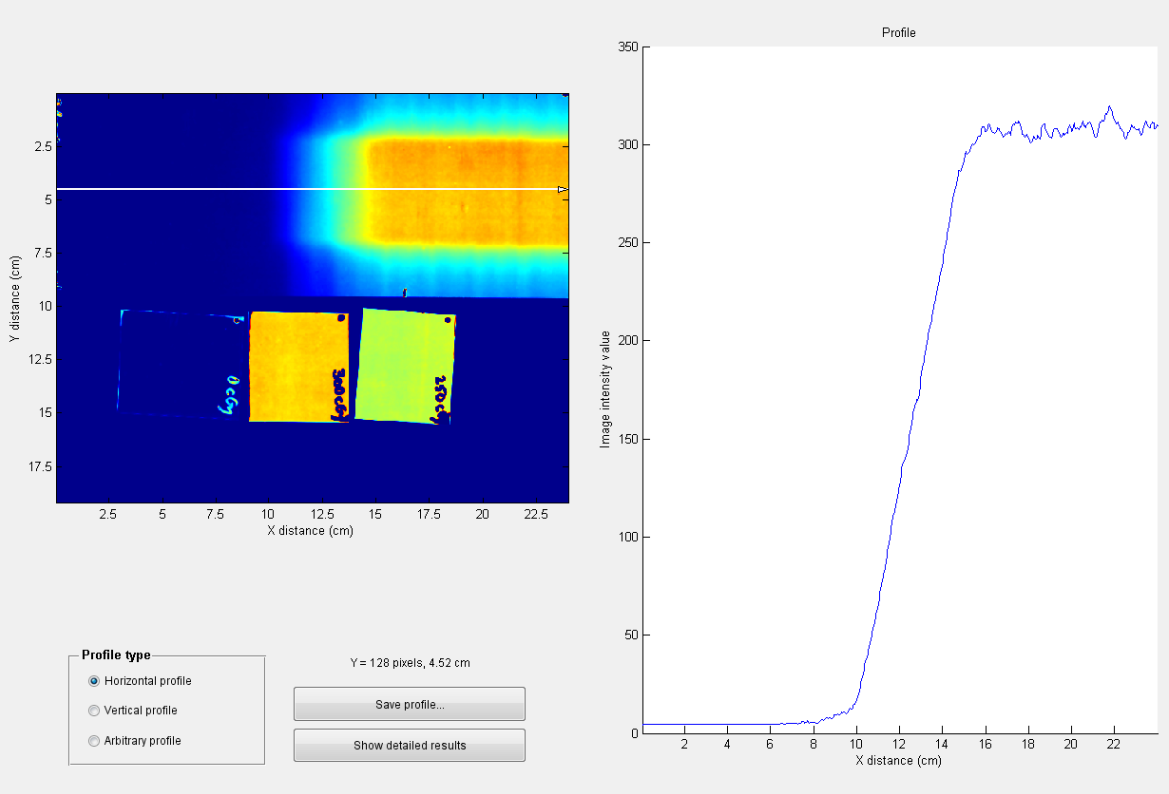

Figure 21. TMI Dose Fall-off Profile.

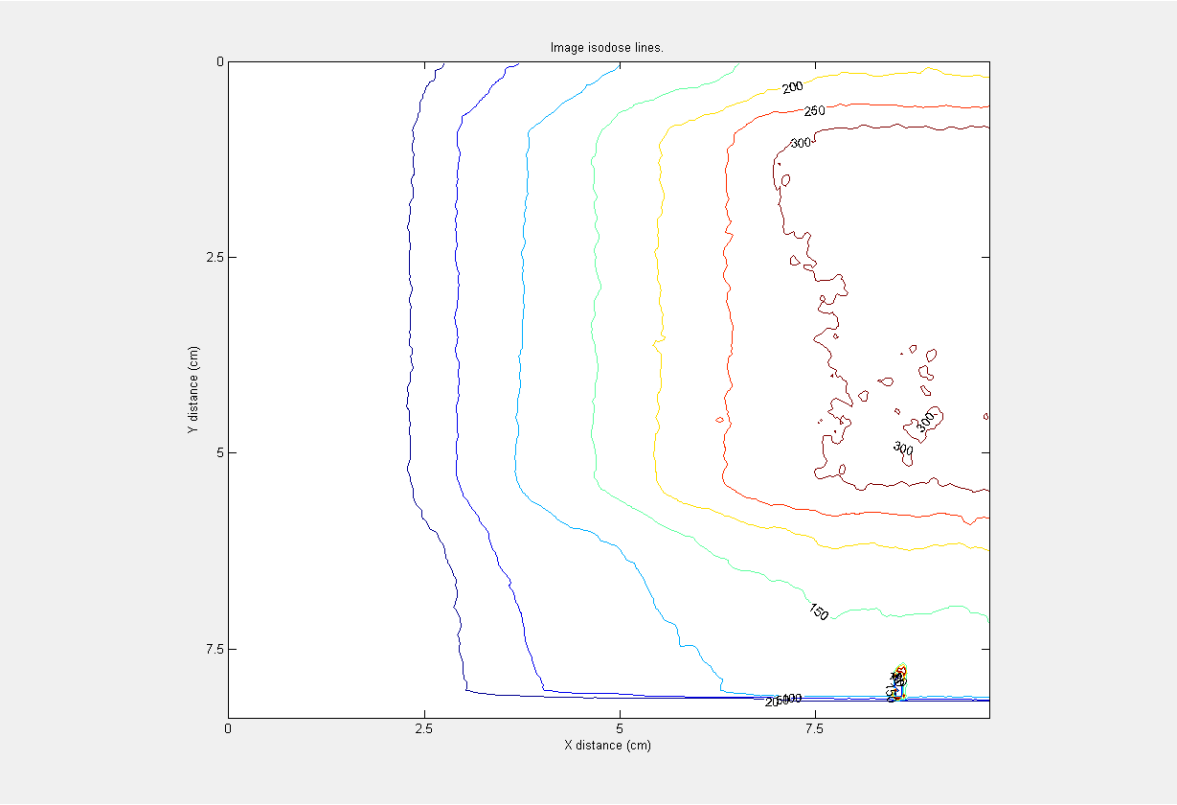

Figure 22. TMI Dose Fall-off Isodose Lines.

Further film measurements with the appropriate number of monitor units delivered are required to determine the accuracy of these conclusions. One such film was acquired at a 0 cm match line, and the dose to each of the regions of interest can be compared with the film receiving 4510 monitor units (Table 10). Profiles taken of these two films can be compared in

Match Line		0 cm	
MU's		4100	4510
TBI	Dose(cGy) ± 1 σ	288.3 ± 4.7	340.6 ± 6.4
Tomo	Dose(cGy) ± 1 σ	330.5 ± 4.7	361.4 ± 5.7
Hot	Dose(cGy) ± 1 σ	303.4 ± 3.8	374.3 ± 8.0
Cold	Dose(cGy) ± 1 σ	212.9 ± 5.9	265.5 ± 6.2

Table 10. Composite Film Dose Comparison Between 4100 MU and 4510 MU.

Figure 23, where it can be seen that the film receiving 4100 monitor units does not have as flat a profile overall. This can possibly be attributed to the greater amount of scatter from the TBI treatment seen in the TMI region than any scatter contribution to the TBI region.

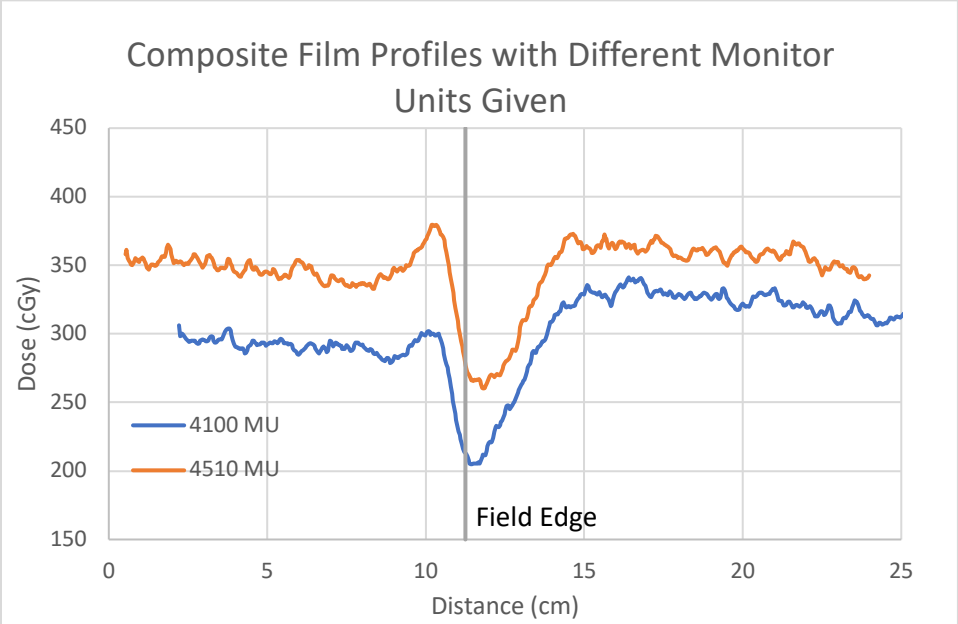

Figure 23. Composite Film Profiles for 4100 MU and 4510 MU.

5. Discussion

The results of this study show that it is feasible to find a match line from a TMI treatment interruption on TomoTherapy. It has been determined that the distance from the interrupt table position to the 50% isodose line is consistently around 4.23 mm. This match line can be used to determine an appropriate setup for the patient's TBI completion treatment. Patient positioning for a TBI treatment cannot be expected to be accurate at a submillimeter level, so any small variation in this distance in an individual treatment plan is not of great concern.

The composite film measurements taken in this study show that a TBI completion procedure is feasible after a TMI treatment interruption on TomoTherapy. The best options found in this study are the match lines of 0 cm or 0.5 cm overlaps, and either of these options

could be used for patient treatment. Although these two options show deviations in dose from the dose prescription of greater than 10%, it is important to keep in mind that this would only be the case for one of the patient's fractions, or 1/8 of the patient's total treatment. For one fraction, a 10% dose inhomogeneity equates to a 1.25% inhomogeneity in the total treatment dose.

Further investigation is needed in order to find a completion procedure that will result in a more homogenous dose distribution across the field matching junction. One option that may result in a more homogenous dose across this junction is field size feathering. With field size feathering, the dose is delivered with two or more different field sizes. Experimenting with different combinations of field sizes to deliver the same completion dose may result in a less pronounced hot spot and a more homogenous dose. To explore this further, TBI plans can be created in Pinnacle and combined with the TomoTherapy Planned Adaptive interruption plan in a software such as Velocity to determine how well this would work. The results from this study would need to be confirmed with further film studies to ensure a smooth dose distribution is delivered across the field matching junction.

Another factor in determining the homogeneity of dose across the field matching junction that may be explored is the field width chosen for TMI treatments on TomoTherapy. Using a smaller field width on TomoTherapy may result in a narrower dose fall-off during treatment interruption, which in turn could result in a less pronounced hot spot after the TBI completion treatment. Further investigation into this idea is required before any conclusion may be made; however, the nature of TMI treatments may limit the choice of field width. Because TMI treatments cover the patient's entire body, the duration of treatment is of concern. Choosing a

larger field width shortens treatment time, and this clinical consideration may constrict the ability to consider shorter field widths for this case.

Working with radiochromic film has proven to result in some variability in dose measurements. One issue that came up during this study was the time left between irradiation and scanning of films. Two hours is the recommended stabilization time,[15] but in a conservative effort, all films were left for 24 hours before scanning. However, over time, the films used for this study seemed to display significantly higher dose measurements when rescanned several days later with the same calibration file. It is unknown if this is due to further development of film, variation in the performance of the scanner used, or some additional factor.

Another issue that came up with respect to the use of radiochromic film dosimetry in this study was variability in the dose measurements from separate films that were irradiated with identical treatments. For example, measurements in the target region of TMI treatments on TomoTherapy resulted in doses ranging from 343 to 363 cGy. It is unknown whether this is caused by variation in the output of TomoTherapy or by variation in film response. One possibility is that small angles in film orientation while scanning were not taken into account. In future film studies, films could be scanned in using a carpenter's square or some similar tool in order to ensure that all films are scanned at the exact same angle.

Another way that the accuracy of absolute film dosimetry can be improved is by using DoseLab's One-Scan Protocol. In this protocol, patient films are scanned in alongside a reference film that has received a known dose. The calibration curve can then be re-scaled according to the scan's response to the reference film. This method reduces variability that may occur from scan to scan, and it reduces error to below 1%.[23]

GAFchromic EBT3 film is specified to have an energy dependence of less than 5% when exposed at energies between 100 keV and 18MeV. The composite films were irradiated at an energy of 6 MV during the TMI treatment on TomoTherapy, and at an energy of 18 MV during the TBI completion procedure on the Elekta linear accelerator. The effect that this may have on the composite film measurements should be explored in future studies to determine the validity of measuring a summation dose from these two different treatments.

6. Conclusion

Finding a match line from a TMI treatment interruption on TomoTherapy using film dosimetry has been determined to be feasible, and the findings from this study match closely with the Planned Adaptive module provided by TomoTherapy.

The composite film measurements combining the TMI treatment interruption on TomoTherapy and the TBI completion procedure show that this type of treatment is clinically achievable at OHSU. Further investigation into field size feathering is required to find an optimal completion treatment, but this initial study proves that the type of completion procedure suggested in this thesis can be performed without compromising reasonable dose homogeneity to the patient.

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8. Appendix

Suggested Protocol for TMI Treatment Interruption on TomoTherapy

Localization Marker Position	A._____
Longitudinal Shift	B._____
Adjusted Localization Marker Position A — B	C._____
Treatment Interruption Position	D._____
Interrupt Position on Patient, Subtract D — C	E._____

Finding the localization marker position

1. Initiate an MVCT.
2. When selecting slices for the MVCT, select the localization marker as the first slice. Then, drag to the right (inferiorly on the patient). The selected slices should start at the localization marker on the left, and extend to the right. Accept these slices.
3. Send the table to the Ready position for the MVCT, and note down the y-coordinate of the Start position (A).
    i. Note: This MVCT does not need to be performed, it is just being used to acquire the Start position. If a different MVCT acquisition is required for the alignment of the patient before treatment, use that setup.

4. Once an MVCT has been performed, check for longitudinal shifts (y-direction), and note them down (B).
    i. If a longitundinal shift has occurred in the +y direction, subtract that amount from (A).
    ii. If a longitudinal shift has occurred in the -y direction, add that amount to (A).

Treatment Interruption

5. Note the y-coordinate of the table position during treatment interruption (D).

Finding the treatment interrupt position on the patient

6. Open up the patient's treatment, so that the lasers are set to align the patient.
7. Align the patient to the localization marker with the lasers.
8. Using the table above, find the distance between the interrupt position and the localization marker position (E).
9. Using a step move on TomoTherapy, move the couch this amount. If E is a positive number, move the couch in the positive direction. If E is a negative number, move the couch in the negative direction.
10. The lasers now point to the interrupt position. This position should be marked and will be used to complete the patient's treatment on the Elekta linear accelerator.