Monte Carlo Techniques for Patient Specific Verification of Complex Radiation Therapy Treatments

including TBI, VMAT and SBRT Lung

by

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Abstract

The main objective of this thesis is to develop Monte Carlo (MC) techniques for verification of complex radiation therapy treatments with emphasis on total body irradiation (TBI) and Volumetric modulated arc therapy (VMAT).

This work was motivated by an initial study including ten non-small cell lung cancer (NSCLC) patients which evaluated the dosimetric consequences of plans optimized using the treatment planning system (TPS) by recalculating them with MC. It was shown that poor modelling of electronic disequilibrium by the TPS lead to underdosage of the planning target volume (PTV) and that quality assurance (QA) procedures should be based on a MC approach.

With the emergence of volumetric modulated arc therapy (VMAT), which is a complex type of treatment delivery, new developments in MC simulations are required. A patient specific MC based QA system for VMAT treatments was developed and implemented clinically. This system is able to assess machine delivery performance and dose calculation accuracy of the TPS. During a substantial portion of the treatment the radiation beam is attenuated by the treatment couch. The impact of the attenuation on QA results is found to be patient specific and is non negligible. A process to create a couch model for MC simulations and its implementation is presented. The accuracy of this system is demonstrated against experimental measurements.

For TBI the most important contributors to mortality is interstitial pneumonitis (IP). Adequate lung shielding and accurate estimation of lung doses is critical to reduce incidence of IP. A MC based TBI verification system including all the treatment delivery characteristics as well as patient specific lung compensators is presented. For the purposes of treatment plan quality improvement, a study including five anonymized image data sets from previously treated patients is performed. It is shown that mean doses to lungs are systematically larger for the prone position treatment compared to the supine position due to anatomical deformation. Improvement in dose distribution is investigated using a new fast inverse dose optimization algorithm combined with a
new treatment delivery technique.
This thesis concludes that MC based verification for complex radiotherapy treatments is clinically feasible and outperforms current methods.
Preface

Chapter 3 is based on work conducted by V. Moiseenko, M. Liu, A. Bergman, B. Gill, S. Kristensen, T. Teke and I.A. Popescu (ethics approval number H06-00051):


My contributions were to modify the actual Monte Carlo (MC) code to expand the number of materials considered (from 4 materials to 55 materials), to modify and implement a dose to water conversion code for the MC system used, generate all the MC data and participated to the preparation of the manuscript.

In Chapter 4 the commissioning of the $^{60}$Co was done in collaboration with Y. Qiu and S. Thomas. The development of the lung compensator software was developed in collaboration with S. Thomas.

A version of chapter 5 has been published:


The identification, design of the research program and data acquisition was carried out by the primary author and Dr. Popescu. Data analysis and preparation of the manuscript were performed jointly.
Preface

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The identification, design of the research program and data acquisition were carried out by the primary author. Data analysis and preparation of the manuscript were performed jointly.
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<td>BEV</td>
<td>Beam’s Eye View</td>
</tr>
<tr>
<td>CC</td>
<td>Collapsed Cone</td>
</tr>
<tr>
<td>CT</td>
<td>Computed Tomography</td>
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<tr>
<td>CM</td>
<td>Component Module</td>
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<tr>
<td>CPU</td>
<td>Central Processing Unit</td>
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<tr>
<td>CSDA</td>
<td>Continuous Slowing Down Approximation</td>
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<tr>
<td>CTV</td>
<td>Clinical Target Volume</td>
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<tr>
<td>DAO</td>
<td>Direct Aperture Optimization</td>
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<tr>
<td>DBS</td>
<td>Directional Bremsstrahlung Splitting</td>
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<tr>
<td>DMLC</td>
<td>Dynamic Multileaf Collimator</td>
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<tr>
<td>DTA</td>
<td>Distance To Agreement</td>
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<tr>
<td>EDW</td>
<td>Enhanced Dynamic Wedge</td>
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<td>EGS</td>
<td>Electron Gamma Shower</td>
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<td>EUD</td>
<td>Equivalent Uniform Dose</td>
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<td>FIDO</td>
<td>Fast Inverse Dose Optimization</td>
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<td>FWHM</td>
<td>Full Width Half Maximum</td>
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<td>GPU</td>
<td>Graphic Processor Unit</td>
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<tr>
<td>GPGPU</td>
<td>General Purpose Graphic Processor Unit</td>
</tr>
<tr>
<td>GTV</td>
<td>Gross Tumour Volume</td>
</tr>
<tr>
<td>HFS</td>
<td>Head First Supine</td>
</tr>
<tr>
<td>HRT</td>
<td>Hypofractionated Radiation Therapy</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>-------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>HU</td>
<td>Housnfield Unit</td>
</tr>
<tr>
<td>IGRT</td>
<td>Image Guided Radiation Therapy</td>
</tr>
<tr>
<td>IMAT</td>
<td>Intensity Modulated Arc Therapy</td>
</tr>
<tr>
<td>IMRT</td>
<td>Intensity Modulated Radiation Therapy</td>
</tr>
<tr>
<td>IP</td>
<td>Interstitial Pneumonitis</td>
</tr>
<tr>
<td>KN</td>
<td>Klein-Nishina</td>
</tr>
<tr>
<td>LQ</td>
<td>Linear Quadratic</td>
</tr>
<tr>
<td>MC</td>
<td>Monte Carlo</td>
</tr>
<tr>
<td>MLC</td>
<td>Multileaf Collimator</td>
</tr>
<tr>
<td>MU</td>
<td>Monitor Unit</td>
</tr>
<tr>
<td>NRC</td>
<td>National Research Council</td>
</tr>
<tr>
<td>NSCLC</td>
<td>Non-Small Cell Lung Cancer</td>
</tr>
<tr>
<td>NTCP</td>
<td>Normal Tissue Complication Probability</td>
</tr>
<tr>
<td>OAR</td>
<td>Organ At Risk</td>
</tr>
<tr>
<td>PDR</td>
<td>Peak Dose Rate</td>
</tr>
<tr>
<td>PSF</td>
<td>Phase Space File</td>
</tr>
<tr>
<td>PTV</td>
<td>Planning Target Volume</td>
</tr>
<tr>
<td>QA</td>
<td>Quality Assurance</td>
</tr>
<tr>
<td>RDF</td>
<td>Relative Dose Factor</td>
</tr>
<tr>
<td>RT</td>
<td>Radiation Therapy</td>
</tr>
<tr>
<td>RTOG</td>
<td>Radiation Therapy Oncology Group</td>
</tr>
<tr>
<td>SBRT</td>
<td>Stereotactic Body Radiation Therapy</td>
</tr>
<tr>
<td>SSD</td>
<td>Source-Surface Distance</td>
</tr>
<tr>
<td>STT</td>
<td>Segmented Treatment Table</td>
</tr>
<tr>
<td>TBI</td>
<td>Total Body Irradiation</td>
</tr>
<tr>
<td>TCP</td>
<td>Tumour Control Probability</td>
</tr>
<tr>
<td>TH</td>
<td>Tissue Heterogeneity</td>
</tr>
<tr>
<td>TPS</td>
<td>Treatment Planning System</td>
</tr>
<tr>
<td>VCU</td>
<td>Virginia Commonwealth University</td>
</tr>
<tr>
<td>VMAT</td>
<td>Volumetric Modulated Arc Therapy</td>
</tr>
</tbody>
</table>
Acknowledgements

Firstly, I would like to thank my supervisors Dr. Cheryl Duzenli and Dr. Tony Popescu for their guidance, their trust and endless support during my PhD. Thank you Cheryl for your encouragements, for the countless 5 minutes meetings and for keeping me on track during all these years. Tony’s enthusiasm and passion for research have been a source of inspiration. Thank you for believing in me even during the darkest days, for encouraging me to pursue my research interests and for your respect. It is a privilege to work with you and to be your friend.

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Thanks to my family for their constant support. Finally, thanks to Marie-Pierre Milette and my son Xander for their unfailing patience, sacrifice and love.
Dedication

To my son Xander and my wife Marie-Pierre Milette
Chapter 1

Introduction

Radiation therapy uses high energy particles (photons, electrons or protons) to damage cancer cells and to stop them from growing and proliferating. The amount of radiation delivered to a location of interest or to the whole patient by a radiation beam is determined by using a dose calculation algorithm. The accuracy of this calculation is critical to assess if the radiotherapy treatment delivers a high dose to the tumour while sparing surrounding healthy tissue.

1.1 Thesis objectives

Monte Carlo methods for radiotherapy are considered to be the gold standard for dose calculation. The unmatched ability of Monte Carlo methods to accurately calculate dose in heterogeneous tissues and in regions of electronic disequilibrium [5-8] is rooted in the fundamental laws of the particle physics interactions used. In contrast, some commercial treatment planning systems (TPS) algorithms have known limitations in their dose calculation algorithms, in particular the handling of lateral electronic equilibrium and the lack of backscatter [9,10]. The importance of accurate tissue heterogeneity dose corrections has been convincingly demonstrated [11-13]. Monte Carlo methods use random sampling from probability distributions and require a large number of events (or histories) for the computed quantity to converge. One limiting factor for clinical implementation and routine clinical use of Monte Carlo simulations in radiotherapy was the computing power necessary to perform simulations within a reasonable amount of time. With new generations of multicore CPU (central processing unit) and graphics processor units (GPU) the necessary computing power is readily available.

The second limiting factor is the commissioning (accurate modelling) of the linear accelerator head for Monte Carlo simulations. This time consuming and tedious pro-
cess requires extensive Monte Carlo expertise. The exact dimensions and material composition of each linear accelerator component is required. This information is often proprietary and sometimes not available from the manufacturer. To circumvent this problem the International Atomic Energy Agency (IAEA) has created a freely available database containing numerical data required to perform MC simulations for each specific linear accelerator. This compilation of existing data has been properly validated. Implementation of Monte Carlo simulations for routine clinical use is therefore within grasp.

In the last two decades the complexity built into radiotherapy planning and treatment delivery has dramatically increased. These advances demand new sophisticated and accurate dose verification methods to validate the treatment plans.

In general, the verification method consists of two stages. In the first step the dose distribution of a given treatment plan is calculated by the TPS on a phantom which simulates the patient. In the second step experimental measurements are performed and results are compared with the calculated dose distribution from step 1. Techniques to measure point doses as well as one, two and three dimensional distributions of dose may be used. Instrumentation includes ion chambers, arrays of diodes, film, gels and more \[2, 14\]. However, all of these methods have certain limitations and none is considered a gold standard for full validation of a treatment plan.

The main objective of this thesis is to develop Monte Carlo (MC) dose simulation techniques for verification of complex radiation therapy treatments. The emphasis is on treatment techniques that pose particular challenges in radiation dosimetry. These include SBRT (stereotactic body radiation therapy) for lung, total body irradiation and volumetric modulated arc therapy, each described in more details below. In the remainder of this chapter a basic introduction to radiation dosimetry, radiobiology and radiation treatment delivery is presented.

In chapter 2 an introduction to Monte Carlo simulations for radiation therapy is presented. A brief description of sampling methods and of the MC code used in this thesis is introduced. Specific modifications to the current code performed are also presented.
1.1. Thesis objectives

In chapter 3, the necessity of Monte Carlo dose calculation in current treatment delivery for tumours located in regions where electronic disequilibrium occurs (lung tumour) is demonstrated. Stereotactic body radiation therapy and hypofractionated radiation therapy are becoming the treatments of choice for early stage non-small cell lung cancer (NSCLC) patients. The BR25 protocol used for clinical trials requires that the dose optimization must be performed without tissue heterogeneity corrections while the quality assurance should include manufacturer provided heterogeneity corrections. The final plans are recalculated with Monte Carlo methods and are shown to have large differences in tumour coverage compared to the original plans calculated with the treatment planning system including tissue heterogeneity.

The feasibility to develop a Monte Carlo based patient-specific quality assurance for the current total body irradiation (TBI) treatment is investigated in chapter 4. The actual planning process relies on hand calculations using basic dosimetric functions. As a consequence treatment plans are very simplistic; inhomogeneity corrections and patient specific geometry (except the lung compensators) are not included. In such situations, an accurate verification must be performed on the patient geometry and not on a water equivalent phantom. Different TBI fractionation schemes and their outcome [15–30] and late toxicity effects have been reported [31–37]. These studies rely on estimated delivered doses without knowledge of the exact dose distribution in patients or to organs at risk. This limited knowledge for a simplistic treatment delivery is in sharp contrast with advanced radiotherapy treatments like intensity modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT). For these type of treatments dose distribution can be precisely calculated by the TPS and accurate verification methods can be performed. A new Monte Carlo source allowing for calculation of dose distributions involving continuous source motion is used to model the $^{60}$Co sweeping beam delivery technique used for TBI. Patient specific verification for each treatment position (supine and prone) is performed on patient CT data, simulations included the tailored lung compensators as well as the beam flattener. Some severe limitations of the current treatment delivery are highlighted.
1.2. Background

VMAT plans have one of the most complex treatment deliveries with continuous linac motion and beam intensity modulation. Quality assurance (QA) on these types of plans is particularly challenging. In chapter 5, a Monte Carlo based VMAT QA is presented. A study on a cohort of 10 patients is carried out. The accuracy of this QA method is demonstrated by comparing results with both the treatment planning system and experimental measurements. This method is now implemented and used clinically in three cancer centres in British Columbia.

During VMAT treatment a portion of the radiation beam is delivered through the couch where the patient lies. In the treatment planning system the couch attenuation can be accounted for. In chapter 6, the necessity to determine experimentally the parameters used to model the couch in the TPS is demonstrated. The effect of couch attenuation on QA results is analyzed by comparing the difference between dose calculated with and without the treatment couch. A systematic method to include the treatment couch into Monte Carlo simulations is also presented. The accuracy of the MC couch model was tested on 6 plans and compared with TPS and experimental measurements.

In chapter 7, the feasibility of improving dose distributions for TBI treatment using Monte Carlo dose calculation and a fast inverse dose optimization (FIDO) algorithm is explored. This new approach avoids the limitations and pitfalls of the current treatment technique as described in chapter 4. The optimization approach is described and some key factors for producing optimal TBI treatment plans are identified.

In chapter 8, a summary and conclusions with recommendations for future work is presented.

1.2 Background

In this section we briefly review the physics of particle interactions used in MC simulations and illustrate their effect on different material types followed by a description of radiation delivery and dose measurements.
1.2. Background

1.2.1 Photon interactions with matter

A radiotherapy photon beam consists of a large number of photons with a range of energies. A photon beam impinging on matter can either be attenuated (photons removed from the primary beam through scattering and absorption processes) or pass through it without interacting. The probability of interaction with a target entity is expressed in terms of cross-section \( \sigma \) which represents the cross-sectional area the target presents to the incident photon and is measured in units of cm\(^2\) or barns (1 barn = \(10^{-28}\) m\(^2\)). For a monoenergetic beam of fluence \( \Phi \) (number of photons crossing an area defined in cm\(^2\)) the expected number of interactions is described by the equation:

\[
\langle N_{\text{int}} \rangle = N_{\text{targ}} \sigma \Phi
\]

where \( N_{\text{targ}} \) is the number of target entities per unit volume.

These targets are either atoms or electrons, thus \( e\sigma \) and \( a\sigma \) represent the cross-section per electron and per atom respectively.

The attenuation is the probability per unit path length that a photon will interact and is described by the quantity called the linear attenuation coefficient \( \mu \). The number of primary photons transmitted without any interaction in a thin layer \( x \) is given by:

\[
N = N_0 e^{-\mu x}
\]

where \( N_0 \) is the number of incident photons. The relation between the cross-section and the attenuation coefficient is given by:

\[
\mu = N_{\text{targ}} \sigma = \frac{N_A}{A} \rho \sigma
\]

where \( N_A \) is the Avogadro’s constant and \( A \) the atomic mass number. The “mass attenuation coefficient” \( \mu/\rho \) is a more fundamental coefficient which is independent of the density of the material and has dimension of g/cm\(^2\). Figure 1.1(a) shows the mass attenuation dependence on the interaction cross sections of the material and on the photon energy.

Five basic types of interactions can occur in the 0–25 MeV energy range produced by clinical linear accelerators:
1.2. Background

Figure 1.1: Total mass attenuation coefficient (a) for several different material used in this thesis. Relative importance of the three major photon interaction types (photoelectric, compton and pair production) as function of energy (b)(adapted from [1]).

- Rayleigh scattering (or coherent scattering, $\sigma_{\text{coherent}}$)
- Compton effect (or incoherent scattering, $\sigma_{\text{incoherent}}$)
- Photoelectric effect ($\tau$)
- Pair production ($\kappa_p$)
- Triplet production ($\kappa_t$)

The total mass attenuation coefficient is the sum of the individual processes.

$$\frac{\mu}{\rho} = \frac{N_A}{A} (\sigma_{\text{coherent}} + \sigma_{\text{incoherent}} + \tau + \kappa_p + \kappa_t)$$  \hspace{1cm} (1.4)

In the radiotherapy range the photoelectric effect ($\tau$), Compton effect ($\sigma_{\text{incoherent}}$) and pair production ($\kappa_p$) occur with the greatest probability. The relative importance of these three interactions is shown in Figure [1].

**Rayleigh (coherent) scattering**

Coherent scattering (or classical scattering) is a process in which a photon is collectively scattered by bound atomic electrons. The electromagnetic wave associated with a photon causes the electrons in the atom to oscillate. These oscillations cause
all electrons to emit electromagnetic waves of the same wavelength as the incident photon. The scattered waves combines with each other hence the name coherent scattering. The photon is seen as being scattered at a small angle. In the process no energy loss, ionization or excitation occurs. This interaction process is negligible for energies above 100 keV and for low-Z material.

**Compton (incoherent) scattering**

The interaction of a photon with a loosely bound electron (binding energy is small compared to the incident photon energy) of an absorber is called Compton scattering. The incident photon transfers part of its energy to the electron which is ejected from the atom with kinetic energy $E_K$ (Figure [I.2]). Using the relativistic conservation of total energy and momentum laws we can derive the Compton wavelength shift:

$$\Delta \lambda = \lambda' - \lambda = \lambda_c (1 - \cos \theta)$$  \hspace{1cm} (1.5)$$

where $\lambda_c = h/(m_e c)$ is called the Compton wavelength.

The same conservation laws are used to derive the energy $E_K$ and the scattering angle $\phi$ of the Compton electron:

$$E_K = h\nu \frac{\alpha (1 - \cos \theta)}{1 + \alpha (1 - \cos \theta)} \hspace{1cm} (1.6)$$

$$\cot \phi = (1 + \alpha) \tan \left( \frac{\theta}{2} \right) \hspace{1cm} (1.7)$$

where $\alpha = h\nu/m_e c^2$. In 1928 Oskar Klein and Yoshio Nishina derived the expression of the differential cross-section using Dirac’s relativistic theory:

$$\frac{d\sigma^K_N}{d\Omega} = \frac{d\sigma_T}{d\Omega} F_{KN} = \frac{r_0^2}{2} (1 + \cos^2 \theta) \ F_{KN} \hspace{1cm} (1.8)$$

where $\sigma_T$ is the classical (Thomson) electron differential cross-section and:

$$F_{KN} = \left( \frac{1}{1 + \alpha (1 - \cos \theta)} \right)^2 \left( 1 + \frac{\alpha^2 (1 - \cos \theta)^2}{[1 + \alpha (1 - \cos \theta)] (1 + \cos^2 \theta)} \right)$$ \hspace{1cm} (1.9)$$
1.2. Background

Figure 1.2: Schematic representation of Compton scattering. An incoming photon interacts with a loosely bound atomic electron. The electron is ejected from the atom and acquires a kinetic energy equal to the energy lost by the photon during the interaction.

\[ E_{tr} = h\nu - h\nu' \]

is the relativistic quantum mechanical correction.

The Compton mass-attenuation coefficient is given by:

\[
\frac{\sigma}{\rho} = \frac{N_A Z}{A} \sigma^{KN} 
\]

(1.10)

with the crude assumption that \( Z/A \) is constant, the Compton mass attenuation coefficient has no dependence on atomic number.

**Photoelectric effect**

The photoelectric effect is a phenomenon where an incident photon interacts with an atom and transfers all of its energy to the bound electrons (Figure 1.3). The kinetic energy of the ejected electron (called photoelectron) is equal to:

\[
E_{tr} = h\nu - E_B 
\]

(1.11)

where \( E_B \) is the binding energy of the electron. The atom, which is in an excited
1.2. Background

Figure 1.3: Schematic representation of the photoelectric effect. An incoming photon (a) interacts and transfers all its energy to a bound electron (b). The energy of the bound electron is equal to the energy of the incoming photon minus the binding energy. The excited atom returns to its ground state by emitting a characteristic photon (c) or by emission of an Auger electron (d).
1.2. Background

Figure 1.4: Mass attenuation coefficient for photoelectric effect for typical material type encountered in this thesis. The attenuation is higher for high Z materials.

state with a vacancy in one of its energy orbitals, returns to a ground state through two mechanisms: emission of characteristic radiation or emission of an Auger electron. Auger electrons are monoenergetic electrons produced by the absorption of characteristic x-rays

In characteristic radiation the vacancy is filled by an outer orbital electron, the energy of the photon emitted is equal to the energy difference of the energy orbitals involved. This energy is unique for each element and for each energy orbital. The mass attenuation coefficient for the photoelectric effect is derived from experimental data and varies with atomic number as $Z^{3.8}$ for materials with $Z > 16$ and as $Z^3$ for lower Z materials. It is proportional to $E^{-3}$ (with E representing the photon energy) and is given by:

$$\frac{\tau}{\rho} \propto Z^3 \frac{1}{A} \frac{1}{E^3}$$  \hspace{1cm} (1.12)

thus it is most important for high Z material and low energy. Figure 1.4 shows
1.2. Background

Figure 1.5: Schematic representation of pair production interaction (a) and triplet production interaction (b). The incoming photon interacts with the field of the nucleus to produce an electron-positron pair. In triplet production the incoming photon interaction occurs in the field of an electron.

the mass attenuation coefficient for photoelectric effect for some of the materials encountered in this thesis. The discontinuities are called absorption “edges” and correspond to the binding energies of the energy orbitals. The probability of ejecting the bound electron is maximum when the incident photon energy is just slightly larger than the energy of the orbital. The difference in Z of various human tissue amplifies the difference of the characteristic radiation produced which plays a significant role in x-ray imaging, more specifically for CT images where photon energies are in the 80-120 keV range.

Pair production

Pair production occurs when a photon interacts with the electromagnetic field of an atomic nucleus. The photon energy is converted into mass by producing and electron ($e^-$) and a positron ($e^+$)(Figure 1.5 (a)). The threshold energy for this interaction to occur is equal to twice the rest mass of the electron ($2m_0c^2 = 1.022 \text{ MeV}$). The excess of energy is shared between the positron and electron thus:
\[ h\nu - 1.022\text{MeV} = E_+ + E_- \]  

(1.13)

where \( E_+ \) and \( E_- \) are the Kinetic energy of the positron and electron respectively.

The mass attenuation coefficient for pair production is:

\[ \kappa \rho \propto \frac{Z^2}{A} \ln (h\nu) \]  

(1.14)

with \( Z/A \) constant. This coefficient increases rapidly with the photon energy and is proportional to \( Z \).

**Triplet production**

Triplet production is similar to pair production except that the photon interaction occurs in the field of an orbital electron as shown in Figure 1.5 (b). In this process two electrons and a positron are produced. The conservation of energy and momentum laws require the threshold energy to be \( 4m_e c^2 \). Triplet production occurs much less frequently compared to pair production.

**1.2.2 Charged particle interactions with matter**

In the previous section we described how charged particles (electrons and positrons) are produced through the photoelectric, Compton, pair production or triplet production process. These secondary particles will deposit energy until they deplete all their kinetic energy and come to rest. Electron transport is characterized by two important mechanisms, energy loss and scattering. Energy loss can occur by “collision energy loss” (electrons colliding with atomic electrons) or by “radiative energy loss” (electron interacting with the electromagnetic field of the nucleus). The transfer of energy from the electron to the medium is quantified by the quantity called “stopping power” (\( S \)) which is defined as the energy loss per unit path length \( S = \frac{dE}{dx} \). The total stopping power can be decomposed into collision and radiative (bremsstrahlung) components. As for the attenuation coefficient, the dependence on density is factored out by using the mass stopping power which has dimensions of MeV cm\(^2\) g\(^{-1}\).
1.2. Background

\[
\left( \frac{S}{\rho} \right)_{\text{tot}} = \left( \frac{S}{\rho} \right)_{\text{col}} + \left( \frac{S}{\rho} \right)_{\text{rad}} \tag{1.15}
\]

The energy loss is described in the following sections.

Collisional energy loss

Electrons deposit their energy to the medium through collisional energy losses. The charged particle can interact with a nearby atomic electron and knock it out of its shell. If the ejected electron is permanently removed the atom becomes ionized. This process is sometimes referred as ionization energy loss. If the atomic electron is elevated to a higher energy level the atom is in an excited state. The charged particle will have a large number of collisional energy loss interactions as it travels through the medium. These interactions involve a small amount of energy transfer. Sometimes the electron can transfer a large amount of energy to the ejected atomic electron. The high energy electrons are called $\delta$-rays. When produced by an electron the interaction process is called Møller scattering; when produced by a positron the process is called Bhabha scattering. The mass collision stopping power characterizing collisional energy loss was determined by Berger and Seltzer and is given by:

\[
\frac{1}{\rho} \left( \frac{dE}{dx} \right)_{\text{col}} = \frac{2\pi r_e^2 m_e c^2 N_A}{\beta^2} \left\{ \frac{Z}{A} \ln \left[ \frac{\tau^2 (\tau + 2)}{2 (I/m_e c^2)^2} \right] + F(\tau) - \delta \right\} \tag{1.16}
\]

with

\[
F(\tau) = 1 - \beta^2 + \frac{\frac{\tau^2}{8} - (2\tau + 1) \ln 2}{(\tau + 1)^2} \tag{1.17}
\]

where:

- $m_e c^2$ is the rest mass of the electron
- $\beta = \frac{v}{c}$ is the velocity relative to the speed of light
- $\tau$ is the ratio of electron kinetic energy to rest mass
- $I$ is the mean excitation energy
• \( \delta \) is the density effect correction

• \( F(\tau) \) accounts for Möller or Bhabha scattering (depending the charge of the particle involve in the interaction)

**Radiative energy loss (Bremsstrahlung)**

We have described in the previous section the interaction of charged particles with atomic electrons. In addition the charged particles may interact with the electric field produced by a nearby atomic nucleus. The electron experiences an deceleration and will radiate energy in the form of a photon. This process is called Bremsstrahlung which means “decelerating radiation” in German. The photon propagates through the medium and will experience one of the five interactions describe in section 1.2.1. Is it also referred as radiative energy loss because the energy will be deposited in a distant location from where the Bremsstrahlung photon was initially produced. Bremsstrahlung processes can also occur through electron-electron interaction in which the Coulomb field of one electron decelerates the other. The rate of his process is small compared to the electron-nucleus reaction. The mass radiative stopping power is given by:

\[
\left( \frac{S}{\rho} \right)_{\text{rad}} = \frac{4N_A Z (Z + 1)}{A} r_0^2 E \frac{183}{Z^4}
\]

and is proportional to \( Z \) and to energy \( E \).

**Electron scattering**

Electron scattering is the process in which the electron interacts with the electric field of a distant nucleus. The interaction is elastic (no energy transfer) and results in the deflection of the electron. The electron can go through a large number of scatterings. These types of interaction are very costly for Monte Carlo simulations (calculation time). Theories to combine the effect of many scatterings are used instead of modelling each single-scattering event.
1.2. Background

Continuous-Slowing-Down-Approximation (CSDA) range

Charged particles lose their kinetic energy through a large number of interactions each involving usually a small energy transfer. These interactions can be modelled as a sum of infinitesimal energy losses. Unlike photons which have a probability of traversing a medium without interacting, electrons have a finite range they can travel in medium and is given by the formula:

\[ r_0 = \int_0^{E_0} \frac{1}{S_{tot}(E)} \, dE \]  \hspace{1cm} (1.19)

where \( r_0 \) is the average path length travelled by the electron with initial kinetic energy \( E_0 \).

1.2.3 Energy transfer and absorbed dose

The energy transfer from a photon beam to a medium takes place in two stages. The first stage involves a photon interaction with an atom (either the atomic electron or the electromagnetic field of an atomic nucleus through one of the processes described in section 1.2.1) resulting in one or more electrons to be set in motion. In the second stage the high energy electrons transfer their kinetic energy to the medium through excitation and ionization processes. The energy is transferred along the electron tracks and does not take place at the same location as the Kerma. The initial energy transfer is described by the quantity called Kerma (Kinetic Energy Released in the Medium) and is defined as

\[ K = \frac{dE_{tr}}{dm} \]  \hspace{1cm} (1.20)

where \( dE_{tr} \) is the kinetic energy transferred by the photons to the electrons in a volume whose mass is \( dm \). The units of Kerma are energy per mass or equivalently Joules per kilogram or Gray where

\[ 1 \text{ Gy} = 1 \frac{\text{J}}{\text{kg}} \]  \hspace{1cm} (1.21)

Kerma applies only to indirectly ionizing particles.

The second step is described by the quantity called absorbed dose which is defined as
1.2. Background

Figure 1.6: Relationship between KERMA and dose as a function of depth in medium.

\[
D = \frac{dE_{ab}}{dm}
\]  

(1.22)

where \( E_{ab} \) is the mean energy imparted by ionizing radiation to a mass \( dm \) of matter.

Due to beam attenuation in the medium, kerma decreases steadily with depth. Close to the surface electrons are set in motion and start depositing energy along their tracks. The number of electrons set in motion increases with depth leading to an increase of absorbed dose. The dose reaches a maximum at a depth characteristic of the photon beam energy closely related to the range of electrons set in motion. This region close to the surface is called the buildup region. At depth of maximum dose (or \( d_{max} \)) the number of electrons entering a small volume is equal to the number of electrons leaving it. This phenomenon is called “electronic equilibrium”. As the depth increases the number of electrons set in motion upstream by Kerma decreases due to the beam attenuation. As a consequence at depths further than \( d_{max} \) the absorbed dose decreases. The relationship between kerma and dose is illustrated in Figure 1.6.
1.2.4 Dose calculation algorithms: convolution method

Two essential components of the convolution method are the terma (first defined by Ahnesjö, Andreo and Brahme [38]) and the kernel. The total energy released per unit mass (terma) is the energy imparted to charged particles by interactions of primary photons and includes the energy retained by the scattered photon. The kernel $K$ represents the fraction of the energy released deposited at point $r$ launched by a primary photon interaction at point $r'$. The kernel can be separated in two or more components (primary kernel and one or multiple scatter kernel(s)) which are used to calculated the primary and the scatter dose respectively.

**Pencil beam approach**

In the pencil beam convolution algorithm the radiation beam is subdivided into small “beamlets” or pencil beams. The energy distribution released from the pencil beam impinging on the patient surface is represented by the pencil-beam kernel $K_{PB}$. The total dose contribution to a point is obtained by convolving the terma with the pencil beam kernel over the field area:

$$D(x, y, z) = \int \int \frac{\mu}{\rho} \Psi_E(x', y') K_{PB}(x - x', y - y', z) dx' dy'$$  \hspace{1cm} (1.23)

where

- $\frac{\mu}{\rho}$ is the mass attenuation coefficient for the medium at point $(x', y')$
- $\Psi_E(x', y')$ is the entrance energy fluence at point $(x', y')$
- $\frac{\mu}{\rho} \Psi_E(x', y')$ is the terma

The pencil beam kernel can be computed with the Monte Carlo method [39] or derived from measurements [40-42]. Ahnesjö et al. [43] determined that polyenergetic pencil-beam kernels could be represented analytically by a sum of two exponentials over the radius:

$$K_{PB}(r, z) = \frac{A_Z e^{-a_Z r}}{r} + \frac{B_Z e^{-b_Z r}}{r}$$  \hspace{1cm} (1.24)

where $r$ is the cylindrical radius from the pencil-beam axis and $A_Z, a_Z, B_Z, b_Z$ are fitting parameters dependent on $z$. 
1.2. Background

The pencil-beam approach suffers from several limitations. Its accuracy is dependent on the precision of the measured data used to determine the Kernel. The most serious disadvantage is its inherent limitation in handling inhomogeneity corrections \cite{44, 45} especially in environments experiencing lateral electronic disequilibrium. However, the acceptable balance between the pencil beam algorithm accuracy and calculation speed has been the major reason for its implementation in many commercial treatment planning systems.

Convolution/Superposition method using point kernels

The convolution/superposition method was presented by several groups in the mid 1980’s differing in their implementation \cite{46–49}. In the point kernel method, the term \( a \) is convolved with a 3D point kernel. The dose in each voxel is the sum of the dose contributions from each irradiated voxel. The dose \( D(r) \) at a point \( r \) is given by:

\[
D(r) = \int_{r'} T(r') \rho(r') \frac{K(r - r', \rho_{ave})}{\rho_{ave}} d^3 r'
\]

(1.25)

where

- \( \rho(r') \) is the density at the point \( r' \)
- \( \rho_{ave} \) is the average density between \( r \) and \( r' \)
- \( T(r') \) is the term \( a \)

and the 3D integration is performed over the patient volume. Monte Carlo methods have been used to calculate the primary kernel (representing the energy deposited by the charged particles set in motion at the primary interaction site) and one or more scatter kernels (representing the energy deposited by all charged particles set in motion by the scattered photons). To account for inhomogeneities, the kernel is scaled using the radiological equivalent path length with respect to the density distribution between the primary interaction site and the point where the dose is calculated. In this approach, the electron tracks are assumed to be straight lines in contradiction with the theory of multiple scattering of electrons. A density scaling method using Monte Carlo generated electron tracks have been proposed \cite{50} leading to longer calculation times. In the convolution/superposition method, the Kernel is no longer
1.2. Background

considered as spatially invariant and therefore the integration must be performed by the superposition method leading to longer calculation times. However, another convolution method, the collapsed cone convolution [51], can reduce the computation time using the rapid fall off of the kernel at large distances from the primary interaction site. The interaction site is at the apex of a series of radially narrow cones spreading out in three dimensions. The kernel represents the energy deposited in the entire cone collapsed onto its central axis and is defined as:

\[ K(r, \Theta) = \frac{A \Theta e^{-a \Theta r} + B \Theta e^{-b \Theta r}}{r^2} \] (1.26)

This method has been implemented in several commercial treatment planning systems.

Details on the implementation of the different convolution/superposition methods into treatment planning systems and their dosimetric accuracy compared to Monte Carlo methods have been reported [52, 53]. Each convolution/superposition method uses some approximation in both the kernel function and in the density scaling method to account for inhomogeneities. The effect of inhomogeneity is accurately modelled only by using Monte Carlo simulations which relies on the fundamental physics of particle interactions. The physics of Monte Carlo simulations and its application to radiotherapy will be described in the next chapter.

1.2.5 Radiation biology

Radiation biology describes the interaction of radiation with biological cells. A tumour is a product of an uncontrolled cell division and failure for self-elimination. Clinical and pathological stages of a tumor are described using the TNM classification of malignant tumors developed by Pierre Denoix between 1943 and 1952 at the Institute Gustave-Roussy. In this nomenclature:

- **T** refers to the size of the tumor
- **N** indicates the status of regional lymph nodes
- **M** denotes the presence of metastasis
1.2. Background

The mechanism of cell killing using radiation is an active field of research. Biological effects from radiation are the result of DNA damage. DNA damage by radiation can occur through direct or indirect action. In direct action the secondary electron produced by absorption of an x-ray photon interacts with the DNA and produces damage to either the helix structure (sugar/phosphate backbone) or to one of the base molecules (cytosine, thymine, adenine, guanine). In indirect action the electron interacts with a water molecule to produce free radicals that are able to diffuse to reach and damage the DNA.

Two types of DNA damage can occur; single strand breaks and double strand breaks. Biological cells have the faculty to repair damaged DNA. In the single strand break the second DNA strand is used as a template for repair. This type of damage has little biological consequences. In the double strand break both DNA strands are damaged. If well separated, they are repaired as independent single strand breaks. If the breaks that occur in opposite strands are separated by only a few base pairs, the chromatin can split in two pieces and lead to chromosomal aberrations.

The proportion of cells that survives a radiation dose is characterized by a cell survival curve as illustrated in Figure 1.7. These curves are derived from clonogenic assay data.
1.2. Background

The shape of the curve can be separated into three regions; the low dose region (where the curve is straight with an initial slope), the high-dose region (where the curve bends), and the very high dose region (where the curve straightens again). The biophysical effects involved in the different shapes of the curve are not well understood. Different models describing these curves exist. The linear-quadratic model assumes that there are two components to cell killing:

\[ \text{Surviving fraction} = e^{-\alpha d - \beta d^2} \]  

where \( d \) is the radiation dose and \( \alpha \) and \( \beta \) are constants. The first component is proportional to dose and describes the probability that one electron will create a two strand break that will lead to lethal chromosome aberration. The second component is proportional to the square of the dose and describes the probability that a two strand break occurs due to damage from two separate electrons.

To reach the tumour the radiation beam goes through healthy tissue. The goal of radiation therapy is to maximize the tumour control probability (TCP) and minimize the normal tissue complication probability (NTCP). Ideally the tumour would be more radiosensitive than healthy tissue as illustrated in Figure 1.8(a)\[2\]. However a more realistic dose response is shown in Figure 1.8(b). The dose response curve has a sigmoidal shape, after a threshold dose is reached the tumour response increases with dose to finally reach 100% asymptotically. The dose delivered must be chosen carefully to achieve a fine balance between tumour control and healthy tissue sparing (maximize TCP and minimize NTCP).

Dose fractionation is used to minimize NTCP without compromising TCP. An example of cell survival curve for fractionated radiation is shown in Figure 1.9. With fractionation a higher dose can be delivered to healthy tissue resulting in a higher fraction of cells surviving. Radiation therapy treatment must therefore minimize as much as possible the dose to normal tissue while delivering a lethal dose to the tumour. This type of treatment is achieved through intensity modulation.
1.2. Background

Figure 1.8: Ideal dose response curve (a) and actual dose response curve (b) for normal tissue and tumour cells (adapted from [2]).

Figure 1.9: Cell survival curve depends on the type of radiation. The effect of fractionation is shown in red. [adapted from http://en.wikipedia.org/wiki/File:Acute-Radiation-Cell-Survival.png].
1.2. Background

1.2.6 Radiation delivery

Delivery of radiation is achieved using a medical linear accelerator or Linac. A schematic diagram is shown in Figure 1.10. Medical Linacs are designed to accelerate electrons to relativistic speeds using an electromagnetic waveguide.

The electron gun is the source of electrons for the waveguide. It consists of a heated cathode that emits electrons at high a temperature. These electrons are accelerated by the anode and exit to the waveguide. Microwave radiation produced by a klystron or a magnetron is used in the waveguide to produce an electromagnetic field. This field accelerates electrons to kinetic energies from 4 to 25 MeV. A high voltage pulsed modulator ensures the synchronicity between the arrival of the electrons produced by the electron gun and the microwaves to the waveguide.

There are two types of accelerating waveguide: the standing waveguide type and the travelling wave guide type. In a travelling waveguide the microwaves reaching the end of the waveguide are absorbed. Only one out of four cavities creates an accelerating electric field for the electrons. In a standing waveguide the microwave that enters on the gun side is reflected at the end of the waveguide giving rise to standing waves.

Figure 1.10: Schematic diagram of a medical linear accelerator.
which oscillate in magnitude with time. Larger electric fields are produced and two out of four cavities create an accelerating electric field.

High energy standing waveguides are typically 1.5 meter long and are mounted horizontally in the gantry. Bending magnets are used to refocus the electron beam to maintain a small radial spread ($\approx 1\text{mm}$) and to redirect the beam towards the target. The exact composition of the target is a well kept secret by manufacturers. A mixture of high Z materials (copper with tungsten) is usually used. Bremsstrahlung photons are produced by the decelerating electrons in the target. This X-ray beam is forward peaked and collimated by the primary collimator. A flattening filter is used to “flatten” the fluence profile of the beam. Its cone shape is designed to have a larger beam attenuation along the central axis where the beam fluence profile is forward peaked. Rectangular radiation fields used to treat patients are shaped using two pairs of jaws. The location of each component within the gantry is shown in Figure 1.11.

For more complex treatments like IMRT or VMAT, field modulation is achieved using a multileaf collimator (MLC). The MLC is composed of two banks of 6 cm thick leaves made of a tungsten alloy. The number, shape and thickness of leaves is manufacturer and model dependent. Each leaf is driven by a high precision motor and they can move independently of each other, allowing complex radiation modulation. Figure 1.12 shows the latest generation of MLC, the Varian HD MLC. A mixture of 1cm, 5mm and 3mm leaf thickness characterizes this MLC. The leaf tip curvature is optimized to minimize the penumbra at both the central axis of the beam as well as off axis.

### 1.2.7 Intensity Modulated Radiation Therapy (IMRT)

The goal of intensity modulated radiation therapy (IMRT) is to deliver a highly conformal dose to tumour while sparing surrounding healthy tissue. IMRT planning is more complex than conventional forward planning. Inverse treatment planning was developed to take advantage of beam modulation. Radiation beam intensity can be modulated using the multileaf collimator leaves. Two types of delivery exist: the first one uses a continuous leaf motion while the beam is on and is called dynamic delivery; the second type of delivery is called step and shoot. The leaves move to their initial position defining a shape or “aperture”. Once in position the radiation
1.2. Background

Figure 1.11: Schematic of a medical linear accelerator. 1) electron gun, 2) standing wave guide, 3) bending magnet, 4) tungsten target, 5) carousel of scattering foils (for electron radiation beam) and flattening filters (for x-rays), 6) monitor ion chamber, 7) secondary collimating system (jaws), 8) beam shaping device (multileaf collimator) (image from varian.mediaroom.com, image courtesy of Varian Medical Systems Inc., All rights reserved).
1.2. Background

Figure 1.12: Picture of the HD-MLC available on Varian TrueBeam Linacs. Each leaf moves independently of each other. The MLC can produce very complex shapes and radiation field modulation. (image from varian.mediaroom.com, image courtesy of Varian Medical Systems Inc., All rights reserved)

beam is delivered. When the beam stops the leaves move to the next position. This process is repeated until all the apertures have been delivered.

Two types of optimization exist. In fluence based optimization the radiation field is divided into beamlets. The optimization algorithm adjusts the beamlet weights until the fluence map produces the desired dose distribution. The optimal fluence needs to be translated into MLC leaf motions taking into account all the mechanical constraints of the leaves. This process is called leaf sequencing. Not accounting for the mechanical constraints in the optimization results in a degradation of the optimal fluence and as a consequence to a degradation of the quality of the plan.

In direct aperture optimization (DAO) the mechanical constraints are included in the optimization process. For each beam the apertures are generated based on the beam’s eye view of the planning target volume. Leaf position and aperture weights are changed randomly until the optimal plan is achieved. The inclusion of the mechanical constraints in the optimization guarantee that the aperture is deliverable, therefore no degradation in the quality of the plan occurs. It is common to use less than 10-15 apertures per radiation field limiting the amount of modulation than can be achieved.
1.2. Background

Figure 1.13: Illustration of a RapidArc treatment. During the treatment the gantry performs one or more full rotation while the beam is modulated using the MLC.

The previous two methods described are used mostly for static radiation beams. Intensity modulated arc therapy was proposed by Yu [54]. In this type of treatment the gantry (radiation beam) is constantly moving while the beam is modulated and several arcs are necessary to deliver the desired dose distribution translating into longer treatment time.

Varian’s RapidArc system (Varian Medical Systems, Palo Alto, CA) is a VMAT type of treatment that delivers the dose in one or more gantry rotations (in general one single arc is sufficient) using dynamic multileaf collimator motion, variable dose rate and variable gantry rotation speed. An illustration of such treatment is shown in Figure 1.13. The planning algorithm is based on the direct aperture optimization method and uses progressive sampling, as described by Otto [55]. The optimization algorithm incorporates the mechanical constraints of the MLC and other linac components and uses a simulated annealing method. The continuous source and MLC motion are modelled as a series of static beams.
1.2.8 Dose measurements

A detector measuring a quantity that can be related to dose with well understood physical principles is called an absolute dosimeter. Ionization chambers are used in this thesis for point dose measurements. The ion chamber can be described as an air cavity bounded by two electrodes having a potential difference and a central collecting electrode as illustrated in Figure 1.14. Electrons crossing the cavity can (if they are energetic enough) transfer energy to the gas and create ion pairs. These particles follow the electric field to opposite electrodes. An electrometer is used to measure the charge collected by the collecting electrode. This charge $Q$ can be related to the absorbed dose in air:

$$D_{air} = \frac{Q}{m_{air}} \left( \frac{W_{air}}{e} \right)$$

(1.28)

where

- $m_{air}$ is the mass of the air in the cavity volume
- $(W_{air}/e) = 33.97\text{eV/ion pair}$ is the energy required to produce an ion pair in air per unit charge

Dose to air can be converted into dose to medium (usually water for clinical applications) using Bragg-Gray cavity theory. For more details about ionization chamber and cavity theory the reader is referred to the following references [1, 14, 56].

1.2.9 Dose comparison

In a clinical environment, quality assurance of complex treatments must be performed. In general, comparison is made between the calculated dose distribution from the treatment planning system and the measured or independently calculated dose distribution. Visual comparison of dose distributions using isodose lines can be used but provide very limited information. Some tools can be used to compare two dose distributions and plot dose profiles to estimate and find the location of the differences. Differences observed are not quantifiable with this subjective method. Another approach proposed by Van Dyk et al. [57] subdivides the comparison into regions of high and low dose gradient. In low gradient regions the acceptance criteria
1.2. Background

Figure 1.14: Diagram of a typical Farmer type ion chamber.

is based on dose difference. They suggested a dose difference of 3% would be clinically acceptable. For high gradient regions the acceptance criteria is based on “distance to agreement”. In the field edge a small spatial error results in large dose differences. For these points the criteria specifies how far one must travel before encountering the same dose value. Van Dyk et al. suggested a value of 3 mm would be clinically acceptable.

**The Gamma factor** A more quantitative method for comparing measured and calculated dose was proposed by Low et al. [58, 59]. This pass/fail method which combines dose difference and distance-to-agreement is called the gamma factor (\( \gamma \)) analysis. The user specifies the acceptability criteria. In this thesis a dose difference of \((\Delta D_M)\) of 3% and distance-to-agreement \((\Delta d_M)\) of 3 mm criteria is used as suggested by Van Dyk et al. [57].

\[
\Gamma(r_m, r_c) = \sqrt{\frac{r^2(r_m, r_c)}{\Delta d_M^2} + \frac{\delta^2(r_m, r_c)}{\Delta D_M^2}} \quad (1.29)
\]
1.2. Background

\[ \gamma(r_r) = \min \{ \Gamma(r_m, r_c) \} \forall r_c \]  

(1.30)

where

- \( r \) is the distance between the calculated \((r_c)\) and the measured \((r_m)\) data points

- \( \Delta d_M \) is the DTA acceptability criteria or equivalently the maximum distance-to-agreement allowed

- \( \delta(r_m, r_c) \) is the dose difference between the measured data point and the calculated data point

- \( \Delta D_M \) is the dose-difference acceptability criteria or equivalently the maximum percentage of dose difference allowed
Chapter 2

Monte Carlo simulation of radiation transport

2.1 Introduction to Monte Carlo

The Monte Carlo method of radiation transport is a numerical solution to the Boltzmann transport equation using the fundamental laws of particle physics interactions. These laws are governed by Quantum Electrodynamics (QED) the most successful field of theoretical physics. Simulation of a particle track (or history) is achieved by random sampling from the probability distributions that govern particle interactions. A large number of histories is necessary before the result of interest converges and leads to small uncertainties. Before the existence of computers, application of random sampling methods to solve complex mathematical problems was unrealistic or limited in the number of histories or events. Some historical examples do exist such as the Comte Buffon needle experiment (1977 [60]) or determining the value of \( \pi \) by Laplace (1886 [61]). Modern application of Monte Carlo methods date from the mid 1940s with the work of von Neumann and Ulam during the Manhattan Project in the Los Alamos National Laboratory. The neutron diffusion in various materials problems they were working on could not be solved with analytical calculations. Stanislaw Ulam recalls his inspiration to use random number as follows:

The first thoughts and attempts I made to practice [the Monte Carlo Method] were suggested by a question which occurred to me in 1946 as I was convalescing from an illness and playing solitaires. The question was what are the chances that a Canfield solitaire laid out with 52 cards will come out successfully? After spending a lot of time trying to estimate them by pure combinatorial calculations, I wondered whether a more practical method than “abstract thinking” might not be to lay it out say

31
one hundred times and simply observe and count the number of successful plays. This was already possible to envisage with the beginning of the new era of fast computers, and I immediately thought of problems of neutron diffusion and other questions of mathematical physics, and more generally how to change processes described by certain differential equations into an equivalent form interpretable as a succession of random operations. Later [in 1946], I described the idea to John von Neumann, and we began to plan actual calculations.

— Stanislaw Ulam

They coined the name *Monte Carlo* after the city of Monte Carlo (capital of Monaco) famous for its casino and one of the centres for gambling. Today, Monte Carlo refers to any method that utilizes sequences of random numbers to perform statistical simulations. In Radiation therapy, Monte Carlo simulations are considered to be the gold standard for dose calculation.

### 2.2 Photon interaction processes

The physics of photon interactions used in MC simulations were described in the previous chapter. A photon can interact with the medium through one of the following processes:

- Rayleigh scattering
- Photonic effect
- Compton scattering
- Pair production
- Triplet production

During a photon history all particles (primary photon and all the daughter particles created) position, direction and energy are stored in a stack of variables. The following steps characterize a photon track:

---

**Distance to next interaction:** The photon is transported from its current position along its current direction to a random distance called mean free path. The mean free path is dependent on the particle energy and the medium in which the photon is currently located.

**Type of interaction:** A random type of interaction is selected with probabilities determined from photon energy and medium type at the interaction location.

**Angle, energy and new particle creation:** Choose randomly from an interaction cross section table the new angle and energy of the photon. If new particles ("daughter particles") are created their angles and energies are randomly chosen and are added on the stack of particles to be simulated.

This process will be repeated for all scattered photons until it either leaves the boundaries of the system or until it reaches the user defined lower energy cut-off. Once the end of the history of the primary photon is reached, then transport of any secondary particles ("daughter particles") are processed. These secondary particles (±electrons) can produce new particles by interacting with the medium. These new particles are in their turn added to the stack to be processed. The energy deposited by the electrons is scored in each voxel of material along their track. For each primary photon, multiple particles are created with secondary charged particles undergoing a larger number of interactions before coming to rest. This is sometimes referred to as a gamma shower.

### 2.3 Electron interactions process

Electrons or positrons can interact with the surrounding medium through the following processes:

- Møller scattering \( e^- e^- \rightarrow e^- e^- \)
- Bhabha scattering \( e^+ e^- \rightarrow e^+ e^- \)
- Bremsstrahlung \( e^\pm N \rightarrow e^\pm \gamma N \)
- positron annihilation \( e^+ e^- \rightarrow \gamma \gamma \)
2.4 Mathematical methods used in Monte Carlo simulations

• elastic scattering $e^\pm N \rightarrow e^\pm N$

A detailed description of these processes can be found in the literature [62–66]. Before coming to rest electrons and positrons can undergo hundreds of thousands of interactions. Computing all the interactions for each charged particle would require a large simulation time given that hundreds of millions of primary photons are necessary for good statistics. However, these interactions involve mostly small energy transfers and small angular deflections and can be treated as “statistically grouped interactions”. One method to perform these simulations was pioneered by Berger [67] and is called the “condensed history method”. In this technique, a large number of electron collisions are “condensed” or grouped into one “step”. The energy loss is either sampled from distribution (dependent on the electron step length) or calculated using the continuous slowing down approximation (CSDA) method. The scattering angle is sampled at the end of the step from multiple scattering distributions [68–71].

2.4 Mathematical methods used in Monte Carlo simulations

2.4.1 Sampling theory

The physics of photon and electron interactions that are used in Monte Carlo simulations for radiotherapy have been described in the previous section. The probability of a specific photon interaction (cross section), the energy loss and scattering angles are sampled from known probability distributions. Two sampling techniques that employ random numbers are reviewed below.

Transformation Method: This method is also called the “direct method”. Consider a probability distribution function $f(x)$ which is defined and normalized over the range $[x_{\text{min}}, x_{\text{max}}]$ and is integrable and positive. The corresponding cumulative probability distribution function is given by:

$$c(x) = \int_{x_{\text{min}}}^{x} dx' \ f(x')$$ (2.1)
2.4. Mathematical methods used in Monte Carlo simulations

with \( c(x_{\text{min}}) = 0 \) and \( c(x_{\text{max}}) = 1 \). Computer generated random numbers \( (r) \) are uniformly distributed and can be transformed into the appropriate probability distribution by inverting equation [2.1]:

\[
x = e^{-1}(r)
\]  

Let’s illustrate this method by using the probability of a photon interaction in a slab of material of thickness \( dz \) as seen in section [1.2.1]:

\[
f(z)dz = \mu e^{-\mu z}dz \quad 0 \leq z \leq \infty
\]  

Mapping between uniformly distributed random number \( (r) \) and the cumulative probability distribution is given by:

\[
r = c(z) = 1 - e^{-\mu z}
\]

\[
z = -\frac{1}{\mu} \ln (1 - r)
\]  

This method is used to calculate the distance to the next interaction in Monte Carlo codes. Frequently, the probability distribution function is not invertible or may not be easy to calculate as in the case of the Klein-Nishina distribution. In such cases the range rejection method is used.

Rejection Method: This method is illustrated using a concrete example: sampling the photon scattering angle for a Compton interaction using the differential Klein-Nishina (KN) cross-section given by

\[
\frac{d\sigma_{KN}(\theta)}{d\Omega} = \frac{r^2}{2} \left( \frac{h\nu'}{h\nu} \right)^2 \left[ \frac{h\nu'}{h\nu} + \frac{h\nu}{h\nu'} - \sin^2 \theta \right]
\]  

The range rejection method consists of three steps:

1. Scale the probability distribution function (Klein-Nishina) such that the maximum value becomes 1.
2. Choose a random number $r_1$ within the range where the probability distribution function is defined. For the KN case it will be between $[0,\pi]$ which corresponds to the photon scattering angle.

3. Choose a second random number $r_2$. If $r_2 < f(x)/f(x_{max})$ then accept $r_1$ as the scattered angle value, otherwise reject it and restart from the second step where $f(x)$ representing the KN differential cross-section.

With this approach half of the random numbers are wasted compared to the direct method but can save computation time if the cumulative probability distribution inversion is complicated. This waste becomes even more significant for distributions having a sharp peak with the extreme case being the dirac delta function. For such cases mixed methods are employed.

**Interaction sampling:** The branching ratio for each photon interaction type is defined as $\sigma_i/\sigma_t$ where $\sigma_i$ is the cross section of the interaction considered (Compton, photoelectric etc...) and $\sigma_t$ is the total cross-section. The type of photon interaction is selected by using a single random number between $[0,1]$ and finding which interaction branching ratio interval it belongs to.

### 2.4.2 Estimating means and variances

Assuming $N$ number of particles are simulated, the estimated value of the mean for a scored quantity $x$ (dose in the case of radiotherapy) is:

$$\langle x \rangle = \frac{1}{N} \sum_{i=1}^{N} x_i$$  \hspace{1cm} (2.6)

The variance associated with the distribution of $x_i$ is given by:

$$S_x^2 = \frac{1}{N - 1} \sum_{i=1}^{N} (x_i - \langle x \rangle)^2$$  \hspace{1cm} (2.7)

The estimated variance of $\langle x \rangle$ is the standard variance of the mean:

$$S_{\langle x \rangle}^2 = \frac{S_x^2}{N}$$  \hspace{1cm} (2.8)

Results reported as the scored quantity:
For more details about Monte Carlo methods applied to radiotherapy the reader is referred to the following reference [72].

2.5 Monte Carlo codes

A large number of Monte Carlo codes for radiotherapy have been developed. One of the most popular and experimentally verified code is the EGS (Electron Gamma Shower) code system. Other codes available are ITS, MCNP, PENEOPE, GEANT4, VMC, VMC++, MCDOSE, MCV, DPM to name a few. Each of these codes differ in the particle transport calculations and in their efficiency and accuracy compared to the EGS code. All of these systems require large computing capabilities such as clusters for routine clinical use. More recently, several groups have successfully implemented Monte Carlo codes on a general purpose graphics processor unit (GPGPU) [73, 74]. Using a single professional GPGPU card (Nvidia Tesla cards) MC simulations can be performed within a few minutes making Monte Carlo simulations accessible for routine clinical use.

2.5.1 EGSnrc

Electron Gamma Shower - National Research Council

EGS stands for electron gamma shower and is named for its ability to simulate the “shower” of electrons and photons produced during an electromagnetic cascade. EGS code was first developed in the 1970s at Stanford Linear Accelerator Centre (SLAC) by Ford and Nelson [75]. In the mid 1980s Nelson et al. [76] improved the performance of the EGS code at low energy and for electron transport. In the late 1980s and throughout the 1990s development of high-accuracy condensed history methods have been implemented [77, 78]. A more detailed history of the EGS code can be found elsewhere [79].

The EGS4 code used in this work uses a Class II scheme for the simulation of electron transport. In this scheme, the energy loss method used for charged particles is the

\[
\langle x \rangle \pm S_{\langle x \rangle}
\]  

(2.9)
2.5. Monte Carlo codes

continuously slowing down approximation (CSDA) where the energy loss is characterized by the stopping power. The multiple scattering theory employed is the Molière theory. A complete review of the photon and electron transport process used in EGS can be found in NRC Technical Report PIRS-701 which is updated with every new release [80].

2.5.2 BEAMnrc code

BEAMnrc code is a system for modelling radiotherapy sources and was developed originally as part of the OMEGA project which was a collaboration between the National Research Council Canada and the University of Wisconsin in Madison. The BEAMnrc code uses the EGSnrc system for modelling coupled electron and photon transport. It receives user input in the form of a text file defining the detailed geometry and composition of each part of the radiotherapy source as well as the physical parameters to be used in the electron and photon transport. Predefined geometrical shapes (called Component Modules or CM) are available to construct the medical linear accelerator. An accelerator is built using several component modules. Each part of the linear accelerator is modeled using the appropriate component module. These modules are oriented perpendicular to the beam axis. Their sizes and compositions are customized based on the radiotherapy source manufacturer specifications.

Modelling a linear accelerator

The linear accelerator simulated for this work is a Varian iX located at the Vancouver Cancer Centre. A schematic representation of the Varian iX linear accelerator model in BEAMnrc is shown in Figure 2.1. A 6 MV x-ray spectrum is generated by using a 6 MeV electron beam energy incident on a tungsten target. The electron beam spread is characterized by a Gaussian with a full-width/half-maximum (FWHM) of 0.75 mm. Both energy and FWHM values are varied until simulated dose to water matches experimental measurements. The details of the modelling and its accuracy can be found elsewhere [81].

Photons and electrons produced in the tungsten target are then transported through each component module. Secondary particles created at each CM are accounted for and transported by the BEAMnrc code.
2.5. Monte Carlo codes

Figure 2.1: Schematic representation of the Varian iX linear accelerator model in BEAMnrc. Each part of the linear accelerator (target, primary collimator, vacuum window, flattening filter, monitor chamber and jaws) is modelled using the appropriate component module (SLABS, CONS3R, CONESTAK, FLATFILT, CHAMBER, JAWS).
The radiation field size is limited by two component modules; the primary collimator and the secondary jaws. The role of the primary collimator is to focus the x-ray beam to a $40 \times 40 \text{ cm}^2$ field size and to reduce radiation leakage outside the primary radiation beam. The CM’s geometrical dimensions are fixed. The role of the secondary jaws (two orthogonal pairs) is to define a variable-shape rectangular radiation field specified at 100 cm from the target (or at isocenter). The x-ray beam intensity profile produced by the target is highly forward peaked (higher intensity along the radiation beam axis). The flattening filter is designed to attenuate the peak to obtain an almost uniform x-ray intensity profile throughout the field size.

**Phase space file**

The Phase Space is a plane perpendicular to the x-ray beam axis. Its position along the beam axis is defined by the user and it can be located only at the end of a CM. For each particle (primary or secondary) reaching this plane, the direction (x-y), kinetic energy, weight and location of last interaction along the beam axis is recorded in the phase space file (PSF). Another variable scored for each particle is the LATCH number. This number contains the charge of the particle, the number of times it crossed the scoring plane and information about particle interactions or transport history. This allows the code to calculate the dose contribution from a specific CM or region. The original purpose of this LATCH variable scored in the PSF has been altered by end-users in recent years (but not adopted by NRC). Bush *et al.* [82] have used this variable to label Monte Carlo beamlets generated from the PSF. More recently, Belec *et al.* [83] reassigned some of the PSF variables to tag the time component of the treatment allowing to perform MC simulations of time dependent continuously moving geometries.

The particles in the PSF can be transported further along a geometry of interest where they may be passed through a tertiary collimator (such as a multileaf collimator) or directed onto a material of interest for dose calculation.

**Particle transport through multileaf collimator (MLC)**

The multileaf collimator is probably one of the most important component modules for accurate Monte Carlo dose calculations in a radiotherapy context. The MLC from each manufacturer are different in shape, size, composition and position relative to the tungsten target. Within the same manufacturer several MLC types can be available, for example Varian Medical Systems offers the Millenium MLC (with the
2.5. Monte Carlo codes

The smallest leaf width of 5 mm projected at isocenter) or the HDMLC (with smallest leaf width of 3 mm projected at isocenter). To accommodate all these different designs several component modules are available (MLCE for Elekta MLC, VARMLC for Varian MLC and DYNVMLC for dynamic Varian MLC motion). More details about the MLC component modules are available in the BEAMnrc user guide [84].

The MLC particle transport code used in this work was developed by Keall and Siebers at the Virginia Commonwealth University [85]. This fast method only accounts for Compton interactions (no electron transport or pair production events) and can simulate both step and shoot and dynamic leaf motion delivery modes. The code outputs a PSF that is located at a distance of 45 cm from the tungsten target (for a Varian MLC). The particles in the PSF can then be directed onto a geometry of interest (e.g. voxelized patient representation) and the dose calculated.

Variance reduction techniques in EGSnrc

The efficiency $\varepsilon$ of a MC simulation is defined as:

$$\varepsilon = \frac{1}{\sigma^2 T}$$  \hspace{1cm} (2.10)

where $\sigma^2$ is the estimated variance of the quantity of interest and $T$ is the CPU time required to obtain this variance. The efficiency quantifies how fast a simulation can calculate a quantity of interest with statistical accuracy of $\sigma^2$. The simulation time is proportional to the number of statistically independent particles (N) while the variance is proportional to $1/N$. Several variance reduction techniques are employed to improved the efficiency.

- **Range rejection and cutoffs**: In range rejection an electron history is terminated whenever its residual energy is lower than the energy required to escape from the current region. In this process the Bremsstrahlung photons produced by the electrons losing energy is ignored. The energy threshold of the range rejection must be kept low to avoid any effect on the dose distribution.

- **Bremsstrahlung splitting**: In this variance reduction technique, each time an electron undergoes an interaction producing bremsstrahlung photons, a large number of photons are set in motion. For each interaction $N_{\text{split}}$ photons are created each having a weight inversely proportional to $N_{\text{split}}$. Three types of
2.5. Monte Carlo codes

Bremsstrahlung splitting method are available in the EGS system, Uniform Bremsstrahlung Splitting (UBS), Selective Bremsstrahlung Splitting (SBS) and Directional Bremsstrahlung Splitting (DBS) with the latest being the most efficient.

- **Russian roulette:** This method is used when there is little interest in the particle produced in an interaction (mostly electrons in the linac head) and is typically used in conjunction with Bremsstrahlung splitting. The low interest particles are eliminated with a given probability and the surviving particles weight are increased by the inverse of that probability. This elimination occurs until one low interest particle remains.

- **Photon forcing:** Photons are forced to interact within a given component module where few interactions occur due to either a low density of the medium or to a thin geometric region. This variance reduction technique is in general used to enhance the production of electrons in the air. This is an effective technique to investigate electron contamination from a region of the linear accelerator.

### 2.5.3 Patient description: densities and material selection

In MC simulations for radiotherapy the dose is scored in a *phantom*. This phantom is a voxelized representation of a patient or a geometry of interest having one or more material types. The standard process of creating a patient phantom requires DICOM CT images. The image data is resampled to match the MC dose calculation grid resolution. Each element (voxel) of the MC dose grid is assigned a Hounsfield Unit (HU) value (CT number) corresponding to the average value from the re-sampled CT image set. The HU are then converted into a physical density using a CT number-to-density conversion curve (sometimes called a CT ramp). In the last step, the densities are converted into material types (e.g. tissue, lung, bone) using a lookup table. This process is illustrated in Figure [2.2](#).

Careful conversion of CT number into material composition and mass density is essential for accurate MC dose calculations. The CT ramp conversion curve must
Figure 2.2: Schematic representation of the creation of a MC phantom. The CT image (a) and MC dose calculation grid (i.e. MC phantom grid resolution) have a different resolution and coordinate system (b). The CT data are re-sampled on the MC dose grid (c). For each voxel of the dose grid, the average HU is used to determine the density and the material type from the CT ramp curve (d) (adapted from [3]).

be determined for each CT scanner to account for their differences in density reconstruction accuracy. Verhaegen and Devic [86] demonstrated that a mis-assignment of media can potentially lead to significant dose errors in MC. They recommended that “careful CT calibration with a suitable phantom is essential”. The effect of tissue composition on MC dose calculations have been reported in the literature [87–89].

Two new CT scanners (GE LightSpeedTM RT16) have been commissioned at the Vancouver Cancer Centre during the course of this thesis. The electron density phantom model 465 (Radiation Measurements Inc.) containing 17 different tissues with known elemental, electron and mass densities was used [90]. For each scanner, the scanner-specific density to CT number conversion was determined by scanning the phantom and reading the HU values for each insert. The data was fit to linear functions in the CT number range from [−725, 225] and from [435, 1200] respectively. For larger mass and electron densities (larger than 1.5 g/cm³) an in-house made phantom with known elemental composition was used. The mass density calibration curve for both CT scanners are shown in Figure 2.3.

Good agreement was observed between both CT scanners except in the larger
Figure 2.3: Mass density calibration of 2 GE LightSpeed CT scanners. Also displayed is the default CT ramp curve from DOSXYZnrc (blue curve) with the material types and their HU range (air \( \leq -950 \) HU; \(-950 \) HU < lung \( \leq -700 \) HU; \(-750 \) HU < tissue \( \leq 125 \) HU; 125 HU < Bone). The average HU value of a voxel is used to determine the mass density (point on the curve) and the material type (by checking in which HU range it belongs).
density region. However, both scanners differ significantly from the default CT to density curve provided by DOSXYZnrc. As highlighted by Verhaegen and Devic [86], careful calibration is essential for accurate Monte Carlo dose calculations.

Most treatment planning systems do not include objects outside of the body contour in the dose calculation process (except for the treatment couch structures if requested by the user). To perform the MC simulations in the same conditions, DICOM CT images must be modified to remove such extraneous objects. Several codes performing such tasks are available [91, 92] but support only “head first supine” (HFS) patient positions to our knowledge.

Python codes using pydicom were developed to purge DICOM CT image datasets of undesirable objects for supine, prone and decubitus patient positions. The program extracts the body contour information from the DICOM RS structure file, tests each image pixel to see if it is inside the contour using a point in polygon algorithm, and reassigns a CT number equal to air if the pixel is outside. Pixels within the body contour are unchanged or the user can reassign a value equal to water if no inhomogeneity correction is desired during the dose calculation. An example is shown in Figure 2.4.

2.5.4 DOSXYZnrc code

DOSXYZnrc is a stand alone code that simulates photon and electron interactions for absorbed dose calculations in a three dimensional Cartesian volume. Every volume element (voxel) can have a different material and density assigned to it. The Cartesian volume (or phantom) can either be produced by the ctcreate code (converts DICOM CT data into density and material composition) or by hand. Radiation beams can be directed onto a phantom from many different angles and can have different characteristics. The properties of each beam geometry are contained within a module called “ISOURCE” (detailed information can be found in the DOSXYZnrc manual [93]). In this work, ISOURCE 2, 20 and 21 are used and they share the same geometry and coordinate system shown in Figure 2.5(a). For patient specific verification, this coordinate system must be translated into the treatment planning system’s coordinate system as shown in Figure 2.5(b).
2.5. Monte Carlo codes

Figure 2.4: Unmodified CT image (a) containing the CT scanner couch in the image. The new DICOM CT image (b) filtered with pydicom does not contain any object outside the body contour. In this example, the arms were not part of the body contour in the TPS.

The relationship between the DOSXYZnrc coordinate system and the treatment planning coordinate system (DICOM system) was determined by Thebaut et al. [94] and more recently by Bush et al. [95, 96]. However, the origin of the phase space file used in these studies is in the negative z direction. This is in contradiction with the origin of ISOURCE 2 where the phase space file is located in the positive z direction for phi=0 and theta=0. For the work presented in this thesis, it was necessary to derive the equations relating the two coordinate systems. The same methodology as Bush et al. was used.

Defining the rotation operators as:

\[
\begin{align*}
\mathcal{R}_X(\alpha) &= \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos(\alpha) & -\sin(\alpha) \\ 0 & \sin(\alpha) & \cos(\alpha) \end{bmatrix} \\
\mathcal{R}_Y(\beta) &= \begin{bmatrix} \cos(\beta) & 0 & \sin(\beta) \\ 0 & 1 & 0 \\ -\sin(\beta) & 0 & \cos(\beta) \end{bmatrix} \\
\mathcal{R}_Z(\gamma) &= \begin{bmatrix} \cos(\gamma) & -\sin(\gamma) & 0 \\ \sin(\gamma) & \cos(\gamma) & 0 \\ 0 & 0 & 1 \end{bmatrix}
\end{align*}
\]
2.5. Monte Carlo codes

the orientation of the radiation beam in the DICOM coordinate system can be related to the initial position (gantry, couch and collimator angles all equal to 0) by a product of rotation matrices along the rotation axis. Similarly, the orientation of the x-ray beam in the DOSXYZnrc ISOURCE 2 coordinate system can be related to the initial position by a product of rotation matrices. The relationship between phi, theta and phicoll with respect to the DICOM angles can be determined by solving the following equation which is slightly different from Bush et al. [95, 96]:

$$\mathcal{R}_Z(\phi)\mathcal{R}_X(-\theta)\mathcal{R}_X(\phi_{Col}) = \mathcal{R}_Y(-\theta_T)\mathcal{R}_Z(\theta_G)\mathcal{R}_Y(-\theta_C)\mathcal{R}_X(\frac{\pi}{2})$$ (2.11)

Two angles must be modified to account for the different origin position between ISOURCE 2 and the DICOM coordinate system. A gantry angle of 0° corresponds to a phi angle of 270°. The second angle to be modified is phicoll. Without modification the orientation of the radiation beam is incorrect as shown in Figure [2.6]
2.5. Monte Carlo codes

Figure 2.6: The MLC pattern created in the TPS for testing is highlighted in yellow and blue. The dose distribution from MC simulation for the unmodified value of phicoll is rotated by 90° (left). The collimator rotation direction was tested (centre) and found to be of opposite sign. Using the corrected phicoll relation the dose distribution overlaps perfectly the MLC pattern (right).

Including these shifts we can rewrite the relation as:

\[ R_Z(\phi + 270)R_X(-\theta)R_X(90 - \phi_{Col}) = R_Y(-\theta_T)R_Z(\theta_G)R_Y(-\theta_C)R_X\left(\frac{\pi}{2}\right) \] (2.12)

The Monte Carlo angles are given by:

\[
\theta = \arccos [\sin \theta_T \sin \theta_G] \\
\phi = 270 + \tan^{-1}\left[\cos \theta_T \sin \theta_G \over \cos \theta_G\right] \tag{2.13}
\]

\[
\phi_{Col} = 90 - \tan^{-1}\left[{-\sin \theta_T \cos \theta_G \cos \theta_C - \cos \theta_T \sin \theta_C \over \sin \theta_T \cos \theta_G \sin \theta_C - \cos \theta_T \cos \theta_C}\right] \tag{2.14}
\]

A python code using pydicom was developed to extract from the DICOM RT file all the characteristics of the treatment plan and create the Monte Carlo input files for Source 20. This code was used in the non-coplanar RapidArc section [5,2,7]. The dose distribution and its uncertainty calculated by DOSXYZnrc is written in an output file called a 3ddose file. The dose is expressed in terms of Gy per incident particle on the target. Conversion to absolute dose is performed following the procedure described by Popescu et al. [97]. This method allows a rigorous calculation of
the absolute dose delivered to the patient for the planned number of monitor units by recording and accounting for the dose to the monitor chamber due to radiation backscatter from the jaws (see Figure 2.7).

**Dose to medium versus dose to water**

MC simulations compute absorbed dose to the medium in which interactions and energy deposited by charged particles is performed. Treatment planning systems compute the dose to the patient assuming a unique material equivalent to water with varying density. To compare both dose distributions fairly, the calculated dose must be performed on the same medium. MC dose to medium can be converted to dose to water by applying the Bragg-Gray cavity theory:

\[
D_w = D_{med}S_{w,med}
\]  

(2.16)

where \(D_w\) is the dose to water, \(D_{med}\) dose to medium and \(S_{w,med}\) is the stopping power ratio. Converting the MC doses into dose to water, or not, is still an on going debate within the radiation therapy community [98].
Figure 2.7: Schematics of the MC linear accelerator setup. The BEAM A simulation (left) involves the patient independent component modules of the linac: target, primary collimator, flattening filter, monitor chamber and mirror. A phase space file is scored above the jaws as well as the forward dose scored in the monitor chamber. This phase space is then used as a source for the BEAM B simulation which includes the patient specific component module (jaws). The output is the backscatter dose scored in the monitor chamber and a phase space file scored below the jaws which can be then used by DOSXYZnrc as radiation source. Image courtesy of T. Popescu.
Chapter 3

Monte Carlo calculation of dose distribution in early stage NSCLC patients

3.1 Accelerated hypofractionated radiation therapy in NCIC-BR25 protocol

Stereotactic body radiation therapy (SBRT) and hypofractionated radiation therapy (HRT) are becoming the treatment of choice for early stage non-small cell lung cancer (NSCLC) patients with a solitary, small, peripheral lesion \[99-101\]. While SBRT and HRT trials (e.g. RTOG 0236/0618 (USA), BR25 (Canada)) vary in fractionation, planning target volume (PTV) definition and prescription isodose line, a requirement commonly found in these protocols is that the dose has to be calculated without tissue heterogeneity (TH) corrections. This ensures that all participants in the clinical trial are consistent in their treatment planning irrespective of what treatment planning system (TPS) and what method of correcting for TH they routinely use (each TPS dose calculation engine and TH method are based or use some type of approximations).

RTOG 0236 and 0618 trials require that for quality assurance (QA) purposes each plan should also be calculated with software vendor supplied heterogeneity corrections for density enabled. This recalculation typically indicates improved PTV coverage compared to the dose distribution calculated with no TH corrections because of less attenuation in the presence of lung. However, some commercial TPS algorithms have known limitations on implemented dose calculation algorithms in particular, the handling of lateral electronic equilibrium and the lack of backscatter \[9, 10\]. Both factors have a pronounced effect for small lung lesions and may cause the dose
distributions calculated for QA purposes to be significantly in error, especially at the periphery of the target volume. The importance of TH corrections implemented in the TPS for dose distributions in the PTV and normal lung for early stage NSCLC patients has been convincingly demonstrated by Schuring and Hurkmans [11] in their recent paper. The authors optimized SBRT plans according to RTOG 0236 guidelines, i.e., 95% of PTV receives the prescription dose of 60 Gy. The authors show that when plans were optimized with no TH corrections and then recalculated with the collapsed cone (CC) algorithm, the D95% of the PTV (averaged over twenty six planned patients) was 57 Gy, which is 5% below the prescribed value.

The Canadian BR25 protocol is similar to the RTOG 0236 and 0618 protocols in patient eligibility, but differs in the hypofractionation schedule (60 Gy in 15 fractions vs. 60 Gy in 3 fractions). One of the planning objectives is to cover 99% of the PTV volume by at least 95% of the prescription dose, with no more than 1% of the PTV volume receiving more than 105% of the prescription dose. This is in contrast to RTOG 0236 and 0618 protocols where the dose of 60 Gy is prescribed to the 60-90% (typically 80%) isodose line, thereby allowing significant dose heterogeneity within the PTV. The tighter constraints associated with the BR25 protocol put extra emphasis on the dosimetric consequences of the dose calculation and validation.

The Monte Carlo (MC) method has been established as the most accurate method to calculate dose in a heterogeneous tissue environment [5-8]. However, the application of MC to SBRT and HRT has thus far received limited attention. Lax et al. [13] and Panettieri et al. [12] compared Monte Carlo simulated dose distributions to TPS pencil beam (PB) and CC calculated distributions in a pentagonal phantom. It was shown that the TPS over-predicts the dose to the periphery of the target volume by up to 10%.

In this study, we evaluated the dosimetric consequences of optimizing dose distributions with a commercial TPS by re-calculating them with MC. Planning guidelines were kept in strict accordance with the specific BR25 protocol. In addition, we found (in agreement with Siebers et al. [102]) that converting the dose-to-medium (tissue) into dose-to-water in MC simulations produces negligible differences for NSCLC and, hence, using the former does not bias the comparison with the TPS doses for lung. We suggest that the current protocol guidelines for SBRT lung, while ensuring a ”con-
3.2 Methods

3.2.1 Patients

The National Cancer Institute of Canada (NCIC) BR25 protocol eligibility requirement is that patients must have medically inoperable NSCLC with stage I/II disease and N0M0 peripheral T1-3 lesions. The requirement for T2-3 stage patients is that the lesion has to be equal or smaller than 5 cm in the largest dimension. For stage T3 patients, only chest wall primary tumours are eligible. Exclusion criteria of significance for this study are that patients with T1-T3 tumours involving mainstem bronchus, or located in the lung apex (thereby putting brachial plexus under risk of receiving prescription dose) are ineligible.

For this study, we used two patients who were treated with the BR25 protocol (the number contributed to the study from Fraser Valley and Vancouver Cancer Centres at the time of manuscript preparation) and seven patients who were retrospectively identified as matching eligibility criteria. One of the retrospectively selected 7 patients presented with two small, distinct, well separated tumours, one in right lung and one in left lung. For this patient, RT plans were produced for one target volume at a time. Therefore, plans were produced for 10 target volumes. Table 3.1 shows location and dimensions of considered gross tumour volumes (GTV) and PTV.

3.2.2 Planning

The primary tumour was defined to be the gross tumour volume (GTV) and this was outlined by an oncologist. According to the BR25 protocol, no expansion from the GTV to the clinical target volume (CTV) was applied. The GTV was expanded by 1.5 cm in all dimensions to obtain the PTV. The prescription dose to the isocentre (PTV centre of mass) was 60 Gy with 99% of the PTV receiving at least 95% of the prescription dose and no more than 1% of the PTV was allowed to receive dose greater than 105% of the prescription dose as required by the BR25 protocol. While the BR25 protocol does not require that specific constraints are applied to V20 for
3.2. Methods

<table>
<thead>
<tr>
<th>ID</th>
<th>Lobe/Ant-Mid-Pot</th>
<th>GTV max dimension, cm</th>
<th>GTV volume, cc</th>
<th>PTV volume, cc</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1*</td>
<td>chest wall</td>
<td>LLL/Post</td>
<td>4.9</td>
<td>33.5</td>
</tr>
<tr>
<td>R2</td>
<td>chest wall</td>
<td>LUL/Mid</td>
<td>4.4</td>
<td>19.1</td>
</tr>
<tr>
<td>R3</td>
<td>mid-lung</td>
<td>LLL/Post</td>
<td>3.4</td>
<td>5.4</td>
</tr>
<tr>
<td>R4,Iso1</td>
<td>chest wall</td>
<td>RUL/Post</td>
<td>4.6</td>
<td>16.9</td>
</tr>
<tr>
<td>R4,Iso2</td>
<td>mid-lung</td>
<td>LUL/Ant</td>
<td>2.7</td>
<td>5.1</td>
</tr>
<tr>
<td>R5</td>
<td>mid-lung</td>
<td>LUL/Mid</td>
<td>3.7</td>
<td>9.7</td>
</tr>
<tr>
<td>R6</td>
<td>mid-lung</td>
<td>LUL/Mid</td>
<td>4.8</td>
<td>24.8</td>
</tr>
<tr>
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<td>mid-lung</td>
<td>LUL/Mid</td>
<td>4.0</td>
<td>18.7</td>
</tr>
<tr>
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<td>chest wall</td>
<td>RUL/Post</td>
<td>3.7</td>
<td>5.9</td>
</tr>
<tr>
<td>BR25,2</td>
<td>mid-lung</td>
<td>LLL/Mid</td>
<td>2.3</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Table 3.1: *Letter R preceding a number indicated patients selected retrospectively. For patients actually treated with BR25 protocol, ID starts with BR25. Chest wall indicates that the GTV extends to the pleura on at least one axial slice, otherwise tumour location is described as mid-lung. LLL left lower lobe; LUL left upper lobe; RUL right upper lobe.

the lung (calculated for normal lung which was defined as both lungs minus GTV), it does require that V20 is reported for each enrolled patient. RTOG 0236 and 0618 protocols require that optimized plans comply with constraints put on V20 (< 15%). A typical field arrangement consisted of three coplanar, isocentrically equally weighted fields. Plans were optimized using the Varian Eclipse TPS (Varian Medical Systems, Palo Alto, CA, USA). The dose calculation algorithm was based on the pencil beam algorithm of Storchi et al. [103]. Optimisations were performed for a Varian EX linear accelerator (6 MV beam with a 120 leaf multi-leaf collimator). Three plans were produced for each PTV in the TPS. Plan 1 followed the BR25 protocol, i.e., planned with no TH corrections. Plan 2 was plan 1 recalculated with TH corrections (Eclipse TPS uses the modified Batho method) as required for QA by the RTOG 0236 and 0618 protocols. Plan 3 was independently produced to achieve BR25 dose specifications with the TH corrections enabled.

MC simulations for plans 2 and 3 were performed. The MC doses were reported as both dose-to-medium and dose-to-water. Doses to the target volumes and normal
3.2. Methods

The BEAMnrc / DOSXYZnrc Monte Carlo system [93, 106] was used to simulate doses to the patient for different treatment plans. This system is based on the EGSnrc particle transport code [80]. Monte Carlo particle transport through the multileaf collimator (MLC) was simulated using a code developed by Siebers et al. [85], while the enhanced dynamic wedge (EDW) was modeled as a BEAMnrc component module, originally developed by Verhaegen and Liu [107]. The information required for the MC simulations was extracted from the TPS DICOM RT files using codes developed by Zavgorodni et al. [108].

The following MC transport parameters were used [109]: AP = PCUT = 0.010 MeV and AE = ECUT = 0.700 MeV, where AP and AE are the low-energy thresholds for the production of secondary Bremsstrahlung photons and knock-on electrons, respectively, while PCUT and ECUT define the global cut-off energy for photon and electron transport, respectively. This choice of electron transport cut-off energy for simulations in lung was also suggested by Ma et al. [110].

The accelerator model simulated was a Varian Clinac 21EX (Varian Medical Systems Inc., Palo Alto, CA, USA) and the physical parameters were defined according to manufacturer specifications. A phase space scored above the linac jaws was used as a source for simulations through the EDW and MLC. The dose accumulated in the monitor chamber of the linac was scored for every simulated field. We used the MC simulation setup described by Popescu et al. [97], which allows a rigorous calculation of the absolute dose delivered to the patient for the planned number of monitor units. In particular, this allowed us to record the dose to the monitor chamber due
3.2. Methods

to radiation backscattered from the moving jaws. Simulations were performed on a cluster of dedicated computers. A phase space above the jaws was obtained using $1.0 \times 10^9$ initial electrons incident on the target and contains $5.1 \times 10^7$ particles. The BEAMnrc runs through the jaws typically used $2.5 \times 10^8$ histories, while the DOSXYZnrc runs on the patient CT data sets used between $2.5 \times 10^8$ and $1.0 \times 10^9$ histories. The number of histories was selected for each simulation, such that the statistical uncertainty in the high dose voxels (GTV) was $\approx 1\%$.

The TPS computes and reports the absorbed dose-to-water, while MC computes and reports (as seen in section 2.5.4) the absorbed dose-to-medium [102]. For a meaningful comparison between the MC and TPS results, the MC dose-to-medium (D2m) has been converted to dose-to-water (D2w), using a stopping-power ratio method based on the Bragg-Gray cavity theory (equation [2.16]). The code used for this conversion (referred as DW) employs 56 materials (body tissue type) [111], thus preventing sharp changes of the stopping-power ratio at material density boundaries, which could lead to substantial errors [112, 113].

The program reads both the MC phantom and the 3ddose file containing the dose distribution. The material type for each voxel is extracted from the MC phantom, the appropriate stopping-power ratio is then applied to the dose in the voxel. A new 3ddose file containing the converted dose is created. The physical density of the 56 materials are selected from ICRU 46 report, the corresponding HU number is determined from the CT calibration curve (Figure 2.3). Several components of the Monte Carlo code have been modified to handle such a large number of material (ctcreate to create the phantoms, DOSXYZnrc itself and dosxyz_show program used to display the dose distribution within the MC phantom). By default DOSXYZnrc supports only 4 material types (air, lung, tissue and bone). The original DW code provided by Siebers et al. was modified to read and write 3ddose file produced from DOSXYZnrc. The changes were tested by comparing dose to medium with dose to water (D2w-D2m). Positive value appear at higher densities due to higher stopping power ratios for higher densities as seen in Figure 3.1.

56
3.3 Results

An overall summary of the PTV coverage for various optimization and forward calculation combinations is presented in Table 3.2. The base plan is defined as having no TH corrections during the optimization (column 2). The planning objective as formulated in the BR25 protocol (i.e., at least 99% of PTV has to receive at least 95% of the prescription dose) was achieved for all 10 PTV regardless of whether or not the TH correction was used during TPS optimization stage (columns 2 and 5). Plans optimized with no TH and recalculated by the commercial TPS with TH showed improved dose coverage compared to the base plan (column 3). In contrast, MC simulations demonstrated that this coverage is compromised (column 4). The planning objective for PTV coverage was not fulfilled for 8 out of the 10 PTV for the case where the optimization did not use a TH correction. This PTV under-dosage was more pronounced for plans optimized with TH corrections as all 10 PTV did not fulfil the planning objective (column 6). In this scenario, the fraction of the volume covered by 95% of the prescription dose (V95%) was as low as 23.3% for the PTV and 80.6% for the GTV.

Figure 3.1: Monte Carlo phantom (left) used to test DW code. Dose difference between dose to water and dose to medium (right) display the correct scaling sign. The dose difference in displayed in Gy.
### 3.3. Results

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>TPS no TH Optimization: Recalculation:</th>
<th>TPS no TH Optimization: Recalculation:</th>
<th>TPS no TH Optimization: Recalculation:</th>
<th>TPS with TH Optimization: Recalculation:</th>
<th>TPS with TH Optimization: Recalculation:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PTV covered with 95% prescription dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R1</td>
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<td>89.3</td>
<td>100.0</td>
<td>85.7</td>
</tr>
<tr>
<td>R2</td>
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<td>99.9</td>
<td>97.0 (95.9%)</td>
<td>99.6</td>
<td>81.1</td>
</tr>
<tr>
<td>R3</td>
<td>100.0</td>
<td>100</td>
<td>98.3 (95.9%)</td>
<td>100.0</td>
<td>93.7</td>
</tr>
<tr>
<td>R4,Iso1</td>
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<td>100.0</td>
<td>90.5</td>
</tr>
<tr>
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<td>100</td>
<td>75.1 (95.8%)</td>
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<td>R5</td>
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Table 3.2: PTV coverage, EUD and V20 for TPS and MC based plans. Dose in parenthesis is for dose-to-water and shows the dose as a percent of the prescription dose covering the same volume as in the dose-to-medium MC calculations for this patient.
3.3. Results

Another indicator for potentially poor PTV coverage after the MC recalculation was when the lung lesion was small and attached or in proximity to the chest wall (3 out of 4 chest wall tumours had $< 89.5\%$ of the PTV volume covered by the 95\% isodose line). For mid-lung lesions, the under-dosing shown in plans optimized with no TH corrections and recalculated with MC was not as severe and was restricted to the periphery of the beam as seen in beams-eye-view. This trend is further reflected in the EUD values. While plans optimized without TH corrections and recalculated in TPS consistently show an increase in EUD (as high as to 67.6 Gy), plans recalculated by MC reveal either a modest increase, or a decrease in EUD, the latter seen for 4 out of 10 PTV.

For plans optimized with TH corrections, the MC recalculation shows that the EUD is consistently lower than in the original base plan (TPS optimized and recalculated with no TH); in the extreme case it is 6 Gy lower than intended 60 Gy. Figure 3.2 shows an example of the PTV coverage on the sagittal slice for various combinations of optimization technique (TPS with/without TH correction) and forward calculations (TPS vs. MC). This figure shows that the planning objective of covering the PTV with the 95\% isodose line was achieved (panel A) and recalculation of the optimized plan with TH corrections indicates no loss of coverage (panel B). In contrast, a MC recalculation of panel A reveals substantial under-dosing as shown in panel C. For plans optimized with TH correction and recalculated in MC this under-dosing is even more severe (panel D). Both panel C and panel D would be considered to be poor plans.

The PTV under-dosing for plans optimized with TH correction (as revealed by MC) is further illustrated in Figure 3.3 which shows the DVH calculated for the patient ‘BR25,1’. This figure shows the original optimized plan (no TH corrections, TPS optimized and recalculated) and the same plan recalculated with TH corrections by the TPS and Monte Carlo. The figure demonstrates that while the TPS recalculation of the optimized plan shows improved PTV coverage, Monte Carlo simulations clearly indicate the opposite. V20 values for normal lung were consistent between MC and TPS calculations with TH corrections, the largest difference was 0.5\%. As expected, V20 was underestimated in calculations with no TH corrections; discrepancies compared to MC were up to 2\%. Data for 5 randomly chosen patients are shown in Table 3.2. Note that while the BR25 protocol requires that V20 values for each patient are
3.4 Discussion

recorded and reported, there are no DVH-based planning constraints for normal lung in this protocol.

As a benchmark test, all patient plans were also optimized and calculated with no TH corrections applied and these plans underwent MC simulation in a corresponding water-filled CT data set. The dose agreement was within the dose uncertainty of the MC simulation (1%). The resulting DVHs were essentially overlapping. Therefore, we conclude that the dose differences reported in the present work are indeed attributable to the TH correction.

Furthermore, to ascertain that the observed differences were not related to the dose-to-water calculation (as performed in the TPS) vs. dose-to-medium calculation (as performed in MC), dose-to-water conversions were performed on the MC data for 5 patients. Results for the PTV coverage are shown in Table 3.2 as values in parenthesis. The volume encompassed by the 95% isodose line in the dose-to-medium calculations is encompassed by the 95% to 95.9% isodose line in the dose-to-water calculations. This indicates a difference of less than 1% of the prescription dose, i.e., 0.6 Gy. Figure 3.4 shows the DVHs calculated for the PTV of patient R4, Iso2. Again, the base plan is one where the optimization and the forward calculation are performed by the TPS with no TH corrections (solid line, Figure 3.4). The shift towards lower doses for plans recalculated by MC is consistent with the previous patient DVHs as shown in Figure 3.3. The difference between the MC DVH calculated as dose-to-medium vs. dose-to-water is minor. All five test patients showed minor differences in PTV coverage. The data demonstrate that regardless of whether the MC calculations were presented as dose-to-medium or dose-to-water, the dose distributions are the same (within uncertainty). This result is consistent with the conclusions reported by Siebers et al. [102] and Fernandez-Varea et al. [114] for a 6MV beam in lung.

3.4 Discussion

Differences in dose calculation for heterogeneous matter between algorithms used by commercial TPS are well documented [115]. Avoiding inconsistencies in planning from contributing institutions due to these differences is one factor leading to the requirement to omit TH corrections in BR25 protocol. The other factor is that it appears reasonable that in the presence of lung, the reduction in attenuation would
3.4. Discussion

Figure 3.2: PTV (red contour) coverage with 95% isodose line (green contour) on the sagittal slice calculated for patient R4, Iso 2. GTV is shown as a blue contour. Panel A Optimize: TPS with no TH correction / Forward Calc: TPS no TH correction; Panel B Optimize: TPS no TH correction / Forward Calc: TPS with TH correction; Panel C Optimize: TPS no TH correction / Forward Calc: MC (yellow line shows 83.3% isodose line actually covering 99% of the PTV); Panel D Optimize: TPS with TH correction / Forward Calc: MC (magenta line shows 78.7% isodose line actually covering 99% of the PTV)
3.4. Discussion

Figure 3.3: DVH for patient BR25,1. The base plan (solid line) was optimized and recalculated by the TPS with no TH corrections. The plan was recalculated first by the TPS using TH corrections (dashed line) and then by MC (dotted lines).
3.4. Discussion

Figure 3.4: DVH for patient R4,Iso2. The base plan (solid line) was optimized and recalculated by the TPS with no TH corrections. MC recalculation of base plan using raw dose-to-medium values (dotted line). MC recalculation using dose-to-water conversion data (dot-dashed line).
make the PTV coverage at least as good as in the plan produced with no TH corrections. Recalculating plans with TH corrections enabled using commercial TPS, as required in RTOG 0236 and 0618 protocols, lends support to this expectation. Our Monte Carlo results show that this expectation is not always fulfilled for the plans produced according to the BR25 protocol and PTV is often under-dosed. The protocol requires that at least 99% of the PTV receives at least 95% of the prescription dose. While this planning objective was achieved in plans produced in TPS with no TH corrections, MC simulations showed that the dose actually covering 99% PTV was 93% of the prescription dose or less for 5 of 10 PTVs. In some cases this under-dosing was substantial. For example, for PTV R4,2 and BR25,1 the isodose lines covering 99% of the PTV were 83.3% and 83.0% of the prescription dose, substantially below the intended 95% (Figures 3.3 and 3.4).

It should be noted that these two PTVs are among the smallest considered in this study, see Table 3.1. This under-dosing was very pronounced for small tumours attached to the chest wall with as low as 75% of the PTV covered by 95% of the prescription dose, instead of the required 99%. While the requirement that at least 99% of the PTV receives at least 95% of the prescription dose was not fulfilled in 8 out of 10 cases after plans optimized with no TH corrections were recalculated with MC, the detriment to the EUD values was modest. For PTV R5, R6 and R7, which are unattached to the chest wall (mid-lung) and relatively large in size, the EUD was > 61.4 Gy.

Fundamentally, under-dosing the PTV compromises local control. The dose-response for SBRT delivered in three fractions has been demonstrated by Timmerman et al. [116]. Local control at 17 months was approximately 50% for a dose of 40 Gy and approaching 95% for a dose of 60 Gy. Also, in a study reporting failures within the PTV (26 patients treated with a three fraction SBRT to doses up to 60 Gy), 7 out of 8 failures were observed in patients treated to 48 Gy or less (Timmerman et al. [116]). Our study, as well as other studies exploring SBRT (e.g., Schuring and Hurkmans [11]) and lung HRT protocols demonstrate that derivation of dose-response is associated with substantial dose uncertainties. Our MC simulations show that EUD values, which quantify the biological consequences of dose distributions in PTV, vary from 57.1 to 63.7 Gy. Therefore, analyzing outcomes data resulting from the BR25 study based solely on the prescribed dose of 60 Gy would not account for diversity in

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dose to target volumes as revealed by MC. The importance of converting the MC results into absolute dose (Popescu et al. [97]) instead of simply normalising them to the prescription dose cannot be overstated. Renormalisation of MC calculated dose distributions (Calvo et al. [117]) for the purposes of comparing relative dose distributions from MC and TPS is misleading. In this study, for plans optimized with no TH corrections and recalculated with MC, the dose to the isocentre in MC simulations varied from 97.5 to 109.4% of prescription dose. It was below 98.5% for three and above 101.5% for five of the PTV. For plans optimized with TH corrections, the dose to the isocentre in MC simulations was always below 100% and as low as 95.7%. In the latter case, renormalisation of the MC results would lead to a gross misrepresentation of PTV coverage.

Our results show that optimizing plans with no TH corrections does not ensure that planning constraints for PTV coverage would be achieved when backscatter and lateral electronic equilibrium are properly accounted for in MC simulations. This revealed under-dosing is not related to the dose being calculated to water by the TPS and to tissue by MC. The observed under-dosing would be even worse if plans were optimized with TH corrections. The extent of this under-dosing depends on the dose calculation algorithm used in a specific TPS. We also question the purpose of recalculating the dose with TH corrections, as required in RTOG 0236 and 0618 protocols. Based on this investigation, this recalculation only assures that the original optimization was performed with no TH corrections. Beyond this, the results of recalculation should not be used to evaluate the quality of the plan. It should be noted that newer dose calculation algorithms for TPS like Acuros XB (Varian Medical system) can more accurately calculate the dose in regions where electronic disequilibrium occurs compared to previous dose calculation algorithms [118, 119]. Such dose calculation engine could potentially be used to optimize plans with TH corrections and ensure that planning constraints for PTV coverage would be achieved satisfying the BR25 protocol. This commercial dose calculation engine is only available for Eclipse TPS and is limiting who can have access to it. Other manufacturer potentially have or are developing dose calculation engines with similar accuracy. Another approach would be to use MC dose calculation which is freely available. Combined with the IAEA phase space file database each clinical centre can have access to the most accurate dose calculation engine.
3.5 Conclusions

Current guidelines in the hypofractionated RT and SBRT protocols for lung cancer patients with small solitary peripheral lesions require that RT plans are optimized with no tissue heterogeneity corrections. Monte Carlo simulations show that this does not ensure the desired PTV coverage, even though recalculation of the optimized plans in a commercial TPS may indicate superior coverage compared to that planned. The data presented supports our view that current clinical protocol guidelines for SBRT lung, while ensuring a “consistency of procedure” between trial participants, actually results in an inconsistency between the reported dose and the actual dose delivered to the patient. Quality Assurance procedures intended to provide accurate dose data should be based on a Monte Carlo approach, and no renormalisation of the dose distributions ought to be allowed.
Chapter 4

Monte Carlo simulations for Total Body Irradiation (TBI)

4.1 Introduction

This work was motivated by an initial study presented in Chapter 3, which demonstrates the necessity of a MC based QA process for treatments involving regions with electronic disequilibrium. Another motivation relies in the lack of an adequate QA process for total body irradiation (TBI) using a cobalt sweeping beam treatment technique.

The most common use of TBI is for patients undergoing bone marrow transplant. TBI plays an important role as the conditioning regimen for hematopoietic cell transplantation. The two main goals are to eradicate malignant cells (leukemias and lymphomas) and to elicit the immunosuppression effect on the host immune system to minimize the risk of engraftment failure. The most common chemotherapy drugs used in combination with TBI are Cyclophosphamide, Etoposide and Busulfan. TBI has major advantages over chemotherapy which include no sanctuary sparing, a homogeneous dose delivery to the entire body, no resistance when combined with other drugs and dose distributions can be altered by shielding organs at risk (lungs or kidneys) or boosting specific locations. In radiation therapy, the use of fractionation is widespread and has proved to be beneficial for normal tissue sparing while maintaining tumour control probability. The fractionation is determined using the linear quadratic model of survival cells. Cell culture studies have shown either no or very small shoulder to the survival curve for lymphocyte [120], leukemic and most human hematopoietic cells [121]. Different TBI fractionation schemes, their outcomes [15,30] and late toxicity effects have been reported [31–37]. Early toxicities of TBI are better known; the two most common acute effects are nausea and vomiting; others include xerostomia,
fatigue and diarrhea. Late toxicities of TBI conditioning regimens are less known. Long term complications include renal dysfunction, cataracts, and growth and cognitive retardation for children. The most important contributor to mortality after bone marrow transplant is interstitial pneumonitis (IP). Experimental and clinical data have confirmed that fractionated TBI reduces the incidence and mortality rate from IP [27–29]. In a study including a cohort of ≃ 1100 patients Sampath et. al. [122] found that lung shielding combined with fractionated TBI (12Gy in 6 fractions) reduces IP incidence from 11% to 2.5%. Correlation between TBI, renal dysfunction [32, 33] and Cataractogenesis [34–37] have also been reported. All these studies rely on estimated doses to the entire body and organs at risk. Performing treatment dose verification for TBI is very challenging since very limited information is available to perform quality assurance. In this chapter TBI fractionation and treatment modalities used in our institution will be described. A feasibility study on developing a robust Monte Carlo based quality assurance process for TBI treatment will be presented. Quality assurance results performed on five previously treated clinical cases are presented and specific areas of improvement will also be discussed.

4.2 TBI treatment with a sweeping cobalt beam

In our institution a prescribed dose of 12Gy at mid-separation along the treatment center axis is used for TBI treatments. This 12Gy dose is delivered in 6 fractions over 3 days, that is, twice daily, separated by at least 6 hours. Treatments are delivered using a parallel-opposed pair sweeping beam technique with extended SSD (source-surface distance ≃ 160 cm) on a Cobalt unit [123] with a $70 \times 70 \text{ cm}^2$ fields size (defined at 160 cm).

During the first part of the treatment the patient is positioned on the low couch in a supine position, while the second part the treatment is delivered with patient lying in a prone position. The cobalt unit head can swivel ±180° away from isocentre, however two micro switches reverse the sweeping direction to limit it from 40° on one side and 50° on the other side. This asymmetric angular sweep is due to the location of the treatment center defined near the umbilicus and covers the entire patient body as seen in Figure 4.1.

The large differences in SSD between the cobalt source and the umbilicus com-
4.2. TBI treatment with a sweeping cobalt beam

Figure 4.1: Schematic diagram of total body irradiation delivery technique using a Cobalt unit. The head swivel to cover the entire body of the patient. A beam flattener is used to provide beam uniformity along the sweep direction. Lung compensators are used to shield the organ and to provide a uniform dose.
Figure 4.2: The beam flattener is positioned right after the collimation system of the Cobalt 60 treatment unit (left). Patient setup using an anthropomorphic phantom is shown in the right. The patient lies on a low couch and the SSD is adjusted by using thick sheets of polystyrene placed under the patient.
4.2. **TBI treatment with a sweeping cobalt beam**

pared to body extremities (head and feet) results in a significant reduction of radiation intensity due to the inverse square law. Beam uniformity along the length of the patient is improved using a beam flattener made of Perspex, with dimensions of $70 \times 30.5 \text{ cm}^2$ and $3.8 \text{ cm}$ thick at its center. A picture of the beam flattener, Cobalt treatment unit and typical treatment setup is shown in Figure 4.2.

The goal of TBI is to deliver a uniform dose (within $\pm 10\%$ of the prescribed dose at mid-separation) to the entire body. The lower density of the lung may translate into significantly larger dose compared to body tissue, thereby compromising the dose uniformity. This overdosing of the lungs must be corrected using one of the listed methods in Task Group 29 [124]. Dose reduction in lungs is achieved using lung compensators. Lung size, shape and density can vary significantly from patient to patient, and can even vary significantly for a given patient depending on whether that patient is lying supine or prone on the couch. Consequently lung compensators are custom made for each patient, and a different set will be made for the supine and for the prone treatment.

The position of the treatment center ($T_X$ or $t_0$) below the umbilicus is adjusted based on the patient height and is identified using a lead marker. The dose prescription point is defined along the treatment centre axis at mid-separation depth. Two more localization marks are identified to position the patient and the lung compensators accurately. The first lead mark ($t_1$) is positioned approximately $3 \text{ cm}$ below the xiphoid process on the sternum and is used to position the compensators. The second lead mark ($t_2$) is placed approximately at the level of the nipples and is used to align the patient along the lasers. These points are shown in Figure 4.3.

Lung toxicity is a key factor to the success of bone marrow transplant [26, 27]. Prior to the treatment day, a radiographic film is place under the low couch, directly beneath the patient’s chest, for each treatment position, supine and prone. The film is processed and the lung compensator contours are outlined by the radiation oncologist, as shown in Figure 4.4. The optical density is measured at several locations within the lungs as well as several locations below the lungs, in a region certain to be tissue. From these optical density values, the thickness of lead compensators required can be calculated [125]. The lead marks for $t_1$ and $t_2$ appear with a higher optical density and are identified manually. A magnification factor is applied to properly scale the
dimensions at the level of the lung compensator holder. The film is also used to create a paper template containing the lung contour and lead marks positions that will be used to accurately position the lung compensators during the treatment.

Before starting the treatment, another film is acquired to verify the adequate position of the lung compensators. If necessary, the lung compensators are moved manually to a better position and another radiographic film is acquired for verification.

On a linear accelerator the treatment time is calculated by the treatment planning system and is defined in terms of monitor units or equivalently in “radiation time”. Despite that modern-day planning systems can generate complex plans, such as volumetric modulated arc therapy, it is not possible to simulate a Cobalt sweeping beam. As a result, TBI treatment time is calculated using basic dosimetric functions. The most important parameters are shown in Figure 4.5.

For each treatment position (supine and prone) the source-surface distance (SSD) is measured with a ruler. The midline separation (or equivalently the thickness of the patient) is measured using a caliper. The mid-separation depth (prescribed dose point) is determined only at the treatment centre level (along the central axis). Variation in patient thickness along the patient body is not accounted for in the treatment time calculation.

Treatment time is calculated using the average SSD and an average midline sep-
Figure 4.4: Radiographic film acquired before treatment day. A radiation oncologist has outlined the desired lung compensators shape. Also visible are the lead marks for $t_1$ and $t_2$ used for positioning.
4.2. TBI treatment with a sweeping cobalt beam

Total Body Irradiation

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Patient Setup

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</tr>
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</tr>
<tr>
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<td>11 cm superior to _t_0, _t_2</td>
<td>22.0</td>
<td>22.0</td>
</tr>
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Treatment time calculations

- Mid separation depth: \( d = \frac{l_1}{f_1} \) \( = 10.25 \) cm
- PDD (d, SSD = 160 cm): From table: 69.48
- PDD (d, SSD): \( \frac{PDD(d, SSD)}{PDD(d_0, SSD_0)} = \left( \frac{d}{d_0} \right)^{1.68} \) \( = 69.66 \)
- Reference dose per field: \( D_2 = D_{200} \cdot \frac{PDD(d, SSD)}{PDD(d_0, SSD_0)} \) \( = 143.55 \) cGy/field
- Output 35x35 @ 80 cm: \( I = \frac{20}{100} \times 35 \times 35 \times 80 \) cGy/min \( = 375.86 \) cGy/min
- TBI sweep factor (P_TBI): 0.216
- Inverse-square factor: \( P_{IS} = \left( \frac{d_0}{d} \right)^{2.0} \) \( = 0.238 \)
- Peak dose rate at treatment center: \( D_{peak} = \frac{I}{P_{IS} \times P_{TBI} \times P_{IS}} \)
- Treatment time per field: \( \tau = \frac{D_{200}}{D_{peak}} \) \( = 7.42 \) min

Figure 4.5: Important parameters used in the calculation of the treatment time and their respective mathematical formulations.
4.3 Monte Carlo Commissioning of a cobalt 60 treatment Unit

Monte Carlo methods are considered as the gold standard for dose calculations. This accuracy is dependent on how accurately the treatment unit dosimetric properties such as percent depth dose, beam profiles and output can be modelled. The virtual Monte Carlo unit must be benchmarked against measured data acquired during the commissioning. The commissioning of the Monte Carlo model for the Cobalt unit was done in collaboration with Dr. Thomas and Y. Qiu. The absolute calibration was generated by the author. The measured data used to benchmark was acquired by clinical medical physicists during the source replacement that occurred in July 2010. The Cobalt Unit (TeraTron 780C, Atomic Energy of Canada Ltd., Ottawa, Canada) was modelled using the manufacturer limited specifications available. Previous studies successfully modelled Cobalt treatment Unit [4, 126, 127] using an isotropic cylindrical source. This approach requires the detailed information of the treatment unit such as accurate dimensions, elemental composition of each component and their exact physical density. In this work the Monte Carlo model for Cobalt unit was modelled using BEAMnrc, dose scoring was performed using DOSXYZnrc code. The NRC swept Beam source was used (ISOURC 15) with the Cobalt 60 spectrum determined.
4.3. Monte Carlo Commissioning of a cobalt 60 treatment Unit

by Mora et al. [4]. The radial intensity distribution of the incident particles is shown in Figure 4.6.

In all simulations the electron and photon cutoff energies (ECUT and PCUT) were set to 0.7MeV and 0.01MeV respectively. All BEAMnrc simulations used directional bremsstrahlung splitting variance reduction (using a splitting factor of 1000). A schematic representation of the Cobalt unit model is shown in Figure 4.7. All DOSXYZnrc simulations were performed using a new source [128] capable of computing dose distributions involving continuously moving radiation source (ISOURCE 21).

The BEAMnrc model of the Cobalt unit was compiled as a shared library to allow DOSXYZnrc to use the full BEAM simulation as a particle source. The statistical error was kept within 1% by using $1.5 \times 10^8$ histories in DOSXYZnrc and a Savitzki-Golay filter. The commissioning of the Monte Carlo model was restricted to a single field size of $35 \times 35$ cm$^2$ (defined at 80 cm) matching the treatment field size used

Figure 4.6: Radial intensity distribution of the incident particles used for ISOURC 15 in BEAMnrc.
4.3. Monte Carlo Commissioning of a cobalt 60 treatment Unit

Figure 4.7: Cobalt 60 treatment unit model for BEAMnrc. The cobalt source capsule is not modelled and replaced by NRC sweeping beam using Mora [4] energy spectrum.
for TBI. The dosimetric properties of the virtual Cobalt model (percent depth dose and beam profiles at several depths) are compared with ion chamber measurements in water. These measurements were performed using a CC13 waterproof ionization chamber (Scanditronix-Wellhofer, Uppsala, Sweden). The source-to-surface distance is set to 80 cm and the field size is defined at 80 cm.

Figure 4.8 compares measured and Monte Carlo simulated percent depth dose. The data is normalized to 100% on the central axis at the depth of maximum dose (0.5 cm). Good agreement is observed between Monte Carlo and measured data.

Figure 4.9 compares measured and Monte Carlo beam profiles for 4 different depths. Good agreement is observed with dose differences within 2% except in the penumbra region.

Monte Carlo simulation reports dose scored in units of dose absorbed per particle incident on target. Linac calibration methods (conversion from dose per particle incident on the target to dose in Gy) have been reported in the literature [97, 129, 130] but are not applicable to a Cobalt unit. The calibration was performed using an experimental set up almost identical to a TBI treatment. Measurement was performed using a PTW Farmer ionization chamber in water at 160 cm SSD and at depth of 5 cm. The beam flattener was centered with the treatment center axis and ten sweep of the beam is delivered.

To create the MC phantom, the original DICOM CT images are modified using pyDicom to assign a fixed HU value inside the beam flattener (whose contour is extracted from the DICOM Structure file) and define pixels outside as air. The phantom is created using a step size CT to material density curve and PMMA material with a density of 1.18 g/cm$^3$. The dose is scored in a volume of water with dimensions of $60 \times 40 \times 140$ cm$^3$. The Beam flattener phantom is fused with the previous one using an in-house C++ code. The conversion factor (between dose per particle incident on target and absolute dose in Gy) is determined by comparison between Monte Carlo predicted dose at depth of 5 cm and measured data.
Figure 4.8: Percentage depth dose (top curve) for the $35 \times 35 \text{ cm}^2$ field size. Solid line: ion chamber data. Red line Monte Carlo simulation data. Dose difference (%) (bottom curve) between ion chamber measured data and Monte Carlo simulated data.
4.3. Monte Carlo Commissioning of a cobalt 60 treatment Unit

Figure 4.9: Off-axis profile curves for the $35 \times 35 \text{ cm}^2$ field size. Solid line: ion chamber measured data. Symbols: Monte Carlo simulated data.
Figure 4.10: Experimental setup for calibration verification. Dose at several depths along the central axis and at a depth of 5cm at several off-axis positions were measured using an ion chamber. Values were compared with Monte Carlo calculated doses.
4.4 Monte Carlo based patient specific dose verification

To verify the accuracy of the calibration, Monte Carlo calculated doses at different depths as well as off-axis were compared with ionization chamber measurements. A schematic representation of the measurement setup is shown in Figure 4.10 and results are reported in Table 4.1. We observed excellent agreement between Monte Carlo and measured data except at depth of maximum dose (0.5 cm) where accurate dose calculation is very challenging even for MC simulations and where accurate experimental measurements are difficult to perform.

<table>
<thead>
<tr>
<th>Off axis distance</th>
<th>Dose difference with calibration point measured</th>
<th>Monte Carlo</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 cm</td>
<td>-1.0 %</td>
<td>-1.0 %</td>
</tr>
<tr>
<td>30 cm</td>
<td>-3.4 %</td>
<td>-3.3 %</td>
</tr>
<tr>
<td>50 cm</td>
<td>-5.6 %</td>
<td>-5.9 %</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Depth at central axis</th>
<th>Dose difference with calibration point measured</th>
<th>Monte Carlo</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 cm</td>
<td>15.3%</td>
<td>12.2%</td>
</tr>
<tr>
<td>2 cm</td>
<td>10.7%</td>
<td>10.4%</td>
</tr>
<tr>
<td>10 cm</td>
<td>-19.0%</td>
<td>-18.2%</td>
</tr>
<tr>
<td>15 cm</td>
<td>-36.2%</td>
<td>-35.1%</td>
</tr>
</tbody>
</table>

Table 4.1: Measured and Monte Carlo calculated dose difference (%) for several different depths and several off-axis position compared to the calibration point (central axis at depth of 5 cm).

4.4 Monte Carlo based patient specific dose verification

The objective of this study is to evaluate the feasibility of developing a MC based patient-specific dose verification that includes all the components of the treatment delivery (such as the lung compensators and the beam flattener) and to estimate dose to lungs. The actual verification process during the delivery consists of a diode system used to monitor exposure during each fraction and film measurements to verify the
correct positioning of lung compensators with respect to the lungs.

4.4.1 Patient specific Monte Carlo phantom

For each case, two sets of CT images are available, one in the supine position and one in the prone position. A slice thickness of 5mm is used. DICOM CT images are modified using pyDicom to keep the original HU values inside the patient only and set all the other pixel values to air (-1000 HU). Two CT scanners are used, each having a specific electron density versus HU units relation. A specific HU to physical density curve was created for each scanner to be used in cttcreate (Figure 2.3). The resolution of the case phantom is selected to be $5 \times 5 \times 5$ mm$^3$. The coordinates of the skin markers visible in the image datasets are determined manually and used to calculate the coordinate shift necessary to align the lung compensator accurately at the lung block holder level.

4.4.2 Lung block compensators

Lung compensators for MC simulation are created from the digitized radiographic film. The contours are outlined by the user using Matlab (Natwick, MA, USA) as well as the two lead markers, $t_1$ and $t_2$, as seen in Figure 4.11. The program uses the coordinates of $t_1$ and $t_2$ manually obtained from the patient CT dataset to align the compensators on the lung block holder plane and apply a magnification factor to the lungs contour. The final step involves creating the lung compensator phantom by resampling the resolution to match the patient phantom voxel resolution and by defining the material as lead with 11.34 g/cm$^3$ density as shown in Figure 4.11.

The beam flattener MC phantom creation was described in the previous sections. In the final step an in-house C++ code is used to combine the beam flattener, the lung compensators and the case phantoms together setting the correct distances between each of these components. The distances used are shown in Table 4.2.

For memory and simulation time efficiency, a variable resolution of the final MC phantom was used in the anterior-posterior direction. For example only one voxel separates the beam flattener and the lung compensators (84.3 cm). A sagittal and axial view of the final phantom is shown in Figure 4.12 (a) and (b) respectively. We
4.4. Monte Carlo based patient specific dose verification

Figure 4.11: Digitized radiochromic film (left). Lung contours are outlined by radiation oncologists; lead markers are manually marked and are used for positioning purposes the day of the treatment. MC lung compensators phantom (right) is created based on the digitized film. The contours were slightly rotated ($t_1$ and $t_2$ are not aligned vertically), the magnification factor applied, the resolution resampled and the phantom was extended in the superior inferior direction to have the same length as the patient MC phantom.

<table>
<thead>
<tr>
<th>Component</th>
<th>Distance from source (Cobalt capsule)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beam flattener</td>
<td>55 cm</td>
</tr>
<tr>
<td>lung block compensator holder</td>
<td>139.3 cm</td>
</tr>
<tr>
<td>TBI Couch surface</td>
<td>184.5 cm</td>
</tr>
<tr>
<td>Digital imager surface</td>
<td>189.7 cm</td>
</tr>
</tbody>
</table>

Table 4.2: Distances between the Cobalt source (capsule) and different components used to create Monte Carlo phantoms.
4.4. Monte Carlo based patient specific dose verification

Figure 4.12: Sagittal (a) and axial (b) view of the final Monte Carlo phantom. Proper alignment of each the beam flattener and lung compensators can be observed.

can observe the correct alignment of the beam flattener with the patient treatment center (at umbilicus) and the correct positioning of the lung compensators on the axial view. The distances between the beam flattener, the lung compensators and patient are not displayed properly due to the inability of the software to handle variable resolution.

4.4.3 Treatment time correction

Treatment time calculation for TBI patients was presented in the previous section. The most important parameter is the peak dose rate of the cobalt source which has to be calculated for the day of the treatment due to the source exponential decay. Two other factors which are patient specific are the source-surface distance and the mid-separation depth. The variation of the treatment time with these two parameters is shown in Figure 4.13.

The midline separation data from the original treatment plan were measured by radiation therapists using a caliper with the patient lying in the treatment position. These values were compared with the midline separation measured from the DICOM
4.4. Monte Carlo based patient specific dose verification

Figure 4.13: Variation of treatment time with respect to SSD and mid-separation depth errors.
4.4. Monte Carlo based patient specific dose verification

Figure 4.14: Measured dose difference due to missing scatter in the caudal direction. For the five cases used in this study differences between 4 – 7% were observed.

CT images. Differences in position of the mid-separation depth was between 0.01 cm and up to 1.14 cm resulting in treatment time difference up to 5.8%. Treatment times were recalculated according to the CT images separation.

The patients CT images were originally acquired from ≃ 5 – 10 cm inferior to the treatment center up to the neck as seen on Figure 4.15. This proximity of the treatment center with the edge of the CT scan data can lead to large dose differences due to the lack of scatter in the caudal direction.

This underdosage was estimated experimentally. An ionization chamber was placed at depth of 13 cm in a solid water phantom. The source-surface distance
4.4. Monte Carlo based patient specific dose verification

<table>
<thead>
<tr>
<th>Plan</th>
<th>Amount of lateral scatter (cm)</th>
<th>dose difference (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>supine</td>
<td>prone</td>
</tr>
<tr>
<td>Case 1</td>
<td>7.25</td>
<td>5.75</td>
</tr>
<tr>
<td>Case 2</td>
<td>6.25</td>
<td>4.75</td>
</tr>
<tr>
<td>Case 3</td>
<td>5.25</td>
<td>9.75</td>
</tr>
<tr>
<td>Case 4</td>
<td>8.25</td>
<td>5.14</td>
</tr>
<tr>
<td>Case 5</td>
<td>6.75</td>
<td>5.25</td>
</tr>
</tbody>
</table>

Table 4.3: Distance between the dose prescription point and the edge of the MC phantom for both supine and prone positions with the corresponding dose differences in %.

was set to 160 cm and the phantom was exposed to one full TBI fraction (10 sweeps). The maximum amount of scatter in the sweeping (caudal) direction was 16 cm; the measured dose was recorded and used as baseline. Measurement was repeated with different amount of scattering material. The dose attenuation due to the missing scatter in the caudal direction is displayed in Figure 4.14.

For each of the five cases used in this study, the amount of lateral scatter in the sweeping direction and the dose difference is shown in Table 4.3. For amounts of scattering material lower than 10 cm, this can lead to differences of over 3%.

4.4.4 Results

Simulations were performed on both a prone and a supine image dataset for each case, one without tissue heterogeneity corrections (equivalent to the patient filled with water) and one with tissue heterogeneity corrections (physical densities determined from the HU values inside the CT DICOM images). Each simulation used ≃3.5 billion histories and Savitzky-Golay filter leading to uncertainties ≃ 1.5%. Simulations were performed on a cluster of six core i7 2.8GHz quad-core CPUs with simulations time ≃ 8 hours using 12 cores only. Monte Carlo calculated doses to the prescription point are shown in Table 4.4. The results presented were corrected for missing scatter and patient thickness difference between CT images and radiation therapist’s measurements.
4.4. Monte Carlo based patient specific dose verification

<table>
<thead>
<tr>
<th>Plan</th>
<th>without heterogeneity</th>
<th>with heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>supine</td>
<td>prone</td>
</tr>
<tr>
<td>Rando</td>
<td>-3.3%</td>
<td>-1.3%</td>
</tr>
<tr>
<td>Case 1</td>
<td>0%</td>
<td>1.0%</td>
</tr>
<tr>
<td>Case 2</td>
<td>-4.1%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Case 3</td>
<td>-4.1%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Case 4</td>
<td>0%</td>
<td>2.5%</td>
</tr>
<tr>
<td>Case 5</td>
<td>-1.2%</td>
<td>1.2%</td>
</tr>
</tbody>
</table>

Table 4.4: Dose difference (%) at the prescribed point between calculated doses using the spreadsheet shown in Figure 4.5 and MC simulations with and without heterogeneities.

Agreement between Monte Carlo doses and prescribed dose at mid-separation is within the TBI treatment tolerance of ±10%.

The calculated treatment time for a prescribed dose of 12 Gy at mid-separation assumes a flat surface and uniform water equivalent density inside the patient. However, patient surface and thickness can have large variations as shown in Figure 4.15 for case 3. For cases with heterogeneity corrections, the mid-separation point for prone position is located inside the spine close to the tissue-bone interface while in the supine position it is consistently in tissue equivalent material.

The MC simulated dose profile along the mid-separation line for the anthropomorphic phantom (Rando) is shown in Figure 4.16. The parallel-opposed pair technique delivers a fairly uniform dose of 12 Gy along the phantom except at the esophagus location where electronic disequilibrium occurs due to the air cavity. We can observe almost no variation in the thickness over the complete length of the phantom for both supine and prone position.

The effect of patient thickness variation on the mid-separation profile is shown in Figure 4.17 for supine position and in Figure 4.18 for prone position for case 3. We observe a large dose variation along the profile in the supine position with a large increase in the neck area. For the prone position, the dose profile varies with the thickness except at the end of the phantom where scattered dose is missing.

These fluctuations, which are not taken into account with the actual TBI treatment planning process, can have a large impact on dose uniformity and on dose

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4.4. Monte Carlo based patient specific dose verification

Figure 4.15: Sagittal view of case 3 in supine position (top) and prone position (bottom). From the CT images the skin markers position can be determined within the resolution of the images. In Prone position the mid-separation is located within the spine close to the tissue-bone interface.
Figure 4.16: Dose profile at mid-separation along the anthropomorphic Rando phantom. Very small variation in the surface shape is observed leading to fairly uniform dose profile along the phantom.
4.4. Monte Carlo based patient specific dose verification

Figure 4.17: Dose profile along the mid-separation axis defined at central axis for case 3. The dose profile increases in the neck region where tissue thickness is minimal.
4.4. Monte Carlo based patient specific dose verification

Figure 4.18: Dose profile along the mid-separation axis defined at central axis for case 3. The dose profile varies with the thickness of the patient.
Table 4.5: MC calculated mean doses to lungs and to the body for both supine and prone treatment. Compared to the prescribed dose (6 Gy for each treatment position) larger doses to lung are occurring with prone treatment and lower dose with supine treatment.

delivered to critical organs such as lungs. The estimated mean doses to the lungs and to the body are shown in Table 4.5. We observed the independence of the mean body dose with respect to the treatment position. Combining both treatment positions, the overall difference with the prescribed dose of 12 Gy to the entire body is between −5% to 0%, well within the TBI ±10% tolerance.

We noticed a systematic overdosing and underdosing of the lungs for the prone and the supine treatment position respectively. This effect is a consequence of the patient anatomy deformation. In supine positions, a larger volume of the lungs is located below the mid-separation while a larger volume of the lung is located above the mid-separation for patients lying in prone position. The left lung deformation and positioning is constrained by the proximity of the heart which tends to push the left lung toward the posterior in the prone position, and in the anterior direction in the supine position. An example is shown in Figure 4.19 for case 5.

This constrained positioning and deformation translates into larger variation of the mean left lung dose with respect to the prescribed dose as seen in Table 4.5. These variation are significant, between −18.4% to −5% for left lung and between −5% to 0% for right lung in supine position. Even larger variation are observed for the prone position with a 10% – 20% difference for left lung and a 8.3% – 18.3% difference for right lung. Combining both treatment positions leads to dose differences between −0.7% and 7.5% within the TBI tolerance. This means that only the mean dose to
4.5 Discussion and conclusion

Figure 4.19: Lung deformation and position variation dependence on treatment position. The heart is pushing the left lung towards the anterior in the supine position and towards the posterior in the prone position.

the whole organ is within the tolerance, large overdosage and underdosage of portion of the lungs could potentially occur. The dose profile in both lungs at mid-separation for case 3 is shown in Figure 4.20 for supine position and in Figure 4.21 for prone position. The lung regions along the profile are highlighted with a gray shaded area. Dose variation along the profile is within the TBI tolerance except around the arms area due to the proximity with the skin surface and to lack of lateral scatter.

4.5 Discussion and conclusion

The aim of this study was twofold: 1) to investigate the feasibility of developing a MC based patient specific QA system for TBI treatments including all the components and 2) to estimate the dose to the lungs. We have demonstrated the possibility of developing a patient specific QA system that includes the beam flattener and the tailored lung compensators. The system designed uses the original patient CT dataset to create the MC phantoms and to get accurate patient thickness at the treatment center. Treatment time (and therefore dose) was found to be very dependent on this patient specific parameter. Another crucial parameter for accurate dose verification at treatment center was found to be the amount of material available between the central axis and the phantom edge for scatter (in the caudal direction). Variation up to 7% have been observed. This limitation could easily be overcome by increasing
4.5. Discussion and conclusion

Figure 4.20: Dose profile at mid-separation across case 3 in supine position. The lung region is highlighted with a gray shaded area.
4.5. Discussion and conclusion

Figure 4.21: Dose profile at mid-separation across case 3 in prone position. The lung region is highlighted with a gray shaded area.
the length of the CT scan for TBI patients. Good agreement was observed between calculated doses to the prescription point and MC simulations with and without tissue heterogeneity corrections. The system presented in this work takes into account all the specificities of the patient anatomy such as patient thickness variation along the sweeping direction, material density inside the patient and anatomical contours. Organ shape and position can experience large variation between the supine and prone position. Moreover, only one CT scan in each position is available making it difficult to correlate voxels between these two scans\(^2\). Therefore, only the mean dose to the entire organ of interest could be accurately estimated without making any approximation as it is the case in using a deformable algorithm. The mean dose to the whole patient body scanned was found to be in good agreement with the prescribed dose for each treatment position. However very large discrepancy for the mean dose to each lung per treatment position was observed. This discrepancy was found to be treatment position specific. In the supine position a larger volume of both lungs are below the mid-separation leading to lower doses (bigger depth). The opposite phenomenon was observed for the prone position. Left lung dose differences was found to be the largest due to the proximity of the heart. Nevertheless the sum of each treatment position lead to good agreement with TBI tolerances of ±10%. The results presented clearly demonstrate that for organs with large motion or deforming potential only the mean dose can be estimated with a parallel-opposed pair treatment technique. Treatment delivery using VMAT with couch motion would be less sensitive to organ motion and deformation. Moreover, this treatment technique would allow to tailor the dose to each organs of interest and deliver a more uniform dose to the whole body for each patient. More stringent dose tolerances could also be applied. This method requires a new MC based verification process for VMAT delivery (e.g. RapidArc) that is presented in the following chapters.

\(^2\)Monte Carlo dose summation of the supine and the prone TBI treatment position using a Cobalt unit was recently reported \([131]\). The total dose was calculated using the VelocityAI software which relies on deformable algorithms.
Chapter 5

Monte Carlo based, patient-specific RapidArc QA using Linac log files

5.1 Introduction

An area of current interest in radiation therapy is the commissioning and quality assurance (QA) of the RapidArc\textsuperscript{TM} (Varian Medical Systems, Palo Alto, CA) treatment delivery system. Clinical studies to assess the benefits of RapidArc over IMRT are being actively investigated \cite{132,134}. Such benefits may include better target coverage homogeneity and shorter delivery time. One of these studies has shown that RapidArc delivers the dose using \sim 40\% less monitor units compared to IMRT for prostate plans \cite{132}. The planning algorithm is based on the Direct Aperture Optimization method and uses progressive sampling as described by Otto \cite{55}.

An arc is approximated by control points representing a set of static fields characterized by their angle, aperture and weight. Between two control points, leaf speed, dose rate and gantry rotation speed remain constant. The optimized dose distribution is delivered in a single 360° gantry rotation. The dosimetric accuracy of the TPS dose calculation is dependent on the sampling of the control points.

A commissioning and QA protocol for RapidArc was recently proposed by Ling et al.\cite{135}. However, few beam delivery accuracy studies have been reported \cite{134,136} to date. Those studies that have been reported use 2D film dosimetry or diode arrays. Using three different dosimetric systems (IBA IMRT MatriXX with MULTICube, PTW 2D-ARRAY seven29 with OCTAVIUS, and Scandidos Delta4), Korreman et al.\cite{136} demonstrated the consistency and accuracy of RapidArc treatment delivery with Gamma values [acceptance criteria of 3%/3mm distance to agreement (DTA)] below 1 in over 90\% of the measured points. Limitations of such experimental devices
5.1. Introduction

include a lack of dosimetric accuracy for film dosimetry and spatial resolution issues for 2D-arrays of diodes. Due to the complexity of RapidArc treatment delivery, an accurate high resolution three dimensional (3D) quality assurance system would be ideal.

Monte Carlo (MC) simulations can be used to provide 3D absolute dose information. Monte Carlo dose verification for Intensity Modulated Arc Therapy (IMAT) was proposed by Li et al.\cite{137} where the gantry rotation was simulated by a series of static beams with 10 degree sampling. Using a similar approach, Bush et al.\cite{138} have shown that a series of 176 static fields was adequate to accurately simulate (within 1%) RapidArc plans. This sampling is similar to that used by the TPS and it does not allow us to assess the discrepancy introduced between the discrete plan and the continuous delivery. Another approach proposed by Chow et al.\cite{139} was to use a modified version of SRCXYZ source code to uniformly sample a continuous gantry rotation using a phase space file. This group demonstrated that this would lead to better agreement between Monte Carlo and measurements (within 2%) compared to the 10 degree sampling used by the TPS. The potential use of DynaLog files for IMRT QA was suggested by Litzenberg et al.\cite{140}. The process was incorporated into Monte Carlo simulations by Luo et al.\cite{141} for static IMRT delivery. Teke et al.\cite{142} applied it to dynamic IMRT delivery and to a pre-cursor to the commercial RapidArc code.

The purpose of this study is to present a Monte Carlo based RapidArc QA process using the Linac log files and to directly assess the dose distribution discrepancy introduced between the discretized plan and the continuous delivery. A new DOSXYZnrc source developed by Popescu and Lobo\cite{128} was used to compute the dose distribution due to a continuously variable beam configuration, involving (as in the case of RapidArc) continuously moving gantry, dynamic multileaf collimator (MLC) motion and variable dose rate. The new Monte Carlo source is capable of simulating both the continuous gantry motion (for actual beam delivery verification) and series of fixed gantry angles (for verification of the Eclipse TPS dose calculation). The method presented in this work can be readily applied by any BEAMnrc/DOSXYZnrc \cite{84,93,106} user.
5.2 Methods and materials

The work presented here was performed with a Varian 21IX CLinac equipped with a Millenium 120 leaf MLC. The treatment sites included prostate, head and neck, brain, as well as several abdominal sites in paediatric cases. All plans were optimized with Eclipse TPS version 8.6 using version 8.2.23 of the analytical anisotropic algorithm for a 6MV photon beam with a grid size of 2.5 mm. The plans consist of a single counterclockwise full arc with 179° to 181° gantry angle range (IEC scale). A RapidArc plan contains the relationships between cumulative dose versus gantry position and MLC leaves position versus gantry angle. This relationship is specified using 177 control points (defining 176 gantry segments) between which the gantry rotation speed, the dose rate and MLC leaf speed remains constant. The treatment is controlled by Clinac and the MLC controller using two Segmented Treatment Table file (STT files) containing respectively gantry angle versus cumulative dose relationship and MLC versus gantry angle relationship.

5.2.1 Monte Carlo codes used and their simulation parameters

For our simulations the BEAMnrc/DOSXYZnrc (National Research Council of Canada, Ottawa, ON, Canada) Monte Carlo system, based on the underlying EGSnrc[80] particle transport code is used. The complete details of the BEAMnrc/DOSXYZnrc parameters used have been presented elsewhere [143]. Plan parameters for the Monte Carlo simulations are extracted from the DICOM plan file exported from the treatment planning system using a modified version of the Vega DICOM library[91]. The dose distributions are calculated with DOSXYZnrc and are converted to absolute dose using a virtual linac calibration method that fully accounts for the backscatter to the monitor chamber of any given treatment field[97]. Denoising of the Monte Carlo dose distributions was performed using a 3D Savitzky-Golay[144] adaptive window digital filter. This method fits the local data to a polynomial curve by minimizing a least squares objective function. The filter coefficients will vary as it moves across the data set as they are influenced by the element values and their associated uncertainty within the smoothing window. The appropriate size for each dimension of the 3D smoothing window is queried based on a chi-squared test. The usefulness of a 3D
Savitzky-Golay filter for Monte Carlo dose calculation applications was first explored by Kawrakow\cite{145}. The final dose distribution is converted into DICOM format\cite{91} and imported into the TPS.

### 5.2.2 Monte Carlo simulations of RapidArc beam delivery

A new DOSXYZnrc source was developed, complementing the existing nine sources of that code and hence referred to as ‘source 20’\cite{128}. This source can be used to compute the dose distribution due to a continuously variable beam configuration, involving (as in the case of RapidArc) continuously moving gantry, dynamic MLC motion, and variable dose rate. In addition, our new source can accommodate collimator rotation, couch rotation and translation in any direction, and arbitrary isocentre motion with respect to the patient, while the beam is on. Intensity modulation is achieved by simulating particle transport through the moving multileaf collimator (MLC), using the code of Siebers\cite{85} here referred to as the ‘VCU code’.

Traditional MC approaches to intensity modulated arc therapy (including RapidArc) presented in the literature involve a superposition of several static simulations. To avoid the pitfalls of poor space and time resolution, such brute-force modelling requires a large number (of the order of 100) of individual simulations, correspondingly involving the reading, writing, storage and transfer of a large number of phase space and 3D dose files. The number of static simulations to be superimposed is arbitrary, but constrained by the computing resources at the disposal of the user. In contrast, our approach using ‘source 20’ is radically different and eliminates the intermediate phase spaces altogether, allowing us to model the actual RapidArc beam delivery, characterized by continuous gantry rotation and MLC movement while the beam is on. To achieve this, the codes that model the linac and the MLC (the BEAMnrc and VCU codes, respectively) are compiled as shared libraries, which are dynamically loaded in the computer memory at run time and deliver particles for the patient dose deposition simulation. This approach was inspired by Kawrakow and Walters\cite{146}, who have discussed the disadvantages of using intermediate phase space files and have shown that efficient MC calculations for photon beams can be performed using DOSXYZnrc with a BEAMnrc source (known as ‘source 9’). A full RapidArc beam delivery is thus simulated in a single DOSXYZnrc run, with only one 3D dose file.
being generated. Our current choice is to have 10,000 control points per gantry arc, but the software allows an arbitrarily high degree of spatial and temporal resolution. A detailed description of ‘source 20’, including other applications besides RapidArc, will be the subject of a separate publication.

### 5.2.3 RapidArc DynaLog files

Two sets of DynaLog files are created separately by the Clinac and the MLC controller. The Clinac DynaLog file contains the treatment setup information, dynamic beam statistics (dose standard deviation and dose-position standard deviation) and both the planned cumulative dose delivered (MU) versus gantry angle (STT) and the actual cumulative dose delivered versus the actual gantry angle. These parameters are only recorded for each STT control point. An extensive summary of the data contained in the MLC DynaLog files can be found elsewhere\[147, 148\]. The most relevant information to this study contained in the log-files are the gantry position (in Varian Standard rotational scale), the beam status (on or off) and the calculated and actual position of each leaf. The data is acquired every 50 ms and recorded at the end of the treatment. For each MLC DynaLog entry the cumulative dose is obtained by interpolation of the Clinac DynaLog file data. Leaf positions are recorded as ‘motor counts’ and need to be converted into physical positions defined at the isocenter plane. The conversion factor was found to be 512 counts/cm which is in agreement with previous studies which used static delivery [141] [147]. Data contained in the DynaLog files is used to create a new MLC file where all the recorded leaf positions and ‘beam hold off’ status are taken into account. Their format is identical to the treatment planning system MLC files. This conversion is done with an in-house developed software written in MATLAB (Natick, MA, USA).

### 5.2.4 RapidArc comparisons

An in-house developed software written in Matlab (Natick, MA, USA) is used to create a DOSXYZnrc input file for ‘source 20’ from the log-files data. Two options are available:

1. Creating an input file using the full benefit of ‘source 20’ where the gantry and
the MLC are constantly moving thus reproducing the real delivery conditions of the treatment.

2. Creating an input file simulating 176 fixed gantry angles where each gantry angle is defined by computing the mean angle between two control points as described by Bush et al. [138].

For each plan three Monte Carlo dose calculations were performed; one using continuous gantry rotation with LINAC log files (referred as S10 Dyna), one using continuous gantry rotation with TPS generated MLC control files (referred as S10 DVA) and one using 176 fixed gantry angles with TPS MLC control files (referred as S10 176GA). Comparison between Eclipse TPS and Monte Carlo using TPS generated MLC files provides us QA on the treatment planning dose calculations, while comparison between Monte Carlo using TPS generated MLC files and Monte Carlo using LINAC log files gives us machine performance QA. The Monte Carlo 176 gantry angle simulation is used to verify that the sampling used in the Eclipse TPS does not introducing additional discrepancy. A schematic representation of the different tests performed is shown in Figure 5.1. The performance of dose-rate and gantry speed variation and MLC position accuracy during delivery was analyzed using DynaLog files.

5.2.5 3D gamma factor

Dose verification of a patients treatment plan prior to therapy is an essential part of a comprehensive quality assurance program. Several tools are available to provide information on how well two dose distributions (e.g. calculated vs. measured) agree. These tools include qualitative isodose overlays, quantitative dose subtraction methods, distance-to-agreement (DTA) methods [149], or some combination of those listed [150, 151]. Low et al. [58, 59] introduced the ‘gamma factor’, \( \gamma \), which is a composite method comprised of the results for a dose difference and a distance-to-agreement comparison. The gamma factor is considered to have a pass rating when the value is \(< 1\).

The gamma-factor analysis can be applied to a 1D profile, or to a n-dimensional gamma map. Typically, quality assurance methods compare a 3D dataset with a
5.2. Methods and materials

Figure 5.1: Schematic representation of the QA tests performed in this study.
5.2. Methods and materials

2D dataset (e.g. 3D calculated v.s. 2D measured film or EPID doses). The quality assurance method used here involves the comparison of two 3D datasets (calculated doses from the TPS v.s. Monte Carlo simulated doses). The availability of two 3D datasets offers a unique opportunity to implement the gamma factor comparison in three dimensions. The user specifies an acceptability criterion for each test; in this study, a 3% dose difference and 3 mm distance-to agreement is used. For the 3D gamma comparison, only absolute dose voxels within a region of interest were considered. This region of interest encompasses dose voxels that have a value higher or equal to 50% of the maximum dose. A PASS status for a given 3D gamma comparison is defined to be when more than 90% of the datapoints have a gamma value < 1. This value was established by reviewing more than 50 test patient IMRT QA datasets. In addition to a 3D gamma factor test, traditional dose comparison methods are also available to the user (e.g. dose difference, distance to agreement and isodose overlays). This study reports 3D gamma values as a measure of agreement between dose distributions.

5.2.6 Comparison with dose measurements

In order to verify the results of the MC simulations presented in this work, we performed measurements in a cylindrical water phantom (28cm in diameter and 30cm in length, consisting of an acrylic shell of about 0.5cm thickness, filled with water), using a calibrated Farmer chamber (PTW-Freiburg, Freiburg, Germany), with an active volume of 0.6 cm$^3$. All experimental results were a ratio of test condition charge readings to calibration conditions charge readings, thus removing any uncertainty due to non-ideal Linac calibration, which could introduce another 1-2% uncertainty. In the TPS, the chamber cavity is visible on the phantom CT dataset. The active chamber volume is contoured and ‘chamber doses’ calculated by the TPS are reported as a mean dose to this volume. The Monte Carlo calculated doses are also imported into the TPS for dose distribution comparison purposes and the MC ‘chamber dose’ is reported as a mean dose to the same contoured chamber volume.
5.2. Methods and materials

5.2.7 Non coplanar SBRT RapidArc

Three RapidArc SBRT lung plan were created. Each plan is composed of three partial arcs with two non coplanar fields (couch rotated). The geometrical details are shown in Table 5.1.

<table>
<thead>
<tr>
<th>Plan</th>
<th>Field size (cm$^2$)</th>
<th>Gantry start angle</th>
<th>Gantry stop angle</th>
<th>Couch angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plan 1</td>
<td>4.4×4.5</td>
<td>180.1°</td>
<td>300°</td>
<td>0°</td>
</tr>
<tr>
<td></td>
<td>40°</td>
<td>300°</td>
<td>30°</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40°</td>
<td>300°</td>
<td>330°</td>
<td></td>
</tr>
<tr>
<td>Plan 2</td>
<td>5.8×7.4</td>
<td>179.9°</td>
<td>60°</td>
<td>0°</td>
</tr>
<tr>
<td></td>
<td>320°</td>
<td>60°</td>
<td>30°</td>
<td></td>
</tr>
<tr>
<td></td>
<td>320°</td>
<td>60°</td>
<td>330°</td>
<td></td>
</tr>
<tr>
<td>Plan 3</td>
<td>7.2×7.1</td>
<td>180.1°</td>
<td>300°</td>
<td>0°</td>
</tr>
<tr>
<td></td>
<td>40°</td>
<td>300°</td>
<td>30°</td>
<td></td>
</tr>
<tr>
<td></td>
<td>300°</td>
<td>40°</td>
<td>330°</td>
<td></td>
</tr>
</tbody>
</table>

Table 5.1: Geometrical properties of the beam arrangement for the SRBT RapidArc plans. Each plan is composed of three partial arcs, one coplanar and two non coplanar.

A three dimensional representation of the trajectories of the partial arcs is displayed in Figure 5.2 for plan 2.

For each plan a Monte Carlo dose calculations using continuous gantry rotation and TPS generated MLC control files was performed. Plan parameters for the Monte Carlo simulations were extracted from the DICOM RT plan file using a python code and pydicom. The AVID IMRT verification phantom (a 18.5cm cube made of solid water-equivalent material) was used for dosimetric verification. Part of the phantom was placed on the over edge of the MedTech S-Frame to avoid any beam attenuation along the beam delivery trajectories, as shown in Figure 5.3.

Ion chamber measurements were performed using a NAC009 TRIAX miniature ionization chamber and A Victoreen Model 530 precision electrometer.

In the TPS, the chamber cavity is visible on the phantom CT dataset. The active chamber volume is contoured and chamber doses calculated by the TPS are reported as a mean dose to this volume. MC predicted dose to chamber were compared with both Eclipse TPS calculated dose and ionization chamber measurements. MC
5.3 Results

5.3.1 RapidArc DynaLog analysis

Ten clinically acceptable RapidArc treatment plans were delivered for various tumor sites and both the Clinac and MLC DynaLog files were recorded to assess the machine performance. The MU and MU-position standard deviation reported in the Clinac Dynalog file beam statistics are listed in Table 5.2; these values are in agreement with Ling et al. [135]. The discrepancy range between actual MU and planned MU (ΔMU range) and between actual MU-position and planned MU-position (ΔGA range) are also listed in this table.

Good agreement was found between actual MU vs. gantry position and planned MU vs. gantry position for all patients (low MU standard deviation values). Figure 5.4 shows this relationship for plan 4 which has large ΔMU and ΔGA range.

MLC log-files contained between 1500 to 2000 recordings. Their analysis showed
5.3. Results

Figure 5.3: Part of the IMRT AVID verification phantom is placed over the edge of the couch to prevent couch attenuation along the radiation beam trajectories.

Figure 5.4: Planned gantry angle as a function of cumulative MU (dashed) and actual gantry angle as a function of cumulative MU (dashed dotted) for plan 4.
5.3. Results

<table>
<thead>
<tr>
<th>Plan #</th>
<th>#MU</th>
<th>MU std (MU)</th>
<th>ΔMU range (MU)</th>
<th>GA std (deg)</th>
<th>ΔGA range (deg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>400</td>
<td>0.05</td>
<td>[-0.01;0.06]</td>
<td>0.35</td>
<td>[-0.47;0.13]</td>
</tr>
<tr>
<td>2</td>
<td>328</td>
<td>0.06</td>
<td>[0.02;0.07]</td>
<td>0.36</td>
<td>[-0.47;0.1]</td>
</tr>
<tr>
<td>3</td>
<td>373</td>
<td>0.03</td>
<td>[-0.17;0.04]</td>
<td>0.35</td>
<td>[-0.5;0.23]</td>
</tr>
<tr>
<td>4</td>
<td>370</td>
<td>0.06</td>
<td>[-0.2;0.07]</td>
<td>0.35</td>
<td>[-0.55;0.13]</td>
</tr>
<tr>
<td>5</td>
<td>258</td>
<td>0.05</td>
<td>[-0.04;0.06]</td>
<td>0.36</td>
<td>[-0.7;0.07]</td>
</tr>
<tr>
<td>6</td>
<td>487</td>
<td>0.05</td>
<td>[0.02;0.07]</td>
<td>0.35</td>
<td>[-0.5;0.12]</td>
</tr>
<tr>
<td>7</td>
<td>533</td>
<td>0.06</td>
<td>[-0.09;0.07]</td>
<td>0.35</td>
<td>[-0.7;0.1]</td>
</tr>
<tr>
<td>8</td>
<td>398</td>
<td>0.06</td>
<td>[0.02;0.06]</td>
<td>0.37</td>
<td>[-0.5;0.1]</td>
</tr>
<tr>
<td>9</td>
<td>480</td>
<td>0.05</td>
<td>[-0.06;0.07]</td>
<td>0.36</td>
<td>[-0.77;0.12]</td>
</tr>
<tr>
<td>10</td>
<td>405</td>
<td>0.05</td>
<td>[-0.19;0.07]</td>
<td>0.35</td>
<td>[-0.57;0.05]</td>
</tr>
</tbody>
</table>

Table 5.2: RapidArc CLinac DynaLog file analysis.

that a few ‘beam off’ events occurred (‘beam on’ flag was set to 0). A surge of beam hold-offs (100-170 hold-off events) was observed during this study. They were caused by a slower gantry rotation speed compared to the recommended specification for RapidArc. A minor tweak of the AMC motor driver board was done to set the gantry speed to exactly 60 s per rotation (recommended specification) and the number of hold-off occurrence reverted to about 10. All the plans were redelivered after tweaking the gantry speed.

These hold-offs were not triggered by the MLC (MLC beam hold-off flags were all set to 0) and leaf position errors were always below the tolerance level (default value is set to 5mm) for each plan, as shown in Table 5.3. Note that ≃80% of position errors are within 0.5 mm and over 95% are within 1 mm which are comparable to results reported by Ling et al. [135].

5.3.2 Monte Carlo dose verification

Throughout this section, the percent difference (% diff) between MC values and experimental ones is calculated as \(\frac{(MC - \text{Exp})}{\text{Exp}}\times100\%\). The comparison between Monte Carlo simulated doses, RapidArc Treatment Planning System calculated doses and chamber measurements is shown in Figure 5.5. MC calculated doses to the active volume of the ionization chamber are in good agreement with experimental measure-
5.3. Results

Table 5.3: RapidArc MLC DynaLog file analysis.

<table>
<thead>
<tr>
<th>Plan</th>
<th># Beam-on set to 0</th>
<th>Leaf Position Errors (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt;0.05 mm</td>
</tr>
<tr>
<td>1</td>
<td>8</td>
<td>58.79</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>60.90</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>63.78</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>60.64</td>
</tr>
<tr>
<td>5</td>
<td>11</td>
<td>67.89</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>61.84</td>
</tr>
<tr>
<td>7</td>
<td>8</td>
<td>59.12</td>
</tr>
<tr>
<td>8</td>
<td>9</td>
<td>60.10</td>
</tr>
<tr>
<td>9</td>
<td>6</td>
<td>57.55</td>
</tr>
<tr>
<td>10</td>
<td>6</td>
<td>58.42</td>
</tr>
</tbody>
</table>

ments, with percent differences less than 2.1% (within the clinical tolerance) demonstrating the accuracy of our system. The agreement between measurements and TPS calculated doses to the chamber was dependent on the dosimetric leaf gap value.

A 2D axial, coronal and sagittal slice dose distribution for plan 1 on a water-equivalent cylinder is shown in Figure 5.6. Good dose distribution agreement between RapidArc and all types of Monte Carlo simulations was observed for all plans. Figure 5.7 shows the dose distribution (isodose lines in %) for plan 4 RapidArc and for all MC simulations. The absolute dose difference between RapidArc and all types of Monte Carlo simulations is shown in Figure 5.8. Larger discrepancies can be observed in high dose gradient regions with differences as large as 8cGy shown with red arrows (a dose of 170.7 cGy was measured for this plan with the ionization chamber).

A thorough analysis of the dose distribution was performed with the 3D gamma test with a 3% and 3mm DTA criteria. These criteria was chosen for comparison purposes with a study assessing the RapidArc delivery accuracy using three different dosimetric systems [136]. In this section the RapidArc TPS plan was used as the reference dose distribution. For all plans good agreement was observed between RapidArc TPS and all types of MC dose distributions with gamma values below 1 in >95% of the points considered. The results are shown in Table 5.4 and are in
5.3. Results

Figure 5.5: RapidArc TPS and Monte Carlo calculated dose to the active volume of the ionization chamber relative to measurements in a water equivalent cylinder phantom. MC uncertainty is $\approx 1.4\%$.

Figure 5.6: Dose distribution comparison between RapidArc TPS (left) and Monte Carlo with DynaLog files (right) on a water-equivalent cylinder for Plan 1.
5.3. Results

Figure 5.7: Dose distribution comparison between RapidArc TPS (top left), S10 Dyna (top right), S10 DVA (bottom left) and 176 GA (bottom right) on a water-equivalent cylinder for Plan 4.
5.3. Results

Figure 5.8: Absolute dose difference between RapidArc TPS and S10 DVA (left), RapidArc TPS and S10 176 GA (center) and RapidArc TPS and S10 DVA (right) on a water-equivalent cylinder for Plan 4. Orange, Purple and white isodose line (respectively -2cGy, -4cGy and -6cGy) correspond to higher RapidArc TPS doses compared to MC while dark blue, red and green isodose lines (respectively +2cGy, +4cGy and +8cGy) correspond to lower RapidArc TPS doses compared to MC.

agreement with Korreman et al. [136].

<table>
<thead>
<tr>
<th>Plan number</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>S10 Dyna</strong></td>
<td>99.2%</td>
<td>97.5%</td>
<td>98.8%</td>
<td>99.4%</td>
<td>98.7%</td>
<td>98.5%</td>
<td>98.4%</td>
<td>99.0%</td>
<td>98.4%</td>
<td>98.7%</td>
</tr>
<tr>
<td><strong>S10 DVA</strong></td>
<td>99.2%</td>
<td>97.5%</td>
<td>95.7%</td>
<td>98.2%</td>
<td>99.1%</td>
<td>97.8%</td>
<td>96.9%</td>
<td>99.2%</td>
<td>96.5%</td>
<td>98.8%</td>
</tr>
<tr>
<td><strong>S10 176GA</strong></td>
<td>99.0%</td>
<td>96.9%</td>
<td>97.2%</td>
<td>96.5%</td>
<td>99.1%</td>
<td>98.6%</td>
<td>95.9%</td>
<td>97.8%</td>
<td>97.3%</td>
<td>98.0%</td>
</tr>
</tbody>
</table>

Table 5.4: 3D Gamma analysis of the dose distributions with 3% 3mm DTA criteria.

An example of the output from the 3D gamma test is shown in Figure 5.9. The program displays the reference dose distribution in the axial [fig.5.9(a)] coronal [fig.5.9(d)] and sagittal [fig.5.9(g)] plane, the MC dose distribution in the same planes (not shown), the dose difference (MC-RapidArc) in the axial [fig.5.9(b)] coronal [fig.5.9(e)] and sagittal [fig.5.9(h)] planes and the gamma test results for the current slice in the axial [fig.5.9(c)] coronal [fig.5.9(f)] and sagittal [fig.5.9(i)] planes.
Figure 5.9: Dose distribution calculated by the TPS, dose difference MC minus TPS, and Gamma value for axial [(a),(b) and (c), respectively], coronal [(d),(e) and (f), respectively] and sagittal slice [(g),(h) and (i), respectively].
5.3.3 Non coplanar SBRT RapidArc

The comparison between Monte Carlo simulated doses, RapidArc treatment Planning system calculated doses, and ionization chamber measurements is shown in Table 5.5. Very good agreement is observed between TPS and MC calculated dose (within 1.6%). A systematic shift between calculated and measured doses was observed and is being investigated. Nevertheless it is within our clinical tolerance of ±5% for SBRT treatment.

For coplanar treatment, the phantom and the ionization chamber can be accurately positioned using the lasers. These lasers cross over at the isocentre position. Monthly QA is performed to verify good position agreement between mechanical isocentre and laser intersection (within a radius of 2mm). However these lasers can no longer be used for accuracy positioning for non coplanar treatments (couch rotation).

The phantom is positioned in the coplanar position and then rotated to the correct position. The couch rotation accuracy is checked monthly but can introduce some errors. Another factor than can play a significant role in this discrepancy is the chamber response for non coplanar modulated beams. As we can see performing accurate chamber measurements for non coplanar SBRT treatment is very challenging.

<table>
<thead>
<tr>
<th>Plan #</th>
<th>measured dose (cGy)</th>
<th>TPS calculated dose (cGy)</th>
<th>MC calculated dose (cGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plan 1</td>
<td>1613.3</td>
<td>1648.6 (+2.2%)</td>
<td>1675.0 (+3.8%)</td>
</tr>
<tr>
<td>Plan 2</td>
<td>1295.4</td>
<td>1337.1 (+3.2%)</td>
<td>1350.6 (+4.2%)</td>
</tr>
<tr>
<td>Plan 3</td>
<td>1301.0</td>
<td>1340.8 (+3%)</td>
<td>1349.9 (+3.7%)</td>
</tr>
</tbody>
</table>

Table 5.5: Measured and calculated dose to chamber. Dose difference (in percent) between calculated and measured is displayed in parenthesis. The measured dose is used as reference.

Good dose distribution agreement between TPS and MC for plan 2 and plan 3 is observed with gamma values below 1 in >92% of the points considered. Larger discrepancies are observed for plan 1, results are shown in Table 5.6. This can be explained by the small field size of this plan leading to a smaller number of slices included in the 3D gamma analysis (meaning a smaller number of voxels). Therefore the weight of each voxels not satisfying the DTA criteria for the total 3D gamma results is greater.
### 5.4. Discussion

<table>
<thead>
<tr>
<th>Plan #</th>
<th>3%/3mm DTA</th>
<th>Maximum field size (cm$^2$)</th>
<th>number of slices</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plan 1</td>
<td>82.9%</td>
<td>$3.5 \times 4$</td>
<td>16</td>
</tr>
<tr>
<td>Plan 2</td>
<td>92.7%</td>
<td>$4.5 \times 6$</td>
<td>24</td>
</tr>
<tr>
<td>Plan 3</td>
<td>96.0%</td>
<td>$6 \times 6.5$</td>
<td>31</td>
</tr>
</tbody>
</table>

Table 5.6: 3D gamma analysis of the dose distribution for non coplanar SBRT plans using 3%/3mm DTA criteria. Maximum field size and number of slice (or volume) considered for the analysis is also displayed.

A 2D axial, coronal and sagittal slice dose distribution for plan 2 and plan 3 on the AVID IMRT verification phantom is shown in Figure 5.10 and Figure 5.11 respectively. Good dose distribution agreement between MC and TPS was observed for all plans.

### 5.4 Discussion

The delivery of RapidArc treatments involves variable dose rate, variable gantry rotation speed and dynamic leaf motion requiring additional QA tests. The CLINAC log files analysis have shown good agreement between cumulative monitor units delivered (MU) and gantry angle positions. The mean MU and MU-position standard deviation were $\simeq 0.052 MU$ and $\simeq 0.355$ degrees respectively and showed no visual significant difference. Analysis of the MLC log file indicated good agreement in the leaf actual positions with respect to the planned positions ($\simeq 95\%$ of the leaves are within 1 mm of the planned positions). A few beam hold-offs occurred with none of them being requested by the MLC. These results indicate that the MLC constraints are properly taken into account during the optimization process and that a $2.5$ mm tolerance could be used without triggering beam hold-offs. A large number of beam hold-offs were observed for gantry rotation speed below the recommended specification for RapidArc. The extensive analysis of the log files has confirmed the delivery accuracy of RapidArc treatments.

The dose differences between MC calculated doses to the active volume of the ionization chamber and measurements in a water equivalent phantom are within the clinical tolerances. Figure [5.5] shows that the three different MC calculated doses to
5.4. Discussion

Figure 5.10: Dose distribution comparison between Monte Carlo (left) and Eclipse TPS (right) on the AVID phantom for Plan 2.

the chamber are within the MC uncertainty and are dosimetrically equivalent. Thus, it validates that the sampling used ($\approx 2^\circ$ per gantry segment) during RapidArc optimization is adequate. More importantly it highlights the machine performance and confirms the log file analysis results.

A previous study has shown the RapidArc delivery accuracy using three different dosimetric system with gamma values below 1 in $> 90 - 95\%$ of the points considered using a $3\%/3\text{mm}$ criteria\cite{136}. Table 5.4 shows similar results for all types of MC calculated dose distributions. This highlights again the accuracy of our method and the machine performance. Also, comparison between RapidArc TPS and Monte Carlo using TPS generated MLC files provides us QA on the treatment planning dose calculations in water-equivalent material.

For the non coplanar SBRT plans very good agreement was observed between MC and Eclipse TPS calculated doses. Larger discrepancies with ion chamber measurement were observed but were within our clinical tolerances of $\pm 5\%$ for SBRT treatments. Performing accurate chamber measurements for this type of treatment is very challenging.
Figure 5.11: Dose distribution comparison between Monte Carlo (left) and Eclipse TPS (right) on the AVID phantom for Plan 3.
5.5 Conclusion

A new Monte Carlo based patient specific RapidArc quality assurance system using the LINAC log files was presented in this work. RapidArc was officially released for clinical use in our center in January 2009 (first center in Canada) and the first experimental results are reported here. Our study included an extended log files analysis, 3D gamma test analysis on the dose distributions and comparison between MC and RapidArc TPS calculated dose with ionization chamber measurements. The majority of leaf position errors were found to be less than 1 mm and leading to no significant dosimetric differences. It is recommended that the conversion factor (converting ‘motor counts’ values to physical leaf positions defined at isocenter plane) should be validated independently and checked routinely. The actual cumulative dose (MU) and the actual MU-position accuracy at the control points resulted in good agreement compared to the planned values. Calculated doses to the active volume of the ionization chamber were within the clinical acceptability range compared to measurements. In addition, 3D gamma tests showed good agreement in the dose distribution between MC and RapidArc TPS. In summary, we have shown that our MC based RapidArc QA using LINAC log files assesses the physical delivery and dose calculation accuracy of RapidArc treatments. This QA process is now used clinically in Vancouver, Fraser Valley and Abbotsford cancer centre.
Chapter 6

A Monte Carlo model of the Varian IGRT couch top for RapidArc QA

6.1 Introduction

RapidArc is a radiation therapy treatment technique that delivers the dose in one or more gantry rotations using dynamic multi-leaf collimator (MLC) motion, variable dose rate and variable gantry rotation speed. The planning algorithm is based on the direct aperture optimization method and uses progressive sampling, as described by Otto[55]. During a substantial portion of the treatment the radiation beam may be attenuated by the couch. This attenuation depends on the modulation of the beam and is therefore specific to each treatment. Several studies have investigated the impact of carbon fiber couch attenuation for radiotherapy using fixed fields and its influence on IMRT treatment ([152–161]. More recently Vanetti et al. [162] studied the impact of Varian IGRT treatment couch modelling on dose calculation accuracy of RapidArc treatment of prostate cancer. They have observed “significant discrepancies of potential clinical impact at the level of the target volumes if calculations are performed without the couch and delivery is performed with couch”. Another study by Popple et al. [163] using the Varian exact couch observed that neglecting the couch in the dose calculation lead to significant error in the quality assurance (QA) results in one case. These studies show the necessity to systematically incorporate the treatment couch into both the optimization and QA process. In recent years several independent Monte Carlo (MC) dose verification systems [138, 142, 164] and GPU based optimization systems [73] for RapidArc treatments reports have been published.

To our knowledge no MC system yet implemented a couch model for RapidArc treatment. This study aims to assess the effect of the IGRT couch attenuation on
6.2 Material and methods

QA results (for both the treatment planning system (TPS) and MC) and to present a systematic method to create an accurate model of the Varian IGRT couch for Monte Carlo QA. This study is limited to only the Varian IGRT couch but the method presented can be readily applied to any couch type, on patient CT datasets and by any DOSXYZnrc [93] user.

6.2 Material and methods

The work presented here was performed with a Varian iX Clinac equipped with a Millennium 120 leaf MLC and IGRT couch top. This study consists of three components. First, both the optimal IGRT couch top HU values for the TPS determined by Vanetti et al. are validated for use in this study. Next, the carbon fiber mass densities for a MC couch model were determined. The impact on TPS quality assurance results using the MC couch model is then assessed for RapidArc treatment plans.

6.2.1 Measurements

The measurement setup is shown in Figure 6.1. The couch top has an inverted trapezoidal shape consisting of a carbon fiber skin surrounding foam inside the couch top. The thickness of the couch top varies between 5 cm and 7.5 cm along its longitudinal direction defining three different sections, the thin part, the transition or medium part and the thick part. Similarly the thickness of the carbon fiber skin varies along the couch length and also varies between the patient face and the rear face. An extensive review of the couch top physical dimensions and material composition was presented by Kunz et al. Dose measurements were performed in a cylindrical phantom (28 cm in diameter consisting of acrylic shell of about 0.5 cm thick, filled with water) using a calibrated Farmer ionization chamber (PTW-Freiburg, Freiburg, Germany), with an active volume of 0.6 cm$^3$. The cylindrical phantom with the ion chamber positioned at isocentre was irradiated using a series of 6MV static beams, with a $10 \times 10$ cm$^2$ field size with varying gantry angles in 5 degree increments. A gantry angle of 180 degrees corresponds with the beam directed posteriorly through the treatment couch. During irradiation through the couch top, the cylindrical phantom was positioned at the couch top center. Measurements referred as “no couch”
6.2. Material and methods

Figure 6.1: Schematic representation of the experimental setup a) End-on view of the phantom placed on the couch for measurement and simulation of dose to chamber when including the couch. The ionization chamber is positioned at isocentre, in the centre of the phantom. b) Side view of the set-up used for dose to chamber measurements referred to as no couch.

were performed using an in-house made phantom holder to extend it over the edge of the couch top as shown in panel b) of Figure 6.1.

6.2.2 TPS modelling

All treatment planning was performed with Eclipse TPS version 8.6 using AAA algorithm for a 6 MV photon beam. The Eclipse TPS provides three simplified models of the IGRT couch top each having different total thicknesses (thin, medium and thick). A constant 4 mm skin thickness is used for each model; the foam thickness varies with the model used. The carbon fiber skin and the inside foam of the couch top are defined as structures having default values of -300HU and -1000 HU respectively. For the purposes of validating the couch top HU values in the TPS, measured and calculated couch attenuation is compared. Couch attenuation is defined as \( \left( \frac{D_{\text{no couch}} - D_{\text{with couch}}}{D_{\text{no couch}}} \right) \times 100 \). The active chamber volume is contoured in the TPS and calculated “chamber doses” are reported as a mean dose to this volume. A dose calculation grid size of 2.5 mm was used. A range of HU values including the TPS default values and the values proposed by Vanetti et al. [162] for both thin and thick couch sections were tested. The set of HU val-
6.2. Material and methods

<table>
<thead>
<tr>
<th>Component</th>
<th>Weight Fraction</th>
<th>Atomic Fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>C (compact)</td>
<td>0.556347</td>
<td>14</td>
</tr>
<tr>
<td>H</td>
<td>0.033349</td>
<td>10</td>
</tr>
<tr>
<td>O</td>
<td>0.317617</td>
<td>6</td>
</tr>
<tr>
<td>N</td>
<td>0.092686</td>
<td>2</td>
</tr>
</tbody>
</table>

Density (g/cm$^3$) 0.052

Table 6.1: Atomic composition and properties of Rohacell 51A material used.

ues minimizing the difference between measured and TPS calculated attenuations for both the thick and thin part of the couch top were determined. These will be referred as the “optimal model” parameters.

6.2.3 Monte Carlo modelling

Monte Carlo simulations were performed using a new DOSXYZnrc source capable of computing dose distributions involving continuously moving gantry, dynamic MLC motion and variable dose rate. A detailed description of this source [128] and its accuracy in modelling RapidArc dose distributions was presented elsewhere [164]. The MC “chamber dose” reported corresponds to the MC calculated mean dose to the contoured chamber volume as defined in the TPS. MC simulations were performed using a 2.5 mm voxel size and the uncertainty for each simulation was kept within 1.4%. The Monte Carlo couch top model is directly related to the TPS model using a constant thickness (2 voxels or 5 mm) carbon fiber skin surrounding a foam core. The physical density of the carbon fiber had to be adjusted to account for the thicker couch top skin in the model compared to the real couch. In this study the carbon fiber skin was simulated as carbon graphite. The material used to model the foam inside of the IGRT couch top was Rohacell 51A as specified by Kunz et al. [165]. The elemental composition used is shown in Table 6.1 and a constant density was used throughout this study.

The MC phantoms were created using ctcreate (code contained in DOSXYZnrc package Walters et al 2006) in a three step process. In the first step, the original CT

3http://personalpages.to.infn.it/~tosello/EngMeet/ITSmat/SDD/Rohacell51A.html
6.2. Material and methods

DICOM images were modified using a python code and PyDicom\(^4\) to keep the original HU values inside the cylindrical phantom only and to define the pixels outside the phantom as air. The phantom contour is extracted from the DICOM structure file. A default DOSXYZnrc CT to material density curve was used to create the cylindrical phantom for Monte Carlo simulations.

The couch top phantom is created in the second step. The contour coordinates of the couch were extracted from the DICOM structure file exported from the TPS using PyDicom. Similarly to the previous step, the original DICOM CT images were modified to assign air to all the pixels outside of the couch top structure. The inside part of the couch was assigned $-800$HU providing a larger range to adjust the ct upper bound parameter for air. This parameter was found to be crucial to properly identify each material. Pixel spacing in a DICOM CT image is smaller than the voxel dimensions for the MC phantom. Pixel values within a voxel will be averaged and assigned to the voxel, which will in turn be converted into physical density. At interface between two medium with large density difference (such as air and water or graphite) this averaging of DICOM CT image pixels produce a gradient in density values that appear as blurred edges. This blurring effect can be removed using the following procedure. Materials are differentiated using the ct upper bound parameter in ctcreate input file. Once the “contours” or the limits of each material are correctly defined the density gradient is removed by having identical upper and lower density bound value in ctcreate input file. The couch phantom was created using a step size CT to material density curve shown in Table 6.2.

<table>
<thead>
<tr>
<th>Material</th>
<th>CT upper bound</th>
<th>Density lower bound</th>
<th>Density upper bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>-861</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Rohacell 51A</td>
<td>-800</td>
<td>0.052</td>
<td>0.052</td>
</tr>
<tr>
<td>Graphite</td>
<td>235</td>
<td>1.7</td>
<td>1.7</td>
</tr>
</tbody>
</table>

Table 6.2: CT to material and physical density conversion parameters used in ctcreate. Density is expressed in g/cm\(^3\).  
\(^4\)http://code.google.com/p/pydicom/
6.2. Material and methods

Figure 6.2: Schematic diagram of the MC couch phantom creation process. The CT upper bound parameter is adjusted through an iterative process until correct material identification is achieved. For time efficiency only one slice of the MC phantom is created during the iterative process. Once the adequate CT upper bound values are defined the complete set of DICOM CT images is used to create the MC phantom.

A two voxel thick couch top skin and adequate material number assignment was achieved by adjusting the CT upper bound parameters in the ctcreate input file using only 2 DICOM CT images. Once the correct upper bound parameters are determined the MC phantom using all the DICOM CT images is created. A diagram of the process is shown in Figure 6.2.

In the third step the phantoms are combined using an in-house C++ code.

This unique approach allows the creation of complex Monte Carlo phantoms (by combining multiple phantoms) that avoid voxel averaging effects (by using a step size CT to material density curve), with materials having similar densities being accurately identified.
6.2. Material and methods

Figure 6.3: Monte Carlo phantom created including the couch top. Materials are perfectly identified with each having a different material number assigned (left side) and having the proper physical density (right side). In this example both the carbon fiber skin and the cylindrical phantom have identical physical density.

It should be noted that values reported in Table 6.2 only works for the CT images used. Couch structure contour coordinates contained in the DICOM Structure file is dependent on the patient orientation and coordinate system. Therefore each CT scan data will have a different coordinate system. Nevertheless, the approach presented here can be used to create properly the couch phantom for MC simulations with different parameter values than reported in Table 6.2. However for QA purpose in our institution we use the same phantom and CT scan data, the MC phantom needs to be created only once. Another approach is to use a MC couch phantom already created and add it directly to another MC phantom of interest. From the DICOM Structure file, coordinate of the extremities of the couch can be extracted and used to perform a coordinate transformation of the existing MC couch phantom to align it properly. This approach is currently being implemented for patient CT dataset.

Figure 6.3 shows one of the phantoms used in this study; we can observe that both the carbon fiber skin and the cylindrical phantom have a similar density but are assigned different material numbers. Using the same series of static fields as used in the TPS modelling section, densities varying between 0.1 g/cm$^3$ and 2.0 g/cm$^3$ were
tested to determine the impact of density of the carbon fiber skin on the calculated couch attenuation. MC calculated chamber doses were compared to TPS calculated chamber doses.

6.2.4 RapidArc quality assurance results

RapidArc treatment planning quality assurance is carried out at this institution by means of a 3D gamma comparison of the TPS dose distribution with a MC generated dose distribution as well as a comparison of TPS calculated chamber doses with ion chamber measurements at selected locations within the cylindrical phantom. For the 3D gamma comparison, only absolute dose voxels within a region of interest are considered. This region of interest is defined as dose voxels having a value higher than 50% of the maximum dose. A PASS status for the QA is given if more than 90% of the data points have a gamma value < 1 and TPS chamber doses and measurements agree within ±3%. The impact of couch modelling parameters on RapidArc QA was assessed using three clinically acceptable RapidArc treatment plans (two abdominal sites in paediatric cases and one head and neck). The plans consist of a single counterclockwise full arc with 179° to 181° gantry angle range (IEC scale), with monitor units (MU) ranging from 409 MU to 511 MU. For each plan the dose was calculated using both the thick and thin couch model (referred to as Thick and Thin respectively).

The effect of the IGRT couch top on chamber doses measured and calculated at isocentre was evaluated first, by comparing ion chamber measurements, MC and TPS calculated chamber doses in the cylindrical phantom. The plan using the optimal TPS couch model was used as a reference in these comparisons. The impact of not including the couch, and of using the default couch HU values in the TPS was demonstrated as well as the impact of varying the carbon fibre density in the MC model.

Finally the impact of carbon fiber density in the MC model on the 3D gamma results was demonstrated by performing the gamma analysis using MC plans generated for a range of carbon fiber densities. In order to separate the effect of couch modelling from other factors that could influence the 3D gamma results, the tests were performed on the homogeneous cylindrical phantom using MC simulation code that had been previously validated for the 6 MV photon beam used.
6.3 Results and discussion

6.3.1 TPS IGRT couch top modelling results

Figure 6.4: Couch attenuation difference between measurements and calculated values by the TPS for a given set of HU. Thick part of the couch is represented with solid lines and dashed lines represent the thin part of the couch.

Figure 6.4 shows the difference between the calculated attenuation for a given set of HU and the measured attenuation for both the thick (solid line) and the thin model (dashed line) of the couch top. The first and second HU value refer to the inside part of the couch (foam) and to the carbon fiber skin respectively. For comparison purposes we have plotted the same set of HU values as Vanetti et al. [162] which also appear to be optimal set of values. The difference between the calculated and measured attenuation is within 1% for all gantry angles except 125 degrees. This discrepancy can be explained by a combination of 3 factors:

1. The simplified couch model differs from the real couch geometry at this location (see Kunz et al.[165])

2. Only a portion of the radiation beam is going through the couch the other portion is missing it.

3. The uncertainty in the fidelity of the positioning of the couch structure relative to the cylindrical phantom and experimental setup. The position of the cylindrical
6.3. Results and discussion

![Figure 6.5: Dose to chamber difference between TPS and MC for a range of density (in g/cm$^3$) of the carbon fiber skin for the MCT model.](image)

phantom on the couch could be offset by $\sim 2$ mm compared to its position in the treatment planning system.

The optimal set of HU values was determined to be (-700,-960) leading to consistently better agreement with measurements and this was used for the rest of this study. Similar findings were found by Vanetti *et al.* [162] using a posterior-anterior and an oblique field. We can observe that the default HU values overestimate the attenuation by up to 2.5% with larger discrepancies found near the couch edge where the beam goes through a thicker part of the carbon fiber skin.

### 6.3.2 Monte Carlo IGRT couch top modelling results

The appropriate physical densities of the carbon fiber skin to be investigated for the MC phantom were determined by comparing MC and TPS calculated doses to chamber for static fields at different gantry angles. Results for the MC thick part
Figure 6.6: Dose to chamber difference between TPS and MC for a range of density (in g/cm$^3$) of the carbon fiber skin for the MCt model.
6.3. Results and discussion

<table>
<thead>
<tr>
<th>Plan</th>
<th>TPS (no couch)</th>
<th>Measured (no couch)</th>
<th>MC (no couch)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plan 1 Thick</td>
<td>2.5%</td>
<td>2.5%</td>
<td>3.4%</td>
</tr>
<tr>
<td>Plan 2 Thick</td>
<td>0.4%</td>
<td>-0.3%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Plan 3 Thick</td>
<td>2.6%</td>
<td>1.5%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Plan 1 Thin</td>
<td>2.3%</td>
<td>2.4%</td>
<td>3.2%</td>
</tr>
<tr>
<td>Plan 2 Thin</td>
<td>0.4%</td>
<td>-0.3%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Plan 3 Thin</td>
<td>2.3%</td>
<td>1.2%</td>
<td>2.3%</td>
</tr>
</tbody>
</table>

Table 6.3: Effect of not including the couch in the dose calculation by comparing dose to chamber differences in percentage. The predicted dose to chamber by the TPS including the optimal couch model is used as reference.

(referred as MCT) and thin part (referred as MCt) models of the couch top are shown in Figure [6.5] and Figure [6.6] respectively. We can observe that carbon fiber physical density ranging between 0.4 g/cm$^3$ and 0.6 g/cm$^3$ leads to good agreement with TPS calculated doses (within 1%). Discrepancies ranging from 6% – 8.5% were observed for the 2g/cm$^3$ density (results are not shown).

6.3.3 QA results

Table 6.3 lists the relative differences in measured and calculated chamber doses for the 3 plans tested, with and without the couch. TPS and MC calculated chamber doses agree with measurement to within 1.2% when the couch is not included. This is within the statistical uncertainly of the MC simulations (1.4%). It is apparent that the effect of the couch on the chamber dose is plan specific, ranging from negligible to approximately 2.5%.

For cases where a significant portion of the treatment dose is delivered through the couch, a non negligible dose difference will be observed. The percentage of the total dose delivered as a function of gantry angle for the 3 plans is shown in Figure [6.7]. The gray shaded area represents the treatment angles going through the couch. It is observed that for plans 1 and 3, larger portions of the total dose are delivered through the couch compared to plan 2 where a significant portion of the dose is delivered at a gantry angle of 45 degrees.
Figure 6.7: Percent of MU delivered per gantry angles for plan 1 (a), plan 2 (b) and plan 3 (c). The gray shaded area correspond to gantry angles going through the couch. For plan 1 and plan 3 the largest intensities are going through the couch. The MLC modulation is not accounted.
6.3. Results and discussion

Table 6.4: Dose to chamber differences in percentage between ion chamber measurement, TPS with default set of couch HU values and TPS with optimal couch model.

<table>
<thead>
<tr>
<th>Plan</th>
<th>Measured (with couch)</th>
<th>TPS with couch (default HU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plan 1 Thick</td>
<td>0.2%</td>
<td>-0.7%</td>
</tr>
<tr>
<td>Plan 2 Thick</td>
<td>-0.8%</td>
<td>-0.2%</td>
</tr>
<tr>
<td>Plan 3 Thick</td>
<td>-0.9%</td>
<td>-0.9%</td>
</tr>
<tr>
<td>Plan 1 Thin</td>
<td>0.7%</td>
<td>-1.0%</td>
</tr>
<tr>
<td>Plan 2 Thin</td>
<td>-0.6%</td>
<td>-0.2%</td>
</tr>
<tr>
<td>Plan 3 Thin</td>
<td>-0.8%</td>
<td>-1.1%</td>
</tr>
</tbody>
</table>

Table 6.4 lists the differences in measured and TPS calculated chamber doses with the couch included. Measured chamber doses and chamber doses calculated using default TPS couch parameters are compared with the chamber doses calculated with optimal TPS couch parameters. The effect of using the default HU values leads to differences of up to 1.1% in the calculated dose to chamber compared to the TPS optimal couch top model. The optimal TPS model agrees with measurement to within 1%. Results are similar for both thick and thin sections of the couch.

The variation in MC chamber dose with choice of physical density of the carbon fiber skin on is shown in Table 6.5. Differences between MCT and MCt models with respect to TPS optimal model for the 3 RapidArc plans are shown. The agreement with TPS was within 1% for all cases when densities of 0.5 g/cm$^3$ or 0.6 g/cm$^3$ are used and within 1.8% for densities ranging from 1 g/cm$^3$ to 0.4 g/cm$^3$. For 2 g/cm$^3$ and 0.1 g/cm$^3$ one of the plans in each case had a discrepancy of greater than 3%.

Dose distribution comparison between TPS with optimal couch model and MC MCT model using 0.5 g/cm$^3$ carbon fiber density for plan 1 is shown in Figure 6.8.

Results for the 3D gamma analysis comparing optimal TPS and MC dose distributions for the same range of density values are shown in Table 6.6. It is interesting to note that with the exception of the MC calculated plans using a carbon fiber density of 2 g/cm$^3$, all plans would have passed the 3D gamma QA criteria having a 90% or greater pass rate. In fact, ignoring the couch completely in the MC calculation would still have resulted in a 3D gamma pass. However, improvement in the 3D gamma
6.3. Results and discussion

Table 6.5: Dose to chamber differences in percentage between TPS optimal models and MC for a range of carbon fiber density.

<table>
<thead>
<tr>
<th>Plan</th>
<th>2g/cm³</th>
<th>1g/cm³</th>
<th>0.6g/cm³</th>
<th>0.5g/cm³</th>
<th>0.4g/cm³</th>
<th>0.1g/cm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plan 1 Thick</td>
<td>-1.7%</td>
<td>-0.8%</td>
<td>0.8%</td>
<td>0.5%</td>
<td>1.1%</td>
<td>1.7%</td>
</tr>
<tr>
<td>Plan 2 Thick</td>
<td>-0.1%</td>
<td>-0.3%</td>
<td>0.4%</td>
<td>0.4%</td>
<td>-0.2%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Plan 3 Thick</td>
<td>-3.4%</td>
<td>-1.3%</td>
<td>-0.8%</td>
<td>0.2%</td>
<td>1.5%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Plan 1 Thin</td>
<td>-2.2%</td>
<td>0.3%</td>
<td>0.9%</td>
<td>0.9%</td>
<td>0.8%</td>
<td>3.1%</td>
</tr>
<tr>
<td>Plan 2 Thin</td>
<td>-0.4%</td>
<td>0.8%</td>
<td>0.4%</td>
<td>0.9%</td>
<td>0%</td>
<td>1.0%</td>
</tr>
<tr>
<td>Plan 3 Thin</td>
<td>-2.8%</td>
<td>-1.8%</td>
<td>0.1%</td>
<td>0.3%</td>
<td>0.6%</td>
<td>2.7%</td>
</tr>
</tbody>
</table>

Figure 6.8: Dose distribution for plan 1 including the thick couch model. TPS optimal model is shown in the left and MC MCT model using 0.5 g/cm³ on the right.
6.4 Conclusion

Table 6.6: 3D gamma analysis of the dose distribution with 3%/3 mm DTA criteria for different carbon fiber densities.

<table>
<thead>
<tr>
<th>Plan</th>
<th>Density in g/cm$^3$</th>
<th>MC (no couch)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Plan 1 Thick</td>
<td>89.5%</td>
<td>97.9%</td>
</tr>
<tr>
<td>Plan 2 Thick</td>
<td>93.6%</td>
<td>98.0%</td>
</tr>
<tr>
<td>Plan 3 Thick</td>
<td>80.3%</td>
<td>95.6%</td>
</tr>
<tr>
<td>Plan 1 Thin</td>
<td>86.6%</td>
<td>98.8%</td>
</tr>
<tr>
<td>Plan 2 Thin</td>
<td>94.2%</td>
<td>97.5%</td>
</tr>
<tr>
<td>Plan 3 Thin</td>
<td>82.0%</td>
<td>94.8%</td>
</tr>
</tbody>
</table>

score is seen when the couch is incorporated in the calculation, with the greatest improvement seen for the 0.5 g/cm$^3$ and 0.6 g/cm$^3$ carbon fiber densities.

6.4 Conclusion

HU values of $-700$ and $-960$ for the carbon fiber skin and inner foam core of the Varian IGRT treatment couch as proposed by Vanetti et al have been validated for use in this study. The study aimed to investigate the effect of the Varian IGRT couch on the RapidArc QA results and to develop and test a MC couch model for use in RapidArc dose calculations for quality assurance on the TPS. Results showed significant differences can be observed between TPS doses including the couch and those without the couch. These differences were treatment specific, and independent of the couch model used (Thick or Thin). Results indicate that a MC model using a 2 voxel (5 mm) thick carbon fiber shell with physical density in the range of 0.4 g/cm$^3$ to 0.6 g/cm$^3$ surrounding a Rohacell 51A foam core of 0.052 g/cm$^3$ is recommended. For consistency, a density of 0.5 g/cm$^3$ will be used by the authors in the MC couch model for the purpose of TPS quality assurance. This model has been tested for use in MC QA of RapidArc treatment plans with excellent results.
Chapter 7

Intensity Modulated Total Body Irradiation (IMTBI) using Fast Inverse Dose Optimization (FIDO)

Intensity modulated radiation therapy (IMRT) treatments have been widely used over the last decade. More recently volumetric modulated arc therapy (VMAT) treatments have offered new capabilities such as dose rate modulation and gantry rotation while the radiation beam is on. These major advances have improved treatment time and dose conformity coverage. With new generations of linear accelerators like the Varian TrueBeam (Varian Medical Systems, Palo Alto, CA), additional degrees of freedom are now available like couch motion (translation and rotation), collimator rotation and jaw motion during the treatment. Using all degrees of freedom of the linear accelerator (gantry rotation and couch translation) it is now possible to deliver a treatment using a helical trajectory. Several studies have investigated using a linear accelerator or a TomoTherapy unit for total body irradiation or total marrow irradiation (TMI) [166–169].

As we have seen in chapter 4, TBI treatment using a parallel-opposed pair of fields with extended SSD is incapable of tailoring the dose for each patient to assure a uniform dose is delivered to the whole body. Moreover quality assurance of such treatment is possible but very limited information can be extracted. Only dose to the prescription point, dose profile along the mid-separation and only mean dose to organs at risk per treatment field can be accurately estimated. TBI treatments can greatly be improved by using all the new degrees of freedom of the linear accelerator and leading to improved accuracy in the QA process. As mentioned in chapter 4 there is currently no TPS system capable of planning total body irradiation treatments on a Linac. In this chapter, the feasibility of delivering a uniform dose to the whole
body using intensity modulated radiation is investigated. In this work, only a two-dimensional problem is considered, generalization to three-dimensional problem could be achieved using the same approach with the total number of beamlets being the limiting factor.

7.1 Material and methods

In inverse treatment planning the desired dose distribution is used to define the treatment goals. During the dose optimization process, plan parameters (such as radiation beam energy, MLC modulation, dose rate etc...) are optimized to achieve these goals. The quality of a treatment plan is evaluated through an objective function or cost function. The lower the value returned by the cost function the closer to the desired dose distribution we get. The goal is to find the optimal set of parameter values for which the cost function reaches the global minimum. Optimization algorithm searching for the global minimum (conjugate gradient or simulated annealing) requires numerous iterations and may be trapped in local minima. Furthermore, these algorithms require longer computing time for each iteration with smaller dose calculation grid size.

In 1940 Birkhoff [170] demonstrated that an arbitrary 2D drawing can be decomposed as a series of straight lines having different directions and different darkness. However some of these lines need to have a negative darkness to obtain a solution. Similarly the desired dose distribution (or equivalently the optimal solution to the quadratic objective function) can be achieved using beamlets having different directions and weights. The optimal solution can be determined through matrix inversion leading to the occurrence of nonphysical negative beamlet weights. In 2005 Goldman et. al. [171] published a new algorithm that determines the optimal solution through matrix inversion and avoiding the appearance of negative beamlet weights. The clinical implementation of this algorithm and comparison with a commercial treatment planning system (Pinnacle, Philips Medical Systems) has been reported [172].
7.1. Material and methods

7.1.1 Introduction to FIDO

The fast inverse dose optimization (FIDO) algorithm \cite{171} reformulates the objective function to reduce it to a linear set of equations. The optimal set of beamlet intensities is found through matrix inversion and avoids negative beamlet weights. First let’s consider a generic (or conventional) type of objective function $O$ defined as:

\[ O = p_{PTV}O_{PTV} + p_{OAR}O_{OAR} + p_{ATR}O_{ATR} \]  \hspace{1cm} (7.1)

where $p_k$ are penalty factors (used to determine the relative importance of the constraint). The conventional objectivity terms are given by:

\[ O_{PTV} = \sum_{x \in PTV} \left( \sum_{i} w_i d_i(x) - d_{PTV} \right)^2 \]  \hspace{1cm} (7.2)

\[ O_{OAR} = \sum_{x \in OAR} \left( \sum_{i} w_i d_i(x) \right)^2 \]  \hspace{1cm} (7.3)

\[ O_{ATR} = \sum_{x \in ATR} \left( \sum_{i} w_i d_i(x) \right)^2 \]  \hspace{1cm} (7.4)

where $w_i$ is the weight of beamlet $i$, $d_i(x)$ is the dose deposited by beamlet $i$ in voxel $x$ and $d_{PTV}$ is the prescribed dose to the PTV. These conventional objectivity terms can reach a minimum value through destructive interference between positive and negative beamlet weights. These negative weights are the result of conflicting requirements, first we require the radiation to pass through the ATR region and possibly through the OAR region to reach the PTV but the objective function also requires the penalty factors of these regions to be zero in order to reach the global minima. In the FIDO algorithm the objectivity terms for organs at risk (OAR) and all the other structures (ATR) are reformulated such that the minimum of the objectivity terms can only be reached if all the weights of all the beamlets depositing dose in these structures are zero:
7.1. Material and methods

\[ O_{OAR,FIDO} = \sum_{x \in OAR} \sum_{i} w_i^2 d_i^2(x) \]  \hspace{1cm} (7.5)

\[ O_{ATR,FIDO} = \sum_{x \in ATR} \sum_{i} w_i^2 d_i^2(x) \]  \hspace{1cm} (7.6)

An additional term called symmetry term is introduced in the cost function to eliminate the interference effect that can generate negative beamlet weights:

\[ O_{sym} = \sum_{i} (w_i - 1)^2 \]  \hspace{1cm} (7.7)

As it will be illustrated later, the priority of this factor is crucial to avoid negative beamlet weights. Another purpose of the symmetry term is to favor “smoother” weight distribution or equal weights for all beamlets. The new objective function can be written as:

\[ O = p_{PTV} O_{PTV} + p_{OAR,FIDO} O_{OAR} + p_{ATR,FIDO} O_{ATR} + p_{sym} O_{sym} \]  \hspace{1cm} (7.8)

The optimal set of beamlet weights which minimizes the objective function is obtained by:

\[ 0 = \frac{\partial O}{\partial w_j} \]  \hspace{1cm} (7.9)

The minimum of the objective function occurs when:

\[ \sum_{i} w_i \left( p_{PTV} \alpha_{ij}^{PTV} + p_{OAR} \alpha_{ij}^{OAR} \delta_{ij} + p_{sym} \delta_{ij} \right) = p_{PTV} \beta_j^{PTV} + p_{sym}(7.10) \]

with
7.1. Material and methods

\[ \alpha_{ij}^{\text{region}_k} = \sum_{x \in \text{region}_k} d_i(x)d_j(x) \quad (7.11) \]

\[ \beta_j^{\text{region}_k} = d^{\text{region}_k} \sum_{x \in \text{region}_k} d_j(x) \quad (7.12) \]

where \( d^{\text{region}_k} \) is the dose required in region \( k \) (in our case the PTV). \( \beta_j^{\text{region}_k} \) is a one dimensional array characterizing the dose deposited by a beamlet \( j \) in all the voxels inside a structure or organ. \( \alpha_{ij}^{\text{region}_k} \) is a two dimensional array containing the dose deposited by both beamlet \( i \) and \( j \) in all voxels contained within region \( k \). Terms of this matrix are non zero if and only if both beamlets deposit dose at the same voxel location.

The optimal beamlet weights are given by:

\[
\begin{align*}
    w_i &= \sum_j \alpha_{ij}^{-1} \beta_j \\
    \text{with} \quad \alpha_{ij} &= p_{\text{PTV}} \alpha_{ij}^{\text{PTV}} + (p_{\text{OAR}} \alpha_{ij}^{\text{OAR}} + p_{\text{ATR}} \alpha_{ij}^{\text{ATR}} + p_{\text{sym}}) \delta_{ij} \\
    \beta_j &= p_{\text{PTV}} \beta_j^{\text{PTV}} + p_{\text{sym}}
\end{align*}
\]

(7.13)

The advantage of the FIDO algorithm is that the optimal set of weights is obtained through a single matrix inversion avoiding unphysical negative weights. Unlike the traditional searching algorithms no iterations are needed and no trapping in local minima occurs. The optimization time depends only the number of beamlets (defining the size of the matrix to be inverted) and is independent of the dose calculation grid size. The \( \alpha_{ij}^{\text{region}_k} \) and \( \beta_j^{\text{region}_k} \) terms need to be calculated only once for each patient. Compared to searching algorithms, a larger number of penalty factors can be investigated therefore leading to a better treatment plan.
7.1. Material and methods

7.1.2 Monte Carlo beamlets dose calculations
The BEAMnrc code (NRC, Ottawa, Canada) is used to simulate the 6MV photon radiation beam from a Varian IX linac. The photon cut-off energy (PCUT) is set to 0.01 MeV and the electron cut-off energy (ECUT) is set to 0.7 MeV. The phase space file is collected under the jaws component module (phase space B in Figure 2.7). The phase space is divided into $5 \times 10 \, \text{mm}^2$ beamlets (size is defined at isocentre) using an in-house software [82]. The beamlet size is matching both the slice thickness of the anthropomorphic phantom CT scan (5 mm) and the maximum leaf width of the MLC (1 cm). A schematic representation of the beamlets and their ordering is shown in Figure 7.1. Details on how to generate beamlets from phase space files, its accuracy and application for direct aperture optimization (DAO) can be found elsewhere [82, 173].

The FIDO algorithm is implemented using Matlab (Natick, MA). The program reads the 3ddose file produced by MC simulations for each beamlet, calculates the $\alpha_{ij}^{PTV}$ and $\beta_j^{PTV}$ terms and determine the optimal set of beamlet weights for a given set of penalty factors by matrix inversion.

7.1.3 Anthropomorphic phantom with no heterogeneity
The MC phantom was generated from DICOM CT images of an anthropomorphic phantom. First the DICOM CT images were modified using pydicom to remove all the artifacts outside of the body contour (eg. CT couch and CT bore). The CT Hounsfield units are converted into physical densities and assigned material type using ctcreate (NRC, Ottawa, Canada). For the homogeneous case considered in this section (water equivalent tissue only) all the voxels inside the body contour were assigned a density of $1 \, \text{g/cm}^3$ and defined as water by using a step size CT to material curve in ctcreate. Dose deposited by each beamlet into the MC phantom is calculated using DOSXYZnrc. For this study 8 equispaced fields were considered with the field distribution shown in Figure 7.2.

For TBI treatments a dose of 12 Gy is prescribed to the whole body. As a consequence the objective function in FIDO contains only the PTV and the symmetry terms. Using the FIDO algorithm optimal beamlet weights were calculated to achieve a uniform dose of 12 Gy to the entire 2D body. Beamlet weights distribution and range
7.1. Material and methods

Figure 7.1: The phase space file for the field size $F_X \times F_Y$ defined at 100 cm SAD is divided into $N$ beamlets of dimension $g_X \times g_Y$. Dose deposited by each beamlet is calculated using DOSXYZnrc.
Figure 7.2: Radiation beam distribution considered for this study. Eight beams were used separated by 45° from each other.
7.2. Results were analyzed.

7.1.4 Anthropomorphic phantom with heterogeneity

For the heterogeneous case considered in this section, voxels inside the body contour were not modified. The HU values were segmented into physical densities and assigned material type using the default CT to density curve provided with DOSXYZnrc. Four types of material are defined, air, lung, tissue and bone. The conversion parameters used in ctcreate are shown in Table 7.1.

<table>
<thead>
<tr>
<th>Material</th>
<th>CT upper bound</th>
<th>Density lower bound</th>
<th>Density upper bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>50</td>
<td>0.001</td>
<td>0.044</td>
</tr>
<tr>
<td>Lung</td>
<td>300</td>
<td>0.044</td>
<td>0.302</td>
</tr>
<tr>
<td>Tissue</td>
<td>1125</td>
<td>0.302</td>
<td>1.101</td>
</tr>
<tr>
<td>Bone</td>
<td>3000</td>
<td>1.101</td>
<td>2.088</td>
</tr>
</tbody>
</table>

Table 7.1: Default CT to material and physical density (provided by DOSXYZnrc) conversion parameters used in ctcreate. Density is expressed in g/cm$^3$.

7.2 Results

7.2.1 No heterogeneity

A total number of 320 beamlets were used to optimize the dose distribution. Reading the 3ddose files takes approximately 1 minute, the calculation of the matrix terms for FIDO between 7 seconds and 10 seconds and the matrix inversion takes only 0.03 seconds.

The relationship between penalty factors and negative beamlet weights appearance has been examined. The threshold was determined by incrementing the PTV penalty factor while the symmetry penalty factor value was fixed at 100. Figure 7.3 shows the weight ratio $w_{min}/w_{max}$ as a function of penalty factors. Once the matrix terms
7.2. Results

Figure 7.3: TBI FIDO results for the weight ratio $w_{\text{min}}/w_{\text{max}}$ as a function of penalty factors for the homogeneous case.

are calculated it takes milliseconds to determine the optimal beamlet weights for a given set of penalty factors. The 500 matrix inversion took only few seconds.

When the penalty factor ratio exceeds 1.43 negative beamlet weights start to occur. For TBI the objective function contains only two terms, the PTV term in FIDO have the same form as in the conventional cost function. Therefore through destructive interference the objective function can be minimized using negative beamlet weights. The only term preventing such behavior is the symmetry term. However this effect can be annihilated if the penalty factor for the PTV term becomes significantly larger compared to the penalty factor of the symmetry term. Figure 7.4 shows the relationship between the minimum, the maximum and the mean dose to the whole body as a function of the penalty factor ratio. Small improvement in the mean dose with higher $P_{\text{PTV}}$ penalty factor was observed.

The optimized dose distribution is shown in Figure 7.5(a) using $p_{\text{PTV}} = 140$ and $p_{\text{sym}} = 100$. Good dose uniformity is observed within the body contour with the exception of the surface dose. The histogram of dose distribution is displayed in Figure 7.5(b). For 92% of the voxels the dose is within the TBI requirements of
Figure 7.4: Maximum, minimum and mean dose to the whole body as a function of penalty factors.
7.3. Heterogeneous case

Figure 7.5: Dose distribution (left) and dose histogram (right) produced by FIDO algorithm.

±10% of the prescribe dose. Only 0.3% of the voxels exceeds the maximum dose allowed of 13.2 Gy, the voxels with dose lower than the minimum of 10.8 Gy are all located at the surface (or in the buildup region) where accurate dose calculations are difficult even for MC simulations.

The weights of the beamlets are shown in Figure 7.6. No negative beamlet weights are observed. Some beamlets have a weight equal to 1 and are located at the edge of the radiation field. These beamlets do not contribute to the dose inside the body contour. However, these beamlets are assigned a weight of 1 by the FIDO algorithm to cancel their contribution to the symmetry term.

Figure 7.7(a) displays the calculated dose to the lungs and Figure 7.7(b) and (c) the dose histograms for the left and right lung respectively. The lung doses are within ±5% of the prescribe dose and well within TBI tolerances. Contrary to the parallel opposed pair delivery technique, the dose to each voxel can be precisely evaluated.

7.3 Heterogeneous case

Similar to the homogeneous case, a total number of 320 beamlets were used to optimize the dose distribution. Figure 7.8 shows the weight ratio $w_{\text{min}}/w_{\text{max}}$ as a function of penalty factors. Negative beamlet weights occur when the ratio is higher than 0.85.
7.3. Heterogeneous case

Figure 7.6: Beamlet weights calculated by the FIDO algorithm. No negative beamlet weights are observed.
Figure 7.7: Dose distribution to the lungs (top) and dose histogram for the left (b) and right lung (c). Each voxel dose is within ±5% of the prescribe dose.
7.3. Heterogeneous case

Figure 7.8: TBI FIDO results for the weight ratio $w_{\text{min}}/w_{\text{max}}$ as a function of penalty factors for the heterogeneous case.

The penalty factors used were $P_{\text{PTV}} = 85$ and $P_{\text{sym}} = 100$.

Dose distribution generated using the new optimal beamlet weights is shown in Figure 7.9. Larger dose fluctuations is observed compared to the homogeneous case seen in the previous section. A larger number of voxels (10.4%) exceed the TBI tolerance limit of ±10%. Lower doses (7% of the voxels) are mostly observed near the lung-tissue interface and on the surface. Higher doses (3.4% of the voxels) are located close to the body surface and also at the location of air cavities (between the “breast” and the body as well as the trachea). The mean dose to the whole body (2D) is 11.92 Gy.

The air cavities exhibit very large doses compared to the rest of the body. These air cavities largely contribute to the objective function and do not belong to body tissue that are prescribe a dose of 12 Gy. The optimal beamlet weights calculated by FIDO are all positive and displayed in Figure 7.10. We want to point out that even in the presence of these air cavities there is no negative beamlet weights generated. The symmetry term successfully prevent such scenario from happening.

If the air cavity is removed from the optimization 2.2% of the voxels have a dose...
7.3. Heterogeneous case

Figure 7.9: Dose distribution using the FIDO optimal beamlet weights (a) and dose histogram (b). Larger dose variation is observed compared to the homogeneous case.

Figure 7.10: Beamlet weights calculated with FIDO algorithm for the heterogeneous case. Even in the presence of large dose fluctuations, no negative weights are observed.
7.4. Discussion and conclusion

higher than 13.2 Gy and 4.9% of the voxels a dose lower than 10.8 Gy. The mean
dose to the whole 2D body is 11.935 Gy. For the left lung 1% of the voxels exceed the
TBI tolerance (0.5% of voxels are higher than the limit and 0.5% are lower). For the
right lung 2.7% exceed the TBI tolerance (1.6% of voxels are higher than the limit
and 1.1% are lower). The dose distribution and dose histograms are shown in Figure
\[7.11\]. An improved dose distribution around the the air cavity is observed.

Achieving uniform dose distribution at lung-tissue-bone interfaces (or high-low
density interfaces) is almost impossible due to electronic disequilibrium. The location
of large density gradients are shown in Figure \[7.12(a)\]. The region with smaller
density receives more scattered dose from the higher density region. At the interfaces
lower density region will therefore exhibit a higher dose compared to the higher den-
sity region as observed in Figure \[7.11(a)\]. Inside the lung regions significant density
fluctuations as large as 100HU occur as seen in Figure \[7.12(b)\]. However no significant
effect on the dose uniformity was observed. The most likely explanation is that these
fluctuations are averaged out due to the large voxel size used to generate the MC
phantom (5 × 5mm\(^2\)).

7.4 Discussion and conclusion

The study aimed to investigate the feasibility of using intensity modulated radia-
tion therapy to create a suitable TBI treatment. This study was limited to a two
dimensional case, extension to a three dimensional case is straightforward. For the
case of a homogeneous phantom, it was demonstrated that the FIDO algorithm was
able to determine the optimal beamlet weights through matrix inversion avoiding
unphysical negative weights. The dose uniformity achieved is within the TBI require-
ments. Moreover, dose to organs at risk such as lungs can be accurately determined
for each voxel. For the heterogenous case larger fluctuations in the dose distribution
was observed. They were due to air cavities and large density gradients located at
the lung-tissue-bone interfaces. The air cavities must be removed in the optimization
process to avoid that it artificially increases the cost function while no dose contraints
are necessary within these regions. Nevertheless all the beamlet weights generated by
the FIDO algorithm were positive. The symmetry penalty term played a crucial role
in avoiding the negative weights. Within the objective function it is the only term
7.4. Discussion and conclusion

Figure 7.11: Dose distribution using the FIDO optimal beamlet weights (a) and dose histogram (b) with the air cavity region excluded from the PTV. Dose histogram for the left (c) and right lung (d).
7.4. Discussion and conclusion

Figure 7.12: Density variation inside the antropomorphic phantom with larger changes occurring at the air cavity boundary (top). Fluctuations inside the lung regions can reach 100HU in variation.
7.4. Discussion and conclusion

that can’t be minimized through destructive interference. The advantage of FIDO over the searching algorithm comes from its ability to determine the optimal beamlet weights through matrix inversion leading to the global minima of the cost function. In theory the beam arrangement used in this feasibility study can be rotated producing similar uniform dose distribution. Combining a rotation of these eight equispaced beams with couch translation one can irradiate the whole body to produce a uniform dose. This approach avoids large organ motion and deformation observed between supine and prone treatment position leading to potentially large non uniform doses inside the organs at risk.
Chapter 8

Conclusions and future work

8.1 Conclusions

The main objective of this thesis was to develop Monte Carlo techniques for verification of complex radiation therapy treatments with an emphasis on total body irradiation and volumetric modulated arc therapy. The feasibility to improve dose distribution for total body irradiation using a fast inverse optimization with Monte Carlo generated beamlets was also investigated. This work was motivated by the availability of a new Monte Carlo source capable of computing dose distributions for a continuously moving radiation source and all the degree of freedom of a linac[128].

The accuracy of the dose calculation plays a crucial role in the outcome of patient studies and helps to develop guidelines for SBRT lung cancer protocols. Current clinical protocol guidelines for SBRT lung, while ensuring a “consistency of procedure” between trial participants, actually resulted in an inconsistency between the reported dose and the actual dose delivered to the patient. This inconsistency is directly related to the lack of accuracy of the dose calculation engine in regions of electronic disequilibrium. The data in this study supports our recommendation that quality assurance procedures intended to provide accurate dose data should be based on a Monte Carlo approach, and no renormalisation of the dose distributions ought to be allowed.

The accuracy of the dose calculation also plays a crucial role in total body irradiation treatments. The current hand planning method uses only basic dosimetric functions and only considers a single point at mid-separation along the central axis for dose calculation. The inhomogeneity correction methods used are very approximate and are applied to the whole lung only. Moreover, only the direction along the beam axis (central axis) is considered for these corrections. Patient thickness was found to
be the most critical parameter for accurately determining the treatment time (and therefore the dose). Using patient CT images is highly recommended for accurate patient thickness measurement thus avoiding treatment time differences of up to 6% compared to hand measurements performed using a caliper. A patient specific Monte Carlo based QA protocol was developed for TBI treatments which incorporates key geometric components of the treatment plan, including the beam flattener, patient specific geometry from the CT dataset and tailored lung compensators. The sweeping beam $^{60}$Co source model was tested versus ion chamber measurements to evaluate its accuracy. This new QA platform provides a new insight to TBI that was not available before.

Five TBI MC based QA were performed on patients treated in our institution. Although the dose to mid-separation was found to be in good agreement with the prescription along the whole body length, large fluctuations were observed outside of this plane. These fluctuations were caused by large variations in distance between the mid-separation plane and the body surface along the patient length. Large differences in lung shape was found between the supine and prone treatment position on the CT images preventing any registration between the two positions and limiting the analysis to the mean dose to lungs only. Compared to the prescribed dose of 6 Gy for each treatment position, large overdosing and underdosing of the lung was observed for prone and supine position respectively. These differences are due to the relative position of the lungs compared to the mid-separation plane. In the supine position, a larger volume of the lungs is located under the mid-separation plane while in prone position, a larger volume is located above. However when both treatment positions are accounted for the mean dose to lungs falls within the TBI tolerances of $\pm 10\%$.

Only the mean dose to the lungs can be accurately evaluated. This severe limitation provide an incomplete evaluation if the treatment is within the TBI tolerances. A more thorough evaluation would require the combined dose to each voxel within the lung; this will necessitate either an anatomical registration-deformation algorithm for such extreme changes or more simply a new treatment delivery method which would only require one treatment position. Considering that the current treatment delivery method does not allow for compensation of the overdosing and underdosing of the lungs, a new treatment technique combined with a new planning method seems to be called for.
8.1. Conclusions

In chapter 7 a feasibility study of a new treatment method combining couch translation and gantry rotation (helical delivery) was presented. The study was restricted to a single axial slice (2D problem). A fairly uniform dose distribution using a fast inverse dose optimization algorithm with MC generated beamlets can be achieved with 8 equispaced fields. The single treatment position permits a detailed analysis of the dose distributions. When no heterogeneity corrections are used, over 92% of the voxels are within the TBI tolerances. The largest benefit of such a treatment and planning method relies in the uniform dose delivered to each voxel within the lungs (within 5% of the prescribed dose at mid-separation). When heterogeneity corrections are used over 98% of the lung voxels are within the TBI tolerance. The 2% of voxels that are out of tolerance are located at the lung-tissue interfaces where electronic disequilibrium occurs and can’t be physically compensated. The FIDO algorithm used for the optimization provides an optimal solution through matrix inversion without appearance of negative beamlet weights provided the symmetry term penalty factor was high enough compared to the PTV one. It was demonstrated that it is possible to deliver a uniform dose to the whole body for a TBI treatment on a single axial slice. In theory it is possible to use the same number of equispaced beam rotated and deliver an equivalent dose distribution. One can imagine the same could be done over the whole length of the patient body to achieve a helical delivery that would include gantry rotation and couch translation. With this treatment delivery type it is possible to develop an accurate Monte Carlo based patient specific QA process.

A Monte Carlo based QA process for RapidArc treatments was presented in chapter 5. A study using 10 patients was performed to evaluate the accuracy of the system. Calculated doses were compared with experimental measurements. The new Monte Carlo source was used to validate the TPS dose calculation accuracy, the discrete sampling method used in the TPS optimization and machine overall performance. Negligible differences were observed between dose distributions from discrete optimization versus continuous delivery. Excellent machine performance was observed with no MLC leaf position errors greater than 2.5 mm and 90% of the errors being less than 1 mm. The established performance and accuracy of the QA method presented in this chapter lead to its clinical implementation in three cancer centres.
8.2. Future work

in British-Columbia (Vancouver, Fraser Valley and Abbotsford). To date, the Monte Carlo based QA method for RapidArc was used on over 335 patients at the Vancouver Cancer Centre. For the SBRT non-coplanar plans, very good agreement between MC and TPS dose distributions were observed. Ion chamber measurements were found to be very challenging to perform in such extreme situations due to the use of such small field sizes and high modulation. Any errors in positioning could result in a drastic change of the chamber reading because of the dose gradient involved. Nevertheless, dose differences between the chamber measurement, TPS and MC were within the clinical tolerances for SRBT.

During a substantial portion of a RapidArc treatment, the radiation beam may be attenuated by the treatment couch. The Eclipse planning system provides a couch model to account for the attenuation. The parameters used to characterize this model need to be determined experimentally. The impact of the couch attenuation on QA results are non negligible and must be properly assessed. The magnitude of the impact is treatment (or patient) specific and seems to correlate with the percentage of MU delivered per gantry angle. A MC model of the couch based on the TPS model can be created to produce good agreement between calculated and measured results. Tweaking of the carbon fiber physical density and keeping the density of the foam constant is sufficient to achieve an accurate model. This model needs to be created only once and can be added to any MC phantom.

Monte Carlo methods can be applied to a multitude of complex treatment verification procedure and can often calculate doses in situations where the commercial treatment planning system cannot (as it was the case for TBI). The variety of applications and the dose calculation accuracy of MC simulations outmatch the treatment planning system capabilities and offer a range of new opportunities in treatment planning and verification.

8.2 Future work

Several avenues for future research and improvement will be or are already investigated by the author. Improvements in ion chamber measurements for non-coplanar
8.2. Future work

SBRT RapidArc plans are currently under active investigation. The clinical implement-
ination of non-coplanar RapidArc QA for SBRT will follow. This work can also
be extended to investigate the use of 4D CT images for 4D RapidArc verification.
3D CT images can be sorted into 10 bins representing phases of the breathing cycle.
Doses for each phase can be to accurately calculated by MC.

Another area of active development from the author is the commissioning and im-
plementation of MC methods for the new Varian TrueBeam linac and more precisely
for the “Developer (research) Mode”. The Varian TrueBeam linear accelerator’s ad-
vanced control features are designed to allow complex three dimensional trajectory
beam delivery. The machine is capable of dynamically moving many components
simultaneously while the beam is on. For example, gantry, collimator, MLC, jaws,
couch translation and rotation may all be performed concurrently with beam delivery.
However, no commercial treatment planning system (including Varian’s own Eclipse)
is able to calculate dose distributions corresponding to this range of beam trajecto-
ries. In Developer Mode, dose delivery is executed via a set of instructions written
in a proprietary XML format which uses a “Trajectory Model”, a central concept
of the TrueBeam control system. In this model all beams are characterized by the
relationship between monitor units (MU) and position of the moving components of
the linear accelerator. The user can design and deliver practically any imaginable
treatment beam by writing an XML script for the linac. During beam delivery, the
control system continuously logs the position of all moving linac components and dose
delivered every 10 msec. The Developer Mode user can request that the logs be per-
manently written in the “trajectory log” file. Using these XML scripts and trajectory
log files to provide input to the Monte Carlo code we will be able to perform highly
accurate dose calculations to validate what was actually delivered by the TrueBeam
and assess machine performance. The implementation of the trajectory log files in-
formation from a TrueBeam linac into Monte Carlo simulations is currently under
active investigation. Future work will also include extending the FIDO optimization
for TBI to three dimensional cases. Early tests have shown very promising results.
The minimum number of beams and optimal arrangement need to be determined to
achieve the optimal performance for treatment delivery. One major constraint that
was not considered in this work is the dose rate limitation for TBI treatments which
adds complexity to the optimization process. These major advances will drastically change the field of TBI treatments and could potentially lead to better outcomes for patients.
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