EVALUATION OF VIRTUAL BOLUS FOR TOMOTHERAPY DOSE OPTIMIZATION IN SUPERFICIAL CANCERS

OOI GIM CHEE

UNIVERSITI SAINS MALAYSIA

2020

EVALUATION OF VIRTUAL BOLUS FOR TOMOTHERAPY DOSE OPTIMIZATION IN SUPERFICIAL CANCERS

by

OOI GIM CHEE

Thesis submitted in fulfilment of the requirements
for the Degree of
Master of Science

June 2020

ACKNOWLEDGEMENT

I'd like to express my appreciation to my supervisor, Associate Professor Dr Iskandar Shahrim Bin Mustafa for his guidance throughout my research. He provided me with constant support and invaluable advises along this meaningful journey.

I wish to thank Mount Miriam Cancer Hospital and the Chief Physicist, Mr. Lum Liang Soo for allowing me to use all available resources and equipment to complete this research. A special thanks to the Clinical Oncologist, Dr Ho Kean Fatt for his generous sharing of knowledge in radiation oncology and his interest in the Physics aspects of radiation oncology which inspired me to conduct this research.

I'd also like to extend my thanks to my colleagues and fellow physicists for their encouragements, support and valuable time especially in the brainstorming sessions with me.

I am sincerely grateful for the love and support from my parents and my family members. Their faith in me empowers me to complete this thesis despite busy working schedule.

Last but not least, my deepest gratitude and loving thoughts go to the love of my life, Yim Wan Sin for her everlasting love, support and enlightenment to me. She is the source of my strength and inspiration.

TABLE OF CONTENTS

LIST OF TABLES

Page

LIST OF FIGURES

Page

LIST OF ABBREVIATIONS

2D	2-Dimensional
CCC	Collapsed-cone Convolution
CCCS	Collapsed Cone Convolution/Superposition
CRT	Chemo-radiation therapy
CT	Computed Tomography
CTV	Clinical Target Volume
DICOM	Digital Imaging and Communications in Medicine
DVH	Dose-Volume Histogram
EHNS	European Head and Neck Society
ESMO	European Society for Medical Oncology
ESTRO	European Society for Radiotherapy and Oncology
FCBB	Fluence-Convolution Broad-Beam
GTV	Gross Tumor Volume
H&N	Head and Neck
IMRT	Intensity Modulated Radiotherapy
KVCT	Kilo-voltage Computed Tomography
LBTE	Linear Boltzmann Transport Equation
MLC	Multi-leaf Collimator
MVCT	Mega-voltage Computed Tomography
NPC	Nasopharyngeal Carcinoma
NVBB	Non-Voxel-based Broad Beam
OAR	Organ at Risk
OD	Optical Density
PTV	Planning Target Volume
QA	Quality Assurance

RT	Radiation Therapy / Radiotherapy
SCC	Squamous Cell Carcinoma
SI Units	International System of Units
TERMA	Total Energy Released per unit Mass
TBI	Total Body Irradiation
TPS	Treatment Planning System
VB	Virtual Bolus

LIST OF APPENDICES

PENILAIAN BOLUS MAYA UNTUK PENGOPTIMUMAN DOS TOMOTERAPI DALAM KANSER SUPERFISIAL

ABSTRAK

Kajian ini menilai kesan dosimetri sinaran menggunakan bolus-maya (VB) dalam Sistem Perancangan Rawatan TomoTerapi (TPS) untuk Perancangan-Sasaran-Isipadu (PTV) yang meluas ke permukaan kulit atau permukaan-badan. PTV dikonturkan pada fantom yang diperluaskan ke permukaan fantom. Bolus maya dengan kombinasi pelbagai ketebalan (0.2 cm / 0.4 cm / 0.6 cm) dan ketumpatan (0.5 g/cm^3 atau 1.0 g/cm^3) dilukis untuk menyediakan rantau tembunan "maya" untuk TPS dan kemudian dioptimumkan dengan TomoTerapi TPS. Film Gafchromic EBT3 ditentukur dan digunakan untuk menganalisis profil dos merentangi PTV dan permukaan fantom, dan untuk melakukan analisis gama untuk kelancaran foton dengan kriteria 3 mm Jarak-ke-Persetujuan (DTA) dan 3 % Perbezaan Dos. Perisian TomoTerapi Dirancang-Mudah Suai digunakan untuk menganalisis hantaran Dos-Isipadu-Histogram (DVH) yang dibina semula daripada perolehan mega-voltan tomografi berkomputer (MVCT). Tanpa penggunaan VB, set kawalan pengoptimuman menunjukkan dos maksimum hampir kepada 110 % di pinggir fantom atau permukaan kerana kekurangan rantau tembunan. VB 0.2 cm menunjukkan tidak dapat menyediakan kawasan tembunan yang mencukupi. Penggunaan VBs 0.4 cm dan 0.6 cm untuk pengoptimuman dos dapat mengawal dos maksimum di TPS dan juga di dalam penghantaran sinaran sebenar. Walau bagaimanapun, VB 0.6 cm mempamerkan pengurangan ketara dalam liputan dos (95%) di dalam penghantaran radiasi sebenar. VB 0.4 cm didapati memberikan liputan dos yang memuaskan untuk pengoptimuman TPS dan juga penghantaran sebenar. VB dengan kombinasi ketebalan 0.4 cm dan

ketumpatan 1.0 g/cm^3 memberikan model yang paling teguh untuk pengoptimuman TomoTerapi TPS bagi mengatasi kekurangan rantau tembunan. Ia dapat menghindarkan lebihan dos terhadap kulit dengan 3 mm anjakan sisian ke dalam kawasan kelancaran foton yang tinggi. Ia mempamerkan perbezaan paling sedikit di dalam dos maksimum dari perancangan TPS dan penghantaran sinaran sebenar; di mana dos maksimum dikekalkan di bawah 105% dan liputan dos diterima secara klinikal di atas 95% dos yang ditetapkan.

EVALUATION OF VIRTUAL BOLUS FOR TOMOTHERAPY DOSE OPTIMIZATION IN SUPERFICIAL CANCERS

ABSTRACT

This study evaluates the radiation dosimetry effects of using virtual-bolus (VB) in TomoTherapy Treatment Planning System (TPS) for Planning-Target-Volume (PTV) that extends to skin or body-surface. PTV was contoured on phantom that extended to the phantom surface. Virtual bolus of various thickness (0.2 cm / 0.4 cm / 0.6 cm) and densities (0.5 g/cm^3 or 1.0 g/cm^3) combinations were drawn to provide "virtual" build-up region for the TPS and then optimized with TomoTherapy TPS. EBT3 Gafchromic Film was calibrated and used to analyze the dose profiles across PTV and the phantom surface, and gamma analysis was peformed for the photon fluence with Distance-to-Agreement (DTA) 3 mm and Dose Difference 3% criteria. TomoTherapy Planned-Adaptive software was used to analyze the delivered Dose-Volume-Histograms (DVHs) reconstructed from the mega-voltage computed tomography (MVCT) acquisition. Without VB used, the control set optimization showed maximum dose close to 110% at the phantom edge or the surface due to lack of build-up region. VB of 0.2 cm was shown to be unable to provide adequate build-up area. The use of VBs of 0.4 cm and 0.6 cm for dose optimization were able to control the maximum dose in the TPS and also in the actual radiation delivery. However, VB of 0.6 cm exhibited large reduction in dose coverage (95%) in the actual radiation delivery. VB of 0.4 cm was observed to provide satisfactory dose coverage for TPS optimization and also actual delivery. VB of thickness 0.4 cm and density 1.0 g/cm^3 combination provided the most robust model for TomoTherapy TPS optimization to account for the lack of build-up region, it is able to prevent over-dosing

the skin with up to 3 mm lateral shift into the high photon fluence area. It exhibited the least difference in maximum dose from TPS planning and actual radiation delivery; where the maximum dose is kept below 105% and the dose coverage is clinically acceptable at above 95% of prescribed dose.

CHAPTER 1

INTRODUCTION

1.1 Background

The use of Intensity-Modulated Radiation Therapy (IMRT) is more prevalent with current healthcare standards, in line with the availability of higher end radiotherapy equipment in Malaysia. As of June 2019, there are total of 33 radiation therapy facilities throughout Malaysia, with most centers providing IMRT services (Hizam *et al*. 2019).

IMRT is almost always recommended as the preferred treatment modality for head and neck (H&N) cancers when radiation therapy (RT) is indicated. IMRT is able to significantly reduce the incidence and severity of xerostomia compared to Three-Dimensional Conformal Radiation Therapy (3D-CRT) for curative-intent irradiation of H&N Squamous Cell Carcinoma (SCC) (Gupta *et al*. 2012). The University of California-San Francisco (UCSF) reported excellent local-regional control for Nasopharyngeal Carcinoma (NPC) was achieved with IMRT with 98% loco-regional progression free rate in 4 years estimate. It is also reported that IMRT provided excellent tumor target coverage with high dose and able to significantly spare the salivary glands and other nearby critical normal tissues (Lee *et al*. 2002).

Besides notable advantages in H&N cancers, IMRT also allow hypo-fractionated RT to be given safely. This is especially important in the use of IMRT for hypo-fractionated RT of 20 fractions for prostate cancers. Hypo-fractionated RT gives similar prostate tumor control outcomes and toxicity compared to conventional RT of 35 fractions, which means patients could save 15 times of visits to the clinic for RT (Morgan *et al*. 2018).

This research was done at Mount Miriam Cancer Hospital (MMCH), the primary modality for IMRT treatments is TomoTherapy (Accuray Inc, Sunnyvale, CA). This system delivers 6 Mega-voltage (MV) photon beams slice-by-slice to the patient, modulated by the binary Multi-Leaf Collimators (MLC) at fixed jaw size and pre-determined constant couch speed (Mackie 2006). The majority of cases treated with IMRT in MMCH was H&N cancers.

1.2 Problem Statement

For clinical target volume (CTV) that are close to the body surface, the skin will be part of the optimization volume when expanded to planning target volume (PTV). PTV expansion is to account for uncertainties during simulation and treatment deliveries, typically 5 mm to 10 mm depending on treatment site (Burnet *et al*. 2004). Superficial PTV is defined as the PTV that is less than 5 mm from the body surface, and this poses a challenge for dose optimization due to insufficient build-up region for photon beam.

TomoTherapy's inverse planning treatment planning system (TPS) through its iterative process, will continuously increase the photon fluence at the superficial PTV region of low electronic build-up, in order to achieve the prescribed dose to the PTV at the skin area. If the patient's position is displaced to the high fluence area, there may be risk of over treating the skin.

In a report by ICRU, the use of artificial build-up material at the skin during optimization but not on the actual treatment was suggested, known as the virtual bolus (VB) method (ICRU Report 62, 1999). This method however creates an uncertainty in the actual dose delivered.

There are not many studies related to the use of VB for IMRT treatment planning optimization for superficial targets. There was a study to compare plans that modified the target to avoid 2 to 3 mm from the body surface and/or use of VB of 2 mm and 5 mm. The study showed target modification caused reduction in actual dose coverage, hence use of VB is more superior solution (Ashburner *et al*. 2014). The use of VB with various thickness and density combination in TomoTherapy optimization for Total Body Irradiation showed larger margin of setup error was achieved with clinically acceptable dose coverage and global hot spots (Moliner *et al*. 2015). The safety and benefit of using VB in breast IMRT planning was studied, and it was shown that plans optimized with VB resulted in improved dose coverage and lower doses to the organ at risk (Tyran *et al*. 2018). There is lack of data reporting on the direct dosimetric effect in terms of dose profiles and dose coverage in actual delivery of plans optimized with VB.

1.3 Scope of Study

Based on current studies, there is lack of measurement data on the changes in delivered dose profile when VB is used and the degree of changes it will introduce with the exact setup. In this research, the main focus was to evaluate the dosimetric effects of utilization of virtual bolus for superficial PTV optimization using TomoTherapy TPS.

TomoTherapy Cheese Phantom was CT-simulated with departmental Head and Neck protocol of 120 kV and 250 mAs with reconstruction of 2.5 mm slice Increment. 2 CTVs were drawn up to phantom surface and expanded 3 mm radially to become the PTVs. The PTVs in air was removed so that the PTVs volumes are all within the phantom volume only. Virtual bolus were drawn over the 2 PTVs at the

surface with uniform thicknesses of 0.2 cm, 0.4 cm and 0.6 cm respectively and were assigned with different densities for the same thickness in TomoTherapy TPS.

Dose optimization to the PTVs was carried out in TomoTherapy TPS to achieve at least 95% of prescribed dose to 95% volume of PTV (ICRU Report 83, 2012). Control set represents optimization without virtual bolus, and experimental data sets include virtual bolus of 2 densities for the 3 respective sets of thickness. The plan quality and dose coverage were evaluated visually throughout the planning CT images and numerically evaluated using DVHs.

Once an acceptable TomoTherapy plan was obtained, dose delivery quality assurance (DQA) was carried out for the exact plan on the exact phantom. EBT3 film was calibrated up to 2.5 Gy and a sensitometric curve was plotted. The delivered dose distributions were evaluated by using EBT3 Gafchromic Film and TomoTherapy Planned Adaptive software which computes the dose delivered using the acquired MVCT.

1.4 Research Objectives

The main objectives of the current research are summarized as follow:

i) To determine the combinations of thickness and density for virtual bolus to be used in TomoTherapy optimization of superficial PTV.

ii) To characterize virtual bolus used in TomoTherapy optimization of superficial PTV, in terms of thickness and density.

iii) To perform an assessment of the actual dose profiles across the PTV and air when virtual bolus is used for optimization.

iv) To propose the optimal virtual bolus thickness and density for TomoTherapy optimization of superficial targets.

1.5 Significance of Study

The importance of this research is to establish the optimal combination of thickness and density of virtual bolus for TomoTherapy optimization of superficial PTV. Whilst there are numerous papers reporting on the use of virtual bolus or other method to overcome the challenge of optimization of superficial targets, currently there is lack of report on the characterization of virtual bolus in terms of thickness and density when used with TomoTherapy.

It is crucial to prevent the TPS from excessively increasing the photon fluence at skin surface, and to obtain the best possible accuracy in actual plan delivery when using virtual bolus during planning optimization. By studying the dose profiles of delivered TomoTherapy plans in phantom, the effect of virtual bolus can be more clearly understood. It is important to understand and minimize the dose difference between optimized planning and actual delivered dose. The Radiation Oncologists have to understand and decide whether it is clinically acceptable for the dose difference reported. It will aid the readers to better discuss and to reach a consensus where virtual bolus utilization is concerned.

Characterization of virtual bolus will also aid the readers to optimally choose the best virtual bolus properties with confidence in order to achieve a desired optimization plan and accurate treatment plan delivery.

1.6 Limitations of the Research

The primary aims of this research are to study the direct dosimetric effects when VB is used during TomoTherapy optimization, hence the optimization was done on a more controlled environment where a homogenous phantom was used, and there was no avoidance or organ at risk structure used in the optimization. This research does not take into account for the dosimetry changes should there be presence of inhomogeneous mediums in the beams' paths when VB is used in such situation.

The CT simulation scan for the phantom was reconstructed with slice thickness of 2.5 mm and in section 4.4.5, it was shown there were relatively larger discrepancies in measured and planned dose for 0.2 cm VB, which may be due to pixel and resolution of the CT images.

This research was solely performed on phantom, and there are no real patients being studied for the use of VB. This research is unable to prove the clinical benefits from the use of VB. The expected clinical benefits of using VB are preventing excessive photon fluence assigned to superficial PTV with minimal build-up region and allowing up to 3 mm of motion and yet still maintain good dose coverage and minimal overdosing (hotspots).

1.7 Thesis Organization

This dissertation evaluates the radiation dosimetry of TomoTherapy delivery when virtual bolus is used during optimization; and to aid Medical Physicists or Dosimetrists who employ virtual bolus technique in IMRT optimization to understand the effect on actual delivery based on the characteristics of the virtual bolus in terms of thickness and density.

Chapter 2 interprets the literature reviews for radiotherapy dose computations and dose calculation algorithm, TomoTherapy dose optimization algorithm, virtual bolus concepts and film dosimetry system.

Chapter 3 describes the experimental setup which includes phantom CT-simulation, target contouring, TPS optimization and film dosimetry protocol developed for this experiment.

Chapter 4 presents the findings of this experiment, based on the film-measured horizontal dose profiles and reconstructed DVHs from MVCTs. Discussions on the results and the limitations of the research are presented in this chapter.

Chapter 5 finalizes this project's findings with a conclusion and further work that could be done is suggested.

CHAPTER 2

LITERATURE REVIEW

2.1 Definition of Photon Beam

Photon is an uncharged particle and considered as an indirectly ionizing radiation because photon liberate directly ionizing particles from matter only after the photon interacts with a matter through the processes of photoelectric effect, Compton Effect and/or pair production (Khan, 2014). Ionizing radiation deposits energy in the medium they interact with, and this deposition of energy is known as radiation dose. Radiation dose is defined as the energy absorbed per unit mass of the medium, J/kg and its SI unit is Gray (Gy) (BIPM, 1975).

2.2 TomoTherapy

TomoTherapy or Helical TomoTherapy is a unique type of IMRT where radiation (6 MV photon) is delivered in slice-by-slice manner, where the patient is simultaneously moved into the gantry bore at predetermined constant speed while the gantry is rotating and delivering radiation dose modulated by binary MLC leaves at a fixed jaw size (Mackie, 2006). TomoTherapy offers higher dosimetry advantages over conventional IMRT. TomoTherapy plans were shown to be able to achieve sharper dose gradients, more conformal coverage and better homogeneity index (HI) for the PTVs compared with IMRT or 3DCRT plans (Chen *et al*. 2007). Helical TomoTherapy plans are able to deliver sharper dose gradients compared with step-and shoot IMRT plans and are expected to be able to significantly reduce the OARs normal tissue complication probability (NTCP) while keeping similar target dose homogeneity (Vulpen *et al*. 2005).

2.3 Treatment Planning System

The treatment planning system (TPS) is the core of the whole modern radiotherapy process, as it provides graphic representation of radiation dose distribution using isodose lines for the PTV(s) defined for a specific patient that would be treated in a particular treatment modality. TPS computes the expected dose distribution in the patient's tissue by accounting for beam attenuation and scatter in types of tissue the beam encounters on its path. The TPS also allows us to configure the beam placements as in the case of 3D conformal radiation therapy or inversely optimize the beam modulation as in the case of IMRT, in order to adequately cover the tumor volume and also to reduce doses to critical structures, hence allowing us to maximize the tumor control and minimize the normal tissue complications for the patients (Podgorsak, 2003).

2.4 Bragg-Gray Cavity Theory

When a dosimeter is placed in a phantom or medium for dose measurement, part of the medium is removed and being replaced by the dosimeter. Bragg-Gray cavity provides a relation between the dose measured by the dosimeter and the actual dose absorbed in the medium. According to the Bragg-Gray theory, the ionization that occurs in a gas-filled cavity situated in a medium is solely related to the energy absorbed in the surrounding medium where the ionizing radiation interactions in the cavity are assumed to be negligible. When the gas-filled cavity is sufficiently small so that its introduction into the medium does not perturbate the fluence of the ionizing radiation in the medium, then the following Bragg-Gray relationship is satisfied:

$$D_{med} = J_g \cdot \frac{\bar{W}}{e} \cdot \left(\frac{\bar{S}}{\rho}\right)_g^{med} \tag{2.1}$$

where D_{med} is the absorbed dose in the medium, J_g is the ionization charge produced per unit mass of the cavity gas, and $\left(\frac{\bar{S}}{\rho}\right)_g^{med}$ is weighted mean ratio of the mass stopping power of the medium to that of the gas for the electrons crossing the cavity. The product of $J_g \cdot \frac{\bar{W}}{e}$ is the energy absorbed per unit mass of the cavity gas (Khan, 2014).

2.5 TPS Dose Calculation Model and Algorithm

Radiation dose calculation is one of the most crucial aspects in radiotherapy treatment planning and dosimetry for verification of delivered dose. The current clinical radiotherapy dose calculations are usually based on two major algorithms which are the model-based algorithm where the commonly used algorithms are Pencil Beam Convolution and Collapsed Cone Convolution (CCC); and Linear Boltzmann Transport Equation (LBTE) solvers, for example the Monte Carlo simulations. The calculation algorithms based on the above models can be commissioned in a clinical setting to give accurate estimation to actual dose in water phantoms, however the accuracies among the models will differ in heterogenic mediums (Krieger *et al*. 2005).

TomoTherapy TPS uses collapsed cone convolution/superposition (CCCS) algorithm for its final dose calculation. The CCCS algorithm combines the primary photon energy fluence and the use of pre-computed calculation kernels to convolve the primary photon transport and secondary electrons and photons transport to model the energy deposition in tissue that accounts for tissue heterogeneities, lateral energy transport, beam hardening and off-axis spectrum softening effect and tilt of kernels. It can be represented by the equation below:

$$D(r) = \int \frac{\mu}{\rho}(r') \times \Psi(r') \times K(r - r') d^3 r' \quad (2.2)$$

in which $\frac{\mu}{\rho}(r')$ is the mass attenuation coefficient, representing the fraction of energy attenuated from the primary photon energy fluence per unit mass as a function of electron density; product of $\frac{\mu}{\rho}(r')$ and $\Psi(r')$ is the total energy released per unit mass (TERMA), representing total amount of energy available at r' for deposition; $K(r - r')$ is the convolution kernel that gives the fraction of the TERMA from a primary interaction point that is deposited to surrounding points as a function of photon energy and direction.

$$D(r) = \int \frac{\mu}{\rho}(p_{r'} \cdot r') \times \Psi(p_{r'} \cdot r') \times K[(p_{r-r'}) \cdot (r - r') d^3 r' \quad (2.3)$$

The above equation 2.3 then represents the CCCS algorithm, where the convolution equation is modified for actual radiological path length to account for heterogeneities (Ahnesjö, 1989).

2.6 TomoTherapy Dose Optimization and Calculation Algorithm

TomoTherapy dose optimization algorithm utilizes Non-Voxel-based Broad Beam (NVBB) framework of low linear and spatial complexity, coupled with adaptive full dose correction approach at fixed intervals of iterations. This adaptive full dose correction approach alternates between two dose engines where one performs accurate full dose calculation with CCCS dose calculation algorithm which is invoked after a number of iterations and another dose engine that performs quick but with compromised accuracy known as fluence-convolution broad-beam (FCBB) algorithm that is invoked in every single iteration (Lu, 2010).

The FCBB algorithm is a fast dose calculation algorithm that estimates approximated dose calculation by applying convolution only on the fluence map without pixelating the radiation beam into beamlets. Its dose calculation accuracy when compared to CCCS is shown to be within 3% for homogeneous medium and within 5% for presence of heterogeneous materials (Lu, 2010).

For the full dose calculation of the optimized plan, CCCS algorithm which comprises of 2 independent parts, TERMA and Convolution/Superposition (C/S) energy deposition are used (Lu, 2010). As mentioned in equation 2.2, TERMA calculation will include the models of fluence phase space, primary photon ray tracing and interaction with medium while C/S energy deposition uses pre-calculated Monte Carlo kernels to model the distribution of the released energy in the medium (Mackie *et al*. 1988).

The NVBB framework is a novel approach that discards the voxel and beamlet models for typical IMRT optimization, enabling it to consume significantly less memory storage and allowing its implementation in a graphic processing unit (GPU) instead of a computer cluster (Lu, 2010).

2.7 Radiotherapy Target Volume Concepts

Tumors and target volumes for radiotherapy have to be carefully defined in order to optimize the treatment. The three (3) fundamental principles of radiotherapy are increasing the radiation dose to the tumor will generally improve the tumor local control probability; improvement of local control of tumor will improve the curability and survivability of the patient; and thirdly reducing the radiation dose to normal tissues will improve the side effect associated with radiotherapy (Suit, 2002).

ICRU Report 50 (1999) describes the concepts of GTV, CTV and PTV. GTV as its name suggests is the gross volume of the primary tumor position and its extent which can be seen on the diagnostic scans, visually observed in the patient or palpable by the clinician. CTV describes the volume around the GTV and additionally covers microscopic and sub-clinical spread of the tumor. The PTV is the volume expansion of CTV to account for statistical uncertainties in the patient setup, organ motion and radiation delivery machine parameters. ICRU Report 50 also specified that minimum dose coverage to the ICRU Reference Point should be higher than 95% and the maximum dose in the PTV should be lower than 107%.

ICRU Report 83 (2010) is published in 2010 to standardize the dose reporting for IMRT while the concept of target volumes remains unchanged. The minimum and maximum dose reporting are replaced with near minimum dose, $D_{98\%}$ and near maximum dose, $D_{2\%}$ instead. This report also recommends reporting the median absorbed dose, $D_{50\%}$ to replace the previously reported dose at ICRU Reference Point due to the complexity of the dose distributions achievable by IMRT technique. The report extensively describes the concepts of IMRT and the coverage of PTV and sub-division of PTVs should there be OAR in vicinity, low build-up regions and/or other special considerations. This is to prevent any alterations to the original PTV and to separate optimization volume from the clinical PTV volume in order to establish a standardize reporting across the regions.

2.8 IMRT Treatment Planning Consideration for Superficial Target

Investigation on acute skin toxicity associated with IMRT for H&N cancers was carried out by Lee *et al*. (2015). They studied the plans where neck nodes are covered up until the skin, neck nodes contoured 5 mm from the skin, and skin being optimized as OAR using anthropomorphic phantom, Rando Phantom (Alderson Research Laboratories, Stanford, CT). The study concluded skin dose may be reduced to a tolerable level by optimizing it as an OAR whilst maintaining good target coverage. This study has shown the need to control the absorbed dose to the skin and to maintain acceptable dose coverage to the targets. In an almost similar study by Thomas *et al*. (2004), they studied on the differences between the use of virtual bolus in addition to PTV modification and the use of skin as an OAR during IMRT dose optimization. When the skin is optimized as an OAR, the TPS will optimize the OAR structure (skin) to a dose limit and at the same time to ensure adequate dose coverage to the target. There will be still be over-fluence effect at the superficial target regions due to lack of build-up area. The study concluded that the use of virtual bolus gives better results.

Ashburner *et al*. (2014) studied on TomoTherapy optimization for superficial target and analyzed three methods to reduce the over-fluence effect by using virtual bolus, PTV clipping to avoid skin and combination of both. From the study, it is observed that the use of either PTV clipping or VB technique, there is large reduction in the fluence boosting effect compared to when there is no intervention. The combined use of clipping and VB have no advantage over solely using clipping or VB by itself. The study concluded that the use of 5 mm virtual bolus gives a more superior solution to account for lack of build-up, however clip distance of 3 mm also provides acceptable results.

Moliner *et al*. (2015) researched on using virtual bolus for Total Body Irradiation (TBI) treating with Helical TomoTherapy. They researched on the optimal density and thickness of virtual bolus to treat TBI using Helical TomoTherapy, and the selection criteria are based on dose coverage and maximum dose in case of setup error, underestimation of delivered dose to the PTV and over-fluence peak. The study concluded that double-layer virtual bolus of 5 mm + 3 mm with density of 0.4 g/cm^3 is best used for TBI planning using Helical TomoTherapy, this combination of double-layer bolus allows setup error up to 2.9 cm and avoids the over-fluence peak effect with the general dose increase of only 1.5% due to dose underestimation by the TPS.

2.9 IMRT Plan Quality and Quantitative Assessment

IMRT is considered one of the most complex techniques in radiation oncology, IMRT aims to deliver highly conformal and homogenous radiation dose to the tumor and to protect the healthy tissues nearby. While reviewing the dose coverage (isodose lines) throughout the CT slices (qualitative assessment) and the DVHs (quantitative assessment) remain as the integral part of plan approval process; Homogeneity Index (HI) can be used to facilitate the plan reviewing process to quantitatively assess the homogeneity of the dose distribution. The concept of IMRT is to deliver highly homogenous radiation dose to the PTV while sparing the OARs, hence HI can be used as an extra tool to gauge the quality of an optimized IMRT plan. Homogeneity index (HI) is defined as the ratio of maximum dose to the prescribed dose and value close to 1 represents good homogeneity (Kataria *et al*. 2012). HI can be calculated using the equation as below:

$$HI = \frac{Dmaximum}{Dprescribed} \tag{2.4}$$

Beside HI, quantitative assessment of an IMRT plan also involves the review of the DVH for the coverage volume, $V_{95\%}$ to be more than 98%, where $V_{95\%}$ is the volume of PTV receiving more than 95% of the prescribed dose; review of the global maximum dose, D_{max} to be less than 105% of the prescribed dose; and the median dose to the PTV is as close to prescribed dose. Apart from target coverage, the OARs doses must also be reviewed based on published data on the dose tolerance for the respective OARs (ICRU 83, 2010).

2.10 IMRT QA (Gamma Analysis)

After treatment planning is done, the optimized and accepted radiation treatment plan needs to be verified before the treatment is given. There are numerous QA to ensure the radiation treatment plan is delivered as planned, such as routine machine output check, mechanical alignment test, and beam profiles measurement and so on. Particularly, we can also perform QA on the radiation treatment plan specific to the patient. This patient specific delivery QA will evaluate the point dose at the center of the highest dose PTV and 2-D gamma analysis of the radiation fluence delivered across a specific plane (Depuydt *et al*. 2002).

The gamma analysis was at first developed to commission TPS by comparing the measured and TPS calculated dose distributions. It was then being applied to patient specific delivery QA as well (Low *et al*. 1998). This analysis is a pass-fail criterion where it evaluates the dose distributions based on user's input parameters for maximum dose difference (D_{max}) and distance-to-agreement (DTA) criteria, usually 3% and 3 mm for IMRT and 2% and 2 mm for Stereotactic Radiosurgery (SRS). The resulting gamma index of more than 1 is considered a failed calculation and vice versa for gamma index below 1. The maximum allowable percentage of gamma index more

than 1 is usually set at 10%, meaning 90% of the pixels have to be passing the gamma analysis (Song *et al*. 2015). The gamma analysis is illustrated in a simplified schematic diagram as shown in Figure 2.1. The gamma evaluation formula can be summarized by the equation as follow:

$$\gamma = \sqrt{\frac{|\Delta r|}{(DTA)^2} + \frac{|\Delta D(r)|}{(Dmax)^2}} \tag{2.5}$$

where DTA is user specified distance, D_{max} is user specified maximum dose difference allowed and Δr is the difference in distance between reference point and point of interest, ΔD(r) is the dose difference between the reference point and point of interest.

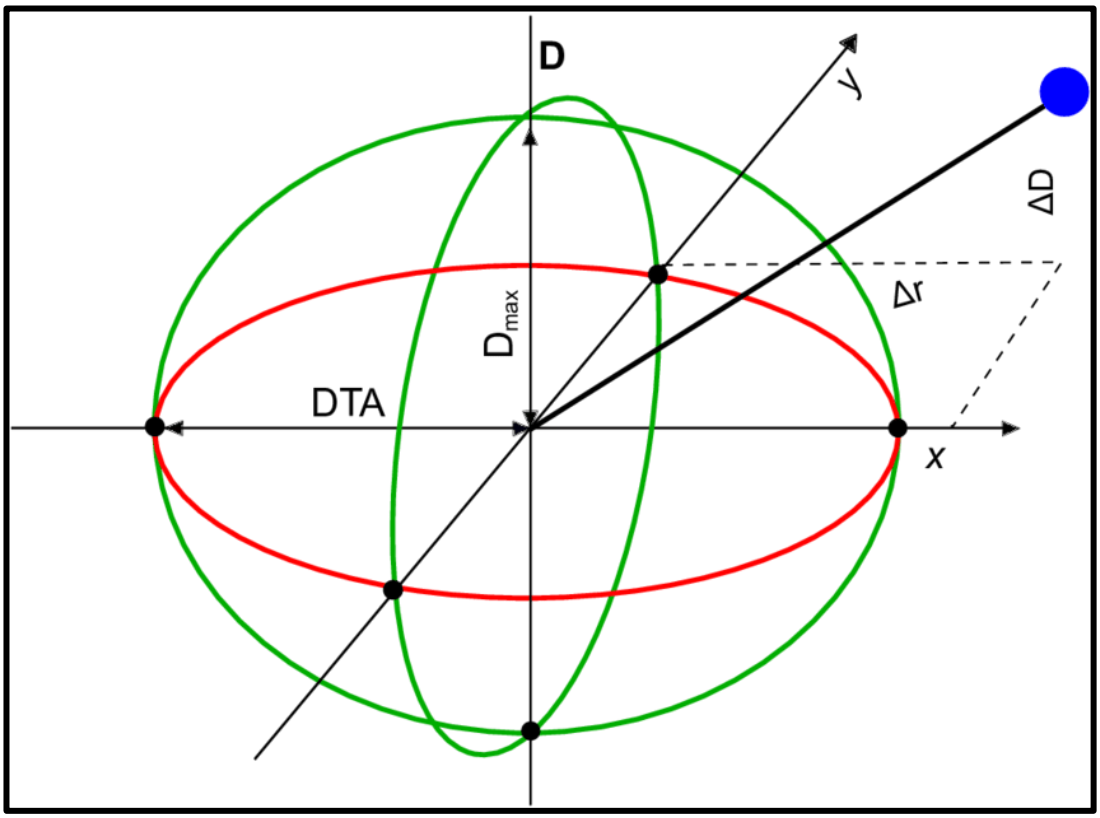

Figure 2.1: A simplified schematic diagram for the combined DD and DTA gamma evaluation. The green and red lines define the ellipsoid area of gamma index below 1. The blue point fails both the DD and DTA criteria. (Tomáö Pavel, 2017)

2.11 Radiochromic Film Dosimetry

Film dosimetry is widely used to measure 2-Dimensional (2D) radiation dose distribution, it can be used for quality assurance of the treatment modality and also for the pre-treatment validation for a treatment plan. There are 2 commercially developed films for film dosimetry, namely silver-halide based and radiochromic. The silver-halide based film responds to radiation by developing a latent image in which it needs to be developed manually or by film processor. Radiochromic film responds to radiation by automatically turning into darker shades at the irradiated areas, and the intensity of darkening increases with increasing absorbed dose (Buston *et al*. 2003). Radiochromic film has several advantages over silver-halide based film, radiochromic film doesn't need post-irradiation processing to develop a visible image, can be handled in visible light condition and has an energy independent dose response from keV to MeV energy range (Stevens *et al*. 1996).

Radiochromic film has to be calibrated to obtain the sensitometric curve that will be used to convert the measured optical densities into absorbed dose. Cheung *et al*. (2006) demonstrated that the calibration curves for EBT Gafchromic film (a type of radiochromic film) are independent of radiation field size of 6 MV X-ray radiation beam, potentially minimizing the uncertainties in doses measurement of small or irregular radiation fields. This makes radiochromic film ideal for 2D dose maps quality assurance.

Radiochromic film EBT3 manufactured by Gafchromic is observed to have stable net Optical Density (OD) after 30 mins for doses below 2 Gy; between 2 hours and 24 hours after exposure the difference in net OD is less than 2.5% at all doses (Borca *et al*. 2013). From the study, the irradiated EBT3 film can be scanned for

analysis after 2 hours, where the post-irradiation development is observed to be stabilized.

2.12 Using MVCT for Dose Re-computations

Theoretically, with an accurate and reliable CT number to electron density calibration curve, MVCT images acquired on TomoTherapy can be used for dose computations. Langen *et al*. (2005) tested the stability of the MVCT numbers by determining the variation of the calibration curve with variable spatial arrangement of the phantom, different time periods of measurement and different parameters for the MVCT acquisition. The author tested two calibration curves with the largest difference to six clinical MVCT images for dose recalculations. The maximum difference from the test was at 3.1%, however the dosimetric endpoints varied by less than 2% in general. Rigid and deformed phantoms are used to perform a series of end-to-end tests and the dosimetric differences observed in all phantom tests were within the range of dosimetric uncertainties observed due to variations in the calibration curves. The authors concluded that the use of MVCT images acquired on TomoTherapy allows the assessment of daily dose distributions that is as accurate as the initial dose calculation performed on the CT-simulation data (KVCT).

2.13 Radiotherapy Fractionation

Fractionation of radiation therapy is the process of dividing a prescribed dose of radiation to multiple times. Fractionation is crucial in order to maximize the destruction of the cancers while minimizing the damage to healthy tissues. Cell survival after being exposed to radiation can be expressed with a logarithmic curve of

survival versus dose. Smaller doses given repeatedly are shown to be less damaging compared to single dose of the same amount (Dale, 1985). Also by taking advantage of the difference in alpha-beta ratio of cancer cells and normal cells, fractionation allows higher total dose to be delivered to the cancer cells while only causing tolerable damage to the normal cells, thereby improving the therapeutic ratio. Therapeutic ratio is defined as the ratio of tumor control probability and normal tissue injury probability (Joiner *et al*. 2009).

CHAPTER 3

EXPERIMENTAL WORK

3.1 Materials

In this section, the instruments and equipment used for this study were introduced and the basic principles of operation of these tools were also explained.

3.1.1 Computed Tomography (CT) Scanner

Siemens Somatom Sensation Open (Siemens Medical Solutions, Erlangen, Germany) CT scanner was used in this experiment to CT simulate the phantom, as shown in the Figure 3.1 below. This CT scanner is a third generation 40-slice helical CT scanner with wider gantry bore of 82 cm aperture. It is powered by a 50 kW generator and features a Straton X-Ray tube. The standard field of view is 50 cm, and it can reconstruct images with extended field of view up to 82 cm, but the image quality will be degraded (Keat *et al*. 2005).

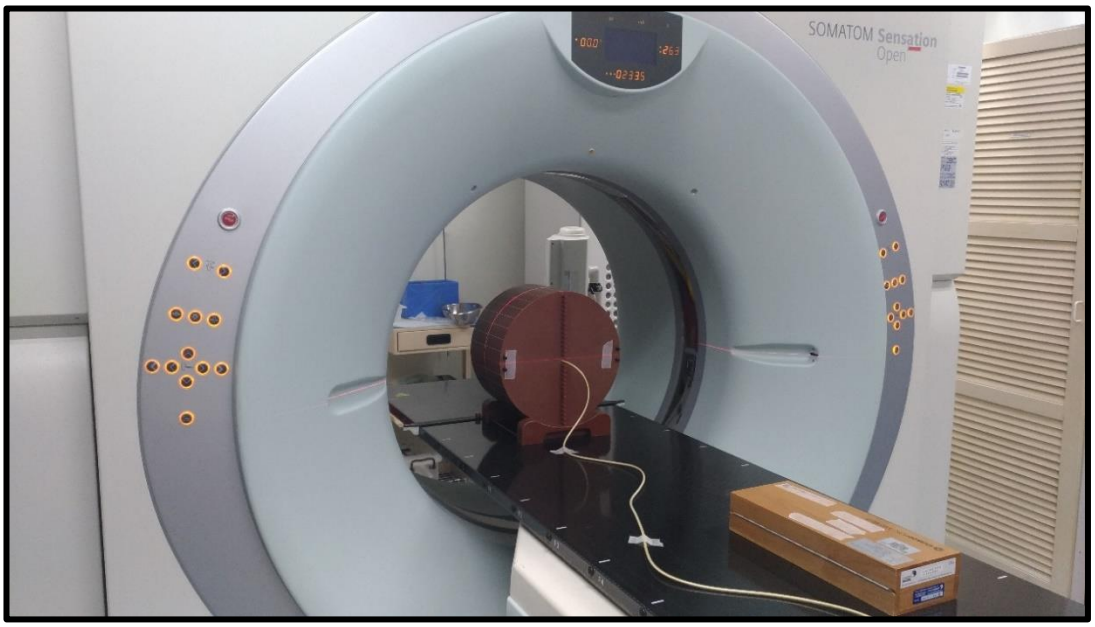

Figure 3.1: The Siemens Somatom Sensation Open CT Scanner with the experimental setup. [Courtesy of Mount Miriam Cancer Hospital]

3.1.2 DICOM Contouring System

Oncentra Master Plan® v4.5.3 (OMP) was used for contouring of the regions of interest (ROI) on the CT-simulated images. The CT scans were exported to OMP in Digital Imaging and Communications in Medicine (DICOM) format. OMP is also a TPS that is capable of calculating dose maps on CT data sets however it was not used for dose calculation in this study. The TomoTherapy final plan dose was exported to this OMP system in order to extract the dose profiles for the respective optimized plans. The Figure 3.2 below shows the OMP system in the contouring module.

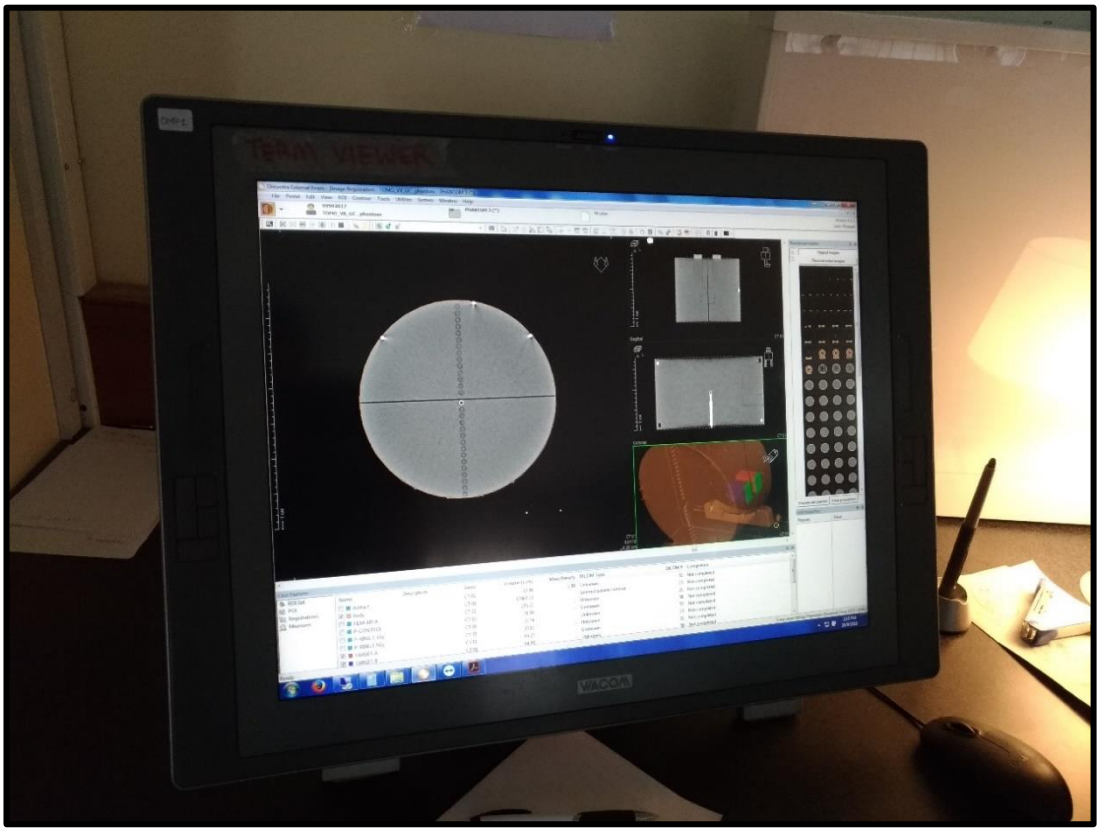

Figure 3.2: OMP to contour the ROI for the experiment. [Courtesy of Mount Miriam Cancer Hospital]

3.1.3 Treatment Planning System (TPS)

TomoTherapy TPS used in this experiment was TomoHD™ Version 2.1.2, it is equipped with the Accuray VoLO™ technology that allows voxel-less optimization

which will increase the optimization speed for treatment planning. It makes use of GPU implementation for parallel computations of beamlets; continuous NVBB representation of beam and patient geometry; combination of CCCS and FCBB dose for fast and accurate dose calculations (Lu, 2010). Figure 3.3 shows the TomoTherapy TPS in the final calculation interface.

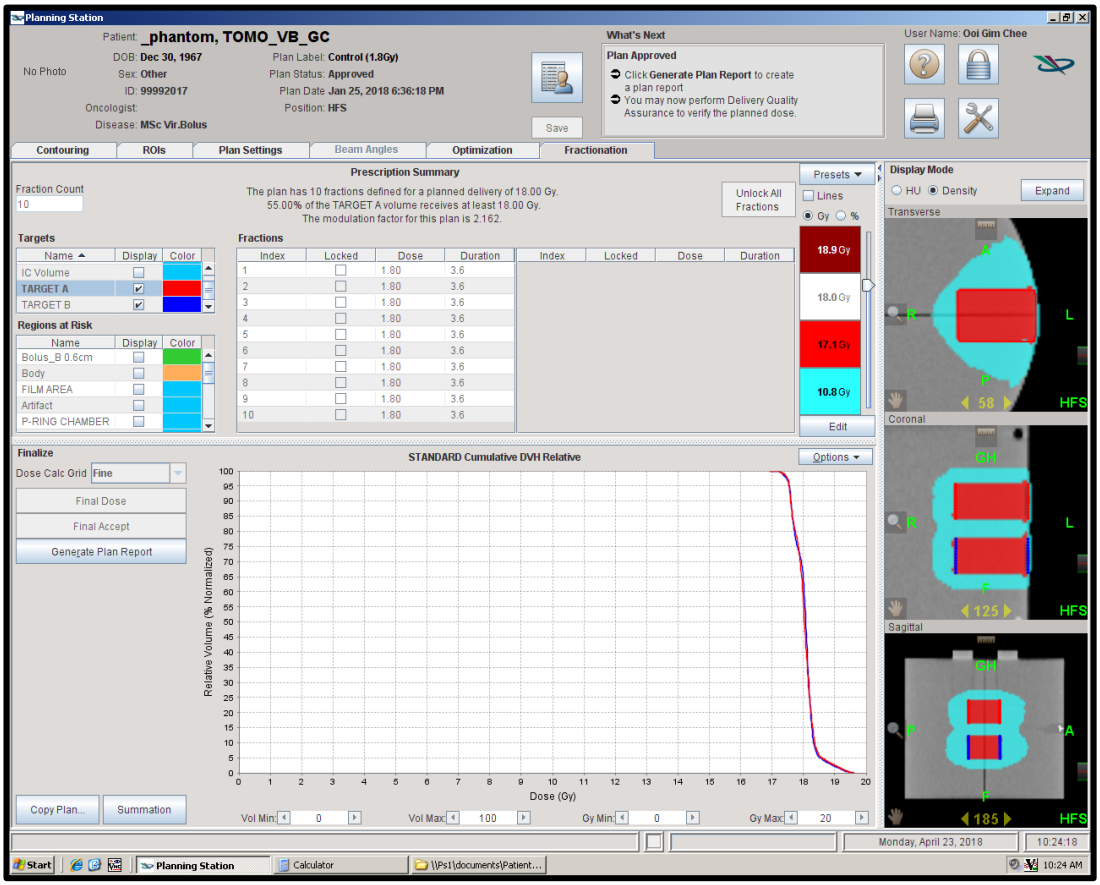

Figure 3.3: The final calculation interface of TomoTherapy TPS.

3.1.4 Radiation Delivery Device (TomoTherapy)

The radiation delivery machine used in this experiment was TomoTherapy Helical/Direct (HD). Helical TomoTherapy (TomoTherapy, Madison, WI) is a unique IMRT-dedicated treatment modality in which 6 MV photon treatment beam is delivered in slice-by-slice manner, where the patient is simultaneously moved into the gantry bore at predetermined constant speed while the gantry is rotating and delivering

radiation dose modulated by binary MLC leaves at a fixed jaw size (Mackie, 2006). This system is also capable in delivering static beams known as Tomo Direct where the gantry is located at a fixed angle while the patient is being moved into the gantry bore with the MLC modulations to deliver a uniform radiation dose. This is relatively similar to that of conventional linear accelerator (LINAC) radiation treatment with more uniform and lesser modulated radiation beam. Figure 3.4 shows the TomoTherapy HD used in this experiment.

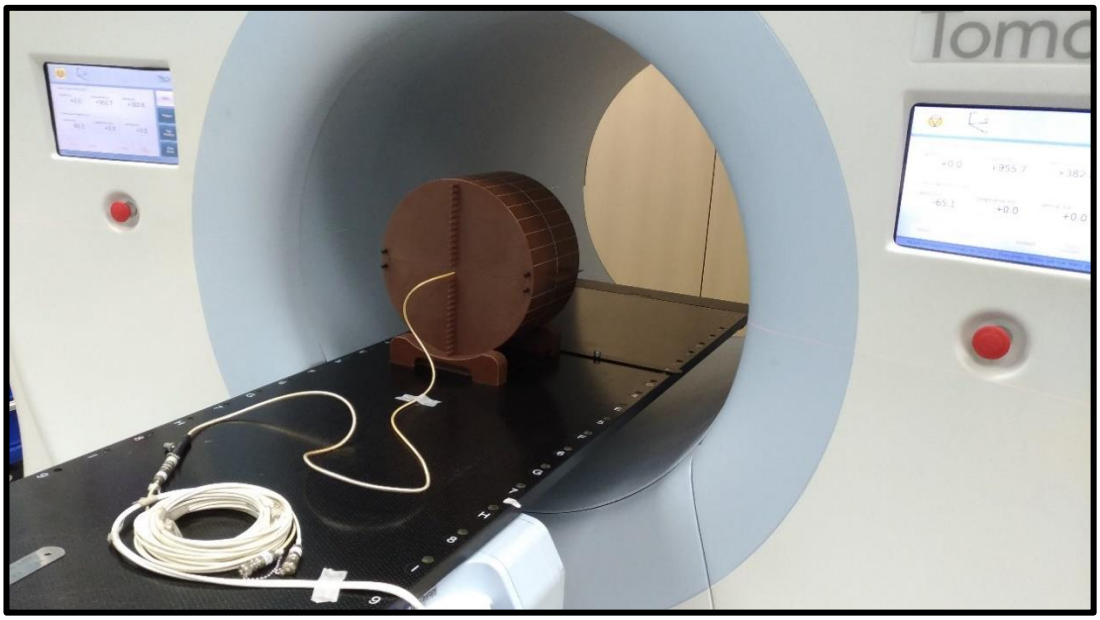

Figure 3.4: TomoTherapy treatment machine with the Cheese® phantom positioned. [Courtesy of Mount Miriam Cancer Hospital]

3.1.5 Phantom

The phantom used in this experiment is known as the TomoTherapy Cheese® Phantom, it is a cylindrical solid-water phantom provided by Accuray, it is made up of water-equivalent materials. The phantom is designed with chamber holes along its central axis and it can be separated into half to accommodate for film placement, it can be used for numerous quality assurance verifications. It can also be used for image quality verifications; it is used to calibrate the Hounsfield Units (HU) of its on-board