Strategies for Reducing the Impact of Tumour Motion During Helical Tomotherapy

Bryan Kim
The University of Western Ontario

Supervisor
Dr. Jerry Battista
The University of Western Ontario

Joint Supervisor
Dr. Jeff Chen
The University of Western Ontario

Graduate Program in Medical Biophysics
A thesis submitted in partial fulfillment of the requirements for the degree in Doctor of Philosophy

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STRATEGIES FOR REDUCING THE IMPACT OF TUMOUR MOTION DURING HELICAL TOMOTHERAPY

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by

Bryan Kim

Graduate Program in Medical Biophysics

A thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy

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The University of Western Ontario
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The thesis by

Bryan Kim

entitled:

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is accepted in partial fulfillment of the requirements for the degree of Doctor of Philosophy

____________________            _________________ ______________
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Abstract

Tumour motion presents a significant limitation for effective radiotherapy of lung cancer, and more specifically for helical tomotherapy. The simultaneous and continuous movements of tomotherapy subsystems (gantry, couch, and binary multi-leaf collimator) can lead to inaccurate dose delivery, when combined with tumour motion. In this thesis, we have investigated the impact of tumour motion and strategies to reduce the resulting dose discrepancies for helical tomotherapy, through computer simulations and film measurements performed in a dynamic body phantom. Three distinctively different types of dose discrepancies have been isolated: dose rounding, dose rippling, and the intensity-modulated radiation therapy (IMRT) asynchronization effect. Each effect was shown to be affected by different combinations of tumour motion and treatment parameters. In clinical practice using a conventional fractionation scheme, the dose rounding effect remains the major concern, which can be compensated by assigning a larger treatment margin around the tumour volume. For hypofractionation schemes, the IMRT asynchronization effect can become an additional concern by introducing dose discrepancies inside the target volume, necessitating the use of a motion management technique.

Two new motion management techniques have thus been developed for helical tomotherapy: loose helical tomotherapy with breath-holding and multi-pass respiratory gating. Both methods require the treatment couch to be reset to its starting position to repeat the entire helical treatment, until nearly all planned dose is delivered. For sinusoidal target motion, employing multi-pass respiratory gating was shown to reduce the dose deviation inside the target volume from 14% to 2% for a single fraction, using 4 gated passes. For non-sinusoidal tumour motion causing a dose deviation of 6% within the tumour volume, the required number of passes to keep the dose deviation below 1% was approximately 4 passes for 30 fractions and 5 passes for 3 fractions, demonstrating the feasibility of the multi-pass respiratory gating approach. Clinical implementation of the multi-pass respiratory gating technique would require a number of electronic control and communication modifications to the existing tomotherapy machine, which would lead to significant improvements in the dose distributions delivered for lung tomotherapy treatments – especially for patients exhibiting large tumour motion who are treated with hypofractionation schemes.
Keywords

Radiotherapy, helical tomotherapy, lung cancer, tumour motion, motion management, breath-holding, respiratory gating
Co-Authorship Statement

The current thesis dissertation contains materials from three publications. The permission for reproducing these publications in this thesis is presented in Appendix B.

Chapter 2 is based on a publication, “Kim B, Chen J, Kron T, and Battista J (2009) Motion-induced dose artifacts in helical tomotherapy. Phys Med Biol 54, 5707-34.” As the main author, I have performed all the experimental and computer simulation work, data analysis, and manuscript preparation. All of these tasks were carried out under the supervision of J Battista and J Chen. T Kron contributed with scientific inputs on an occasional basis. All the co-authors were involved in the editing process of the published manuscript.

Chapter 3 is based on a publication, “Kim B, Kron T, Battista J, and Van Dyk J (2005) Investigation of dose homogeneity for loose helical tomotherapy delivery in the context of breath-hold radiation therapy. Phys Med Biol 50, 2387-404.” As the main author, I have performed all the experimental and computer simulation work, data analysis, and manuscript preparation. All of these tasks were carried out under the supervision of T Kron and J Battista. J Van Dyk contributed with scientific inputs on an occasional basis. All the co-authors were involved in the editing process of the published manuscript. The concept of loose helical tomotherapy delivery was concocted by T Kron and J Battista.

Chapter 4 is based on a publication, “Kim B, Chen J, Kron T, and Battista J (2010) Feasibility study of multi-pass respiratory-gated helical tomotherapy of a moving target via binary MLC closure. Phys Med Biol 55, 6673-94.” As the main author, I have performed all the experimental and computer simulation work, data analysis, and manuscript preparation. All of these tasks were carried out under the supervision of J Battista and J Chen. T Kron contributed with scientific inputs on an occasional basis. All the co-authors were involved in the editing process of the published manuscript. T Kron was responsible for the concept of employing multi-pass respiratory gating for helical tomotherapy, as well as the experimental method of simulating a gated beam delivery by modifying the plan leaf opening sinogram.
In dedication to God, who has continuously reminded me that

“For I am the LORD, your God, who takes hold of your right hand and says to you, Do not
fear; I will help you.”

(Isaiah 41:13)

And

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Joon Kim and Inok Kim
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<td>1D</td>
<td>One-Dimensional</td>
</tr>
<tr>
<td>2D</td>
<td>Two-Dimensional</td>
</tr>
<tr>
<td>3D</td>
<td>Three-Dimensional</td>
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<tr>
<td>3D-CRT</td>
<td>Three-Dimensional Conformal Radiation Therapy</td>
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<td>4D</td>
<td>Four-Dimensional</td>
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<tr>
<td>4D-CT</td>
<td>Four-Dimensional Computed Tomography</td>
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<tr>
<td>4D-CBCT</td>
<td>Four-Dimensional Cone Beam Computed Tomography</td>
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<tr>
<td>ABC</td>
<td>Active Breathing Control</td>
</tr>
<tr>
<td>AP</td>
<td>Anterior-Posterior</td>
</tr>
<tr>
<td>b-MLC</td>
<td>binary Multi-Leaf Collimator</td>
</tr>
<tr>
<td>CBCT</td>
<td>Cone Beam Computed Tomography</td>
</tr>
<tr>
<td>CT</td>
<td>Computed Tomography</td>
</tr>
<tr>
<td>CTV</td>
<td>Clinical Target Volume</td>
</tr>
<tr>
<td>DRR</td>
<td>Digitally Reconstructed Radiograph</td>
</tr>
<tr>
<td>DSR</td>
<td>Dynamic Stereotactic Radiosurgery</td>
</tr>
<tr>
<td>EPID</td>
<td>Electronic Portal Imaging Device</td>
</tr>
<tr>
<td>FPI</td>
<td>Flat Panel Imager</td>
</tr>
<tr>
<td>FSB</td>
<td>Forced Shallow Breathing</td>
</tr>
<tr>
<td>GTV</td>
<td>Gross Tumour Volume</td>
</tr>
<tr>
<td>HT</td>
<td>Helical Tomotherapy</td>
</tr>
<tr>
<td>ICRU</td>
<td>International Commission on Radiation Units and Measurements</td>
</tr>
<tr>
<td>IGTV</td>
<td>Internal Gross Tumour Volume</td>
</tr>
<tr>
<td>IM</td>
<td>Internal Margin</td>
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<tr>
<td>IMRT</td>
<td>Intensity Modulated Radiation Therapy</td>
</tr>
<tr>
<td>IMAT</td>
<td>Intensity Modulated Arc Therapy</td>
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<tr>
<td>ITV</td>
<td>Internal Target Volume</td>
</tr>
<tr>
<td>kV</td>
<td>kilo-Voltage</td>
</tr>
<tr>
<td>LR</td>
<td>Left-Right</td>
</tr>
<tr>
<td>MIP</td>
<td>Maximum Intensity Projection</td>
</tr>
<tr>
<td>MV</td>
<td>Mega-Voltage</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>MVCT</td>
<td>Mega-Voltage Computed Tomography</td>
</tr>
<tr>
<td>MLC</td>
<td>Multi-Leaf Collimator</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>MU</td>
<td>Monitor Unit</td>
</tr>
<tr>
<td>Non-IMRT</td>
<td>Non-Intensity Modulated Radiation Therapy</td>
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<tr>
<td>NSCLC</td>
<td>Non-Small Cell Lung Cancer</td>
</tr>
<tr>
<td>OAR</td>
<td>Organ At Risk</td>
</tr>
<tr>
<td>OBI</td>
<td>On-Board Imager</td>
</tr>
<tr>
<td>OD</td>
<td>Optical Density</td>
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<tr>
<td>PTV</td>
<td>Planning Target Volume</td>
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<tr>
<td>QA</td>
<td>Quality Assurance</td>
</tr>
<tr>
<td>RPM</td>
<td>Real-Time Position Management</td>
</tr>
<tr>
<td>RMS</td>
<td>Root-Mean-Square</td>
</tr>
<tr>
<td>RMS_AD</td>
<td>Root-Mean-Square of Dose Deviations</td>
</tr>
<tr>
<td>ROI</td>
<td>Region of Interest</td>
</tr>
<tr>
<td>RTOG</td>
<td>Radiation Therapy Oncology Group</td>
</tr>
<tr>
<td>SAD</td>
<td>Source-to-Axis Distance</td>
</tr>
<tr>
<td>SI</td>
<td>Superior-Inferior</td>
</tr>
<tr>
<td>SBRT</td>
<td>Stereotactic Body Radiotherapy</td>
</tr>
<tr>
<td>SM</td>
<td>Set-up Margin</td>
</tr>
<tr>
<td>TPR</td>
<td>Tissue-Phantom Ratio</td>
</tr>
<tr>
<td>TPR 20/10</td>
<td>Ratio of TPR Values at Depths of 20 cm and 10 cm in Water</td>
</tr>
<tr>
<td>VMAT</td>
<td>Volumetric Modulated Arc Therapy</td>
</tr>
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<th>Symbol</th>
<th>Description</th>
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<tr>
<td>$A$</td>
<td>tumour motion amplitude</td>
</tr>
<tr>
<td>$b$</td>
<td>on-axis fan beam thickness</td>
</tr>
<tr>
<td>$b'$</td>
<td>off-axis fan beam thickness</td>
</tr>
<tr>
<td>$\beta$</td>
<td>dose rippling parameter</td>
</tr>
<tr>
<td>$\beta_{eff}$</td>
<td>effective dose rippling parameter</td>
</tr>
<tr>
<td>$D$</td>
<td>total couch travel during a treatment</td>
</tr>
<tr>
<td>$D(y)$</td>
<td>dose at a given longitudinal position</td>
</tr>
<tr>
<td>$dc$</td>
<td>duty cycle</td>
</tr>
<tr>
<td>$\Phi(y)$</td>
<td>normalized fluence at a given longitudinal position</td>
</tr>
<tr>
<td>$H$</td>
<td>number of helices</td>
</tr>
<tr>
<td>$K$</td>
<td>dose kernel</td>
</tr>
<tr>
<td>$L$</td>
<td>target length</td>
</tr>
<tr>
<td>$n$</td>
<td>number of beam projections per gantry rotation (Chapter 2, 3)</td>
</tr>
<tr>
<td>$N_b$</td>
<td>number of beam projections delivered after couch movement of one fan beam thickness</td>
</tr>
<tr>
<td>$p$</td>
<td>pitch factor</td>
</tr>
<tr>
<td>$\theta$</td>
<td>gantry angle</td>
</tr>
<tr>
<td>$\rho$</td>
<td>density</td>
</tr>
<tr>
<td>$R$</td>
<td>number of gantry rotations</td>
</tr>
<tr>
<td>$t$</td>
<td>time</td>
</tr>
<tr>
<td>$\Delta t(y)$</td>
<td>total radiation exposure time at a given longitudinal position</td>
</tr>
<tr>
<td>$T_0$</td>
<td>relative leaf opening time per beam projection</td>
</tr>
<tr>
<td>$T_a$</td>
<td>actual leaf opening time per beam projection</td>
</tr>
<tr>
<td>$T_g$</td>
<td>gantry rotation period</td>
</tr>
<tr>
<td>$T_l$</td>
<td>gantry rotation period for loose helical delivery</td>
</tr>
<tr>
<td>$T_m$</td>
<td>maximum leaf opening time per beam projection</td>
</tr>
<tr>
<td>$T_r$</td>
<td>tumour motion period</td>
</tr>
<tr>
<td>$T_{r, eff}$</td>
<td>effective tumour motion period</td>
</tr>
<tr>
<td>$T_l$</td>
<td>gantry rotation period for tight helical delivery</td>
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<tr>
<td>$X, Y, Z$</td>
<td>3D Cartesian coordinates in the room coordinate system</td>
</tr>
<tr>
<td>Symbol</td>
<td>Description</td>
</tr>
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<td>----------</td>
<td>----------------------------------------------------------------------------</td>
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<tr>
<td>x, y, z</td>
<td>3D Cartesian coordinates in the tumour coordinate system</td>
</tr>
<tr>
<td>Y(t)</td>
<td>Tumour position at time $t$ in the room coordinate system</td>
</tr>
<tr>
<td>$Y_{couch}(t)$</td>
<td>Treatment couch position at time $t$</td>
</tr>
<tr>
<td>$Y_{tumour}(t)$</td>
<td>Tumour position on the treatment couch at time $t$</td>
</tr>
<tr>
<td>$y_L(t)$</td>
<td>Position of the leading longitudinal beam edge at time $t$</td>
</tr>
<tr>
<td>$y_T(t)$</td>
<td>Position of the trailing longitudinal beam edge at time $t$</td>
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Chapter 1

1 Introduction

This chapter provides a background overview of the research work presented in this thesis dissertation, as well as the research objectives, hypothesis, scope, and the roadmap of this thesis work.

1.1 General Overview

In 2009, there were an estimated 171,000 new cancer cases and 75,300 cancer-related deaths in Canada. Lung cancer accounted for 14% of all cancer incidences, but caused 27% of all cancer deaths, making it the leading cause of cancer deaths in Canada. The 5-year overall survival rate for lung cancer has been historically very low at 15%, compared to the average value of 62% for all cancer sites [1]. There is a clear need to improve the treatment of this disease.

Three different approaches routinely used for treating cancer are surgery, radiotherapy, and chemotherapy. For non-small cell lung cancer (NSCLC), these treatment methods may be used individually, or in combinations. Surgery has shown to yield highly successful clinical outcomes, with 5-year overall survival rates in the range of 50-70% [2,3]. However, surgery is suitable for only one-third of all patients, who are mostly in the early stages of the disease. The inoperable NSCLC patients may be treated with radiotherapy alone, or in combination with chemotherapy. For medically inoperable NSCLC, early stage patients account for 10-15%, while locally advanced cases make up for 30-40% of the patient population [4].\(^1\) When radiotherapy with conventional dose prescription is used alone, the 5-year overall survival rates are in the range of 6-32% for the early stage cases, while generally not exceeding 5% for the locally advanced cases [5,6]. Although different treatment schemes may be employed to improve the

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\(^1\) The remaining 12-27% of NSCLC patients account for more advanced cases.
effectiveness of traditional radiotherapy, the resulting clinical outcomes still remain far inferior to those achievable with surgery [2-5].

Recently, stereotactic body radiotherapy (SBRT) has emerged as a promising technique to improve clinical outcomes for early-stage NSCLC, achieving results comparable to surgery through intensified dose regimens [7-14]. There have been a number of clinical studies in North America, Europe, and Asia, investigating the effectiveness of stereotactic body radiotherapy (SBRT), employing a very small number of dose fractions (hypofractionation) for treating NSCLC. From the currently on-going clinical trial (RTOG 2306), 2-year and 3-year overall survival rates of 54.7% and 42.7% have been reported, respectively [9,10]. In a different study, 5-year overall survival rates as high as 72% and 83% have been observed [11], while 3-year overall survival rates of 47-60% were reported in several multi-institutional studies [12-14]. However, there are remaining concerns for normal tissue complications in the areas of skin, chest wall and rib, due to the high dose given during each fraction [15]. Thus, more long-term data will be required to determine whether SBRT can be adopted as the new standard radiotherapy practice for early stage NSCLC.

Local recurrence is the major reason for high failure rates of lung cancer radiotherapy [7]. Local relapse rates of 6 to 70%, with a median of 40%, have been reported from various studies [16,17]. The major contributing factor for high local recurrences is the insufficient dose given to the tumour volume, limited by the dose tolerance of surrounding organs at risk (OAR), such as normal lungs, heart, and spinal cord. Radiosensitivity of surrounding lung tissues places a limit on the maximum dose deliverable to the tumour volume, so that radiation-induced complications, such as radiation pneumonitis and radiation fibrosis, can be avoided [18]. The effort to spare lung tissues, however, comes at the expense of local tumour control. Local tumour control has been shown to improve with dose escalation [2,4,5,12]. The presence of tumour motion driven by patient breathing [19-22] further limits the maximum dose deliverable to the tumour volume, as an additional margin is generally assigned around the tumour volume to encompass the entire range of tumour motion. This significantly increases the total irradiated volume of normal lung tissues [20]. In addition, the
presence of tumour motion during dose delivery can generate unwanted dose discrepancies inside the tumour volume [20].

Thus, for lung radiotherapy, the use of a highly conformal dose delivery technique becomes essential for improving normal tissue sparing, while simultaneously enabling dose escalation. In the presence of tumour motion, it is crucial to minimize the required margin size and the magnitude of motion-induced dose discrepancies, by employing an effective motion-management method for the chosen dose delivery technique. In this dissertation, helical tomotherapy was selected as the dose delivery technique for lung cancer, due to its highly conformal dose delivery capability. Motion management for helical tomotherapy becomes the focal point of this thesis, as motion management is currently not available clinically for helical tomotherapy. In this work, we have identified and systematically categorized the different types of motion-induced dose discrepancies for helical tomotherapy, while investigating their characteristics in relation to different treatment and respiratory parameters. Feasibility of breath-holding and respiratory gating techniques for helical tomotherapy was then investigated, in terms of their effectiveness for reducing the magnitude of the different motion-induced dose discrepancies.

1.2 Radiation Therapy Techniques

The goal of radiation therapy is to concentrate the dose of radiation to the tumour volume, while minimizing the dose to surrounding normal structures. During the course of a radiation treatment, the prescription dose is usually divided up and delivered in multiple fractions, over a period of weeks, rather than completed in its entirety in a single fraction. The purpose of dose fractionation is to preserve the normal tissues, while allowing cell cycle redistribution and reoxygenation of the tumour cells for more effective tumour cell killings [23]. For conventional lung radiotherapy, a prescription dose of 60 Gy is typically delivered over 30 fractions with 2 Gy given per fraction.

For radiotherapy, a linear accelerator (Figure 1.1) is conventionally used to deliver radiation dose distribution conformal to the target volume. A patient is placed on the treatment couch, while a mega-voltage x-ray beam is generated and emitted from the
gantry head. The gantry can be rotated to treat the tumour volume from various angles. In Figure 1.2, the radiation is shown to be delivered to the lung tumour volume, outlined by the yellow contour, using four treatment beams from different gantry angles. In the resulting dose distribution shown in percentage of the prescription dose, the tumour volume is being covered by the high dose region shown in red (95%), while the other normal structures such as lungs, heart, and spinal cord are located in the low dose regions, depicted in cyan (40%) and blue (20%). Various radiation delivery techniques have been proposed and used over the years, in an effort to improve dose conformity and normal tissue sparing. The different techniques will be described in the order of complexity in following sections.

Figure 1.1: Photograph of a Varian Clinac iX linear accelerator (Varian Medical Systems, Palo Alto, CA) at London Regional Cancer Program.
Figure 1.2: Dose distribution of a 4-beam plan for a lung lesion (yellow). The red colour represents high dose region receiving more than 95% of the prescription dose, while the low dose regions are depicted with cyan (40%) and blue (20%). The ‘red’ beam profiles depict the unique fluence patterns (i.e. intensity modulation) for each of the treatment beams.

1.2.1 Three-Dimensional Conformal Radiation Therapy (3D-CRT)

Three-dimensional conformal radiation therapy (3D-CRT) is performed by shaping each treatment beam according to the projected target shape at a given gantry angle [24]. The beam aperture can be modified with shielding blocks, or by utilizing a multi-leaf collimator (MLC) [25,26]. An example of a MLC system is shown in Figure 1.3, which consists of 120 collimator leaves for shaping a radiation field and/or generating intensity modulation within the field.
1.2.2 Fixed Gantry Intensity Modulated Radiation Therapy (IMRT)

Intensity modulated radiation therapy (IMRT) is an advanced form of 3D-CRT that utilizes conformal radiation fields with non-uniform fluence, with an intent to deliver uniform dose to the tumour volume [27]. The built-in MLC system of the conventional linear accelerator allows for an IMRT delivery to be carried out either in a “step-and-shoot” or “sliding window” mode [28]. In the “step-and-shoot” approach, a sequence of static segments shaped by the MLC leaves is delivered at a fixed gantry angle, while in the “sliding window” mode, also known as the “dynamic MLC” approach, the MLC leaves move continuously during irradiation at a fixed gantry angle.

The dose conformity and normal tissue sparing can be further improved by increasing the number of fixed gantry angles, from which radiation is delivered. In Figure 1.3, a conformal dose distribution is generated by assigning each of the four treatment beams with unique and non-uniform fluence patterns represented by the ‘red’ beam profiles. An additional degree of freedom may be introduced by using the couch angle for non-coplanar treatments [29].
1.2.3 Rotation Therapy

The benefits of using multiple beams to improve dose conformity can be fully exploited by employing continuous gantry rotation during radiation delivery. The treatment may consist of a single or multiple arcs, where each individual arc may cover up to a full $360^\circ$ rotation [30-36]. Traditional rotation therapy used a fixed beam aperture shaped according to the target volume for the entire dose delivery [30]. In a specialized case with a fixed beam aperture, both gantry and couch rotations may occur simultaneously, as in dynamic stereotactic radiosurgery (DSR) [37,38].

For conformal arc therapy, rotational dose delivery is made with a dynamic MLC to adapt the beam aperture according to the projected target shape at each gantry angle [31]. Intensity modulated arc therapy (IMAT) utilizes a dynamic MLC to deliver a single level of fluence to the target volume during each individual arc [32-34]. Thus, multiple arcs are normally required to generate more complex fluence patterns for IMAT. Volumetric modulated arc therapy (VMAT) is capable of achieving the planned dose distribution in a single rotation, by introducing additional degrees of freedom of varying the gantry rotation speed and dose rate [35,36]. The currently available commercial systems employing the VMAT technique include Varian RapidArc (Varian Medical Systems, Palo Alto, CA), and Philips SmartArc (Philips Healthcare, Andover, MA). Varian Medical Systems has recently upgraded their RapidArc system to allow for the delivery of multiple arcs to generate even more sophisticated fluence patterns for radiation therapy.

1.2.4 Tomotherapy

In contrast to the use of a cone beam of radiation that covers the entire target volume, the target volume may also be treated in slices by utilizing a fan beam of radiation. Such delivery techniques can further improve the capability of producing more sophisticated in-plane fluence patterns, but at the expense of prolonged treatment time.

1.2.4.1 Serial Tomotherapy

For serial tomotherapy, each slice within the target volume is treated with a full or partial gantry rotation. After completing the dose delivery to each target slice, the treatment
couch is indexed to the next target slice position for irradiation [39]. The fluence within the fan beam is modulated by two rows of 64 binary MLC ($b$-MLC) leaves that either move in or out of the fan beam field. Intensity modulation is achieved by varying the duration of each leaf opening as a function of beam projection. However, the treatment couch indexing between target slices introduces couch positional uncertainty, which can lead to unwanted “hot or cold” dose spots at the junctions of slices. This problem can be resolved by employing a continuous couch motion that occurs simultaneously with the gantry rotation, as in the case for helical tomotherapy.

1.2.4.2 Helical Tomotherapy

Helical tomotherapy combines continuous gantry rotation and linear couch motion to deliver a 6 MV x-ray fan beam to the target volume in a helical manner [40-42]. A Hi-Art II helical tomotherapy unit (TomoTherapy Inc., Madison, WI) is currently being used clinically at London Regional Cancer Program (Figure 1.4 a). The fan beam has a projected width ($X$) of 40 cm at the isocenter ($SAD = 85$ cm), which is further divided into 64 beamlets by a single row of binary multi-leaf collimator ($b$-MLC) leaves (Figure 1.4 b). There are three different available fan beam thickness ($b$) of 1.05 cm, 2.5 cm, and 5.0 cm projected at the isocenter along the longitudinal direction ($Y$).

Other helical tomotherapy parameters include pitch factor, and gantry rotation period. Pitch factor ($p$) is defined as the longitudinal ($Y$) distance advanced by the treatment couch per gantry rotation, in units of fan beam thickness ($b$). Gantry rotation period ($T_g$) is the time required to complete one full $360^\circ$ rotation. Gantry rotation periods of less than 20 s are typically used clinically for lung tomotherapy. For dose calculation purposes, each gantry rotation is virtually divided into 51 equally-spaced beam projections (each spanning $\sim 7^\circ$), during which the individual $b$-MLC leaves either travel into and out of the fan beam field. Intensity modulation is achieved by varying the durations of individual leaf openings for each beam projection.
The helical tomotherapy unit was the first radiotherapy machine to incorporate an on-line CT imaging capability for patient set-up verification at the start of each treatment fraction. The mega-voltage CT (MVCT) images of a patient acquired with the downshifted energy of 3.5 MV are compared to the planning kilo-voltage (kV) CT images to ensure that the patient is appropriately positioned [43,44].

### 1.3 Image Guidance Techniques

Historically, for radiotherapy, the patient position used during the treatment planning process was replicated mainly with the help of skin tattoos at the start of each treatment fraction [45,46]. However, the internal anatomy can change in relation to the patient surface, between the time of CT imaging for treatment planning and the start of a treatment fraction [47,48]. Thus, relying solely on the skin tattoos for patient set-up is insufficient, due to the tumour position uncertainty arising from the interfraction variation of patient anatomy. Although the dosimetric errors caused by the interfraction variation of tumour position may average out over multiple fractions with the use of a proper
margin [49-51], the use of image guidance to directly verify tumour position at the start of each treatment fraction becomes essential in accurately delivering the planned dose distribution to the tumour volume. This will allow for a possible margin reduction to lower radiation toxicity, as well as dose escalation for an increased local tumour control [52,53]. In some instances, it also becomes necessary to track the tumour position in real-time to account for the intrafraction variation of the tumour position. In this section, the different methods to monitor the interfraction and intrafraction variation of tumour position will be described.

1.3.1 Two-Dimensional (2D) Mega-Voltage (MV) Imaging

Using the mega-voltage (MV) x-ray treatment beam, two-dimensional projection images of the patient can be acquired with film or digitally with an electronic portal imaging device (EPID) [54-56]. The resulting projection images can then be aligned with the digitally reconstructed radiographs (DRR) generated from the planning CT datasets [57]. During the comparison process, positions of visible bony landmarks relative to the radiation field edge are used to verify the tumour position indirectly [58,59]. However, possibilities still exist for the tumour position to change with respect to the bony structures [19]. Direct verification of the tumour position can be achieved with the use of fiducial markers implanted into the tumour volume at the risk of potential surgical complications, such as pneumothorax [46,47]. Although various technologies have been available for electronic portal imaging, the majority of the currently available systems utilize amorphous silicon flat panel imagers (FPI) [54]. The commercial FPI-based systems include Varian PortalVision (Varian Medical Systems, Palo Alto, CA) and Elekta iViewGT (Elekta Oncology, Stockholm, Sweden).

1.3.2 Two-Dimensional (2D) kilo-Voltage (kV) Imaging

Projection images exhibiting better contrast can be generated with the use of kilo-voltage (kV) x-ray sources in the treatment room. However, direct verification of tumour position may still require the use of fiducial markers implanted into the tumour volume [58,59]. Multiple x-ray tubes may be used, so that the orthogonal projection images produced by the corresponding detectors can be combined to provide some 3D
information [54]. In the commercially available robotic radiosurgery systems [60,61], such as BrainLAB Novalis (BrainLAB AG, Feldkirchen, Germany) and Accuray Cyberknife (Accuray, Sunnyvale, CA), two x-ray tubes are mounted on the ceiling, while the flat panel imagers are located in the floor. Conversely, the system developed by the Shirato group utilizes four floor-mounted x-ray tubes and x-ray image intensifiers installed on the ceiling [62-64].

1.3.3 Three-Dimensional (3D) kilo-Voltage (kV) CT Imaging

Direct 3D imaging of soft tissues can be achieved by performing CT imaging inside the treatment room. In the “CT-on-rails” approach, a separate CT scanner is installed inside the treatment room, such that the treatment couch can be shared between the treatment unit and the CT scanner [65,66]. The commercial systems include Varian ExaCT (Varian Medical Systems, Palo Alto, CA), and Siemens Primatom (Siemens AG, Erlangen, Germany).

The existing linear accelerator can also be modified to incorporate cone beam CT (CBCT) imaging, where an additional kV x-ray tube is mounted orthogonal to the gantry head to rotate with the gantry, sharing the same axis of rotation [67-71]. By employing a cone beam geometry that covers the entire region of interest within the patient, a 3D CT image can be acquired in a single rotation. However, the increased scattered x-rays generated due to the large field size must be accounted for to obtain better quality and quantifiable CT number data for dose computations. The commercial linear accelerators equipped with the CBCT system include Elekta Synergy (Elekta Oncology, Stockholm, Sweden), Varian On-Board Imager (OBI) (Varian Medical Systems, Palo Alto, CA), and Siemens Artiste (Siemens AG, Erlangen, Germany). These commercial systems also provide electronic portal and kV-fluoroscopic imaging capabilities. Alternatively, the linear accelerator can also be designed to generate both kV and MV x-ray beams from the same source position. In the Siemens Artiste system (Siemens AG, Erlangen, Germany), the kV beam is generated by utilizing a carbon target instead of tungsten target, while retracting the beam flattening filter.
1.3.4 Three-Dimensional (3D) Mega-Voltage (MV) CT Imaging

Cone Beam CT (CBCT) imaging can also be performed with the treatment MV x-rays, requiring fewer modifications to the existing linear accelerator design [72-76]. An example of such system is Siemens MVision (Siemens AG, Erlangen, Germany). As noted previously, helical tomotherapy is capable of providing MVCT imaging, using a fan beam similar to that of the diagnostic CT units. With a gantry rotation period of 10 s [39], the current TomoTherapy Hi-Art II system (TomoTherapy Inc., Madison, WI) offers three different MVCT acquisition modes with slice spacing of 6 mm (coarse), 4 mm (normal), and 2 mm (fine) [77-79].

1.3.5 Real-Time Tumour Tracking Methods

The 2D-kV imaging system described in Section 1.3.2 can be used to directly monitor the tumour position in real-time. Projection images are acquired periodically during the treatment to track the fiducial markers implanted into the tumour volume [60-64]. However, this approach is not applicable for helical tomotherapy, due to the ring gantry configuration of the tomotherapy machine restricting the access of the fluoroscopic tubes. Direct monitoring of the tumour volume can also be carried out without the use of radiation. With the Calypso system (Calypso Medical Technologies, Inc., Seattle, WA), electromagnetic transponders implanted into the tumour volume are tracked electromagnetically by the localization array panel mounted onto the treatment couch [80,81]. The relatively compact size of the localization array panel also makes the use of the Calypso system feasible for all radiotherapy machines, including helical tomotherapy.

The tumour volume can also be monitored indirectly in real-time by tracking a tumour surrogate that represents the tumour position. The examples of tumour surrogates include chest or abdominal motion, lung volume and/or speed of air flow measured by spirometry [82,83], or pressure measured by an abdominal strain gauge [84]. In the Real-time Position Management (RPM) system (Varian Medical Systems, Palo Alto, CA), the movement of an infrared reflective plastic box placed on patient’s chest or abdomen is monitored by an in-room camera. A commercial example of an abdominal strain gauge is the fixation belt used for the AZ-733V respiratory gating system (Anzai Medical Co.,
Ltd, Tokyo, Japan), that is wrapped around the patient abdomen. The resulting abdominal pressure changes are then measured with a pressure sensor attached to the fixation belt. Although indirect monitoring removes the surgical complication risks of implanting fiducial markers, an accurate correlation must be established between the actual tumour position and the tumour surrogate. In addition, one must ensure that the same correlation is being maintained throughout the course of treatment. The internal-external correlation between the tumour position and tumour surrogate may be verified with the use of 4D-CT imaging [85-89].

1.3.6 Future Outlook

Currently, both the CBCT and MV imaging techniques are being used only for geometric verification of the tumour position. The next step would be to perform dose calculations using the acquired CT data, to determine whether the planned dose distribution is being delivered to the tumour volume, and if the existing plan needs to be re-optimized during the course of treatment. However, the CT numbers generated by these imaging modalities are not yet reliable enough for dosimetric adaptations [90-96]. With the use of four-dimensional (4D) CT imaging [85-89] becoming more prevalent for treatment planning, employing a four-dimensional (4D) image guidance technique may become a clinical practice of the future. Direct comparisons could then be made between the planning 4D-CT and 4D-CBCT images generated at the same phase of the respiratory cycle [97]. A MRI system may also be incorporated into the linear accelerator to provide superior soft tissue contrast, while avoiding the need for giving additional radiation dose to the patient. However, significant technological hurdles still remain, such as the interference between the electromagnetic fields of the linear accelerator and the MRI system [98,99].

1.4 Tumour Motion and Motion-Induced Dose Discrepancies

Tumour motion resulting from patient breathing is a significant problem for lung radiotherapy. It forces the clinicians to use a larger margin around the tumour volume, in an effort to encompass the full extent of tumour motion. As a result, a significant volume
of surrounding normal lung tissues is irradiated, increasing radiation toxicities and placing a limit on the maximum dose that can be prescribed to the tumour volume. In addition, the presence of tumour motion during dose delivery can produce dose discrepancies between the planned and delivered dose distributions to the tumour volume, affecting the accuracy of dose delivery. These major issues caused by tumour motion can compromise the clinical benefits of radiotherapy and lead to suboptimal local tumour control of lung cancer. In this section, the mechanics of breathing and extent of lung tumour motion will be described, as well as the impact of tumour motion for different radiation treatment modalities, including helical tomotherapy.

### 1.4.1 Mechanics of Breathing

Breathing is a physiological process alternating between inspiration and expiration to facilitate gas exchanges between blood and air inside the lungs. Lungs are located within the thoracic cavity, surrounded by a fluid-filled pleural cavity. The inner membrane of the pleural cavity envelops the lungs, while its outer membrane is attached to the thoracic wall, holding the lungs in place. Due to this unique anatomical arrangement, volume of the thoracic cavity directly affects the pressure inside the pleural cavity (intrapleural pressure) and the lungs (alveolar pressure). During breathing, the alveolar pressure varies from being slightly below or above the atmospheric pressure, causing the air to either flow in or out of the lungs. On the other hand, the intrapleural pressure always remains far below the atmospheric pressure to keep the lungs from collapsing [20].

During inhalation, the expansion of the thoracic cavity occurs in all dimensions, driven by the active contractions of the diaphragm and the intercostal muscles connecting the ribs. The superior-inferior (SI) dimension of the thoracic cavity is expanded with the diaphragm descending inferiorly, while the contracting intercostal muscles pull the ribs superiorly and anteriorly to increase the anterior-posterior (AP) and lateral diameters of the thoracic cavity. The thoracic cavity expansion is then accompanied by a volumetric increase of the pleural cavity, and a simultaneous decrease in intrapleural pressure. Due to the decrease of pressure just outside the lungs, the lungs also undergo volumetric expansions, causing the alveolar pressure inside the lungs to drop below the atmospheric pressure. Thus, air is drawn into the lungs, until the alveolar pressure reaches the
atmospheric pressure. During the exhalation, both diaphragm and intercostal muscles passively return to their pre-inhalation states, restoring the previous lung volume and pressure, pushing air out of the lungs. The complex elastic property of the lung also contributes to its volume-pressure relationship exhibiting hysteresis, where the inhalation lung volume is always smaller than the exhalation lung volume at the same transpulmonary pressure, i.e. the difference between the alveolar pressure and intrapleural pressure [100]. In relations to dose computations and dose delivery, the lung is a complex dose absorber due to its variable shape and density.

### 1.4.2 Measurements of Tumour Motion

Various studies have employed different imaging modalities, such as fluoroscopy, CT and MRI to investigate tumour motion at different locations with the lung (upper, middle and lower lung) [19,20]. Fluoroscopy techniques included film radiography, MV portal imaging, and kV fluoroscopy, with and without the use of fiducial markers. Parameters of lung tumour motion, such as magnitude, period, regularity, and baseline variation were shown to vary widely between individual patients. Although it was difficult to establish a strong correlation between tumour displacement and tumour location within the lung, the greatest 3D tumour displacements were observed for the lower lung tumours, due to the influence of diaphragmatic motion. Mean displacements of up to 18.5 mm, 7 mm, and 12.6 mm were reported in the superior-inferior (SI), anterior-posterior (AP), and left-right (LR) direction, respectively [19-21]. Thus, proximity of the tumour position to the diaphragm may serve as a strong indicator for the presence of predominant SI tumour motion. In some studies, the diaphragm position was used as the tumour surrogate for monitoring, due to the difficulty of viewing the actual tumour volume [101-104]. For lower and middle lung tumours, the displacements of up to 38.7 mm and 26.1 mm were observed in the SI direction [21]. However, the largest tumour displacement was reported for an upper lung tumour, which exhibited a displacement of up to 50 mm in the SI direction [19].
1.4.3 Motion-Induced Dose Discrepancies for Helical Tomotherapy

The presence of tumour motion during dose delivery can lead to significant dose discrepancies between the planned and delivered dose distributions. This motion-induced dosimetric problem may not be simply resolved by assigning a larger margin around the tumour volume, as the dose distribution within the tumour volume and surrounding region is being affected. Thus, it becomes crucial to understand the relationships between the treatment and tumour motion parameters, and discover ways to minimize the magnitude of overall dose discrepancies.

Motion-induced dose discrepancies have been reported in the literature for different IMRT techniques. The interplay between the MLC motion and tumour motion prevent the intended dose distribution from being delivered to the tumour volume, as the interplay effect is not modelled during treatment planning [49,50,105,106]. The problem becomes even more complicated for helical tomotherapy, which employs three simultaneously moving subsystems (gantry, couch, and b-MLC). As a result, possibilities for a greater number of interplay and interactions with tumour motion can exist. The impact of tumour motion during helical tomotherapy has been studied [49,107-109]. Gradual changes in amplitude, period, and baseline of tumour motion over a period of time were also shown to generate significant dose discrepancies [110,111].

However, no work has yet to isolate and systematically categorize the different types of dose discrepancies resulting from tumour motion during helical tomotherapy. Different types of motion-induced dose discrepancies should be investigated individually, in relations to different treatment and tumour motion parameters to gain better understanding for their causes. Once a clear understanding for all potential types of dose discrepancies is established, the appropriate strategies to address these effects can be proposed and investigated. Study of different types of motion-induced dose discrepancies due to tumour motion during helical tomotherapy is one of the most essential components of this thesis.²

² Different motion-induced dose discrepancies investigated in this thesis are summarized in Table 5.1.
1.5 Motion Management of Lung Tumours during Radiation Delivery

In this section, both the traditional and new methods of defining motion-encircling tumour volume will be discussed. The different motion management techniques will then be described for both conventional radiotherapy techniques and helical tomotherapy.

1.5.1 Use of Margins to Encompass Tumour Motion

Traditionally, target volume delineation process follows the guidelines provided by the ICRU 62 [112]. A gross tumour volume (GTV) is defined as “the gross demonstrable extent and location of the malignant growth” that is visible on the planning images [98]. A clinical target volume (CTV) expands on the GTV to include microscopic extensions surrounding the GTV, which are invisible on the images but nonetheless exist. A planning target volume (PTV) is then produced by adding a margin around the CTV to account for all sources of intrafraction and interfraction uncertainties arising over the course of a radiation treatment. There are a number of PTV margin “recipes” currently available, which propose the different weighting factors for the various systematic and random components of uncertainties to calculate the required PTV margin size [113].

In the presence of tumour motion, the PTV margin may be further divided into internal margin (IM) and set-up margin (SM). An internal margin (IM) encompasses the intrafraction tumour motion, and interfraction variations of the CTV size, shape and position. A set-up margin (SM) accounts for the patient set-up and beam positioning uncertainties. One of the currently available image guidance methods discussed in Section 1.3 may be employed to minimize the PTV margin size.

With the availability of more advanced imaging techniques, however, a new way of defining GTV to encompass tumour motion has emerged. This motion-encircling tumour volume may be referred to as the tumour motion envelope [114], or the internal gross tumour volume (IGTV) [115-119]. The philosophy behind this approach is to commence the tumour delineation process with a “correct” GTV, rather than accounting for tumour motion using internal margin (IM) at a latter stage. “Slow” CT imaging utilizes a gantry rotation period comparable to a tumour motion period to capture the
entire motion extent of a tumour volume [120-122]. The slow CT scan is performed multiple times to ensure that the resulting tumour motion envelope represents the sum of tumour volumes at all of its probable positions. Due to the use of a relatively slow gantry speed and large amount of data, however, the resulting slow CT images are subjected to significant motion-induced image artifacts, interfering greatly with an accurate delineation of the tumour envelope [114,123-125]. Gagne et al has demonstrated that the tumour envelope can still be determined accurately in the presence of image artifacts by only accepting a volume of pixels with intensity above a specific threshold [105].

With the advent of 4D-CT imaging technique, multiple CT datasets at different respiratory phases have become available clinically [85-89]. Thus, the GTV’s contoured from all respiratory phases can be combined to generate an internal gross tumour volume (IGTV). Currently, at London Regional Cancer Program (LRCP), contouring is done at the end-expiration and end-inspiration phases to capture the tumour volume at its most extreme positions. The two GTV’s are then combined with the GTV contoured on the “average” CT of all phases to generate the IGTV. It has been shown that the IGTV produced from the end-expiration and end-inspiration phases alone may significantly underestimate the IGTV generated from all phases [119]. Alternatively, the IGTV can also be delineated on the maximum intensity projection (MIP) image from the different phases [116-119]. However, the MIP approach is not capable of isolating the tumour volumes that are located close to other structures, such as the diaphragm or mediastinum [116].

1.5.2 Tumour Motion Management for Conventional Radiotherapy Techniques

Accurate determination of the planning target volume (PTV) encompassing the entire tumour motion alone is not sufficient to account for the motion-induced dose discrepancies generated inside the PTV. Thus, employing tumour motion management will be required to reduce the magnitude of dose discrepancies. The currently available motion management techniques can be classified into breath-holding, respiratory gating, and tumour tracking.
1.5.2.1 Breath-Holding

During a radiation treatment employing breath-holding, treatment beam is only turned on during breath-holds, and turned off between breath-holds to allow patients to resume normal breathing. Patients undergo breath-holding at a planned respiratory phase, during which the tumour volume is temporarily immobilized inside the treatment field [126-139]. To achieve breath-holding in a reproducible manner, patients are provided with assistance in the form of verbal instructions [130], a breathing-aid such as the active breathing control (ABC) device [131-135], a visual display of the patient’s own respiration trace [82,83], or different combinations of these aids.

The respiratory phase for breath-holding may occur at deep-inspiration [126-134], normal inspiration [136,137], or end-expiration [131,138]. Deep-inspiration breath-holding has generally shown to yield high tumour position reproducibility, and displace the critical structures within the thoracic cavity, such as the heart and major blood vessels, away from the treatment field. In addition, the total mass of normal lung tissues within the treatment field may decrease, as the lung tissue density approaches its minimum at deep-inspiration. However, patient discomfort remains a big issue for breath-holding, due to the poor pulmonary conditions of lung patients. At Memorial Sloan-Kettering Cancer Center (MSKCC), a compliance rate of only 40% was reported for deep-inspiration breath-holding in 2000 [127]. Patient compliance rate may improve with normal inspiration breath-holding, but the aforementioned clinical advantages of deep-inspiration breath-holding may be greatly reduced. With end-expiration breath-holding, tumour coverage may improve due to the increased lung tissue density, but at the expense of greater mass of normal tissues being irradiated. However, it has been shown that the improved lung tissue sparing at deep inspiration is likely to outweigh the improved tumour coverage at end-expiration [139].

Due to the patient compliance issue for breath-holding, forced shallow breathing (FSB) may be employed to allow limited normal breathing [140-143]. In this approach, pressure is applied to the patient’s abdomen by a small plate attached to a stereotactic frame, thus limiting the extent of diaphragmatic motion. Negoro et al has observed the
range of tumour motion to decrease from 8-20 mm (12.3 mm mean) to 2-11 mm (7.0 mm mean) with abdominal compression [142].

1.5.2.2 Respiratory Gating

During a radiation treatment employing respiratory gating, the treatment beam is only turned “on” during a pre-determined portion of a tumour motion cycle, placing no constraints on patient breathing. This pre-set portion of a tumour motion cycle, namely the gating window, may cover a range of tumour positions (amplitude gating) or phases within a respiratory cycle (phase gating), during which radiation delivery is enabled [144-148]. Once the tumour volume moves out of the gating window, the treatment beam is turned off, until it returns again inside the gating window for a subsequent beam delivery. As the magnitude of tumour motion during radiation delivery becomes restricted to the residual motion [148] within a gating window, the impact of tumour motion during a gated dose delivery is greatly reduced.

Selecting an appropriate gating window size is based on a tradeoff between accuracy and efficiency of dose delivery. Use of a very small gating window will effectively “freeze” the tumour motion during radiation delivery, allowing for an accurate dose delivery to be made to the tumour volume. However, this occurs at the expense of significantly prolonging the treatment session time. The gating window is normally positioned around the end-expiration phase, as a moving tumour volume typically slows down during expiration and reaches its minimum velocity at the end-expiration. Thus, placing a gating window around the end-expiration phase yields a smaller residual motion, compared to other respiratory phases [144].

1.5.2.3 Tumour Tracking

During a radiation treatment employing tumour-tracking, the moving tumour volume is continuously irradiated by dynamically moving a treatment beam according to tumour position [149-155]. As a result, no constraints are placed on patient breathing, and unlike breath-holding and respiratory gating, the treatment session time is comparable to a radiation treatment session time without motion management. Beam repositioning may be achieved through the use of a dynamic MLC [149-154], or a robotic arm [155] moving
a miniature linear accelerator. In the remainder of this thesis, the MLC repositioning method will be referred to as the tumour tracking method.

Clinical implementation of tumour tracking dose delivery requires the use of a real-time tumour monitoring system (Section 1.3.5), and a predictive algorithm [156-161]. A predictive algorithm is used to anticipate the “near-future” tumour position in advance, accounting for the time required to determine and execute appropriate MLC movements after detecting the tumour location. For a conventional MLC system, the leaf response latency and the actual leaf transition time combine to yield a total latency in the range of 100-200 ms [20]. Thus, the accuracies of tumour monitoring and the predictive algorithm become crucial to ensure an appropriate synchrony is established between tumour motion and corresponding leaf actions, so that significant dose discrepancies can be avoided.

1.5.3 Tumour Motion Management for Helical Tomotherapy

Employing any of the aforementioned motion management techniques in Section 1.5.2 becomes more complicated for helical tomotherapy, due to its continuously moving subsystems (gantry, couch, and b-MLC). In the past, different motion management methods [162-167] have been proposed for helical tomotherapy, but none of them have been implemented clinically as of yet.

In the “gating-by-rotation” approach, dose delivery during each gantry rotation occurs, while the patient undergoes breath-holding. Each gantry rotation with breath-holding is then followed by a “non-treatment” gantry rotation, during which the couch movement is temporarily halted and the b-MLC leaves remain fully closed to permit normal breathing [162,163]. At the start of the subsequent gantry rotation, both breath-holding and couch motion resume for dose delivery. The same process is repeated, until the entire tumour volume is treated.

Tumour motion information may be incorporated a priori during the plan optimization process, allowing for a pre-planned tracking of the tumour volume by the binary MLC (b-MLC) during treatment [164,165]. However, the same tumour motion pattern used
during planning must be reproduced during each treatment fraction to avoid significant dose discrepancies. Real-time tumour tracking has also been proposed for helical tomotherapy [166,167]. In this method, the longitudinal motion component is compensated by “shuffling” and executing the sequence of planned beam projections assigned with the same gantry angles out-of-order, according to the detected longitudinal tumour location. The change in lateral tumour position is accounted for by delivering the same planned fluence through different leaves.

1.5.4 Limitations of the Proposed Tumour Motion Management Approaches for Helical Tomotherapy

With the “gating-by-rotation” approach, halting the couch motion during treatment introduces an additional couch position uncertainty and potential beam junctioning, as well as potentially altering the patient position. Although the couch position uncertainty introduced during each stoppage may be small, the uncertainty accumulated over multiple start-stops may become significant. The use of a large pitch factor to reduce or eliminate the interruptions of couch movement may be more feasible clinically, and this becomes another objective of this thesis.

Although incorporating tumour motion information during the plan optimization process is an innovative way to track the tumour volume in a pre-planned manner, it will be very difficult to reproduce the identical tumour motion pattern during each treatment fraction. For real-time tumour tracking method, “shuffling” the beam projections to treat the different slices within the volume out-of-order does not compensate for the radiological pathlength differences encountered by the original and shifted beam projections. As each spatially shifted beam projection encounters different tissue density and thickness, the beam attenuation will be affected, preventing the intended dose from being delivered to the tumour volume – especially for large amplitudes of tumour motion. This tissue attenuation issue may be avoided by employing respiratory gating over tumour tracking. Feasibility study of respiratory gating for helical tomotherapy is one of the primary objectives of this thesis.
Due to the continuous motions of the gantry and treatment couch during helical tomotherapy, the dose undelivered at a particular gantry angle and couch position cannot be recovered, unless the gantry rotation and couch motion are interrupted. The only way to make up for the “missing” dose without introducing treatment interruptions is to repeat the entire treatment. Thus, the two new approaches presented in the current thesis utilize multiple passes of helical tomotherapy dose delivery to complete the planned dose distribution to the tumour volume.

1.6 Research Objectives
The research work done in this thesis was focused on the following objectives:

1. Define the different types of dose discrepancies resulting from tumour motion during helical tomotherapy, and investigate the characteristics of each dose discrepancy individually, in relations to different treatment and tumour motion parameters, through computer simulations and experimental measurements using film dosimetry.

2. Describe and investigate the dosimetric characteristics of the loose helical tomotherapy delivery with breath-holding, simulated on a linear accelerator (prior to the arrival of the helical tomotherapy unit at LRCP), through treatment planning and experimental measurements using film dosimetry.

3. Describe and investigate the feasibility of employing multi-pass respiratory gating technique for helical tomotherapy, through computer simulations and experimental measurements using film dosimetry on the helical tomotherapy machine.

1.7 Research Hypothesis
Respiratory gating or breath-holding techniques can be applied to helical tomotherapy to reduce the different sources of dose discrepancies caused by tumour motion.
1.8 Scope of the Thesis and Thesis Roadmap

Target volume investigated in this thesis work represents a lower lung tumour located close to the diaphragm, thus exhibiting predominant motion along the superior-inferior (SI) direction, driven by diaphragmatic motion. Thus, all motion patterns investigated in this thesis displayed 1D target motion, only along the SI direction. All the experimental measurements were performed with sinusoidal target motion, while both sinusoidal and non-sinusoidal motion patterns were employed for computer simulations. No inhomogeneity was introduced by assuming a target volume that is surrounded by water-equivalent tissues, instead of lung tissues.

In Chapter 2: “Motion-induced dose artifacts in helical tomotherapy”, the different types of dose discrepancies resulting from tumour motion during helical tomotherapy are defined, and their characteristics are investigated individually, in relations to different treatment and tumour motion parameters. The work in this chapter is based on a publication, “Kim B, Chen J, Kron T, and Battista J (2009) Motion-induced dose artifacts in helical tomotherapy. *Phys Med Biol* 54, 5707-34.” In Chapter 3: “Investigation of dose homogeneity for loose helical tomotherapy delivery in the context of breath-hold radiation therapy”, the loose helical tomotherapy delivery with breath-holding is described, along with its dosimetric characteristics. The work in this chapter is based on a publication, “Kim B, Kron T, Battista J, and Van Dyk J (2005) Investigation of dose homogeneity for loose helical tomotherapy delivery in the context of breath-hold radiation therapy. *Phys Med Biol* 50, 2387-404.” In Chapter 4: “Feasibility study of multi-pass respiratory-gated helical tomotherapy of a moving target via binary MLC closure”, the multi-pass respiratory gating technique is described. The proposed technique is investigated, in terms of its effectiveness for reducing the magnitude of different motion-induced dose discrepancies described in Chapter 2. The work in this chapter is based on a publication, “Kim B, Chen J, Kron T, and Battista J (2010) Feasibility study of multi-pass respiratory-gated helical tomotherapy of a moving target via binary MLC closure. *Phys Med Biol* 55, 6673-94.” In Chapter 5: Summary and Conclusions, major findings from each of Chapter 2, 3, and 4 are summarized. The
clinical implications and the limitations of the proposed methods and the work done in this thesis are discussed, as well as the future work.

1.9 References


Chapter 2

Motion-Induced Dose Artifacts in Helical Tomotherapy


2.1 Introduction

2.1.1 Helical Tomotherapy

Helical tomotherapy [1,2] is a novel radiation therapy technique, which utilizes a continuously rotating gantry and a linearly moving couch to irradiate a target volume in a helical manner. As the treatment couch advances into the gantry bore along the longitudinal direction (Y), the target volume is irradiated in slices using a fan beam of radiation. At the axis of gantry rotation (SAD = 85 cm), a two-stage collimation produces a fan beam field with a projected width of 40 cm (X = 40 cm) and a selectable fan beam thickness of 1.05 cm, 2.5 cm, or 5.0 cm along the longitudinal direction (Y). The fan beam is further divided into 64 beamlets with each beamlet being 0.625 cm wide at the axis of gantry rotation (40 cm / 64 = 0.625 cm), using a binary multi-leaf collimator (b-MLC). The b-MLC consists of 64 interlaced binary leaves (32 on each side of the axis of gantry rotation), which can be either fully open or fully close with a leaf transit time of about 15 ms [3,4]. Radiation fluence passing through each beamlet is thus controlled by the duration of time for which its corresponding leaf remains open (i.e. leaf opening time). Every gantry rotation during a helical tomotherapy treatment is divided into 51 equally-spaced beam projections (each spanning ~7°) for the purpose of intensity modulation. Intensity modulation is then achieved by assigning a specific value of leaf opening time as a function of beam projection and leaf number. The duration of leaf opening time is centered about the mid-point of each beam projection period, with the leaf remaining closed during the start and end of the beam projection period.
2.1.2 Tumour Motion

The presence of tumour motion during the radiation therapy of lung cancer is a well-documented problem. In the past, various approaches have been proposed to minimize the effect of respiratory-driven tumour motion during conformal radiation therapy [5-8], IMRT [9,10], and helical tomotherapy [4,11-13] treatments. Inferiorly positioned lung tumours typically exhibit the greatest range of motion along the superior-inferior (SI) direction of the patient, due to their proximity to the diaphragm and the resulting influence of the diaphragmatic motion. Peak-to-peak magnitude of such tumour motion can approach several cm’s with a typical period of 3-5 s [14-17]. The SI motion component coincides with the longitudinal direction of the couch motion, and thus interferes directly with the “slice-to-slice” irradiation of the target volume during a tomotherapy delivery. This motion-induced interference can lead to various types of dose discrepancies between the delivered and plan dose distributions [18-21]. Dose discrepancies can also result from the anterior-posterior (AP) and left-right (LR) components of tumour motion. Although the correct slices of the target volume are still being irradiated in the presence of these motions, the plan dose is not correctly deposited in the planning target volume (PTV). In this work, however, we will be focusing on the SI target motion only, as it is the predominant motion component that can potentially produce the most significant dose discrepancies.

2.1.3 Different Types of Motion-Induced Dose Discrepancies

In the present study, three different types of motion-induced dose discrepancies are defined specifically for helical tomotherapy, namely (1) dose rounding, (2) dose rippling, and (3) IMRT leaf opening asynchronization effect. Dose rounding [18,21] is the penumbral widening of a delivered dose distribution near the edges of a target volume along the direction of tumour motion. In the presence of longitudinal target motion, the penumbral increase leads to the under-dosing of the target volume near its longitudinal boundaries, and over-dosing of the surrounding normal structures just outside the target volume. Dose rounding becomes more pronounced with the increasing amplitude of tumour motion.
Dose rippling [18-20] is a series of periodic dose peaks and valleys present within the target region along the direction (Y) of couch motion. Dose rippling is observed for tomotherapy cases both with and without intensity modulation (i.e. IMRT and non-IMRT cases). Dose rippling occurs due to an asynchronous interplay between the couch motion and the longitudinal tumour motion with a fixed frequency. When the interplay is synchronous, dose rippling becomes absent for the non-IMRT cases, while being significantly reduced for the IMRT cases. For the non-IMRT cases, constant leaf opening time means that the dose losses due to motion are always compensated by the identical dose gains (and vice versa) for synchronous conditions, which leads to the absence of dose rippling. On the other hand, the variable durations of leaf opening time during an IMRT delivery cause the dose gains to differ from the dose losses. Thus, although the magnitude of dose rippling is significantly reduced for synchronous conditions, the differences still exist between the planned and delivered dose distributions.

The IMRT leaf opening asynchronization effect is an additional effect caused by an asynchronous interplay between the temporal patterns of leaf openings and the longitudinal target motion. Unlike dose rippling, the IMRT leaf opening asynchronization effect does not exhibit any periodicity, and its resulting dose distribution pattern is highly specific and unique to each tomotherapy plan (i.e. leaf opening pattern). The paper by Kanagaki et al [21] was the only study that investigated the effect of tumour motion for IMRT helical tomotherapy deliveries. However, the IMRT leaf opening asynchronization effect was not observed in this particular work, and hence we characterized a new and significant dose discrepancy associated with IMRT tomotherapy deliveries.

2.1.4 Purpose

In the present study, the characteristics of the three aforementioned dose discrepancies were investigated as functions of target motion amplitude and period for both non-IMRT and IMRT helical tomotherapy cases in the presence of sinusoidal target motion. The non-IMRT cases were investigated to allow for the dose rounding and dose rippling effects to be studied separately. A computer simulation model was developed to
calculate longitudinal dose profiles along the axis of gantry rotation inside a body phantom, and to be used as a tool to predict the dosimetric effect of tumour motion during a helical tomotherapy delivery. Experimental verification was then carried out on the helical tomotherapy unit, using a motion body phantom and dosimetric film. The dosimetric characteristics of dose rounding and dose rippling were also studied as a function of target motion amplitude.

2.2 Materials and Methods

2.2.1 Helical Tomotherapy Plans

In this section, the parameters related to helical tomotherapy and tumour motion will be defined. The nature of leaf opening sinogram will be explained. The non-IMRT and IMRT helical tomotherapy plans used in this study to investigate the effect of target motion will be also described.

2.2.1.1 Helical Tomotherapy and Tumour Motion Parameters

The treatment parameters associated with helical tomotherapy include pitch factor \((p)\), fan beam thickness \((b)\), gantry rotation period \((T_g)\), and number of gantry rotations \((R)\). Pitch factor \((p)\) is defined as the progression distance of the longitudinal couch motion per gantry rotation in units of fan beam thickness \((b)\). Gantry rotation period \((T_g)\) is the time required to complete one full gantry rotation; the current helical tomotherapy unit allows for selectable periods \((T_g)\) between 15 and 60 s, with a gantry rotation period of 15 to 20 s being used clinically for the helical tomotherapy of lung cancer [22]. Number of gantry rotations \((R)\) is the number of gantry rotations required to treat the target volume during the treatment. The parameters related to tumour motion are amplitude \((A)\) and period \((T_r)\). Amplitude \((A)\) is defined as the one-half of the peak-to-peak amplitude \((2A)\) of tumour motion along the longitudinal direction \((\pm Y)\), while tumour motion period \((T_r)\) is the time required to complete one full cycle of tumour motion.

2.2.1.2 Leaf Opening Sinogram

During a helical tomotherapy treatment, intensity modulation is carried out according to the leaf opening time information stored in the form of a leaf opening sinogram. The leaf
opening sinogram is a two-dimensional matrix of leaf opening time values, where the row and column indices represent leaf number and beam projections, respectively. In this study, a user-created leaf opening sinogram was utilized for the non-IMRT cases, while a leaf opening sinogram for the IMRT cases was generated by the helical tomotherapy plan optimizer (TomoTherapy version 2.2.2, TomoTherapy Inc., Madison, WI).

2.2.1.3 Non-IMRT Helical Tomotherapy Plan

The current helical tomotherapy unit (HI-ART II) allows the user to enter a leaf opening sinogram directly at the treatment console for a radiation delivery. In order for the leaf opening sinogram to be accepted at the treatment console, the leaf opening sinogram must contain values of relative leaf opening time. Relative leaf opening time \( T_0 \) is defined as the ratio of the actual leaf opening time \( T_a \) for a beam projection to the maximum leaf opening time per beam projection \( T_m \):

\[
T_0 = \frac{T_a}{T_m}, \quad T_m = \frac{T_g}{n}
\]  

(2.1)

where \( T_0 \) is the relative leaf opening time for a beam projection, \( T_a \) is the actual leaf opening time for the beam projection, \( T_m \) is the maximum leaf opening time per beam projection, \( T_g \) is the gantry rotation period, and \( n \) is the number of beam projections per gantry rotation (\( n = 51 \)).

For the non-IMRT plan, the planning target volume (PTV) was assumed to be a 5.5 cm-long cylinder centered along the axis of gantry rotation inside the body phantom (Modus Medical Devices Inc., London, Canada) shown in Figure 2.1 a), which mimicked a human torso. The four central leaves were assigned with the maximum leaf opening time \( T_0 = T_m = 1.00 \) for all beam projections, while the rest of the leaves remained fully closed \( T_0 = 0.00 \) during the entire treatment, using a fan beam thickness \( b \) of 2.5 cm. A fixed value of leaf opening time was assigned for each individual leaf, so that a uniform fluence was delivered only along the central axis of the PTV. Using a pitch factor of 0.8 \( (p = 0.8) \), four full gantry rotations \( (R = 4) \) were required to treat the PTV, and a gantry rotation period of 16 s \( (T_g = 16 \text{ s}) \) was selected. A pitch factor of 0.8 was
selected rather than the typically used pitch factor of less than 0.3 for lung cancer tomotherapy [22], in order to produce specific conditions for studying the dose rippling effect described in Section 2.1.3.

### 2.2.1.4 IMRT Helical Tomotherapy Plan

An IMRT helical tomotherapy plan was generated using the CT images of a body phantom (\( \rho = 1.18 \, \text{g/cm}^3 \), length = 12 cm, width = 30 cm, height = 20 cm) in Figure 2.1 a). On the CT images of the body phantom (Figure 2.1 b), a virtual 3.6 cm-long cylindrical organ at risk (OAR) was delineated to be wrapped around by a 6.6 cm-long C-shaped planning target volume (PTV). Contouring of the PTV, the OAR, and the phantom outline was performed in a commercial treatment planning system (Pinnacle 8.0d, Philips Medical Systems). The CT images and contours were then exported to the tomotherapy treatment planning system (TomoTherapy version 2.2.2, TomoTherapy Inc., Madison, WI), where a dose of 2.0 Gy was prescribed to 95% of the PTV with the maximum OAR dose being limited to 0.8 Gy. A pitch factor (\( p \)) of 0.287 (i.e. 0.86 / 3) was selected to minimize the “thread artifact” [23], and a fan beam thickness of 2.5 cm was chosen. During the tomotherapy plan optimization process, the values of leaf opening time needed to optimize the plan were calculated for each of the 64 b-MLC leaves as a function of beam projection, yielding the planned dose distribution shown in Figure 2.1 c).

At the end of the plan optimization, the generated leaf opening sinogram contained sums of leaf opening time for all fractions of a treatment (i.e. actual leaf opening time per fraction * number of fractions) over 819 beam projections (\( R \sim 16 \)), with the matrix rows and columns representing beam projections and leaf number, respectively. The leaf opening sinogram was then truncated to shorten the length of the PTV from 6.6 cm to 3.24 cm, so that the resulting PTV region fell well within the length of the body phantom with the motion amplitudes used in this study. This was done by eliminating the first 252 and the last 159 beam projections, yielding a plan with 408 beam projections (\( R = 8 \)) and a plan dose of 1.75 Gy instead of 2.0 Gy. This was deemed acceptable, as the objective of this study was not to reproduce a particular plan, but to investigate how motion affects
In order to make the modified leaf opening sinogram to be accepted at the treatment console, each value of leaf opening time was converted to relative leaf opening time, and the entire leaf opening sinogram matrix was then transposed (i.e. indexed by leaf number, beam projection).

Figure 2.1: IMRT helical tomotherapy plan for a stationary target a) Photograph of the lucite body phantom (\(\rho = 1.18 \text{ g/cm}^3\), length = 12 cm, width = 30 cm, height = 20 cm) mimicking a human torso, b) Transverse (top) and coronal (bottom) CT images of the body phantom with the contours of the PTV (dark), OAR (light), and the phantom outline. The film insert remained stationary inside the body phantom at its mid-position during the CT scanning process. c) Plan dose distributions on the transverse and coronal planes. Dose of 2.0 Gy was prescribed to 95% of the PTV with the maximum OAR dose being limited to 0.8 Gy.

---

3 The delivered dose distribution in Figure 2.7 (b) for the (i) “no motion” case appears different from the plan coronal dose distribution shown in Figure 2.1 (c), due to the truncation process as well as the resulting shift in gantry angle.
2.2.2 Computer Simulation

A computer simulation program was developed in MATLAB (Mathworks, Natick, MA), as a tool to study and predict the dosimetric effect of longitudinal target motion during a helical tomotherapy delivery. The computer simulation model was designed to calculate dose profiles along the axis of gantry rotation for both non-IMRT and IMRT helical tomotherapy irradiations of the body phantom (Figure 2.1 a). A similar study for helical tomotherapy was first published by Kissick et al [20], which was an extension of the work done by Yu et al [19] for the sliding window technique. The concept used by Yu et al [19] was applicable to the present study and to the study by Kissick et al [20], since the set-up for the sliding window technique in the presence of lateral motion was analogous to that of helical tomotherapy in the presence of longitudinal motion. For simplicity, we investigated the effect of target motion with a sinusoidal pattern, and this model was general enough to handle any type of motion pattern.

2.2.2.1 Coordinate System

The tumour coordinate system (Figure 2.2 b) was adopted for the computer simulation model in this study, instead of the room coordinate system (Figure 2.2 a) used by Kissick et al [20]. In the room coordinate system (Figure 2.2 a), the tumour position, $Y(t)$ is determined by the linear motion of the treatment couch combined with the periodic motion of the tumour volume itself:

$$Y(t) = Y_{couch}(t) + Y_{tumour}(t) = \frac{p \cdot b}{T_g} t + A \sin \left( \frac{2\pi}{T_r} t \right)$$

(2.2)

where $Y_{couch}(t)$ is the position of the treatment couch as a function of time, $Y_{tumour}(t)$ is the position of the tumour volume on the treatment couch as a function of time, $p$ is the pitch factor, $b$ is the fan beam thickness, $T_g$ is the gantry rotation period, $T_r$ is the period of tumor motion, and $A$ is the amplitude of tumour motion along the longitudinal (+Y) direction.

In the tumour coordinate system (y) shown in Figure 2.2 b), the tumour volume remains stationary, while the “moving” treatment field assumes the roles of both couch motion
and tumour motion. The two fan beam edges, leading beam edge $y_L(t)$ and trailing beam edge $y_T(t)$ move along the longitudinal direction ($+y$) with respect to the center of the tumor volume according to the following equations:

$$
y_T(t) = \frac{p \cdot b}{T_g} t + A \sin \left( \frac{2\pi}{T_r} t - \frac{D}{2} \right) - b = \frac{p \cdot b}{T_g} t + A \sin \left( \frac{2\pi}{T_r} t - \frac{p \cdot b \cdot R}{2} \right) - b
$$

$$
y_L(t) = \frac{p \cdot b}{T_g} t + A \sin \left( \frac{2\pi}{T_r} t - \frac{D}{2} \right) + b = \frac{p \cdot b}{T_g} t + A \sin \left( \frac{2\pi}{T_r} t - \frac{p \cdot b \cdot R}{2} \right) + b
$$

where $y_T(t)$ and $y_L(t)$ are the positions of the trailing and leading beam edges as functions of time, respectively, $D$ is the total couch travel during the treatment, and $R$ is the number of gantry rotations used during the treatment.

Figure 2.2: Coordinate systems for a moving target: a) In the room coordinate system, the tumour position ($Y$) with respect to the stationary fan beam is governed by the linear motion of the treatment couch, combined with the periodic motion of the tumour volume itself, as summarized in Equation 2.2, b) In the tumor coordinate system ($y$), the target volume remains stationary, while the “moving” treatment field assumes the roles of both couch motion and tumor motion. The two fan beam edges (trailing beam edge, $y_T(t)$ and leading beam edge, $y_L(t)$) move along the longitudinal direction ($+y$) with respect to the center of the tumor volume according to Equation 2.3.
2.2.2.2 Computer Simulation Model

The dose received by each longitudinal point \((y)\) along the axis of gantry rotation was determined by first calculating the radiation exposure time. In Figure 2.3, a set of solid lines observed at each longitudinal position represents the irradiation time ("ON") of the corresponding point, while the dotted lines indicate the time spent outside the longitudinal beam edges ("OUT"). Thus, the radiation exposure time \(\Delta t\) was calculated by summing up the temporal lengths of all solids lines:

\[
\Delta t(y) = \sum_{i=1}^{m} \Delta t_i(y)
\]  

(2.4)

where \(\Delta t(y)\) is the radiation exposure time at a given longitudinal position \((y)\), \(m\) is the number of solid lines at each longitudinal position \((y)\), and \(\Delta t_i\) is temporal length of the \(i^{th}\) solid line.

For the non-IMRT helical tomotherapy cases shown in Figure 2.3 a) and b), the irradiated time ("ON") was equal to the time spent inside the two fan beam edges ("IN"), since the radiation beam was fully on during the entire treatment by assigning the maximum leaf opening time for all beam projections \((T_0 = 1.00)\). For the IMRT helical tomotherapy delivery in Figure 2.3 c), the irradiated time ("ON") was the temporal overlaps between the time spent inside the beam edges ("IN") and the "Beam ON" windows, making "ON" a subset of "IN". The widths of the "Beam ON" windows were determined by the values of leaf opening time assigned as a function of leaf number and beam projection. The temporal length \((\Delta t_i)\) of each solid line ("ON") was calculated numerically by comparing the longitudinal position of the given point to the positions of the beam edges and the "Beam ON" windows in temporal increments of 1 ms. The radiation exposure time \((\sum \Delta t_i)\) of each point was then determined by summing up the lengths of all the irradiated time segments \((\Delta t_i)'s\). The radiation exposure time calculation was repeated in spatial increments of 0.01 cm to produce a radiation exposure time versus position profile.
Figure 2.3: (a) Position vs. time curves of the longitudinal beam edges for a non-IMRT helical tomotherapy ($p = 0.8, T_g = 16 \text{ s}, R = 4$) of a central target ($T_r = 4 \text{ s}, A = 0.5 \text{ cm}$) in the tumour coordinate system ($y$), under a synchronous interplay condition ($\beta = \text{integer} = 5$). A set of solid lines observed at each longitudinal position represents the irradiated time (“ON”) of the corresponding point, while the dotted lines indicate the time spent outside the longitudinal beam edges (“OUT”). In non-IMRT cases, the irradiated time (“ON”) is equal to the time spent inside the two fan beam edges (“IN”), since the radiation beam remains fully on during the entire treatment ($T_0 = 1.00$). The temporal length ($\Delta t_i$) of each solid line (“ON”) was calculated numerically by comparing the longitudinal position of the given point to the positions of the beam edges in temporal increments of 1 ms. The radiation exposure time ($\Delta t$) of each point was then determined by summing up the lengths of all irradiated time segments ($\Delta t_i$’s). (b) Position vs. time curves of the longitudinal beam edges for a non-IMRT helical tomotherapy ($p = 0.8, T_g = 16 \text{ s}, R = 4$) of a central target ($T_r = 8 \text{ s}, A = 0.5 \text{ cm}$) in the tumour coordinate system ($y$), under an
asynchronous interplay condition ($\beta \neq \text{integer} = 2.5$). (c) Position vs. time curves of the longitudinal beam edges for an IMRT helical tomotherapy ($p = 0.287$, $T_g = 15$ s, $R = 8$) of a central target ($T_r = 8$ s, $A = 1.0$ cm) in the tumour coordinate system $(y)$. The irradiated time ("ON") was the temporal overlaps between the time spent inside the beam edges ("IN") and the “Beam ON” windows, making “ON” a subset of “IN”. The widths of the “Beam ON” windows were determined by the values of leaf opening time assigned as a function of leaf number and beam projection.

The resulting longitudinal exposure time versus position profile was converted directly into a longitudinal fluence profile by assuming a constant fluence rate. The fluence profile, $\Phi(y)$ was then converted to a longitudinal dose profile, $D(y)$ via one-dimensional convolution using an empirically determined dose kernel, $K(y)$:

$$D(y) = K(y) \otimes \Phi(y)$$

where $D(y)$ is the dose profile, $K(y)$ is the dose kernel, and $\Phi(y)$ is the normalized fluence profile.

The normalized fluence profile $\Phi(y)$ was assumed to be rectangular in shape along the direction. The dose kernel, $K(y)$ was then derived using a dose profile along the axis of gantry rotation, acquired experimentally using Kodak EDR2 film. A piece of film was placed inside the stationary film insert within the body phantom (Figure 2.1 a), and irradiated for one full gantry rotation ($T_g = 15$ s) with the treatment couch remaining stationary during the radiation delivery. The dose kernel was a set of exponential functions resembling the primary beam penumbra equations defined by Cunnigham [24] and used by a commercial treatment planning system (Theraplan Plus v.3.0, 1998) [25].

The dose profile calculated with the dose kernel, $K(y)$ was fitted manually to the measured dose profile by continuously varying the coefficient values of the different parameters in the dose kernel, $K(y)$. The fitting process was repeated until the root-mean-square (RMS) of the absolute differences between the entire calculated and measured dose profiles was less than 1.2 %. 
2.2.2.3 Dose Rippling Parameter (β)

Dose rippling was one of the three motion-induced dose discrepancies investigated in this study. The dose rippling parameter, β was defined as a tool to quantify the presence of dose rippling by determining the nature of interplay (asynchronous or synchronous) between the couch motion and tumour motion. The dose rippling parameter, β was defined as the ratio of the time required \( (T_g / p) \) for the couch to travel a distance of one fan beam thickness \( (b) \) to the target motion period \( (T_r) \):

\[
\beta = \frac{T_g}{p \cdot T_r}
\]

where \( p \) is the pitch factor, \( T_g \) is the gantry rotation period, and \( T_r \) is the period of tumour motion.

A synchronous interplay is established when there is an integer number of target motion cycles completed during the time span \( T_g / p \) (i.e. \( \beta = \) integer).\(^4\) For a non-IMRT tomotherapy delivery, a synchronous condition leads to the uniform irradiation of the target along the axis of gantry rotation, and thus the absence of dose rippling – proved mathematically in Appendix A.\(^5\) A similar mathematical relationship to Equation (2.6) was also defined for the sliding window technique in the study by Yu et al [18]. In Figure 2.3 a), the uniform irradiation of the target under the synchronous condition (\( \beta = 5 \)) is indicated by the identical radiation exposure time for the target points, \( y = -1.8 \) cm and \( 0.5 \) cm, i.e. \( \sum \Delta t (-1.8) = \sum \Delta t (0.5) \). At the target point, \( y = -1.8 \) cm, the temporal lengths of the five solid lines add up to the sum of the three solid lines at \( y = 0.5 \) cm. At \( y = -1.8 \) cm, the dotted line between the first two solid lines is the same length as the fourth solid line, making them interchangeable with each other in position. The dotted line between the second and third solid lines is then switched with the fifth solid line due

\(^4\) An example of a synchronous interplay condition is shown in Figure 2.5 (b), while an asynchronous condition is presented in Figure 2.6 (b).

\(^5\) The absence of dose rippling under a synchronous condition also applies for periodic, non-sinusoidal target motion.
to their identical lengths, overall yielding a single solid line ranging from $t = 4.55$ s to $t = 24.55$ s for the radiation exposure time of 20 s, i.e. $\sum \Delta t_i (-1.8) = 20$ s. At $y = 0.5$ cm, the dotted line between the first and second lines could be interchanged with the third solid line, while the dotted line between the second and third solid lines is switched with the first solid line. As a result, a single solid line covering from $t = 26$ s to $t = 46$ s is produced for the radiation exposure time of 20 s as well, i.e. $\sum \Delta t_i (0.5) = 20$ s = $\sum \Delta t_i (-1.8)$. In Figure 2.3 b), the asynchronous interplay condition ($\beta \neq $ integer = 2.5) results in the non-uniform radiation delivery to the target volume. This is illustrated by the two selected target points, $y = -2.0$ cm and 0.4 cm receiving different radiation exposure, i.e. $\sum \Delta t_i (-2.0) \neq \sum \Delta t_i (0.4)$, which leads to the presence of dose rippling.

2.2.3 Experimental Verification

2.2.3.1 Motion Body Phantom

A motion body phantom (Modus Medical Devices Inc., London, Canada) shown in Figure 2.4 was used to verify the simulation results for the non-IMRT and IMRT helical tomotherapy cases listed in Table 2.1. The motion phantom consisted of a lucite body phantom ($\rho = 1.18$ g/cm$^3$, length = 12 cm, width = 30 cm, height = 20 cm), and a sinusoidally moving lucite film insert ($\rho = 1.18$ g/cm$^3$, length = 18 cm, diameter = 8 cm) representing a tumour mass. The film insert was designed to hold a piece of film (length = 15 cm, width = 6 cm) inside it, and contained five pins at its inside corners (2 at one corner and 1 at each of the three corners) to generate pinprick landmarks on each film. These fiducial marks were later used in the data analysis stage to align a pair of scanned film images for directly comparing the two dose distributions. The film insert was positioned to move through the central opening of the body phantom, with the film placed on the coronal plane. The amplitude of the film insert motion was set by adjusting the position of the translation stage holding film insert. The motion phantom was also equipped with a “chest-height” platform, whose vertical up-and-down motion represented the anterior-posterior (AP) motion of a “chest wall”. The “chest-height” platform moved with an identical period as the film insert. Thus, the period of the film insert motion was verified by measuring the positions of the optical markers placed on the platform, using an optical tracking camera (NDI, Waterloo, ON) with a sampling frequency of 60 Hz.
Table 2.1: List of non-IMRT and IMRT helical tomotherapy cases.

<table>
<thead>
<tr>
<th></th>
<th>p</th>
<th>$T_g$ (s)</th>
<th>R</th>
<th>D (cm)</th>
<th>L (cm)</th>
<th>$T_r$ (s)</th>
<th>$\beta$</th>
<th>A (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>non-IMRT</td>
<td>0.8</td>
<td>16</td>
<td>4</td>
<td>8.0</td>
<td>5.5</td>
<td>8</td>
<td>2.5</td>
<td>1.0</td>
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<td></td>
<td></td>
<td></td>
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<td>1.5</td>
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<td>4</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>IMRT</td>
<td>0.287</td>
<td>15</td>
<td>8</td>
<td>5.8</td>
<td>3.3</td>
<td>8</td>
<td>$\sim$6.5</td>
<td>1.0</td>
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<td></td>
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<td></td>
<td>1.0</td>
</tr>
</tbody>
</table>

Figure 2.4: Experimental verification setup for a moving target. The motion body phantom (Modus Medical Devices Inc., London, ON) consisted of the lucite body phantom, and a sinusoidally moving lucite film insert (length = 18 cm, diameter = 8 cm) representing a tumour mass. The film insert was designed to hold a piece of film (length = 15 cm, diameter = 6 cm) inside it. The motion phantom was also equipped with a “chest-height” platform that moves with an identical period as the film insert. The period of the film insert motion was verified by measuring the positions of the optical markers placed on the platform, using an optical tracking camera (NDI, Waterloo, ON) with a sampling frequency of 60 Hz.
2.2.3.2 Calibration of Film Dosimetry

For each film experiment, a calibration procedure was carried out with a 6 MV helical tomotherapy X-ray beam, using a cylindrical solid water “Cheese” phantom (TomoTherapy Inc., Madison, WI, length = 18 cm, diameter = 30 cm). A 10” x 12” EDR2 film was placed inside the phantom, and the couch height was adjusted to position the film on the isocentric coronal plane. The calibration procedure delivered eight 3 cm$^2$ square fields with known dose of 30.5 cGy, 65.2 cGy, 100.9 cGy, 128.2 cGy, 159.5 cGy, 188.9 cGy, 215.0 cGy, and 244.4 cGy. The calibration film was processed along with a blank film to enable background subtraction. The developed films were then scanned with a Vidar VXR-16 DosimetryPro scanner (Vidar Systems Corporation, Herndon, VA) and analyzed with the RIT113 V4 software (Radiation Therapy Dosimetry Software, Colorado Springs, CO). A region of interest (ROI) of 2 cm$^2$ was placed inside each of the eight different fields on the calibration film and within the blank film. The average optical density (OD) was then calculated for each ROI to generate an OD versus dose calibration curve.

2.2.3.3 Radiation Delivery

All the film experiments were carried out in the non-clinical mode at the helical tomotherapy unit. An electronic communication was established between the tomotherapy machine and the motion phantom through a cable, such that the film insert motion would commence once the gantry angle reached zero. The initial phase of the film insert motion was set at zero for all non-IMRT and IMRT cases by positioning the film insert in its mid-position before the start of each radiation delivery.

2.2.3.4 Uncertainty Analysis

Five repeated “no motion” measurements for the non-IMRT cases ($\rho = 0.8$, $T_g = 16$ s) were used to calculate the dose uncertainty inside the PTV. The measured dose profiles were realigned to ensure that the center of the PTV in each dose profile matched with those from the other dose profiles. A standard deviation was calculated for each dose point, and then the mean of all the standard deviations values were determined to represent the dose uncertainty of the film experiment in this study.
2.3 Results and Discussion

2.3.1 Non-IMRT Helical Tomotherapy Cases

2.3.1.1 Dose Rounding Effect

In Figure 2.5 a), dose rounding effect\(^6\) was illustrated in the measured coronal dose distribution of a non-IMRT helical tomotherapy delivery. In the “no motion” dose distribution (i), thread artifact\(^7\) was manifested as a series of dose ripples near the outer edges of the dose distribution along the longitudinal direction (y). In the “motion” dose distribution (ii), the dose rounding effect due to the longitudinal target motion led to the “blurring” of a thread artifact, reducing the magnitude of off-axis dose ripples. The presence of dose rounding effect was illustrated in the dose difference map (iii) between the two dose distributions (“motion” dose distribution (i) – “no motion” dose distribution (ii)). Underdosing was observed near the longitudinal PTV boundaries, while the regions both superior and inferior to these boundaries experienced overdosing. Dose profiles along the axis of gantry rotation (dotted line, x = 0 cm) were generated from the dose distributions (i) and (ii) to further characterize the dose rounding effect.

As shown in Figure 2.5 b), the measured and simulated dose profiles both exhibited dose rounding near the PTV boundaries due to the large peak-to-peak amplitude of target motion (2\(A = 2.0\) cm). The dose rounding effect resulted in the underdosing of the PTV near its boundaries, and overdosing of the surrounding normal structures just outside the PTV boundaries. As shown in Figure 2.5 b), dose rippling was absent due to the synchronous interplay condition (\(\beta = \text{integer} = 5\)) between the couch motion and longitudinal target motion. The dose rippling-like feature present inside the PTV region for the measured “no motion” dose profile was attributed to the oval shape of the body phantom (width = 30 cm, height = 20 cm), which yielded a different attenuation path length as a function of gantry angle. A difference of 2.5 % was observed between the

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\(^6\) Dose rounding is manifested as dose blurring in the direction of tumour motion, occurring near the longitudinal boundaries of the target volume

\(^7\) Thread effect is an off-axis beam junctioning effect inherent to helical tomotherapy, which arises mainly due to beam divergence. Please refer to Section 3.3.1, 5.2.2.1, 5.3.2, and 5.4.3 for further explanations.
maximum and minimum dose values of this dose rippling-like feature for the “no motion” dose profile, while the difference was reduced to 1.5 % for the “motion” dose profile. The decrease in the dose difference was attributed to the “blurring” effect, caused by the target motion along the longitudinal direction. The measured dose profile exhibited a dose uncertainty of ±0.5 %, calculated as the mean of standard deviations of the dose values from the five re-aligned “no motion” profiles acquired under the same delivery conditions. The simulated dose profile agreed with the measured dose profile within a standard deviation of 0.5 % inside the PTV region.

The magnitude of dose rounding was quantified by the penumbral size, which was calculated as the average of the distance between the 20 % and 80 % dose points (P_{20/80}) and the distance between the 80 % and 20 % dose points (P_{80/20}). The simulated data were generated for the different amplitudes of target motion, while using the same treatment parameters and target motion period (T_r). The plotted data in Figure 2.5 c) showed that the penumbral widening worsened with increasing amplitude (A) of target motion. At the target motion amplitude of 1.0 cm, the penumbra size started to increase linearly with the target motion amplitude for both target motion periods. The smaller penumbral size was observed for the target motion period of 8 s (T_r = 8 s), as the presence of dose ripples inside the PTV (Figure 2.6 b) led to the sharpening of the penumbra.\(^8\) All the experimental data points agreed with the simulated data points within 1 mm.

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\(^8\) Dose rippling (Section 2.3.1.2) inside the target is manifested as dose undulations along the dose ramp-up and ramp-down regions, which may increase or decrease the penumbral size, depending on the phase of tumour motion. In the absence of dose rippling, however, longer tumour motion period (T_r) will always lead to an increase in penumbral size.
Figure 2.5: (a) Measured film dose distributions on the central coronal plane for a non-IMRT helical tomotherapy \((p = 8, T_g = 16 \text{ s}, R = 4)\) of a central target: in the (i) absence and (ii) presence of target motion \((T_r = 4 \text{ s}, A = 1.0 \text{ cm}, \beta = 5)\). (i) “no motion” dose distribution, (ii) “motion” dose distribution \((T_r = 4 \text{ s}, A = 1.0 \text{ cm}, \beta = 5)\), and (iii) dose difference map between (i) and (ii). The dotted lines represent the axis of gantry rotation \((x = 0 \text{ cm})\). (b) Normalized longitudinal dose profiles along the axis of gantry rotation for a non-IMRT helical tomotherapy \((p = 0.8, T_g = 16 \text{ s}, R = 4)\) of a central target \((T_r = 4 \text{ s}, A = 1.0 \text{ cm})\). \(P_{20/80}\) is the distance between the 20 \% and 80 \% dose points, used to quantify penumbral size. (c) Penumbral size vs. amplitude of target motion for two different target motion periods \((T_r = 4 \text{ s} \text{ and } 8 \text{ s})\) for a non-IMRT helical tomotherapy \((p = 0.8, T_g = 16 \text{ s}, R = 4)\) of a central target.
2.3.1.2 Dose Rippling Effect

In Figure 2.6 a), dose rippling effect was illustrated in the measured coronal dose distribution of a non-IMRT helical tomotherapy delivery. In the “motion” dose distribution (ii), the asynchronous interplay condition generated between the couch motion and target motion yielded a dose rippling pattern inside the PTV along the longitudinal direction (y). The thread artifact present in the “no motion” dose distribution (i) was effectively absent in the “motion” dose distribution, as the larger peak-to-peak motion (2A) of 3.0 cm compared to the peak-to-peak motion of 2.0 cm in Figure 2.5 a), leads to an increased “blurring” of dose ripples, and the resulting absence of thread artifact. In the dose difference map (iii), the presence of both dose rippling and dose rounding effects are apparent. Dose profiles along the axis of gantry rotation (dotted line, x = 0 cm) were generated from the dose distributions (i) and (ii) to further study dose rippling effect.

As shown in Figure 2.6 b), both dose rounding and dose rippling were observed for the measured and simulated dose profiles. Significant dose rounding occurred due to the very large peak-to-peak amplitude of target motion (2A = 3.0 cm). The asynchronous interplay condition (β ≠ integer = 2.5) produced a dose rippling pattern with the dose variation of 3.0%. The dose variation was measured as the difference between the lowest dose valley and the highest dose peak found inside the PTV region. The simulated dose profile agreed with the measured dose profile within a standard deviation of 0.5% inside the PTV region.

As shown in Figure 2.6 c), the dose profiles were generated by the simulation program for different combinations of pitch factor (p) and gantry rotation period (Tg), while keeping the β value at 2.5. The target motion period (Tr) was fixed at 8 s. The magnitude of dose ripples remained at ~2.5% for all cases, demonstrating that the dose rippling effect is independent of the individual parameters governing the β value.9

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9 Although the effect of varying the tumour motion period was not presented here, the magnitude of dose ripples remains comparable for the same β value acquired with different Tr values.
effect of target motion amplitude \((A)\) on the magnitude of dose ripples was also investigated using the simulation results. In Figure 2.6 d), the dose variations are plotted as a function of target motion amplitude for a fixed \(\beta\) value of 2.5. The dose variation plot exhibits a sinusoidal-like pattern with the peak of each cycle decreasing with the target motion amplitude. This particular pattern is rather non-intuitive as the largest dose variation of 8% is observed at a relatively small target motion amplitude of 0.30 cm.

In the initial rise \((0 < A \leq 0.3 \text{ cm})\), the dose variation increases with the target motion amplitude \((A)\), due to the respective increase and decrease of the maximum and minimum dose inside the PTV. The maximum dose is received by the PTV points that move into the beam both at the start and end of their irradiations, thus increasing the overall exposure time compared to the static case. On the other hand, the minimum dose points recede away from the beam at the start and move past the beam near the end of their irradiations, resulting in the decrease of the overall radiation exposure time. When the target motion increases beyond \(A = 0.3 \text{ cm}\), the maximum dose points start to spend time outside the beam during their irradiations, with the duration of time outside the beam increasing with the target motion amplitude. The decrease in the maximum dose is then compensated by the minimum dose points spending additional time inside the beam. As a result, the dose variation starts to decrease with the amplitude of target motion \((0.3 < A \leq 0.6 \text{ cm})\).

The respective decrease and increase of the maximum and minimum dose continue, until the dose received by the “old” minimum dose points surpasses the dose received the “old” maximum dose points, thus leading to switches between the positions of the maximum and minimum dose points. The same trend previously observed in the initial rise \((0 < A \leq 0.3 \text{ cm})\) is then repeated for \(0.6 < A \leq 0.85 \text{ cm}\), explaining the periodic nature of the dose variation pattern. The dose variation peaks at the different amplitudes \((A = 0.3, 0.85, 1.35,\text{ and } 1.85 \text{ cm})\) decrease with the amplitude of target motion, as the maximum dose points move out of the beam more frequently during their irradiations.
with increasing target motion amplitude, thus reducing the maximum exposure time and the corresponding dose variation.\textsuperscript{10}

In Figure 2.6 e), the dose rippling magnitude was plotted as a function of dose rippling parameter ($\beta$) for the different target motion amplitudes, exhibiting patterns similar to “sinc” functions. “Nodes” were observed at all the integer $\beta$ values, as dose rippling becomes absent at these values. The dose rippling magnitude does not change monotonically with the target motion amplitude, but rather changes up and down in a sinusoidal-like manner related to the pattern illustrated in Figure 2.6 d). The dose rippling magnitude declined rapidly with increasing value of dose rippling parameter ($\beta$), approaching less than 1% at the $\beta$ value of 4.5 for all the target motion amplitudes.\textsuperscript{11}

The largest dose rippling magnitude of ~25% was observed for the target motion amplitude of 0.5 cm and the $\beta$ value of 1.5, where the target motion period ($T_r$) approached an unusually high value of 10 s. Dose rippling parameter values lower than one ($\beta < 1$) were not applicable to helical tomotherapy, and thus were not investigated in this study. For the sliding window technique, however, higher velocities of the jaw motion (compared to the couch motion) lead to faster radiation beam movements than helical tomotherapy, which in turn yield lower the dose rippling parameter values. In the study by Yu et al\textsuperscript{[18]}, the employed jaw motion velocities produced $\beta$ values ranging from 0.035 to 1. The dose rippling magnitude approached as high as 400% for $\beta$ values close to 0.1.

\textsuperscript{10}The maximum dose points moving out of the beam more frequently simultaneously translates into the minimum dose points moving into the beam more frequently, overall reducing the dose variation.

\textsuperscript{11}A non-integer $\beta$ value indicates the presence of an incomplete tumour motion cycle during the time for the treatment couch to advance by one fan beam thickness ($T_g / p$). The incomplete portion of a tumour cycle leads to the different points within the target to experience different radiation exposure time. With increasing $\beta$ value, the absolute time of this incomplete portion decreases, thus reducing the variation in radiation exposure time between different points, which in turn leads to a reduction in dose rippling magnitude.
Figure 2.6: (a) Measured film dose distributions on the central coronal plane for a non-IMRT helical tomotherapy ($p = 0.8$, $T_g = 16$ s, $R = 4$) of a central target: (i) “no motion” dose distribution, (ii) “motion” dose distribution ($T_r = 8$ s, $A = 1.5$ cm, $\beta = 2.5$), and (iii) dose difference map between (i) and (ii). The dotted lines represent the axis of gantry rotation ($x = 0$ cm). (b) Normalized longitudinal dose profiles along the axis of gantry rotation for a non-IMRT helical tomotherapy ($p = 0.8$, $T_g = 16$ s, $R = 4$) of a central target ($T_r = 8$ s, $A = 1.5$ cm, $\beta = 2.5$). The dose variation was measured as the difference between the lowest dose valley and the highest dose peak found inside the PTV region. (c) Simulated longitudinal dose profiles along the axis of gantry rotation for a non-IMRT helical tomotherapy of a central target ($T_r = 8$ s, $A = 1.5$ cm, $\beta = 2.5$). Four different dose profiles were generated using different combinations of pitch factor ($p$) and gantry rotation period ($T_g$), while keeping the $\beta$ value at 2.5. (d) Simulation study: Dose variation vs. target motion amplitude ($T_r = 8$ s) for a non-IMRT helical tomotherapy ($p = 0.8$, $T_g = 16$ s, $R = 4$) of a central target under the asynchronous interplay condition ($\beta \neq$ integer = 2.5). (e) Simulation study: Dose rippling magnitude vs. dose rippling parameter ($\beta$) for different amplitudes of target motion for a non-IMRT helical tomotherapy ($p = 0.8$, $T_g = 16$ s, $R = 4$) of a central target.
2.3.2 IMRT Helical Tomotherapy Case

As shown in Figure 2.7 a), simulated longitudinal dose profiles were generated for the different values of target motion periods for an IMRT helical tomotherapy delivery. The unusually large target motion period of 15 s yielded a dose rippling pattern inside the PTV with a magnitude of 2.0 % ($\beta \sim 3.5$). Meanwhile, the dose profile resulting from the target motion period of 4 s showed little differences from the “no motion” dose profile. While no major dose discrepancies were observed for $T_r = 15$ s and 4 s, one couldn’t interpolate or predict the major dose perturbations at $T_r = 8$ s, based on the results from the other target motion periods. The IMRT leaf opening synchronization effect was observed, producing the largest dose discrepancies of 11.3 %\(^{12}\) for the motion amplitude of 0.3 cm. Further investigations with other target motion periods (not presented here) showed that the IMRT leaf opening asynchronization effect was plan-specific. The artifact was present at a wider range of tumour motion periods than the dose rippling effect, with the largest dose discrepancies observed at a particular target motion period, 8 s for the particular IMRT helical tomotherapy case investigated in this study.

In Figure 2.7 b), the effect of target motion is illustrated in the coronal dose distribution of an IMRT helical tomotherapy delivery for a target motion period of 8 s. The dose difference map (iii) between the planned (“no motion”) and delivered (“motion”) dose distributions demonstrated significant motion-induced dose errors. The longitudinal dose profiles were then obtained along the axis of gantry rotation for the “no motion” and “motion” dose distributions to further examine the different dose discrepancies present. In Figure 2.7 c), the measured and simulated dose profiles exhibited IMRT leaf opening asynchronization effect and dose rounding effect. The IMRT leaf opening asynchronization effect was observed inside the PTV region, where the difference between the measured “motion” and “no motion” dose profiles ranged from -29 % to 7 %.

\(^{12}\) The dose discrepancy of 11.3% was calculated as the total variation in dose differences between the planned and delivered dose profiles inside the target, which ranged from -6.1 to 5.2% for tumour motion period ($T_r$) of 8 s.
motion is the cause of this effect. The simulated dose profile agreed with the measured dose profile within a standard deviation of 1.7% inside the PTV region.

Significant dose rounding was also observed near the PTV boundaries due to the very large peak-to-peak amplitude of target motion ($2A = 3.0 \text{ cm}$). However, dose rippling was not observed despite the asynchronous interplay condition ($\beta \neq \text{integer} \sim 6.5$), as the use of a tighter pitch factor ($p = 0.287$) compared to the non-IMRT cases ($p = 0.8$) yielded a much higher non-integer $\beta$ value ($\beta \sim 6.5$ versus $\beta = 2.5$). It was previously shown in Figure 2.6 c) that the dose rippling magnitude started to become insignificant at $\beta = 4.5$ for all the target motion amplitudes, thus explaining the absence of dose rippling at $\beta \sim 6.5$. Dose rippling was also not observed in the study by Kanagaki et al [20], where a pitch factor of 0.3 was assigned for all the IMRT helical tomotherapy cases, yielding high $\beta$ values varying from 10 to $\sim 67$. Therefore, dose rippling should not be a concern clinically, unless the breathing patterns exhibit unusually lengthy tumour motion periods ($T_r$). In the clinical setting, pitch factors ($p$) of less than 0.3 are typically used along with the gantry rotation periods ($T_g$) ranging from 15 to 20 s, likely driving the $\beta$ values well above 4.5.

The characteristics of the IMRT leaf opening asynchronization effect were further investigated by studying its relationship with the target motion amplitude, and also the effect of having multiple fractions. In Figure 2.7 d), underdosing of the PTV and dose rounding both worsened with increase in the target motion amplitude, while the PTV overdosing was significantly reduced for the amplitude of 2.0 cm. In Figure 2.7 e), the effect of delivering multiple dose fractions on the IMRT leaf opening asynchronization effect was investigated by introducing a random starting phase of target motion for each fraction for the total of 30 fractions. The resulting dose profiles were then summed up to generate a single composite profile. When compared to the “no motion” profile, the “random phase” dose profile exhibited significant dose differences ranging from -16.5% to 1.5%. The “random phase” dose profile was also quite symmetrical in shape. This was attributed to the fact that most of the 30 randomly generated dose profiles had dose profiles that were roughly mirror images of themselves. In Figure 2.7 e), the dose
profiles with the starting phases of $0^\circ$ and $180^\circ$ were essentially the mirror images of each other.\textsuperscript{13}

\textsuperscript{13} The dose profiles with the starting phases of $0^\circ$ and $180^\circ$ were identical to their corresponding single-fraction dose profiles.
Figure 2.7: (a) Simulated longitudinal dose profiles along the axis of gantry rotation for an IMRT helical tomotherapy ($p = 0.287$, $T_g = 15$ s, $R = 8$) of an off-axis target ($A = 0.3$ cm) for different target motion periods ($T_r$). (b) Measured film dose distributions on the central coronal plane for an IMRT helical tomotherapy ($p = 0.287$, $T_g = 15$ s) of an off-axis target: (i) “no motion” dose distribution, (ii) “motion” dose distribution ($T_r = 8$ s, $A = 1.5$ cm), and (iii) dose difference map between (i) and (ii). The dotted lines represent the axis of gantry rotation ($x = 0$ cm). (c) Normalized longitudinal dose profiles along the axis of gantry rotation for an IMRT helical tomotherapy ($p = 0.287$, $T_g = 15$ s, $R = 8$) of an off-axis target ($T_r = 8$ s, $A = 1.5$ cm). (d) Simulated longitudinal dose profiles along the axis of gantry rotation for an IMRT helical tomotherapy ($p = 0.287$, $T_g = 15$ s, $R = 8$) of an off-axis target ($T_r = 8$ s) for different target motion amplitudes ($A$). (e) Simulated longitudinal dose profiles along the axis of gantry rotation for an IMRT helical tomotherapy ($p = 0.287$, $T_g = 15$ s, $R = 8$) of an off-axis target ($T_r = 8$ s, $A = 1.5$ cm) for 30 fractions.
2.3.3 Potential Solutions for Minimization of the Three Dose Discrepancies

Various approaches have been proposed to minimize the effect of tumour motion during helical tomotherapy [4,11-13]. Increasing the PTV margin size along the direction of target motion is the simplest way to compensate for the dose rounding effect, at the expense of increasing the integral dose to the patient. In Figure 2.5 c), the penumbral widening due to dose rounding was shown to be proportional to the target motion amplitude ($A$), thus making the PTV margin size directly dependent upon the target motion amplitude. However, the dose rippling and IMRT leaf opening asynchronization effects cannot be resolved by this approach alone, as the asynchronous interplay conditions still remain. The effects of all three dose artifacts could be minimized effectively by immobilizing the target volume only during the “beam ON” time through breath-holding [11,13]. However, breath-holding may not be feasible physically for all lung cancer patients, due to their compromised lung functions. In the “motion-incorporated helical tomotherapy”, the tumour motion information acquired prior to the treatment is utilized during the plan optimization process [12,26]. As a result, the tumour motion is accounted for during the treatment, while the patient is still allowed to breathe normally. This method, however, requires the patient to reproduce the identical breathing pattern used for planning during the treatment, which may not be guaranteed in practice. Failure to reproduce the same breathing pattern can result in significant dose discrepancies between the planned and delivered dose distributions.

Respiratory gating can be incorporated into helical tomotherapy in the form of the “multi-pass respiratory gating technique” [27], without placing any constraints on the patient breathing. Due to the continuous motion of the treatment couch, multiple passes of helical tomotherapy deliveries are required to complete the helical tomotherapy plan, instead of the conventional single pass. During each pass, only the beam projections overlapping with the gating windows are delivered, while the remaining beam projections are “blocked” by the complete closure of all 64 binary MLC leaves. After each pass, the couch is reset to its starting position, and the treatment commences at a different phase of tumor motion for the gating windows to cover the previously undelivered beam
projections. This process is repeated until all of the planned beam projections are delivered. Respiratory gating reduces the magnitude of target travel during the “beam ON” time, leading to the decrease in both the penumbral size and the PTV margin size required to compensate for dose rounding. Respiratory gating also alters the periodicity of the target motion during the “beam ON” time. Thus, the asynchronous conditions existing for the dose rippling and IMRT leaf opening asynchronization effects can be altered into the synchronous conditions, resulting in the minimization of both effects. The disadvantages of respiratory gating include the escalations in the treatment time and the patient integral dose, resulting from the multiple passes. The feasibility of this approach continues to be investigated in our laboratory. In the “real-time motion-adaptive delivery” [4], the beam projections of a planned leaf opening sinogram are delivered out of order (“shuffled”) according to the tumour motion, rather than sequentially. This means that in place of each planned beam projection, a past or future beam projection corresponding to the position of the tumour volume at a given time is selected and delivered. This particular method also places no constraints on the patient breathing. Each of the proposed techniques relies on various assumptions about the nature of tumour motion, and offers advantages and disadvantages for the helical tomotherapy treatment of a moving target.

2.4 Conclusions

In this study, three different dose discrepancies arising from the presence longitudinal tumour motion during helical tomotherapy were identified. Their characteristics were investigated through both computer simulation modeling and experimental verification using a motion phantom with film. The characteristics of the three different motion-induced dose discrepancies were illustrated, and the dosimetric significance of each effect was described. The computer simulation model was shown to be a valuable tool for predicting the dosimetric impact of target motion during helical tomotherapy, as the calculated dose profiles agreed with the measured data within ±0.5 % and ±1.5 % inside the PTV region for the non-IMRT and IMRT tomotherapy deliveries, respectively. Various potential solutions to minimize the effect of target motion were also discussed, and each proposed method needs to be investigated for its effectiveness in suppressing
the three dose discrepancies described here. The computer simulation model could also prove useful during the patient selection process for the different approaches of minimizing dose artifacts.

2.5 References


Chapter 3

3 Investigation of Dose Homogeneity for Loose Helical Tomotherapy Delivery in the Context of Breath-Hold Radiation Therapy


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3.1 Introduction

3.1.1 Helical Tomotherapy

In helical tomotherapy (HT) [1,2], an intensity-modulated fan beam of radiation is delivered to the patient in a helical manner, as a result of gantry rotation occurring simultaneously with linear couch motion (Figure 3.1). Each gantry rotation is divided into 51 equally-spaced beam projections with each projection spanning over ~7°. Beam modulation is facilitated by a binary multi-leaf collimator (b-MLC) consisting of 64 leaves. Overall, these features provide tomotherapy with the ability to sculpt a highly conformal dose distribution. The gantry rotation period \(T_g\) can be set between 10 s and 60 s, depending on the dose that needs to be delivered per rotation. In the standard tomotherapy practice, the couch advances by less than the fan beam thickness during each gantry rotation (i.e. pitch factor < 1), in order to avoid problems of abutment regions which may occur in serial tomotherapy [3]. Pitch factor \(p\) is defined as the amount of couch translation that occurs during one gantry rotation, divided by the fan beam thickness \(b\). Fan beam thickness \(b\) is defined as the distance between the 50% of the maximum dose value along the axis of gantry rotation in the direction of couch translation. Other tomotherapy parameters include the number of beam projections per gantry rotation \(n\), and number of gantry rotations \(R\) required to cover the entire target length along the direction of couch motion.
Figure 3.1: Helical tomotherapy (HT): The helical line depicts the path of beam projections (stars) during a tomotherapy treatment. The Y-axis indicates the direction of couch motion. HT-specific parameters include fan beam thickness ($b$), number of beam projections per gantry rotation ($n$), and number of gantry rotations ($R$) required to cover the entire target. The distance travelled during one gantry rotation is determined as the product of fan beam thickness and pitch factor ($b \times p$).

3.1.2 Target Motion

Respiration-driven target motion is a major problem in radiation therapy of lower lobe lung cancer, as larger target margins are required to compensate for the target’s range of motion, which may reach up to several cm’s [4-6]. As a result, a significant volume of healthy lung tissues is exposed to radiation, which in turn limits the maximum dose that can be delivered to the tumour. Thus, it is crucial to address target motion in order to take full advantage of highly conformal dose delivery provided by HT. Four motion mitigation methods are currently available for conventional radiation therapy and IMRT (Table 3.1). Of these choices, breath-holding appears to be the easiest one to implement for HT. Other techniques would require a complex control mechanism to co-ordinate the movement of the three HT subsystems (gantry, $b$-MLC, and couch) with respect to the target motion. In contrast, breath-holding requires no such effort as the target motion is
significantly reduced within the treatment field during radiation delivery. Breath-holding also allows one to choose the phase within the breathing cycle, which is most ideal for an effective treatment. Thus, we propose a different HT approach, namely loose helical delivery, which is ideally suited for breath-hold HT. Although loose helical delivery has been suggested [15], it has never been fully studied or described in the literature. In the present study, the dosimetric characteristics of loose helical delivery are investigated in comparison to standard HT. Standard HT \((p < 1)\) is referred to as tight helical delivery throughout this paper. Different HT cases have been simulated in the treatment planning software and then verified experimentally with film.

### Table 3.1: Motion mitigation methods.

<table>
<thead>
<tr>
<th>Method</th>
<th>Description</th>
<th>Advantage</th>
<th>Disadvantage</th>
<th>Applicable to HT?</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breath-holding</td>
<td>Beam ‘on’ during breath-holding, Beam ‘off’ during free-breathing</td>
<td>Normal tissue sparing for deep-inspiration breath-holding</td>
<td>Patient tolerance issue regarding breath-holding, increase in total session time</td>
<td>Yes</td>
<td>[4,6-8]</td>
</tr>
<tr>
<td>Beam-gating</td>
<td>Beam ‘on’ window set to a specific portion of breathing cycle</td>
<td>Normal breathing for patient</td>
<td>Increase in total session time</td>
<td>Very difficult due to continuous rotational beam delivery</td>
<td>[4,9,10]</td>
</tr>
<tr>
<td>Real-time target tracking</td>
<td>MLC leaf motions adjusted in real-time to track target</td>
<td>No increase in total session time, normal breathing for patient</td>
<td>Tracks linear rigid body motion only due to MLC mechanical limitation</td>
<td>The binary MLC of a HT unit cannot track targets moving in the SI direction</td>
<td>[11,12]</td>
</tr>
<tr>
<td>Target anticipation based on 4D CT</td>
<td>Change in target position is accounted for during plan optimization</td>
<td>Applicable to all treatment techniques, results in the best possible solution for breathing</td>
<td>Only works under the condition that the patient will breathe identically as planned with the help of the breathing guide</td>
<td>Yes, if the patient can maintain the same breathing pattern on the given treatment day as planned</td>
<td>[13,14]</td>
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### 3.1.3 Loose Helical Delivery

Loose helical delivery consists of a number \((H)\) of individual interlaced “loose” helices commencing at different gantry angles. The starting gantry angles are equally divided around the gantry, while the same starting couch position is assigned to all loose helices
Each loose helix covers the entire target length in a single gantry rotation \( R = 1 \) by utilizing a pitch factor of greater than 1 \( (p > 1) \), during which breathing-holding takes place. This way no interruptions are required during beam delivery except for cases such as coughing where the target accidentally moves out of the treatment field. The gantry rotation period \( (T_g) \) should be set to the minimum allowed time of 10 s in order to maximize the number of patients who can tolerate this approach. After the completion of each loose helix, the couch travels back to its starting position for the next loose helix to begin. It is during the time slots between the helices when the patient is allowed to breathe normally. The required pitch factor for loose helical delivery is calculated by Equation 3.2, which is derived from Equation 3.1. It is directly dependent on the length of target \( (L) \) along the axis of gantry rotation and the fan beam thickness \( (b) \):

\[
R = \text{# of rotations needed} = \frac{\text{target length} + \text{fan beam thickness}}{\text{fan beam thickness} \times \text{pitch factor}} = \frac{L + b}{b \cdot p} \quad (3.1)
\]

Therefore, for loose helical delivery:

\[
R = 1 = \frac{L + b}{b \cdot p} \Rightarrow p = \frac{L + b}{b} \quad (3.2)
\]

Figure 3.2: Loose helical delivery: each loose helix \( (p > 1) \) with a different starting gantry angle covers the entire target in one gantry rotation \( (R = 1) \), during which breath-holding takes place. Required pitch factor is dependent on target length and fan beam thickness. In this example, loose helical delivery consists of four helices \( (H = 4) \).
3.2 Materials and Methods

HT treatments were simulated in the conventional linear accelerator environment, since the current HT planning software does not allow for the optimization of loose helical delivery. The HT beam was represented by the 6 MV x-ray beam from a conventional linear accelerator (Varian Clinac 2100 C/D) collimated to a fan beam geometry. The normalized photon spectrum of a HT beam is comparable to that of the 6MV Varian Clinac beam with the similar maximum photon energy of 6 MV, although the peak of the energy spectrum shifts from 0.4 MeV to 0.5 MeV for the HT beam [16]. The absence of the flattening filter and the shorter source-to-axis distance (85 cm versus 100 cm) of the HT machine (TomoTherapy Inc., Madison, WI) were not modelled in this study. As a result, the 6MV beam used in this study has a slightly different TPR 20/10\textsuperscript{14} value of 0.67 compared to the TPR 20/10 value of 0.63 for the HT beam.

During a HT delivery, each gantry rotation is equally divided into 51 beam projections by momentary closing of all leaves between the beam projections. Radiation delivery remains continuous over the span of each beam projection. In study, however, the individual beam projections were depicted as “snap-shots” of radiation occurring at different gantry angles. Each beam projection was modelled as an open beam with no beam intensity modulation. In order to mimic the continuous couch motion of a HT machine, each beam projection was assigned a unique couch position. The displacement between beam projections, termed here as “projection increment” was calculated as follows:

\[
\text{projection increment} = \frac{\text{couch translation per gantry rotation}}{\text{# of beam projections per gantry rotation}} = \frac{p \cdot b}{n}\]  \hspace{1cm} (3.3)

In the present study, both loose and tight helical deliveries with limited numbers of beam projections (i.e. less than 51) were chosen to investigate the dosimetric impact of the tomotherapy parameters. The different HT cases studied are summarized in Table 3.2. A

\textsuperscript{14} Tissue-phantom ratio (TPR) is the ratio of the dose at a given point in phantom to the dose at the same point at a reference depth for the same field size. TPR 20/10 is the TPR ratio at depths of 20 cm and 10 cm in water.
fan beam thickness of 4.5 cm (Y) and a fan beam width of 10 cm (X) were selected to treat an arbitrary cylindrical target (10 cm in diameter, 4.5 cm (Y) in length) inside a cylindrical phantom with a diameter of 20 cm (Lucite, ρ = 1.18 g/cm³). Central axes of both the target and the phantom were aligned to the axis of gantry rotation of the linear accelerator.

Table 3.2: Tomotherapy scenarios.\(^\text{15}\)

<table>
<thead>
<tr>
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<th>R</th>
<th>H</th>
<th>Total number of projections ((n \times R \times H))</th>
<th>MU per projection</th>
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Tight helical delivery (\(p = 0.5\))

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<th>H</th>
<th>Total number of projections ((n \times R \times H))</th>
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</tbody>
</table>

Loose helical delivery (\(p = 2\))

\(^a\) It is not possible to deliver a monitor unit of this magnitude accurately. Thus, it was not performed experimentally, and only simulated in the treatment planning software.

3.2.1 Computer Simulations

The HT cases summarized in Table 3.2 were planned with Theraplan Plus (TPP) v.3.0 software (MDS Nordion, Kanata, Canada). The treatment planning software uses a pencil-beam algorithm, and the equivalent tissue-air ratio (TAR) method [17] including electron transport [18] for inhomogeneity corrections when using photon beams. The 6 MV photon beam model was specifically commissioned for the fan beam dimension (10 cm (X) x 4.5 cm (Y)) based on film data.\(^\text{16}\) Film data were obtained for three different

\(^15\) For loose helical delivery, number of loose helices was selected such that the total number of beam projections remains the same as tight helical delivery.

\(^16\) Film data were acquired to provide depth dose profile information for different field size.
square field sizes (4.5 cm, 6.2 cm, and 10 cm) at five different depths (0.5 cm, 1.5 cm, 3 cm, 5 cm and 10 cm), as TPP only allows square field data for beam modelling [19].

Instead of using the CT images of the actual phantom where a slice spacing (Y) of 3 mm would be used, a virtual phantom was created within TPP to produce a finer slice spacing of 1 mm (Y), thus allowing dose calculation at that interval. A relative electron density of 1.146 [20] was assigned to the whole phantom to represent Lucite ($\rho = 1.18$ g cm$^{-3}$). All dose calculations were performed using a pencil beam size of 1 mm with inhomogeneity corrections. The dose calculation grid spacing of 1 mm was used along all axes (X, Y, Z). Dose profiles were obtained along $X = 0$ cm, $+2$ cm, $+4$ cm axes on the calculated dose distribution plane ($Z = 0$ cm) bisecting the target.

The calculated dose distributions were normalized to the sum of beam weights, each of which represented the dose at the isocentre. Percentage dose values were then renormalized to the average dose along the central section (3.9 cm) along the axis of gantry rotation. The length of 3.9 cm was determined by subtracting 3 mm from each side of the target length (4.5 cm) to account for the rounding of dose profile.

### 3.2.2 Experimental Verification

Experiments were carried out on the linear accelerator to verify the dose distributions calculated by Theraplan Plus. Each experiment was performed with a film placed inside the cylindrical phantom (Lucite, $\rho = 1.18$ g/cm$^3$, 20 cm in diameter and length), which is shown in Figure 3.3. Kodak EDR2 film was chosen for the relatively large linear dose response range of 25-400 cGy [21-24]. A 10” x 12” film was cut in half and placed inside the film cassette of the phantom. The film cassette is made of black-coloured Lucite ($\rho = 1.18$ g/cm$^3$) in order to prevent light from reaching the film. Inside the film cassette, two film pieces are separated by a 6 mm film divider to provide dose distribution results for two planes ($Z = 0$ cm and $Z = -0.6$ cm). However, only the outcomes for $Z = 0$ cm plane are presented in this study. Three trials were performed for Case 1 of loose helical delivery ($n = 5$) to determine the reproducibility of the experiment.
The number of monitor units (MU) delivered per beam projection is calculated so that the total number of monitor units remains approximately the same for all cases:

\[ n \times R \times MU \approx constant \]

After each beam projection, the couch was unlocked and manually translated to the next couch position, according to the projection increment calculated using Equation 3.3. Rulers taped on both sides of the phantom were used to verify the position of the phantom with the cross-sectional laser. Each film was scanned and analyzed using film dosimetry system software (RIT 113 v.3.13). Dose profiles were obtained along X = 0 cm, ±2 cm, ±4 cm axes on the Z = 0 cm coronal plane. A calibration film was taken on each experimental day using an open 6 MV photon beam. A calibration film was taken on each experimental day using an open 6 MV photon beam. The calibration film was exposed at the isocentre with four 4 x 4 cm² fields with different monitor units (25 MU, 100 MU, 175 MU, 250 MU) with a 5 cm buildup of solid water.

### 3.3 Results

Both computer simulations and film experiments were used to study the dose homogeneity for loose helical delivery compared to standard HT in a cylindrical target. Two major effects were observed: the “thread” effect and the “beating” effect. In this section, results defining and characterizing these two effects are presented.
3.3.1 “Thread” Effect

In Figure 3.4, the dose distribution results based on the TPP and the film data are presented for the two delivery methods: tight (Case 2, \( n = 5 \)) and loose helical delivery (Case 3, \( n = 10 \)). The dose patterns observed in the TPP data are supported by the film data. In Figure 3.4 a) and c), the dose distribution for Case 2 (\( n = 5 \)) of tight helical delivery is characterized by the presence of higher dose regions, occurring away from the axis of gantry rotation – known as the “thread” effect [25]. The higher dose regions consisted of dose values greater than 100 % and in this case, the maximum dose value reached ~105 %. The positions of these higher dose regions followed a helical path with respect to the axis of gantry rotation. This particular dose pattern due to the thread effect was observed in all tight helical delivery cases in this study. The thread effect was also manifested as ripples in the isodose plots of HT plans produced for complex lung cases at our institution [26], confirming that the thread effect is indeed an inherent characteristic of HT.

The presence of higher dose regions led to dose modulations in the off-axes dose profiles (\( X = \pm 2 \) cm, \( \pm 4 \) cm). Dose modulation is defined as the peak-to-trough difference in percent dose within the target region, while off-axes include all longitudinal axes parallel to the axis of gantry rotation, except the axis of gantry rotation. It was observed the magnitude of dose modulations increased away from the axis of gantry rotation, while no dose modulations were observed along the axis of gantry rotation (\( X = 0 \) cm) for all tight helical delivery cases.
Figure 3.4: Dose distribution results on the coronal plane $Z = 0$ cm for: (a) Case 2 ($n = 5$) of tight helical delivery ($p = 0.5$), Theraplan Plus (TPP). (b) Case 3 ($n = 10$) of loose helical delivery ($p = 2$), Theraplan Plus (TPP). (c) Case 2 ($n = 5$) of tight helical delivery ($p = 0.5$), film. (d) Case 3 ($n = 10$) of loose helical delivery ($p = 2$), film. The dotted line in each dose distribution represents the axis of gantry rotation ($X = 0$ cm). The solid arrows in (a) are pointed to the higher dose regions, which are spaced by $b \times p$ (fan beam thickness times pitch factor). The white circular annulus observed in (d) is an artifact due to the underlying mechanical couch structure.
The thread effect and the absence of dose modulations along the axis of gantry rotation are due to beam divergence. It causes the magnitude of fan beam thickness to vary away from the axis of gantry rotation. Along the axis of gantry rotation, the fan beam thickness \( b \) remains the same (i.e. 4.5 cm) at all gantry angles. However, at the off-axes, the magnitude of fan beam thickness \( b' \) changes as a function of the off-axis position \( (X) \) and the beam gantry angle \( (\theta) \) according to:

\[
b'(X, \theta) = \left( \frac{SAD - X \sin \theta}{SAD} \right) b = \left( \frac{100 \, cm - X \sin \theta}{100 \, cm} \right) 4.5 \, cm \quad (3.4)^{17}
\]

At the off-axes, beam projections with different fan beam thickness lead to peaks and troughs in the primary fluence profiles. In Figure 3.5, the schematic illustration is presented for the primary fluence profile along an off-axis, \( X = 4 \) cm for Case 2 \((n = 5)\) of tight helical delivery. Each beam projection is represented by a rectangle, whose width and height represent fan beam thickness and primary photon fluence, respectively. The main purpose of this schematic illustration was to show the variation in the intensity pattern due to beam projection overlaps, as change in fluence according to the distance from the source was not modeled.

The overall pattern of the fluence profile shown in Figure 3.5 supports the dose modulation pattern observed in the dose profiles (Figure 3.6) obtained from the TPP and the film data. The fluence profile consists of a set of two troughs and two peaks, followed by another set, where each set contributes to a dose peak. The two sets of troughs and peaks in the fluence profile are separated by the same distance as the two dose peaks, which is the couch distance travelled during one gantry rotation \( (b \times p) \).

\[\text{17} \quad \sin \theta = \cos(90^\circ - \theta)\]
Figure 3.5: Schematic fluence profile along the X = 4 cm axis for Case 2 (n = 5) of tight helical delivery (p = 0.5). The target (4.5 cm) is treated over 4 gantry rotations (R = 4) with a fan beam thickness (b) of 4.5 cm. Each rotation is comprised of 5 beam projections with following gantry angles: 0°, 72°, 144°, 216°, 288°. The fan beam thickness (b') along the X = 4 cm axis changes as a function of gantry angle according to Equation 3.4.

Figure 3.6: Dose profile along the X = 4 cm axis for Case 2 (n = 5) of the tight helical delivery based on the Therplan Plus (TPP) data, and the film data.
Along the axis of gantry rotation inside the cylindrical target, both the fan beam thickness and the primary photon fluence remain the same at all gantry angles. These conditions result in a primary fluence profile with homogenous fluence without any modulations inside the target region (Figure 3.7). Homogenous fluence within the target profile in turn produces dose profiles exhibiting no dose modulations (Figure 3.8). The absence of dose modulations along the axis of gantry rotation was true for all tight helical delivery cases.

In Figure 3.4 b) and d), higher dose regions are noticeably absent in the dose distribution for Case 3 \((n = 10)\) of loose helical delivery. In Figure 3.9, it is illustrated that along the off-axis \(X = 4\) cm, the change in fan beam thickness due to beam divergence is counteracted by the presence of multiple beam gantry angles at each couch position. As a result, the off-axes dose modulations inherent in tight helical delivery are eliminated (Figure 3.10), and a more homogenous dose distribution is produced, illustrating the dosimetric advantage of loose helical delivery.

In Figure 3.4, the five narrow strips\(^\text{18}\) observed near the boundaries of high dose region (between \(X = \pm 4\) cm and \(\pm 5\) cm) resulted in the maximum dose modulation of 1\% and 2\% for TPP and film, respectively. The strips were separated by a distance equal to the projection increment, which was 0.9 cm for this case. This dosimetric feature is attributed to the fact that each beam projection undergoes different amount of attenuation before reaching a point along the off-axis. As a result, a different dose is deposited by each beam projection. As the off-axis position moves away from the axis of gantry rotation, the variation in the depth dose of the different beam projections becomes greater – thus producing small dose variations observed near the boundaries of the high dose region. The same feature was observed for Case 5 of loose helical delivery \((n = 18)\). However, due to the overlaps of the strips (0.5 cm apart), no discernable dose modulations were observed from the TPP data, while only a maximum dose modulation of 1\% was observed from the film data.

\(^{18}\)The five narrow strips refer to the thin white strips observed near the edges of the high dose region in Figure 3.4 (d) for loose helical delivery.
Figure 3.7: Schematic fluence profile along the axis of gantry rotation ($X = 0 \text{ cm}$) for Case 2 ($n = 5$) of tight helical delivery ($p = 0.5$). The target ($4.5 \text{ cm}$) is treated over 4 gantry rotations ($R = 4$) with a fan beam thickness ($b$) of $4.5 \text{ cm}$. Each rotation is comprised of 5 beam projections with following gantry angles: $0^\circ$, $72^\circ$, $144^\circ$, $216^\circ$, $288^\circ$.

Figure 3.8: Dose profile along the $X = 0 \text{ cm}$ axis for Case 2 ($n = 5$) of the tight helical delivery based on the Theraplan Plus (TPP) data, and the film data
Figure 3.9: Schematic fluence profile along the X = 4 cm axis for Case 3 (n = 10) of loose helical delivery (p = 2). The target (4.5 cm) is treated with 4 interlaced loose helices (H = 4). Each helix is comprised of 10 beam projections (n = 10) with a different starting gantry angle (0°, 90°, 180°, 270°). The off-axis position (X = 4 cm) results in different fan beam thickness (b'') at each gantry angle. Fluence variations due to inverse square law and beam attenuation were not modelled.
Figure 3.10: Dose profile along the X = 4 cm axis for Case 3 (n = 10) of loose helical delivery based on the Theraplan Plus (TPP) data, and the film data

3.3.2 “Beating” Effect

The dose homogeneity within a dose distribution by loose helical delivery was affected however, when the ratio between the number of beam projections (n) and pitch factor (p) was not an integer. A non-integer \( \frac{n}{p} \) value produced unwanted dose modulations along all off-axes as well as on the axis of gantry rotation, resulting in the “beating” effect (Figure 3.11). The separation between dose peaks was equal to the projection increment. As seen in Figure 3.11 and Table 3.3 (loose helical delivery case), increasing the \( \frac{n}{p} \) ratio reduced the magnitude of dose modulations.

The maximum dose modulations for all tight and loose helical deliveries are summarized in Table 3.3. An experimental uncertainty of 2 \% (2\( \sigma \)) dose modulation was calculated based on the relative standard deviation of the three trials performed for Case 1 of loose helical delivery (\( n = 5 \)). The dose modulations according to film data were consistently higher than the TPP calculations, where an average difference of 3 \% was found with 4 \% being the maximum. The difference was attributed to the fact that the treatment planning software overestimates the tail regions of 6 MV beam profiles for different field sizes and depths, thus yielding smaller dose modulations.
Figure 3.11: Film results and dose profiles for loose helical delivery of (a) Case 1 \((n = 5), n / p = 2.5\); (b) Case 4 \((n = 15), n / p = 7.5\). The dose profiles were taken along the dotted line, representing the Y-axis axis.
Table 3.3: Maximum dose modulations.

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3.4 Discussion

3.4.1 Comparison of Loose and Tight Helical Delivery

3.4.1.1 “Thread” Effect

Tight helical delivery is characterized by the thread effect [25], which results in dose modulations away from the axis of gantry rotation. In this study, the thread effect produced dose modulations as high as 14% inside the target region along the off-axes X = ±4 cm for n = 3 (Table 3 (tight helical delivery case)). Dose modulations were present even at n = 45 according to the TPP data, indicating that the thread effect takes place regardless of the number of beam projections. Thus, dose modulations due to the thread effect are expected to be present for the current HT unit (n = 51). This is indeed confirmed by our experience with the unit and its treatment planning software [26].

The advantage of loose helical delivery lies in its ability to produce a homogeneous dose distribution by eliminating thread effect. This was seen in Case 3 and 5 of loose helical delivery, where the absence of higher dose regions resulted in dose profiles with no dose modulations. This is due to the fact that loose helical delivery treats the target with helices commencing at different gantry angles. We expect this advantage to persist also
for intensity modulated HT deliveries as long as the different starting angles can be included in the plan optimization.

### 3.4.1.2 Sensitivity to the Uncertainty of Couch Movement

The study by Yang et al [27] reported that the HT delivery is much less sensitive to the uncertainty in couch position compared to serial tomotherapy [3]. A 1.0 mm error in couch position resulted in 5% dose modulations, whereas in serial tomotherapy, dose modulations could be as high as 20%. This is attributed to the difference in the dose profiles (in the direction of couch motion) produced by the two techniques after each gantry rotation. The resulting dose profile of the HT delivery after a single gantry rotation is triangular in shape containing the “ramp-up” and “ramp-down” regions, in contrast to the sharp drop-offs present in the dose profile of a serial tomotherapy beam. As a result, the HT delivery can produce a uniform longitudinal dose distribution as long as the dose profiles from the different gantry rotations are matched within a few mm, while serial tomotherapy requires a more critical matching of the dose profiles.

For loose helical delivery, each loose helix produces a dose profile that is trapezoidal in shape. There are no junction issues as in the tight helical delivery since the dose profiles produced by the individual loose helices are being overlaid onto one another. At the same time, loose helical delivery is more sensitive to systematic uncertainty compared to the tight helical delivery, as the same starting couch position must be reproduced multiple times. An uncertainty in the gantry repositioning is also introduced since loose helical delivery requires different starting gantry angles for the individual helices. However, the starting couch position is reproducible within an accuracy of 0.5 mm, and thus the impact of the starting position uncertainty on the final dose distribution should be negligible. The HT unit is capable of repositioning the gantry at the cardinal angles (0°, 90°, 180° and 270°) within 1°, and the uncertainty of this magnitude should have minimal effect on the dose distribution. During a HT treatment, the couch position is accurate with ±0.5 mm, and due to the higher couch velocity, loose helical delivery is less sensitive to the impact of random uncertainty in the actual couch position compared to tight helical delivery. Thus, overall loose helical delivery should be less sensitive to couch position errors.
3.4.1.3 “Beating” Effect and its Impact on Pitch Factor Selection

A non-integer \( n / p \) ratio results in the beating effect (first described in this work), which creates dose modulations along all \( X \)-axes in the direction of couch motion inside the target region. ICRU Reports 50 and 62 recommend the dose given to the planning target volume (PTV) to be kept within +7% and -5% of the prescription dose, providing room for 12% dose variation [28,29]. In clinical practice, it would be desirable to keep the dose variation due to dose modulations under 5% in order to provide room for the other sources of uncertainty. The film data suggest that the dose modulations will remain under 5% when the \( n / p \) ratio is greater than 7.5.

With the number of beam projections fixed at 51 for the current tomotherapy unit, most loose helical delivery cases will experience dose modulations, since pitch factors other than 3 and 17 yield non-integer \( n / p \) ratios. As a result, a restriction must be imposed on the maximum allowed pitch factor in order to keep the dose modulations below 5%. This condition in turn places a limit on the maximum treatable target length, which depends directly on the pitch factor (\( p \)) and the fan beam thickness (\( b \)) as shown in Equation 3.2.

Assuming that the findings in this paper are applicable to the current HT unit, the pitch factor must be selected below 7 in order to keep the \( n / p \) ratio above 7.5 and the dose modulations under 5%. This in turn limits the maximum treatable target length to 15 cm and 30 cm, when using currently available fan beam thickness of 2.5 cm and 5 cm, respectively (according to Equation 3.2).

In the future, improving the current MLC transit time (~30 ms) will increase the number of beam projections deliverable per gantry rotation. As a result, the maximum treatable target length will become larger as well. If the option of adjusting the MLC transit speed ever becomes available, one would be able to fix the rotation period to the breath-holding capability of the patient and select the number of beam projections according to the target length.

In a recent study, HT plans with two different planning target volumes were generated for each of ten patients with stage 3 inoperable non-small cell lung cancer [30]. PTV2 was created with a 2 cm margin around the gross tumour volume (GTV), while PTV1
included regional lymph nodes in addition to the GTV. The cranial/caudal extensions of these PTVs were $12.8 \pm 4.5$ cm for PTV2 and $17.5 \pm 2.8$ cm for PTV1. Considering the ranges of target lengths for these two PTV volumes, loose helical delivery with a fan beam thickness of $2.5$ cm should be sufficient for most PTV cases containing the lung tumour only, while a loose helical delivery plan including elective nodal treatment would likely require a fan beam thickness of $5$ cm.

The beating effect was not found to be an issue for the tight helical delivery cases in this study, since their $n/p$ ratios were all integers. Even if they were not integers, dose modulations will always be smaller than 5% due to their large $n/p$ values, except for Case 1 where $n/p$ is only 6. For the current tomotherapy unit ($n = 51$), the beating effect will never be a concern for tight helical delivery ($p < 1$), since the $n/p$ ratio will always be larger than 51, which is significantly higher than 7.5.

### 3.4.2 Practical Considerations for the Use of Loose Helical Delivery

The additional treatment time required for loose helical delivery arises from the sum of couch re-set time between the helices. Thus, the increase in treatment time directly dependent on the number of loose helices ($H$) used. Each re-set time is expected to last for $30$ s provide sufficient recovery time for the next breath-hold. The re-set time slots are represented as the dark bands within the treatment time in Figure 3.12.

The number of loose helices ($H$) should be selected such that the total “beam-ON” time ($H \times T_l$) required to cover the target is comparable to the total “beam-ON” time ($R \times T_l$) for tight helical delivery. This ensures that the planned dose is delivered to the target while performing an equivalent degree of beam intensity modulation. For loose helical delivery, it can be assumed that the gantry rotation period will be set to the minimum gantry rotation period of $10$ s to account for compromised lung functions of patients. Therefore, if the gantry rotation period in tight helical delivery is larger than $10$ s, the number of required helices ($H$) needs to be greater than the number of gantry rotations ($R$) used in tight helical delivery. $H$ is larger than $R$ by the ratio of gantry rotation periods used for the two deliveries:
\[ H \times T_l = R \times T_t \implies H = R \times \frac{T_l}{T_t} = R \times \frac{T_l}{10 \text{ s}} \] 

(3.5)

where \( T_l \) is the gantry rotation period for loose helical delivery and \( T_t \) is the gantry rotation period for tight helical delivery.

If one assumes a target length of 10 cm, tight helical delivery using a fan beam thickness of 2.5 cm with the recommended pitch factor of 0.3 requires 17 gantry rotations to cover a target of this magnitude. As a typical gantry rotation period ranges from 20 s to 30 s, the treatment time should last anywhere from 5 to 10 minutes (Figure 3.12). In order to achieve a similar beam-ON time with loose helical delivery, 34 to 51 loose helices are needed. This yields a total couch re-set time of 15–25 minutes, increasing the total treatment time to 20–35 minutes. However, the treatment time is only a portion of session time as shown in Figure 3.12. Adding the time for set-up and MVCT (20 minutes) the total session time increases from 25–30 minutes to 40–55 minutes. This is an increase by a factor of \(~2\), which may be acceptable given the dosimetric advantages of loose helical delivery.

**Figure 3.12:** Total session time for: the tight helical delivery (top), loose helical delivery (bottom). The dark bands within the treatment segment for loose helical delivery represent couch re-set time between loose helices, during which the patient breathes normally.
The overall treatment time may be reduced by utilizing a fan beam thickness of 5 cm, as a smaller number of helices will be required. Olivera et al [31] have shown that the use of a larger fan beam thickness yields better dose uniformity. However, it also compromises the ability to perform beam intensity modulation and the accuracy of dose conformation to the target in the longitudinal direction. Therefore, using a fan beam thickness of 5 cm would not reduce the number of helices by a factor of 2, but by a factor between 1 and 2. At present, the HT treatment planning system does not allow for the planning of loose helical delivery. However, if the loose helical delivery option ever becomes available, the time and effort spent for planning and optimization remains the same, since the overall number of projections stays the same as in tight helical delivery. Loose helical delivery is also applicable to all tumour targets driven by respiratory motion. The tumour sites may include liver and other sites within in the thoracic cavity.

3.4.3 Other Methods for Accounting for Respiration-Driven Motion in HT

Table 3.1 gives a summary of all methods, which could be used for mitigation of motion in radiation therapy. In the context of HT, both breath-holding and planning for motion prospectively appear to be possible. In the present study, we have investigated loose helical delivery as a potential means to combine breath-holding with improved dose distributions. However, breath-holding may be incorporated into tight helical delivery as well. In the proposed “gating-by-rotation” approach, each rotation of breath-hold treatment is followed by a rotation of non-treatment where the patient breathes freely [32]. During non-treatment rotations, the couch motion is halted and the treatment beam is blocked by the closure of all MLC leaves. This on-off strategy is repeated for the full treatment volume. The dose distribution outcomes of this approach essentially represents those of tight helical delivery presented in this study, assuming breath-holding has been carried out as planned.

Recently, the tomotherapy group in Madison, WI has proposed a method that incorporates respiratory motion during the optimization process [13,14]. In this approach, beamlet calculations are performed at the different phases of the CT data, once the correlation between beam delivery and breathing is established. The calculated
beamlets are then mapped back to the primary phase according to the displacement maps, and the plan optimization is carried out. The displacement maps are generated during deformable image registrations of the lung at different phases. However, this method only works under the condition that the patient’s breathing can correctly follow the breathing guide on the given treatment day.

3.5 Conclusions

- Loose helical delivery allows incorporation of breath-holding into helical tomotherapy for a more effective treatment of respiration-driven tumour target.

- The advantage of loose helical delivery lies in its ability to produce a homogenous dose distribution by eliminating the “thread” effect – an inherent characteristic of tight helical delivery.

- Loose helical delivery, however, results in the “beating” effect, when the $n/p$ ratio is a non-integer. The magnitude of dose modulations due to the beating effect decreases with an increasing $n/p$ ratio. Thus, a pitch factor must be selected such that the magnitude of dose modulations remains below 5%.

- The planning effort remains the same for loose helical delivery, and the total treatment time increases only by a factor of 2, making loose helical delivery clinically practical.

- Overall, loose helical delivery is promising solution that should be strongly considered for the future HT treatments of respiration-driven targets.

3.6 Acknowledgements

The author would like to thank Jeff Chen and Eugene Wong for their help with beam modeling in the Theraplan Plus system. The author would also like to acknowledge Andrea McNiven for providing the phantom for the film experiment and the Ontario Research and Development Challenge Fund (OCITS project) for the source of funding.
3.7 References


Chapter 4

4 Feasibility Study of Multi-Pass Respiratory-Gated Helical Tomotherapy of a Moving Target via binary MLC Closure


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4.1 Introduction

Helical tomotherapy [1,2] utilizes a continuously rotating gantry and a linearly moving couch to deliver an intensity-modulated fan beam of radiation in a helical manner. Helical tomotherapy has been used extensively in the clinics, due to its IMRT dose delivery capability combined with the on-line megavoltage CT available for image guidance. Intensity modulation is performed by the binary multi-leaf collimator (b-MLC), consisting of 64 interlaced binary leaves that either move into or out of the fan beam field. The radiation fluence is then determined by the duration of leaf openings for each of the 51 equally-spaced beam projections per gantry rotation. However, the fan beam geometry and the movements of the three subsystems (gantry, couch, and collimator) also make helical tomotherapy more susceptible to producing dose artifacts in the presence of target motion [3-7].

Three major motion-induced dose discrepancies have been defined previously for helical tomotherapy; (1) dose rounding, (2) dose rippling, and (3) IMRT leaf opening asynchronization effect [7]. Dose rounding [3,6,7] is the penumbral widening of a delivered dose distribution along the direction of tumour motion. Dose rippling [3-5,7] is a series of periodic dose undulations inside the target volume along the direction of couch motion, due to an asynchronous interplay between the couch motion and tumour motion. The IMRT leaf opening asynchronization effect [7] is caused by an asynchronous
interplay between the temporal leaf opening patterns of the b-MLC leaves and tumour motion, yielding a dose discrepancy pattern unique to each tomotherapy plan.

In the past, various approaches have been proposed to compensate for tumour motion during radiotherapy, in the form of breath-holding [8-10], respiratory gating [11-13], and tumour-tracking [14,15]. Breath-holding may be incorporated to minimize tumour motion during helical tomotherapy, although breath-holding may not be feasible for all lung cancer patients due to their compromised lung functions [16,17]. Alternatively, the tumour motion information acquired prior to the treatment may be included during the plan optimization to allow normal breathing during the actual treatment [18,19]. However, this method assumes that patients can reproduce the breathing patterns used for planning during treatments. Failure to reproduce the same breathing patterns can lead to significant dose discrepancies. Real-time motion-adaptive delivery [20,21] was proposed recently, where the sequence of planned beam projections is “shuffled” and executed out-of-order according to the tumour motion, thus placing no constraints on patient breathing patterns. The desired dose distributions, however, may not always be achieved, as this method does not account for the radiological pathlength differences between the original and shifted beam projections. The spatially shifted beam projections may encounter different tissue thicknesses and densities, thus affecting the beam attenuation – especially for large amplitudes of target motion.

We propose a new way to implement respiratory gating for helical tomotherapy, namely multi-pass respiratory gating [22]. In this approach, the tumour motion during the radiation delivery is restricted to the residual motion within the gating window. Thus, this method reduces the beam attenuation differences caused by the relative motion between the tumour volume and the surrounding normal tissues. Due to the continuous couch motion during helical tomotherapy, the planned beam projections must be delivered over multiples passes of radiation deliveries. The multiple passes may consist of all gated passes (“full gating”) or multiple gated passes and one final ungated pass (“partial gating”). In the present study, we investigated the feasibility and effectiveness of the proposed technique for sinusoidal motion (“ideal” scenario) and a patient respiratory motion pattern (“realistic” scenario). Full gating was tested for sinusoidal
motion, through experimental measurements with film and computer simulation for a single fraction. For the patient waveform, both full and partial gating methods were investigated for various fractionation schemes (1, 3 and 30 fractions), through computer simulation. The fractionation effect on the magnitude of dose discrepancies was investigated, as the motion-induced dose deviations were previously shown to “smear out” over multiple fractions of IMRT treatments [4, 23, 24]. It was assumed that each treatment fraction commenced at a random phase of tumour motion. The interest for hypofractionation (3 fractions) was prompted by the recent clinical trials on hypofractionated stereotactic radiotherapy, which is current being regarded as a promising treatment option for lung cancer [25-27].

4.2 Materials and Methods

4.2.1 Multi-Pass Respiratory Gating Technique

4.2.1.1 Helical Tomotherapy, Tumour Motion, and Gating Parameters

The helical tomotherapy parameters include fan beam thickness ($b$), pitch factor ($p$), gantry rotation period ($T_g$), leaf opening time per beam projection ($T_a$), and number of gantry rotations per fraction ($R$). At the axis of gantry rotation (i.e. isocenter, SAD = 85 cm), the fan beam is projected to be 40 cm wide ($X$) with a selectable fan beam thickness ($b$) of 1.05 cm, 2.5 cm, or 5.0 cm ($Y$). Pitch factor ($p$) is defined as the longitudinal ($Y$) progression distance of the treatment couch per gantry rotation, in units of fan beam thickness ($b$). Gantry rotation period ($T_g$) is the time required to complete one full gantry rotation, which consists of 51 equally-spaced beam projections. During the different beam projections, each binary leaf remains open for a planned duration ($0 \leq T_a \leq T_g / 51$). In the current study, the gantry rotation periods of 15 s and 16 s were used for different test cases. Gantry rotation periods of less than 20 s are typically used clinically for lung tomotherapy. The total treatment time per fraction is thus the product of the gantry rotation period ($T_g$) and the number of gantry rotations per fraction ($R$).

The tumour motion parameters consist of amplitude ($A$) and tumour motion period ($T_t$). Amplitude ($A$) is defined as one-half of the peak-to-peak amplitude ($2A$) of tumour
motion, while tumour motion period ($T_r$) is the time elapsed for one full cycle. In this study, the effectiveness of the proposed technique was tested for the superior-inferior motion only, as it is the predominant direction of tumour motion [24,28-30].

The gating parameters are number of passes ($n$), duty cycle ($dc$), and gating window size. Duty cycle ($dc$) is a parameter used for phase gating, which is defined as the fraction of tumour motion period ($T_r$) during which radiation is delivered. Gating window size is a parameter for amplitude gating, which is the magnitude of target motion allowed during gated radiation delivery.

4.2.1.2 Leaf Opening Sinogram

During a helical tomotherapy delivery, intensity modulation is performed by the $b$-MLC, consisting of 64 interlaced binary leaves. The binary leaves travel along the longitudinal direction ($\pm Y$) to either move into or out of the different sections of the fan beam. The radiation fluence passing through the different beamlets is determined by the durations of leaf openings during each beam projection. The leaf opening time information is stored in the form of a leaf opening sinogram, which is a two-dimensional matrix of relative leaf opening time values ($T_0$), with the row and column indices representing leaf number and beam projection number, respectively. The relative leaf opening time is defined as the ratio of the actual leaf opening time ($T_a$) for a beam projection to the maximum leaf opening time per beam projection ($T_m = T_g / 51$). In this study, a user-created leaf opening sinogram was utilized for the non-IMRT cases, while a leaf opening sinogram for the IMRT cases was generated via the helical tomotherapy plan optimizer (TomoTherapy v. 2.2.2, TomoTherapy Inc., Madison, WI).

4.2.1.3 General Concept of Multi-Pass Respiratory Gating

In the multi-pass respiratory gating technique, the gated helical tomotherapy is achieved by delivering only the beam projections that occur within a respiratory gating window, while blocking the remaining beam projections via the complete closure of all MLC leaves. After each pass, the couch is reset to its starting position, and the treatment recommences at a different phase of tumor motion for the previously blocked beam projections to coincide with the gating window. This process is repeated until the entire
plan dose is delivered (“full gating”). However, this approach may not be clinically feasible, as the number of passes \( n \) required may become too high, due to the complexities of tumour motion patterns. Thus, an alternative approach is halting the gating process after a certain number of passes, and delivering the entire remaining planned dose in a subsequent final pass without gating (“partial gating”).

In Figure 4.1, the multi-pass respiratory gating method with the full gating approach is illustrated for a simple non-IMRT case. In Figure 4.1 a), the displayed leaf opening sinogram (right panel) is designed to treat an off-axis target (left panel). For illustrative purposes, we assume a uniform fluence from all beam projections. The gating window is centered at the end-expiration phase with an unusually high duty cycle \( dc \) of 50%, where the entire leaf opening sinogram is completed over two gated passes (Figure 4.1 b and c). The peak-to-peak amplitude (2\( A \)) of target motion in this example was 2.0 cm, yielding a residual motion of 1.0 cm within the gating window.

### 4.2.1.3.1 Ideal Scenario: Sinusoidal Waveform

The feasibility of the full gating approach was first tested for sinusoidal motion with a constant amplitude \( A \) and target motion period \( T_r \), through experimental measurements using film (Section 4.2.3) and computer simulation (Section 4.2.4) for a single fraction. The test cases included a non-IMRT helical tomotherapy case (Section 4.2.2.1) exhibiting the dose rippling and dose rounding effects, and an IMRT helical tomotherapy case (Section 4.2.2.2) displaying the IMRT leaf opening asynchronization and dose rounding effects. Phase gating was used with the gating window centered at the end-expiration phase for two different duty cycles \( dc \) of 50% and 25%. The duty cycle of 25% represents the clinical scenario, while the duty cycle of 50% was chosen as the “stress” case for the proposed gating method.

### 4.2.1.3.2 Realistic Scenario: RPM Waveform

Both full and partial gating methods were then investigated for a patient respiratory motion pattern, through computer simulation (Section 4.2.4) for the IMRT helical tomotherapy case (Section 4.2.2.2). The patient waveform was acquired by the Real-time Position Management (RPM) system (Varian Medical Systems, Palo Alto, CA). In this
study, it was assumed that the anterior-posterior motion of the RPM block placed on the patient’s abdomen represented the actual tumour motion. Amplitude gating was employed due to the constantly changing amplitudes of the RPM trace, including two large erratic peaks that may represent unexpected physiological events such as patient coughing. For different fractionation schemes (1, 3 and 30 fractions), we determined the optimal gating parameters to keep the root-mean-square of dose deviations ($\text{RMS}_{\Delta D}$) from the planned dose profile below 1.0%, both inside the PTV and for the entire profile. The amplitude gating window size ranged from 4 to 7 mm, in an increment of 1 mm.
Figure 4.1: Multi-pass respiratory gating technique with the full gating approach ($dc = 50\%$). (a) Left panel: Off-axis target, Right panel: Leaf opening sinogram. (b) First gated pass. Only the beam projections occurring within the gating window are delivered. (c) Second gated pass. The treatment commences at a different starting phase of the tumour motion to deliver the previously blocked beam projections.
4.2.2 Treatment Planning

4.2.2.1 Non-IMRT Helical Tomotherapy Plan

A non-IMRT plan was designed to deliver uniform fluence to the central axis of a 5.5 cm-long cylindrical target volume, aligned with the axis of gantry rotation. The target volume was located inside the film insert that moves through an opening of the body phantom (Modus Medical Devices Inc., London, Canada), shown in Figure 4.2 a). Maximum leaf opening time \( t_o = 1 \) was assigned to the four central leaves with the rest of the leaves remaining fully closed \( t_o = 0 \) for all beam projections over four gantry rotations \( R = 4 \). A fan beam thickness \( b \) of 2.5 cm was used with a pitch factor \( p \) of 0.8 and a gantry rotation period \( T_g \) of 16 s. A pitch factor of 0.8 was chosen instead of typical pitch factors of less than 0.3 for lung cancer tomotherapy [31], in order to intentionally generate dose rippling.

4.2.2.2 IMRT Helical Tomotherapy Plan

The IMRT helical tomotherapy plan was generated using the stationary CT images of the body phantom \( \rho = 1.18 \text{ g cm}^{-3}, \text{ length} = 12 \text{ cm}, \text{ width} = 30 \text{ cm}, \text{ height} = 20 \text{ cm} \). On the CT images of the body phantom (Figure 4.2 b), a virtual C-shaped PTV (length = 6.6 cm) was delineated to wrap around a cylindrical OAR (length = 3.6 cm), using a commercial treatment planning system (Pinnacle 8.0d, Philips Medical Systems). The CT images and contours were then exported to the tomotherapy treatment planning system (TomoTherapy version 2.2.2, TomoTherapy Inc., Madison, WI), where a dose of 2.0 Gy was prescribed to 95% of the PTV with the maximum OAR dose being limited to 0.8 Gy. A pitch factor \( p \) of 0.287 (i.e. \( 0.86 / 3 \)) was selected to minimize the “thread artifact” [32] with a fan beam thickness of 2.5 cm. The optimized dose distribution in a transverse plane is shown in Figure 4.2 c). The leaf opening sinogram generated through the plan optimization consisted of 819 beam projections \( R \sim 16 \).

The plan leaf opening sinogram was then truncated to 408 beam projections \( R = 8 \) by eliminating the first 252 and the last 159 beam projections, decreasing the plan dose from 2.0 Gy to 1.75 Gy. This was done to shorten the length of the PTV from 6.6 cm to 3.24 cm, so that the resulting PTV region fell well within the length of the body phantom.
while in motion. This was deemed acceptable, as the objective of this study was not to reproduce a particular plan, but to investigate how the multi-pass gating technique can effectively minimize the dose discrepancies between the gated and planned dose distributions.

Figure 4.2: IMRT helical tomotherapy plan for a stationary target. Dose of 2.0 Gy was prescribed to 95% of the PTV with the maximum OAR dose being limited to 0.8 Gy. (a) Photograph of the lucite body phantom ($\rho = 1.18 \text{ g cm}^{-3}$, length = 12 cm, width = 30 cm, height = 20 cm) mimicking a human torso. The different features of the motion phantom are labelled in the “zoomed-in” picture. (b) Transverse CT image of the stationary body phantom with the contours of the PTV (dark), OAR (light), and the phantom outline. The coronal film insert remained stationary inside the body phantom at its mid-position during the CT scanning process. (c) Plan dose distribution in the transverse plane.
4.2.2.3 Gated Leaf Opening Sinograms

A series of gated leaf opening sinograms was generated for each plan leaf opening sinogram, to experimentally simulate a multi-pass gated delivery. The plan leaf opening sinograms for the non-IMRT and IMRT cases were modified according to the gating parameters, using a code written in MATLAB (Mathworks, Natick, MA). For the modification process, the plan leaf opening sinogram must be first transposed, as shown in Figure 4.3 a). Only the beam projections occurring within the gating window are left unchanged, while the remaining beam projections are replaced with a relative leaf opening time value of ‘0’ to “block” the radiation delivery (Figure 4.3 b). When more than half of a beam projection overlaps with the gating window, the beam projection is deemed to be inside the gating window, and vice versa. Thus, the actual “Beam ON” time per tumour motion cycle may be either longer or shorter than the intended duration set by the gating window. For each investigated case in this study, however, the cumulative difference over the entire treatment was zero. For the subsequent passes, the beam projections completed during the previous passes are now “blocked” to avoid replication, while the previously undelivered beam projections are assigned with their original leaf opening time (Figure 4.3 c). The resulting gated leaf opening sinograms were then re-transposed and converted to the tomotherapy file format for deliveries at the treatment console.
Figure 4.3: Leaf opening sinograms for the full gating method. (a) “Transposed” plan leaf opening sinogram. The row and column indices now represent projection number and leaf number, respectively. (b) Gated leaf opening sinogram for the first pass. Only the beam projections occurring within the gating window are left unchanged, while the remaining beam projections are replaced with a relative leaf

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dark grey - beam projections "blocked"
light grey - beam projections "allowed"
opening time value of ‘0’ to “block” the radiation delivery. (c) Gated leaf opening sinogram for the second pass. The beam projections completed during the first pass are “blocked”, while the previously undelivered beam projections are assigned with their original leaf opening time.

4.2.3 Experimental Measurements for a Sinusoidally Moving Target

The experimental measurements were carried out on the helical tomotherapy machine (Hi-Art II, TomoTherapy Inc., Madison, WI) to investigate the effectiveness of the multi-pass gating technique, using a body phantom with a moving film insert (Figure 4.2 a). The film insert travelled in a sinusoidal manner with a fixed target motion period \( (T_r) \) and amplitude \( (A) \).

4.2.3.1 Motion Body Phantom

The motion phantom (Figure 4.2 a) consists of a lucite body phantom \( (\rho = 1.18 \text{ g cm}^{-3}, \text{length} = 12 \text{ cm}, \text{width} = 30 \text{ cm}, \text{height} = 20 \text{ cm}) \) mimicking a human torso, and a sinusoidally moving lucite film insert \( (\rho = 1.18 \text{ g cm}^{-3}, \text{length} = 18 \text{ cm}, \text{diameter} = 8 \text{ cm}) \). The film insert was positioned to move through the central opening of the body phantom. The film \( (\text{length} = 15 \text{ cm}, \text{width} = 6 \text{ cm}) \) was placed on the coronal plane centered along the axis of gantry rotation, inside the film insert. The film insert contains five pins at its inside corners (2 at one corner, and 1 at each of the three corners) to generate pinprick landmarks on each film, which were later used to align a pair of scanned film images for direct dosimetric comparisons. The amplitude of the film insert motion is set by adjusting the position of the translation stage holding film insert. The motion phantom is also equipped with a “chest-height” platform, whose vertical up-and-down motion represents the anterior-posterior (AP) motion of a “chest wall”, and moves with an identical frequency as the film insert. The period of the film insert motion was verified by measuring the positions of the optical markers placed on the platform, using an optical tracking camera (NDI, Waterloo, ON) with a sampling frequency of 60 Hz.
4.2.3.2 Calibration for Film Dosimetry

The calibration process was performed at the helical tomotherapy, on the same day of the experiment. A cylindrical solid water phantom ("Cheese" phantom, length = 18 cm, diameter = 30 cm, TomoTherapy Inc., Madison, WI) was used. A 10” x 12” EDR2 film was placed on the coronal plane bisecting the "Cheese" phantom, which was centered along the isocentre. The calibration procedure delivered eight 3-cm$^2$ square fields with known dose of 30.5 cGy, 65.2 cGy, 100.9 cGy, 128.2 cGy, 159.5 cGy, 188.9 cGy, 215.0 cGy, and 244.4 cGy. The calibration film was processed along with a blank film to enable background subtraction. The developed films were scanned with a Vidar VXR-16 DosimetryPro scanner (Vidar Systems Corporation, Herndon, VA), and analyzed with the RIT113 V4 software (Radiation Therapy Dosimetry Software, Colorado Springs, CO). A region of interest (ROI) of 2 cm$^2$ was placed inside each of the eight different fields on the calibration film and within the blank film. The average optical densities (O.D.) of the ROIs were then used to generate an O.D. versus dose calibration curve.

4.2.3.3 Radiation Delivery

All the film experiments were carried out in the non-clinical “service” mode at the helical tomotherapy unit. For each case, three different delivery scenarios were performed: (1) “no motion”, (2) “motion, no gating”, and (3) “motion, gating”. An electronic communication was established between the tomotherapy machine and the motion phantom, such that the film insert motion would commence once the gantry angle reached zero. For the “no motion” and “motion, no gating” scenarios, the starting phase of the film insert motion was set to zero, by positioning the film insert at its mid-position before the start of radiation delivery. For the “motion, gating” scenario, the film insert position was adjusted to commence at a different phase for each pass.

Ideally, the starting positions of the film insert for Scenario (1) & (2) should correspond to the average film insert position inside the gating window for Scenario (3). However, this will require a separate CT scan of the body phantom for each case, with the film insert positioned according to the target motion amplitude ($A$) and gating parameters. In this particular situation, the anatomy of the body phantom does not vary radiologically
along the longitudinal direction. Thus, the stationary (1) and non-gated (2) dose profiles can be aligned with the gated dose profiles (3) by simply applying a rigid shift ($\Delta y$) along the longitudinal direction, which was equal to the average target position inside the gating window.

### 4.2.3.4 Experimental Data Analysis

During the experimental data analysis, the dose deviations from the planned dose profile were evaluated inside the PTV. This task was performed to determine the combined effects of the different dose discrepancies, and the resulting improvements with the multi-pass gating technique. For the non-IMRT helical tomotherapy case, penumbral size and dose rippling magnitude were introduced as the metrics to quantify dose rounding and dose rippling effects, respectively. Penumbral size was defined as the average of two distances between the 20% and 80% dose points ($P_{20/80}$), and the 80% and 20% dose points ($P_{80/20}$). Dose rippling magnitude was measured as the dosimetric difference between the highest dose peak and the lowest dose valley inside the PTV.

The dosimetric uncertainty of the film experiment for the non-IMRT helical tomotherapy case ($p = 0.8$, $T_g = 16$ s, $R = 4$) was measured from the five measured “no motion” dose profiles. Standard deviations were calculated for all dose points, once the dose profiles were aligned by the center of the PTV regions. The mean of all standard deviations values was then determined to yield a dosimetric uncertainty of $\pm 0.5\%$. For the IMRT helical tomotherapy case ($p = 0.287$, $T_g = 15$ s, $R = 8$), the dosimetric uncertainty of $\pm 1.0\%$ was calculated from the standard deviation of the maximum PTV dose for the three “no motion” film dose distributions.

### 4.2.4 Computer Simulation

A computer program was developed to calculate simulated longitudinal dose profiles along the axis of gantry rotation inside a body phantom. The simulation program described in a previous publication [7] was used to generate the longitudinal dose profiles for a sinusoidally moving target. Additional parameters such as the number of passes ($n$) and duty cycle ($dc$) were added to allow dose calculations for phase gating. The exposure time at each longitudinal position was determined by iteratively calculating the total time
spent simultaneously within the gating window, leaf opening window and the two jaws defining fan beam thickness \((b)\). The fluence profile for each gating case was produced by summing up the fluence profiles calculated from the different passes, which was then converted to a dose profile through the convolution process using a dose spread kernel.

The computer program was further modified to accept a RPM trace as a numerical input waveform, and to perform dose calculations for amplitude gating. For amplitude gating, partial deliveries of the beam projections were allowed, whereas the beam projections were either delivered or blocked entirely for phase gating. In order to study the fractionation effect, a random tumour motion phase was introduced at the start of each fraction. The resulting dose profiles for the individual fractions were then accumulated to yield a dose profile for multiple fractions.

4.3 Results

4.3.1 Non-IMRT Helical Tomotherapy Case, Sinusoidal Waveform

In Figure 4.4 a) and b), the non-gated and gated longitudinal dose profiles along the axis of gantry rotation are presented for the non-IMRT helical tomotherapy case \((p = 0.8, T_g = 16\ s, R = 4)\). Without gating, a penumbral size of 22 mm was measured, which corresponded to an increase of 6 mm over the penumbral size of the planned dose profile. With full gating \((dc = 25\%, n = 4)\), the penumbral size decreased by 5 mm to 17 mm, which was within 1 mm of the planned penumbral size. The dose rippling magnitude was also reduced from 3 to 0.5% by gating. In Figure 4.4 a), the dose deviations inside the PTV ranged from -10 to 2%, with the mean dose difference of -2%. The dose deviation of -10% was observed near the PTV boundary, due to the dose rounding effect. The maximum dose deviation of 2% was less than the dose rippling magnitude of 3%, due to the “dose rippling-like” feature present inside the PTV of the planned dose profile. This dosimetric feature was attributed to the oval shape of the body phantom. In Figure 4.4 b), the dose deviations inside the PTV were reduced to within \(\pm 1\%\), with the mean dose difference of 0.5%. In both Figure 4.4 a) and b), the simulated dose profiles agreed with the corresponding measured dose profiles within a standard deviation of 0.6% inside the PTV.
Figure 4.4: Non-IMRT helical tomotherapy case ($p = 0.8, T_g = 16\ s, R = 4$) delivered in the presence of sinusoidal target motion ($T_r = 8\ s, A = 1.5\ \text{cm}$) over a single fraction. (a) Non-gated measured and simulated longitudinal dose profiles along the axis of gantry rotation. (b) Gated measured and simulated longitudinal dose profiles along the axis of gantry rotation ($dc = 25\%, n = 4$).
4.3.2 IMRT Helical Tomotherapy Case, Sinusoidal Waveform

In Figure 4.5 a), the measured coronal dose distributions are shown for the IMRT helical tomotherapy case ($p = 0.287$, $T_g = 15$ s, $R = 8$) under four different radiation delivery conditions. Significant dose discrepancies were evident in the “motion, no gating” dose distribution (ii), due to the IMRT leaf opening asynchronization effect. In Figure 4.5 b), the corresponding longitudinal dose profile along the axis of gantry rotation showed significant dose deviations ranging from -29 to 5%, with the mean dose difference of 8%. Dose rounding effect was also observed near the PTV boundaries. The measured and simulated dose profiles agreed within a standard deviation of 2.5% inside the PTV. In Figure 4.5 c), the renormalized non-gated dose profiles summed over 30 fractions and 3 fractions with three different sets of random starting phases of target motion are plotted. For the 30 fraction scenario, the dose discrepancies of -29 to 5% observed for the single fraction case (Figure 4.5 b) decreased to range from -16 to 1%. For the 3 fraction case, however, it was illustrated that the dose variations were dependent upon the values of random starting phases. The first set of random starting phases yielded dose deviations (-31 to 9%) larger than the single fraction case, while the second set of random starting phases produced dose differences (-18 to -1%) that were close to the 30 fraction scenario. On the other hand, the dose discrepancies values for the third set of random starting phases (-19 to -10%) fell between the single fraction and 30 fractions cases.

In Figure 4.5 a), significant reductions of dose discrepancies were observed in the “motion, 50% gating” dose distribution (iii), while the planned “no motion” dose distribution (i) was nearly restored in the “motion, 25% gating” dose distribution (iv). In Figure 4.5 d), the dose deviations of the measured “50% gating” profile ($dc = 50\%, n = 2$) ranged from -5 to 2 %, with the mean dose difference of -2%. In Figure 4.5 e), the use of a lower duty cycle ($dc = 25\%, n = 4$) further decreased the measured dose deviations to range from -1 to 3%, with the mean dose difference of 2%. In Figure 4.5 d) and e), the measured and simulated dose profiles agreed with a standard deviation of 1.0% inside the PTV.
Figure 4.5: IMRT helical tomotherapy case ($p = 0.287$, $T_g = 15\ s$, $R = 8$) delivered in the presence of sinusoidal target motion ($T_r = 8\ s$, $A = 1.5\ cm$) over a single fraction. (a) Measured coronal dose distributions under four different radiation delivery conditions: (i) “no motion”, (ii) “motion, no gating”, (iii) “motion, 50\%\ gating”, and (iv) “motion, 25\%\ gating”. The dotted lines ($x = 0\ cm$) represent the axis of gantry rotation. (b) Non-gated measured and simulated longitudinal dose profiles along the axis of gantry rotation. (c) Non-gated simulated longitudinal dose profiles along the axis of gantry rotation for 30 fractions and 3 fractions with three different sets of random starting phases of target motion. (d) Gated measured and simulated longitudinal dose profiles along the axis of gantry rotation ($d_c = 50\%$, $n = 2$). (e) Gated measured and simulated longitudinal dose profiles along the axis of gantry rotation ($d_c = 25\%$, $n = 4$).

4.3.3 IMRT Helical Tomotherapy Case, RPM Waveform

In Figure 4.6, the simulated longitudinal dose profiles acquired over 3 fractions are plotted. Without gating, the RMS values of dose deviations ($\text{RMS}_{\Delta D}$) were 2.42\% inside the PTV and 1.61\% for the entire profile. For full gating with 6 mm gating window and 4 passes, the $\text{RMS}_{\Delta D}$ values were 2.50\% inside the PTV and 1.31\% for the entire profile.
Although the full gating approach improved the alignment of the resulting dose profile to the planned dose profile, the RMS$_{\Delta D}$ inside the PTV remained high as only 97.9% of the plan dose was completed over 4 passes. With the 6 mm gating window, the full gating method required a total of 6 passes to keep the RMS$_{\Delta D}$ values below 1.0%. For partial gating, it was possible to achieve RMS$_{\Delta D}$ values of less than 1.0%, using 4 passes that consisted of 3 gated passes and 1 ungated pass (3 + 1). The RMS$_{\Delta D}$ values were 0.67% inside the PTV and 0.48% for the entire profile.

In Table 4.1, the optimal gating parameters are summarized for both gating approaches for three different fractionation schemes. For a single fraction, 4 mm was the maximum residual motion allowed to keep the RMS$_{\Delta D}$ values below 1.0%. With the small gating window of 4 mm, large numbers of passes were needed for both full (12) and partial

Figure 4.6: IMRT helical tomotherapy case ($p = 0.287$, $T_g = 15$ s, $R = 8$) delivered in the presence of non-sinusoidal target motion (RPM trace) over 3 fractions with random starting phases of target motion. Simulated longitudinal dose profiles are calculated for planned radiation delivery, radiation delivery without gating, full gating with 6 mm gating window and 4 passes, and partial gating with 6 mm gating window and 3 + 1 passes.
gating \((7 + 1)\) methods. For 3 fractions, the required numbers of passes were reduced significantly to 6 passes for full gating and 3 + 1 passes for partial gating, with a 6 mm gating window. For 30 fractions, the numbers of passes used were 5 and 2 + 1, with the gating windows of 7 mm and 6 mm for full and partial gating methods, respectively.

Table 4.1: Optimal gating parameters for different fractionation schemes.

<table>
<thead>
<tr>
<th>Methods</th>
<th>Window size</th>
<th>Number of passes</th>
<th>MU delivered (%</th>
<th>RMS(_{\Delta D})(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) 1 fraction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No gating</td>
<td>—</td>
<td>—</td>
<td>100.0</td>
<td>6.03 3.40</td>
</tr>
<tr>
<td>Full gating ((n))</td>
<td>4 mm</td>
<td>12</td>
<td>100.0</td>
<td>0.72 0.46</td>
</tr>
<tr>
<td>Partial gating ((n-1) + 1)</td>
<td>4 mm</td>
<td>7 + 1</td>
<td>95.7 + 4.3</td>
<td>0.86 0.47</td>
</tr>
<tr>
<td>(b) 3 fractions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No gating</td>
<td>—</td>
<td>—</td>
<td>100.0</td>
<td>2.42 1.61</td>
</tr>
<tr>
<td>Full gating ((n))</td>
<td>6 mm</td>
<td>6</td>
<td>99.8</td>
<td>0.80 0.50</td>
</tr>
<tr>
<td>Partial gating ((n-1) + 1)</td>
<td>6 mm</td>
<td>3 + 1</td>
<td>92.9 + 7.1</td>
<td>0.67 0.48</td>
</tr>
<tr>
<td>(c) 30 fractions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No gating</td>
<td>—</td>
<td>—</td>
<td>100.0</td>
<td>1.47 1.09</td>
</tr>
<tr>
<td>Full gating ((n))</td>
<td>7 mm</td>
<td>5</td>
<td>99.9</td>
<td>0.65 0.46</td>
</tr>
<tr>
<td>Partial gating ((n-1) + 1)</td>
<td>6 mm</td>
<td>2 + 1</td>
<td>82.1 + 17.9</td>
<td>0.64 0.82</td>
</tr>
</tbody>
</table>

4.4 Discussion

4.4.1 Treatment Planning

Treatment planning for the multi-pass gating delivery will require the acquisition of a 4D-CT data set [33-35]. The CT data set reconstructed at the phase corresponding to the gating window must be used for target delineation and plan optimization. During the CT-scanning, the anterior-posterior (AP) position of the patient’s abdomen should also be monitored with the RPM system. The correlation between the internal tumour motion and the motion of the RPM block must be verified, so that the tumour position can then be monitored reliably during the treatment.
4.4.2 Selection of Gating Parameters

The selection of the gating parameters is based on the trade-off between the accuracy and efficiency of the gated dose delivery. Decreasing the duty cycle or the gating window size will reduce the residual tumour motion during radiation delivery, thus potentially improving the accuracy of dose delivery. However, this occurs at the expense of increasing the number of passes and the treatment time. This was the motivation behind the proposal of the partial gating approach. The results presented in Table 4.1 shows that the partial gating approach requires fewer passes than the full gating method for all three fractionation schemes. Full gating always needs nearly 100% of the plan dose to be delivered, regardless of the fraction number. For partial gating, the required percents of plan dose delivered before the last ungated pass were much smaller than 100%, with the delivered percent of the plan dose decreasing with the fraction number. The percents of plan dose completed before the last pass were 95.7% for a single fraction, 92.9% for 3 fractions, and 82.1% for 30 fractions.

For a single fraction, large numbers of passes were needed for both gating methods to keep the RMS\(\Delta D\) values below 1.0%. The number of required passes was greatly reduced for 3 and 30 fractions, due to dose averaging over multiple fractions. However, the differences in the numbers of passes used between 3 and 30 fractions for both gating approaches were only one pass. This indicated that the multi-pass gating technique may be applicable to hypofractionation employed in stereotactic radiotherapy [25-27], although further studies will be required to validate its suitability.

4.4.3 Hardware and Software Requirements for Clinical Implementation

Clinical implementation of the multi-pass gating technique will require the following three components: (1) Real-time tumour position monitoring system, (2) Communication interface for real-time feedback of tumour position, and (3) Gantry startup synchronization.
4.4.3.1 Real-Time Tumour Position Monitoring Systems

Currently, there are different types of indirect and direct tumour monitoring systems available. The RPM system provides advantages in terms of its wide availability, ease of use and non-invasiveness. Like other indirect monitoring techniques, however, the system works under the assumption that the correlation established prior to a treatment will be maintained throughout the treatment. This may be especially dangerous for lung sites, where establishing stable and reliable correlations were shown to be very difficult [36]. Monitoring an additional tumour surrogate such as the lung air flow [37-39] may work as an assurance check during the treatment.

The tumour position may be monitored directly with the use of electromagnetic transponders implanted into the tumour volume [40,41]. With the Calypso system (Calypso Medical Technologies, Inc., Seattle, WA), the electromagnetic transponders are tracked electromagnetically by the localization array panel mounted onto the treatment couch. The relatively compact size of the localization array panel also makes the use of the Calypso system feasible for the ring gantry configuration of the tomotherapy machine. However, there are added risks of complications, due to the surgical implantation procedure of the transponders.

4.4.3.2 Communication Interface for Real-Time Feedback

A communication interface must be established between the real-time tumour monitoring system and the tomotherapy b-MLC control centre. In addition, the software interface must be programmed to trigger emergency maneuvers such as full b-MLC closures, under unexpected respiratory circumstances such as patient coughing, thereby accounting for temporary tumour excursions. It should be noted that there is a total b-MLC latency time of 45 ms, which consists of the leaf response latency time of 30 ms and the leaf transit time of 15 ms [20]. Thus, in order to execute the intended leaf motions in a timely manner, the tumour position must be anticipated 45 ms in advance. In the past, various algorithms have been described in the literature to account for system latency during the tumour tracking dose deliveries [42-47].
4.4.3.3 Gantry Startup Synchronization

At the start of each gated pass, the start of the tomotherapy treatment must be synchronized with a particular phase of tumour motion, so that the previously blocked beam projections can potentially occur within the gating window. One may continue to rotate the gantry, until the start of the first undelivered beam projection coincides with the start of the gating window. However, significant time may elapse before the synchronization is established, making this “waiting” approach impractical. Alternatively, the tomotherapy gantry may be modified to allow for a variable gantry speed to be used within its physical limits, only before the start of the radiation delivery. The freedom to accelerate or decelerate the gantry will significantly reduce the “wait” time required for synchronization. The “near-future” tumour position calculated by one of the aforementioned predictive algorithms may be used to determine the required speed changes. At the start of the treatment, the gantry must resume its planned speed, and maintain it throughout the treatment.

4.4.3.4 Potential Issues and Risks of the Proposed Method

Successful execution of multi-pass respiratory gated helical tomotherapy strongly depends on the accurate monitoring of tumour position. Incorrect synchronizations between the gated beam deliveries and tumour motion can potentially yield worse dose discrepancies than the non-gated approach, as the gated beam deliveries will be biased towards the wrong tumour positions.

Similar to the gating techniques implemented for linear accelerators, an accurate and efficient gated dose delivery will depend on a consistent correlation between a tumour surrogate and the actual tumour position, and a fairly regular and predictable breathing pattern. For gated helical tomotherapy, an additional determining factor becomes the accuracy of a predictive algorithm for anticipated tumour position. This will allow for timely execution of $b$-MLC opening and closure according to the observed breathing pattern, as well as effective gantry startup synchronization using gantry speed control.

For the different indirect tumour monitoring techniques mentioned in Section 4.4.3.1, however, numerous opportunities exist for the correlation between a tumour surrogate
and the tumour position to change over the course of treatment. The correlation changes can occur between the different fractions, between the gated passes within a single fraction, or during an individual gated pass. Thus, the correlation must be periodically confirmed or updated with the observed changes in the tumour motion pattern. However, measuring the internal tumour motion will require the patient to be removed from the treatment couch for a 4D-CT acquisition [33-35], unless a CT scanner is placed in the treatment room [48,49] to minimize the internal variations between the imaging verification and treatment processes. The use of fluoroscopic tubes [50-54] to monitor the tumour position in the treatment room becomes complicated for helical tomotherapy, because the ring gantry configuration of the helical tomotherapy machine hinders the access of these fluoroscopic tubes.

Direct monitoring approaches such as the use of the magnetic transponders are thus recommended to allow for continuous monitoring of tumour position, at the risk of potential surgical complications such as pneumothorax. Fixation rates of the magnetic transponders to lung tissues were initially shown to be low in the canine lung [40], but addressed with a modified transponder design with stability features [41]. For patients who can not tolerate the surgical implantation of the magnetic transponders, indirect tumour monitoring methods may still be employed, as long as patients can maintain consistent respiratory patterns. This makes the patient selection process critical for the gated helical tomotherapy treatment. The patient breathing reproducibility was also shown to improve significantly with patient coaching [55-57].

Appropriate emergency maneuvers are essential for clinical implementation of the proposed methods, in order to cope with unexpected situations. Physiological events such as coughing that cause sudden and significant changes in the respiratory motion pattern must trigger an interlock, in the form of full leaf closures to halt the radiation from reaching the patient. Treatment will only resume, once the patient regains the normal breathing pattern. Both the partially delivered beam projection and undelivered beam projections during this suspended time period will be compensated during the subsequent gated passes. However, frequent interruptions during the treatment will
significantly increase the treatment session time, making gated helical tomotherapy impractical for a particular group of patients.

4.5 Conclusion

In this study, the feasibility of multi-pass respiratory gating technique was investigated for both ideal and realistic tumour motion patterns. For sinusoidal motion, the PTV dose deviations of -29 to 5% observed without gating were reduced to range from -1 to 3% for a single fraction, using full gating with 4 passes. For a patient waveform, partial gating required fewer passes than full gating for all fractionation schemes. For a single fraction, the maximum allowed residual motion was only 4 mm, thus requiring large numbers of passes for both full and partial gating methods. The number of required passes decreased significantly for 3 and 30 fractions, allowing residual motion up to 7 mm. Overall, the multi-pass respiratory gating method was shown to be an effective way to reduce the various motion-induced dose discrepancies present in helical tomotherapy. Its clinical implementation will require modest modifications to the current helical tomotherapy control system.

4.6 Acknowledgements

The authors would like to thank the LRCP engineering staff, Jim Allin, Greg Berryhill, Waldemar Dabrowski, Steve Gibson, and Randy McVittie for their helps with establishing the communication between the helical tomotherapy machine and the motion phantom. The current work was made possible through the Ontario Research and Development Challenge Fund (ORDCF) as a project supported by the Ontario Consortium of Image-guided Therapy and Surgery (OCITS), and the Canadian Institute of Health Research (CIHR) Strategic Training Program in Oncology.

4.7 References


Chapter 5

5 Summary and Conclusions

This chapter summarizes all the major findings of this thesis work, and includes discussion related to clinical implications, limitations, and future work.

5.1 Summary

In the introductory chapter, it was stated that tumour motion due to breathing presents a significant limitation for radiotherapy of lung cancer, and more specifically for helical tomotherapy. The research objectives were addressed in the three subsequent chapters, investigating the nature of different motion-induced dose discrepancies for helical tomotherapy, developing two new motion management methods to reduce these effects, and testing the feasibility of the multi-pass respiratory gating technique, in terms of its effectiveness and practicality, through computer simulations and film measurements with a motion body phantom. In this final chapter, all the major findings from these chapters are summarized, and discussed in terms of clinical implications, limitations, and required future work.

5.2 Motion-Induced Dose Discrepancies and Beam Junctioning Effects

In the presence of tumour motion, a number of different interactions can arise between tumour motion and the three continuously moving subsystems (gantry, couch, and b-MLC) of a helical tomotherapy unit. Our research focused on a detailed investigation of the resulting dose discrepancies and development of challenging solutions to reduce these effects. In addition, there are inherent dosimetric effects arising from helical dose delivery, unrelated to tumour motion. Beam divergence and the resulting partial beam overlaps between different gantry rotations can lead to a “threading” dose pattern being produced away from the axis of gantry rotation. Under special circumstances, beam junctioning “beating” effect may also be generated along the axis of gantry rotation. In Table 5.1, the three motion-induced dose discrepancies and two inherent beam junctioning effects are summarized, in terms of their causes and related key parameters.
5.2.1 Dose Discrepancies in the Presence of Tumour Motion

In this thesis, motion-induced dose discrepancies for helical tomotherapy were categorized into three different types: (1) dose rounding, (2) dose rippling, and (3) IMRT leaf opening asynchronization.

**Table 5.1: Summary of different dosimetric effects in the presence and absence of tumour motion in helical tomotherapy.**

<table>
<thead>
<tr>
<th>Section</th>
<th>Dosimetric Effect</th>
<th>Cause</th>
<th>Key Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.2.1</td>
<td>Dose Discrepancies in the Presence of Tumour Motion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.2.1.1</td>
<td>Dose Rounding Effect</td>
<td>Dose blurring due to tumour motion</td>
<td>tumour motion amplitude ( (A) ), secondary effects due to dose rippling (below)</td>
</tr>
<tr>
<td>5.2.1.2</td>
<td>Dose Rippling Effect</td>
<td>Interplay between couch and tumour motion</td>
<td>gantry rotation period ( (T_g) ), pitch factor ( (p) ), tumour motion period ( (T_r) )</td>
</tr>
<tr>
<td>5.2.1.3</td>
<td>IMRT Leaf Opening Asynchronization Effect</td>
<td>Interplay between IMRT leaf opening pattern and tumour motion</td>
<td>dominant frequency of leaf opening sinogram ( (f_s) ), tumour motion period ( (T_r) ), tumour motion phase</td>
</tr>
<tr>
<td>5.2.2</td>
<td>Inherent Dosimetric Effects in the Absence of Tumour Motion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.2.2.1</td>
<td>Thread Effect</td>
<td>Off-axis helical beam junctioning</td>
<td>pitch factor ( (p) )</td>
</tr>
<tr>
<td>5.2.2.2</td>
<td>Beating Effect</td>
<td>On-axis helical beam junctioning</td>
<td>pitch factor ( (p) ), number of beam projections per gantry rotation ( (n) )*</td>
</tr>
</tbody>
</table>

*Not to be confused with number of gated passes, also represented by ‘n’ in Chapter 4.
5.2.1.1 Dose Rounding Effect

Dose rounding is defined as the dose blurring of a delivered dose distribution relative to the planned dose distribution, in the direction of tumour motion, and is especially manifested at the edges of a treated volume. In Figure 2.5 (a), the resulting ‘softer’ dose gradient led to the simultaneous under-dosing of the tumour volume near its boundary and over-dosing of normal tissues just outside the tumour volume. In addition, the superior-inferior (SI) component of tumour motion, which coincides with the direction of couch motion, further widens the “build-up” and “build-down” of dose associated with helical tomotherapy dose delivery, as illustrated in Figure 2.5 (b). In Chapter 2, the magnitude of dose rounding effect was characterized by a penumbral width, calculated as an average of two distances between the 20% and 80% dose points ($P_{20/80}$) within the “build-up” region and the 80% and 20% ($P_{80/20}$) dose points within the “build-down” region. Dose rounding effect was shown to be mainly dependent upon tumour motion amplitude ($A$), with other parameters making smaller contributions. In Figure 2.5 (c), the magnitude of dose rounding effect was shown to increase with tumour motion amplitude. Small differences of 0.4 to 2.7 mm were observed between the two tumour motion periods ($T_r$) at different tumour motion amplitudes, as the dose rippling effect (Section 5.2.1.2) present inside the target volume for $T_r = 8$ s led to the sharpening of the penumbral region. Depending on the phase of tumour motion, the penumbral width can also further increase in the presence of dose rippling effect. Additionally, use of a smaller pitch factor may contribute to the widening of the penumbral region.\footnote{Dose rounding becomes more sensitive to tumour motion amplitude ($A$), as the treatment couch slows down. Treatment couch velocity can be reduced by either decreasing the pitch factor ($p$) or increasing the gantry rotation period ($T_g$).}

5.2.1.2 Dose Rippling Effect

Dose rippling is caused by the interplay between the couch motion and periodic tumour motion along the direction of couch movement. The superior-inferior (SI) component of tumour motion directly interferes with the irradiation of tumour volume, as its direction of motion coincides with the longitudinal movement of the treatment couch. In the
presence of SI motion, tumour volume is forced to move in and out of the passing treatment beam, preventing the planned tumour volume slices from being fully treated in a sequential manner, thus leading to non-uniform dose deposition within the tumour volume. In Figure 2.6 (a) and (b), when a sinusoidally moving target volume is irradiated with an unmodulated beam (i.e. non-IMRT helical tomotherapy plan), the dose rippling effect was shown to be manifested as a series of equally-spaced dose peaks and valleys inside the target volume, resembling a wave “interference” ripple. The successive peaks or valleys are separated by the distance travelled by the treatment couch during one cycle of tumour motion. However, uniform dose delivery to the target volume could still be achieved for a special condition between the linear couch motion and periodic tumour motion. Under this “dose equilibrium” condition, the excess or deficient dose delivered to a particular tumour point, caused by the movement of the leading beam edge in the tumour coordinate system, is compensated exactly by the movement of the trailing beam edge, as illustrated in Figure 2.3 (a). In the remainder of this section, a dose equilibrium condition for dose rippling effect will be referred to as a synchronous interplay condition.

In Chapter 2, the dose rippling parameter ($\beta$) (defined in Equation 2.6) was introduced as a key metric to predict the presence ($\beta \neq \text{integer}$) or absence ($\beta = \text{integer}$) of dose rippling effect. The $\beta$-parameter represents the number of tumour motion cycles completed while advancing the treatment couch by one fan beam thickness. The relationship between an integer $\beta$ value and a synchronous interplay condition was mathematically derived in the Appendix of Chapter 2. In Figure 2.6 (c), a common $\beta$ value from different combinations of treatment and tumour motion parameters was shown to yield comparable dose modulations, further affirming $\beta$ as an appropriate metric for dose rippling effect.

The magnitude of dose rippling was defined as the difference between the maximum dose peak and the minimum dose valley observed inside the target region, along the axis of gantry rotation. The dose rippling effect was then investigated as functions of tumour motion amplitude ($A$) and dose rippling parameter ($\beta$). In Figure 2.6 (d), the relationship between the magnitude of dose rippling and tumour motion amplitude exhibited a
complex periodic pattern, with the maximum value decreasing with the tumour motion amplitude, perhaps contrary to intuition. The observed periodicity was attributed to the use of pure sinusoidal target motion. In Figure 2.6 (e), the magnitude of dose modulation was plotted against $\beta$ for different tumour motion amplitudes. The magnitude of dose rippling was shown to decline rapidly with increasing $\beta$ to less than 1% at $\beta = 4.5$ for all tumour motion amplitudes. At each non-integer $\beta$ value, the relationship between the magnitude of dose rippling and tumour motion amplitude was shown to be different, while dose rippling was absent at integer $\beta$ values, as expected. In Figure 2.7 (a), it was shown that dose rippling effect could also be observed for an IMRT helical tomotherapy plan. The phase of tumour motion was shown to affect the positions of the dose peaks and valleys, as well as the penumbral width, although the magnitude of dose modulation remained unchanged.

### 5.2.1.3 IMRT Leaf Opening Asynchronization Effect

The IMRT leaf opening asynchronization effect arises from the interplay between the $b$-MLC motion and periodic tumour motion. When the dominant frequency of superior-inferior (SI) tumour motion approaches the dominant frequency ($f_s$) of the plan leaf opening sinogram along the direction of couch movement, dose discrepancies unique to an IMRT helical tomotherapy plan can be generated, as illustrated in Figure 2.7 (b). In Figure 2.7 (c), the longitudinal dose profile acquired along the axis of gantry rotation exhibited dose deviations ranging from -29% to 7% inside the PTV, yielding a root-mean-square of dose deviations ($\text{RMS}_{\Delta D}$) equal to 14%. In Figure 2.7 (d), the IMRT leaf opening asynchronization effect was shown to worsen with tumour motion amplitude, while its sensitivity to the phase of tumour motion was also demonstrated in Figure 2.7 (e). The IMRT leaf opening asynchronization effect was shown to decrease significantly, however, in the presence of more complex tumour motion. When a tumour surrogate waveform acquired with the Real-time Position Management (RPM) system (Varian Medical Systems, Palo Alto, CA) for a real patient was employed to represent tumour motion, dose deviations ranging from -9% to -2% were observed inside the PTV, yielding a $\text{RMS}_{\Delta D}$ value of 6%. The great reduction in dose deviations may be attributed to the
absence of dominant tumour motion frequency close to the $f_s$ value, as well as the presence of multiple frequency components making up the RPM waveform.

The presence of the IMRT leaf opening asynchronization effect could be anticipated prior to a helical tomotherapy treatment by performing a Fourier analysis of the plan leaf opening sinogram, as well as the tumour motion pattern to determine their respective dominant frequencies. In Figure 5.1, a frequency spectrum was generated for the intensity modulation pattern of a central binary leaf from the plan leaf opening sinogram$^{20}$ generated in Chapter 2 and 4. The observed dominant frequency ($f_s$) of 0.133 Hz closely matched the tumour motion frequency of 0.125 Hz ($T_r = 8$ s) employed in Figure 2.7 (c), thus explaining the significant dose discrepancies observed in this figure.

The IMRT leaf opening asynchronization effect was not generated however, when tumour motion frequencies close to the other frequency components of the plan leaf opening sinogram were selected, as illustrated in Figure 5.2. Only dose rounding was present for these tumour motion frequencies. Thus, Fourier analysis may serve as a quick quality assurance (QA) check to ensure that no major resonance exists between the IMRT leaf opening pattern and tumour motion. The Fourier analysis may even be performed for a newly acquired patient waveform before each treatment fraction to account for the inter-fraction variability of tumour motion pattern $^{1,2}$ – possibly caused by changes in tumour volume and shape, as well as patient’s respiratory capacity over the course of radiotherapy treatment.

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$^{20}$ This plan leaf opening sinogram refers to the truncated version of the plan leaf opening sinogram generated in Figure 2.1 and 4.2. Truncation process is explained in both Section 2.2.1.4 and 4.2.2.2.
Figure 5.1: Frequency spectrum for the intensity modulation pattern of a central binary leaf. Its dominant frequency ($f_s$) was observed at 0.133 Hz.

Figure 5.2: Simulated longitudinal dose profiles along the axis of gantry rotation for the IMRT helical tomotherapy plan ($p = 0.287$, $T_g = 15$ s, $R = 8$) generated for different tumour motion periods ($T_r$) with a tumour motion amplitude ($A$) of 1.5 cm. The IMRT leaf opening asynchronization effect was observed only for $T_r = 8$ s.
5.2.2 Dosimetric Effects in the Absence of Tumour Motion

The two inherent beam junctioning effects for helical tomotherapy, unrelated to tumour motion are the (1) thread effect, and (2) beating effect. These effects are not classified as dose discrepancies (i.e. dose differences between the planned and delivered dose distributions), because they are clinically accounted for during the dose calculations of the treatment planning system. In this work, they have been observed experimentally, as other investigators have [3], and hence are only discussed here briefly.

5.2.2.1 Thread Effect

The thread effect is a well known off-axis helical beam junctioning effect, inherent to helical tomotherapy [3]. Even with perfect beam overlaps along the axis of gantry rotation for a uniform dose delivery, the thread effect can still be generated away from the axis of gantry rotation, due to beam divergence. As the projected fan beam thickness changes according to the distance from the x-ray source, alternating beam overlap and gaps are created off-axes. The resulting dose peaks and valleys both follow a helical trajectory, resembling a screw thread. Fluence also changes according to an inverse-square of distance from an x-ray source; attenuation and scatter are other contributing factors for the thread effect [3]. The successive dose peaks and valleys along off-axes are separated by a distance equal to the couch translation during each gantry rotation (i.e. pitch factor \( p \) * fan beam thickness \( b \)), as illustrated in Figure 3.4. Dose difference between dose peaks and valleys was shown to increase with off-axis position, as expected with greater divergence distance, according to the results from Table 3.3.

5.2.2.2 Beating Effect

The beating effect is an on-axis beam junctioning effect generated only under highly specific treatment conditions. In Chapter 3, \( n / p \) ratio was used as a metric for predicting the presence \((n / p = \text{non-integer})\) and absence \((n / p = \text{integer})\) of the beating effect, as indicated by the results summarized in Table 3.3, where \( n \) is the number of beam projections per gantry rotation and \( p \) is the pitch factor. The \( n / p \) ratio represents the number of beam projections delivered \((N_b)\), after the treatment couch moves a distance equal to one fan beam thickness:
\[ N_p = \frac{n}{p} \times b = \frac{n}{p} \]  

(5.1)

With a non-integer \( n / p \) ratio, the total number of beam projections encountered by different parts of a target volume alternates between two values, leading to the periodic dose peaks and valleys along the direction of couch motion, observed in Figure 3.11. The magnitude of beating effect was shown to decrease with an increasing \( n / p \) ratio, as the relative dosimetric contribution of the extra beam projection decreases with an increasing number of beam projections. The decreasing separation distance between dose peaks with increasing \( n / p \) ratio, further contributes to the dose peak reduction. The separation distance between the successive dose peaks or valleys is equal to the couch increment per beam projection (i.e. projection increment defined in Equation 3.3).

The work in Chapter 3 was done before the arrival of the Hi-Art II helical tomotherapy machine (TomoTherapy Inc., Madison, WI) at the London Regional Cancer Program (LRCP) in May of 2004. Helical tomotherapy dose delivery was experimentally simulated using a linear accelerator x-ray beam by delivering a series of static beams from different gantry angles and couch positions. The results in Chapter 3 could be replicated with the current helical tomotherapy unit by assigning a very short leaf opening time per beam projection, mimicking a static beam projection, and a pitch factor larger than 7 to keep the \( n / p \) value below 7.5. However, the magnitude of dose peaks may still be reduced slightly, due to the presence of continuous couch motion.

### 5.3 Clinical Implications

In this section, the clinical implications for each of the motion-induced dose discrepancies produced in the presence of tumour motion, and the two beam junctioning effects inherent to helical tomotherapy dose delivery will be discussed.

#### 5.3.1 Presence of Tumour Motion

Dose rounding is a clinically-relevant effect that worsens with tumour motion amplitude, as shown in Figure 2.5 (c). The reduced tumour dose delivered near the tumour boundary can be compensated by increasing the treatment margin according to the magnitude of
dose rounding. For large amplitudes of tumour motion, however, the resulting margin expansion would significantly increase the total irradiated volume of surrounding normal tissues, potentially increasing radiation toxicity and necessitating the use of a motion management technique. It is highly unlikely that the dose rippling effect would yield significant impact in clinical practice, where pitch factors of less than 0.3 are typically used with gantry rotation periods of 15-20 seconds. Use of such treatment parameters would likely yield $\beta$ values much greater than 4.5, where the magnitude of dose rippling was shown to become negligible in Figure 2.6 (e) – unless unusually long tumour motion periods are exhibited by the patients. The IMRT leaf opening asynchronization effect could introduce significant dose discrepancies within the tumour volume, as illustrated in Figure 2.7 (b) and (c). For a conventional fractionation scheme, however, the dose deviations resulting from the IMRT leaf opening asynchronization effect may “wash out” over multiple fractions. In Figure 2.7 (e) and Figure 5.3, the simulated dose profiles accumulated over 30 fractions exhibited only dose rounding in the presence of sinusoidal and non-sinusoidal target motion, respectively. A randomly selected tumour motion phase was assigned at the start of each fraction for calculation of these cumulative dose profiles. On the other hand, the IMRT leaf opening asynchronization may still have a clinical impact, when hypofractionation schemes are employed. In Figure 4.6, the simulated dose profile accumulated over 3 fractions without gating for non-sinusoidal target motion, exhibited both IMRT leaf opening and dose rounding effects, yielding an $RMS_{AD}$ of 2.4% within the PTV. Thus, for clinical practice, the use of a motion management technique may become necessary during helical tomotherapy treatments, especially for patients displaying large amplitudes of tumour motion being treated with hypofractionation schemes.
Figure 5.3: Simulated longitudinal dose profiles along the axis of gantry rotation for the IMRT helical tomotherapy plan \( (p = 0.287, T_g = 15 \text{ s}, R = 8) \) accumulated over 30 fractions in the presence of a non-sinusoidal target motion (RPM trace). A randomly selected tumour motion phase was assigned at the start of each fraction.

5.3.2  Absence of Tumour Motion

It is highly unlikely that the beating effect will be clinically relevant for helical tomotherapy. With the number of beam projections per gantry rotation fixed at 51 and pitch factors of less than 0.3 typically used clinically, the \( n / p \) ratio would become extremely high and well above the value of 7.5, where a maximum dose modulation of approximately 5% was observed, according to the results in Table 3.3. The thread effect is accounted for during the treatment planning process. The current clinical practice at LRCP follows the finding by Kissick et al [3], which has shown that thread effect can be minimized by using a pitch factor that satisfies the following condition:

\[
p = 0.86 \left( \frac{1}{a} \right), \quad a \in I
\]  

(5.2)
5.4 Tumour Motion Management Techniques

In this section, the feasibility of employing respiratory gating and breath-holding for helical tomotherapy will be discussed, in terms of their effectiveness to reduce the magnitude of each individual motion-induced dose discrepancy.

5.4.1 Multi-Pass Respiratory Gating Technique

In Chapter 2, dose rounding and the IMRT leaf opening asynchronization effect were both shown to worsen with tumour motion amplitude \( A \). In addition, target motion period \( T_r \) was shown to be the determining parameter for yielding interplay conditions that can generate dose rippling or the IMRT leaf opening asynchronization effect. When multi-pass respiratory gating is employed, the magnitude of tumour travel during beam delivery becomes restricted to the residual motion within the gating window. Additionally, delivering the treatment beam only during a pre-determined portion of the tumour motion cycle introduces an effective “beam ON” tumour motion period that is different from the actual tumour motion period \( T_r \). In Figure 5.4, it is illustrated that the effective tumour motion period \( T_{r \text{eff}} \) “seen” by the treatment beam during a multi-pass gated treatment is calculated as the product of duty cycle \( dc \) and tumour motion period \( T_r \). Duty cycle \( dc \) is defined as the fraction of tumour motion cycle during which the radiation delivery is made. Thus, the multi-pass respiratory gating technique has the potential to address all three types of dose discrepancies by effectively reducing the magnitude and period of tumour motion during radiation delivery. The emergence of the \( T_{r \text{eff}} \) parameter also means the original definition of the dose rippling parameter \( \beta \) in Equation 2.6 needs to be modified to accommodate for both gated and non-gated situations, yielding a newly defined dose rippling parameter, namely the effective dose rippling parameter \( \beta_{\text{eff}} \):

\[
\beta_{\text{eff}} = \left( \frac{1}{0.01 \, dc} \right) \beta = \frac{1}{0.01 \, dc} \frac{T_g}{p \cdot T_r} = \frac{T_g}{0.01 \, p \cdot dc \cdot T_r} = \frac{T_g}{0.01 \, p \cdot T_{r \text{eff}}} \tag{5.3}
\]

In Figure 4.4 (b), the multi-pass respiratory gating technique was shown to effectively reduce both dose rippling and dose rounding observed in Figure 4.4 (a). In Figure 4.4 (a),
the two effects combined to yield an RMS$_{AD}$ of 4% inside the PTV, with a dose rippling magnitude of 3%. In Figure 4.5 (b), the RMS$_{AD}$ inside the PTV was reduced to 0.7%, while decreasing the dose rippling magnitude to 0.5%. The significant reduction in dose rippling magnitude was attributed to establishing a synchronous interplay condition by using a duty cycle of 25%, which changed the $\beta_{eff}$ value from 2.5 to 10. In Figure 4.5 (b), the presence of the IMRT leaf opening asynchronization effect and dose rounding produced dose deviations ranging from -29% to 5% inside the PTV, with an RMS$_{AD}$ of 14%. In Figure 4.5 (d), 2 gated passes were employed with a duty cycle of 50% to significantly reduce the RMS$_{AD}$ to 2.4%, with the dose deviations varying from -5% to 2%. In Figure 4.5 (e), employing 4 gated passes with a duty cycle of 25% further decreased the RMS$_{AD}$ to 2%, with the dose deviations ranging from -1.5% to 3.5%.

The practicality of the multi-pass respiratory gating technique was then investigated for more complex non-sinusoidal target motion, represented by a patient RPM waveform (Table 4.1). For a conventional fractionation scheme consisting of 30 fractions, the number of required passes was shown to range from 3 to 5 to keep the RMS$_{AD}$ inside the PTV below 1%. For 3 fractions, the number of required passes was shown to increase by only a single pass over the 30-fraction scheme. Thus, the treatment session time required for a multi-pass respiratory gated helical tomotherapy treatment may remain comparable between different fractionation schemes. Currently, at London Regional Cancer Program (LRCP), each helical tomotherapy treatment is assigned with a treatment session time of 30 minutes. The first half of the treatment session is dedicated to patient set-up, MVCT acquisition for patient position verification, and patient repositioning, while the second half consists of 5-10 minutes of “beam-ON” time and the time needed for the patient to leave the treatment room. The use of 4 to 5 gated passes would yield a “beam-ON” time of 20-50 minutes, and with the couch reset time totaling up to 5 minutes, the treatment session time may last up to 75 minutes – representing an increase by a factor of 2.5.
Figure 5.4: Position vs. time curves of the leading and trailing beam edges in the tumour coordinate system for a multi-pass respiratory gated helical tomotherapy treatment ($p = 0.8$, $T_g = 16$ s, $R = 8$), employing phase gating ($dc = 50\%$, $n = 2$). The gating window is centered around the end-expiration phase. The effective tumour motion period ($T_{r\,eff}$) “seen” by the treatment beam is calculated as the product of duty cycle ($dc$) and tumour motion period ($T_r$).
5.4.2 Loose Helical Tomotherapy with Breath-Holding

With the breath-holding strategy, the dose rounding effect is expected to be minimized to a negligible level, as the magnitude of tumour motion approaches zero during breath-holding. The residual motion during breath-holds will vary between patients, according to their abilities to tolerate and perform breath-holding in a reproducible manner. In addition, minimal tumour motion during radiation delivery would likely yield negligible interplay effects, leading to the absence of dose rippling and IMRT leaf opening asynchronization effect.

5.4.3 Thread Effect

Although the impact of different motion-induced dose discrepancies could be minimized by employing a motion management technique, dosimetric effects previously present in the absence of tumour motion may resurface. In Figure 5.5, thread effect observed in the planned “no motion” distribution (i) becomes blurred by the presence of tumour motion in the “motion” dose distribution (ii). Interestingly, the thread effect starts to reappear in the “gated” dose distribution acquired with a duty cycle of 50% (iii). The threading pattern then becomes clearly visible in the “gated” dose distribution obtained with a duty cycle of 25% (iv), as the magnitude of target motion during radiation delivery is further reduced. The dose distributions in Figure 5.5 were generated using four fully-open central \( b \)-MLC leaves (i.e. non-IMRT helical tomotherapy plan) with the helical tomotherapy treatment parameters of \( p = 0.8, T_g = 16 \) s, and tumour motion parameters of \( T_r = 8 \) s, \( A = 1.0 \) cm, yielding \( \beta = 2.5 \).

For loose helical tomotherapy with breath-holding, the thread effect is expected to be absent due to the use of multiple “interlaced” helices. Interlaced helices are generated by assigning different gantry start angles (i.e. phases) to the individual helices. As the different helices are out-of-phase from one another, the off-axes dose modulations produced by the individual helices are averaged out. In Figure 3.4 (b) and (d), employing four “interlaced” helices \( 90^0 \) out-of-phase from one another was shown to eliminate the thread effect observed in the original dose distributions in Figure 3.4 (a) and (c), acquired by using a conventional tight helix. The work by Kissick et al [3] has also demonstrated
significant reduction of the thread effect by using double helices that were $180^\circ$ out-of-phase from each other.

Figure 5.5: Central coronal dose distributions produced by a non-IMRT helical tomotherapy plan ($p = 0.8$, $T_g = 16 \text{ s}$, $R = 4$): (i) “no motion” dose distribution, (ii) “motion” dose distribution ($T_r = 8 \text{ s}$, $A = 1.0 \text{ cm}$), (iii) “gated” dose distribution ($dc = 50\%$, 2 passes), (iv) “gated” dose distribution ($dc = 25\%$, 4 passes). The tread effect previously observed in the “no motion” dose distribution (i) resurfaces in the “gated” dose distributions ((iii) and (iv)).

5.5 Limitations and Future Work

In this section, limitations of the two proposed motion management techniques, namely loose helical tomotherapy with breath-holding and multi-pass respiratory gating techniques will be discussed, including recommendations to the manufacturer of the helical tomotherapy unit. In addition, limitations of the work done in this thesis will be described, as well as the required future work to address these limitations.
5.5.1 Limitations of Proposed Methods

Both loose helical tomotherapy with breath-holding and multi-pass respiratory gating techniques require much longer treatment session time because of the use of multiple passes. In addition, patient position uncertainty could also be introduced, as the treatment couch is retracted back to its starting position between passes and patient discomfort may ensue. Fortunately, the helical tomotherapy machine provides the on-board MVCT imaging capability to verify patient position and minimize corresponding positional uncertainty between passes, at the expense of further increasing the treatment session time and dose received by patients.

There are other patient-related factors. Patient compliance for breath-holding remains a significant issue for loose helical tomotherapy. Although breath-holding at either normal inspiration or expiration could yield higher patient compliance than the 40% rate reported for deep-inspiration breath-holding by Memorial Sloan-Kettering Cancer Center (MSKCC) [4], nevertheless the proposed breath-holding technique for helical tomotherapy is not applicable for all patients. The use of active breathing control device may improve the patient compliance rate [5-7]. Effectiveness of the multi-pass respiratory gating technique also requires the patient to maintain a fairly regular tumour motion, in terms of tumour motion period, amplitude, and baseline position. This way, the undelivered beam projections from each gated pass can coincide with the gating window more easily. With extremely irregular tumour motion patterns, completing all planned beam projections under a reasonable number of gated passes will become very difficult, making the patient selection process crucial. For practical purposes, the partial gating approach described in Chapter 4 should be strongly considered over the full gating method. For partial gating, once a certain percentage of beam projections are delivered, all remaining beam projections are delivered without gating, thus keeping the total number of passes used under a reasonable limit. In Table 4.1, it was shown that partial gating required 8 passes to achieve an $\text{RMS}_{\text{AD}}$ of less than 1% for a single fraction, compared to 12 passes for full gating. For 3 and 30 fractions, the partial gating approach needed 2 less passes than full gating, requiring 4 and 3 passes, respectively.
5.5.2 Recommendations to the Manufacturer

For clinical implementation of loose helical tomotherapy, modifications to the current treatment planning platform must be made by the manufacturer to provide the treatment planning capability for multiple helices with large pitch factors. However, concerns remain as conformality of dose distribution to tumour volume may be greatly compromised from the use of extremely large pitch factors. Thus, an extensive treatment planning exercise must be performed with large pitch factors to determine its clinical feasibility, in terms of dose delivery accuracy and number of loose helices required to satisfy different clinical criteria.

Clinical implementation of respiratory gating for helical tomotherapy would require an electronic communication to be established between the tumour monitoring system and the $b$-MLC control center. An automatic emergency maneuver in the form of full $b$-MLC closure would also be required, in the event that the tumour motion pattern undergoes an unexpected change, triggered by a physiological event such as coughing. As most patients would exhibit some degree of irregularity in their tumour motion patterns, it is recommended for the manufacturer to provide variable speed capability for both the gantry and the treatment couch. Having these additional degrees of freedom would make it easier for the undelivered beam projections to be placed within the gating window during subsequent passes.

5.5.3 Limitations of Current Work and Future Work

A major limitation of the computer simulation model used in this thesis was that the calculation of each dose profile was restricted to the axis of gantry rotation. A capability to generate dose profiles along off-axes would enable one to investigate the 3D impact of tumour motion on helical tomotherapy dose delivery. Different factors such as beam divergence and fluence change according to an inverse-square of distance from the x-ray source should be accounted for during the calculations of off-axes dose profiles. For experimental measurements, a gel dosimeter [8-10] may be used instead of film to acquire 3D dose distributions.
The dosimetric impact of more complex non-sinusoidal tumour motion should be investigated experimentally. The motion body phantom used in this thesis was only capable of producing sinusoidal motion in one direction, with adjustable tumour motion amplitude ($A$) and period ($T_r$). The most recent version of the Modus respiratory motion phantom is equipped with a programmable motor capable of replicating different patient-related motion waveforms (Modus Medical Devices Inc., London, ON), such as the RPM waveform used for computer simulation results in Table 4.1. The dosimetric impact of tumour motion components along different directions should also be investigated individually or in combination. Motion along the anterior-posterior (AP) direction would affect the fluence reaching the target volume, while motion along the lateral the left-right (LR) direction would directly interfere with the $b$-MLC motion, as it runs perpendicular to the movement of each leaf. In a simplified setup, 1D target motion could be made to yield 3D motion components by rotating and tilting the entire motion body phantom assembly used in Chapter 2 and 4. A commercially available dynamic thorax phantom (CIRS, Norfolk, VA) provides 3D target motion by simultaneously applying translational and rotational motions to a cylindrical insert made of lung equivalent material, containing a spherical target volume.

Lung deformation has been modelled by utilizing deformable lung-equivalent material surrounding a target volume, such as sponge [11,12], as well as employing a balloon connected to a piston to mimic a human diaphragm [12]. Finally, a non-spherical target volume with a more realistic tumour shape has been produced using flexible resin [13]. The effect of lung deformation on the resulting dose distributions can also be investigated, using a deformable gel dosimeter currently being developed at the London Regional Cancer Program (LRCP). A deformable gel dosimeter is created by producing gel inside a latex balloon. Dose calculations on 4D-CT datasets at different phases can also be performed to investigate the effect of lung deformation on the resulting dose distributions, one phase at a time. Robust optimization approach [14] may be used to account for anticipated motion-induced dose discrepancies in advance during the plan optimization process, in addition to other types of uncertainties. The current approach by Heath et al, however, does not account for the interplay between the MLC motion and tumour motion, while providing dose rounding reduction, thus requiring further improvements.
5.6 Conclusions

In this thesis, we have isolated three distinctively different types of motion-induced dose discrepancies for helical tomotherapy, namely dose rounding, dose rippling, and the IMRT leaf opening asynchronization effect. Each effect was shown to exhibit unique characteristics, in relation to the different tumour motion and helical tomotherapy treatment parameters. The major dose discrepancies to be considered in clinical practice are dose rounding and the IMRT leaf opening asynchronization effect. For a conventional fractionation scheme, the dose rounding effect remains the major concern, which can be compensated by assigning a larger treatment margin around the tumour volume. For hypofractionation schemes, the IMRT leaf opening asynchronization effect can become an additional concern by introducing dose discrepancies within the tumour volume, necessitating the use of a motion management technique.

Two new motion management methods have thus been developed for helical tomotherapy, in the form of loose helical tomotherapy with breath-holding and multi-pass respiratory gating. The feasibility of the multi-pass respiratory gating technique was demonstrated in terms of its effectiveness and practicality, through computer simulations and film measurements performed in a motion body phantom. For sinusoidal target motion, the proposed method was shown to reduce the $\text{RMS}_{\text{AD}}$ inside the PTV from 14% to 2.7% and 2% for respective duty cycles of 50% and 25% requiring 2 and 4 gated passes. For more realistic non-sinusoidal tumour motion causing an $\text{RMS}_{\text{AD}}$ of within the PTV, the required numbers of passes to keep the $\text{RMS}_{\text{AD}}$ below 1% were shown to range from 3-5 passes for 30 fractions, and 4-6 passes for 3 fractions, demonstrating the feasibility of the multi-pass respiratory gating approach. In conclusion, employing multi-pass respiratory gating during helical tomotherapy was shown to greatly reduce the different types of dose discrepancies, and decrease the required margin size, potentially reducing radiation toxicity and allowing dose escalation for better tumour control. Clinical implementation of the multi-pass respiratory gating technique would require a number of electronic control and communication modifications to the existing helical tomotherapy machine, which would lead to significant improvements in the dose
distributions delivered for lung tomotherapy treatments – especially for patients exhibiting large tumour motion who are treated with hypofractionation schemes.

Unique breathing patterns exhibited by each patient warrant a patient-specific approach during the treatment planning and dose delivery processes of a helical tomotherapy treatment. The fundamental understanding of the different motion-induced dose discrepancies acquired in this thesis work will greatly help with the patient selection process to extract maximum clinical benefit with or without the use of a motion management technique. The knowledge gained in this work on different interplay effects can also be applied to other treatment modalities, including traditional cone beam radiotherapy techniques, as well as more specialized techniques such as stereotactic body radiotherapy employing hypofractionation. Thus, it is hoped that the results of this thesis will help improve the clinical outcomes for radiotherapy of lung cancer – a disease that continues to remain a challenge for conventional treatment techniques.

5.7 References


Appendices

Appendix A: Supplementary Material for Chapter 2

Mathematical condition (β = integer) for a synchronous interplay between the couch motion and the longitudinal target motion for a non-IMRT helical tomotherapy delivery

In the tumour coordinate system (Figure 2.2 b), the longitudinal boundaries of the fan beam $H(y)$ can be defined by the two Heaviside step functions, $H_T(y)$ and $H_L(y)$ along the axis of gantry rotation. $H_T(y)$ and $H_L(y)$ represent the trailing and leading beam edges respectively, whose positions are determined by the functions, $y_T(t)$ and $y_L(t)$. In the tumour coordinate system, the fan beam position changes with respect to the stationary target volume:

$$H(y) = H_T(y) - H_L(y)$$  \hspace{1cm} (1)

$$H_T(y) = H(y - y_T(t)) = \begin{cases} 
1 & \text{for } y > y_T(t) \\
1/2 & \text{for } y = y_T(t) \\
0 & \text{for } y < y_T(t) 
\end{cases}$$  \hspace{1cm} (2)

$$H_L(y) = H(y - y_L(t)) = \begin{cases} 
1 & \text{for } y > y_L(t) \\
1/2 & \text{for } y = y_L(t) \\
0 & \text{for } y < y_L(t) 
\end{cases}$$

where $H_T(y)$ and $H_L(y)$ represent the trailing and leading beam edges, respectively, and $y_T(t)$ and $y_L(t)$ are the positions of the trailing and leading beam edges as functions of time in the tumour coordinate system, defined as following:

$$y_T(t) = \frac{p \cdot b}{T_g} t + A \sin \frac{2\pi}{T_r} t - \frac{D}{2} - b = \frac{p \cdot b}{T_g} t + A \sin \frac{2\pi}{T_r} t - \frac{p \cdot b \cdot R}{2} - b$$

$$y_L(t) = \frac{p \cdot b}{T_g} t + A \sin \frac{2\pi}{T_r} t - \frac{D}{2} + b = \frac{p \cdot b}{T_g} t + A \sin \frac{2\pi}{T_r} t - \frac{p \cdot b \cdot R}{2} + b$$  \hspace{1cm} (3)
where \( p \) is the pitch factor, \( b \) is the fan beam thickness, \( T_g \) is the gantry rotation period, \( D \) is the total couch travel during the treatment, \( R \) is the number of gantry rotations competed during the treatment, \( T_r \) is the period of tumour motion, and \( A \) is the one-half of the peak-to-peak amplitude (2A) of tumour motion along the longitudinal direction (+y).

Each longitudinal point \( y \) is irradiated at a given time \( t \), while the point is located between the fan beam edges. The radiation exposure time \( (\Delta t) \) is calculated for each point by integrating the fan beam function \( H(y) \) over the treatment time \((0 \leq t \leq R \times T_g)\):

\[
\Delta t(y) = \int_{t=0}^{R \times T_g} H(y) \, dt = \int_{t=0}^{R \times T_g} (H_T(y) - H_L(y)) \, dt
\]

\[
= \int_{t=0}^{R \times T_g} (H(y - y_T(t)) - H(y - y_L(t))) \, dt
\] (4)

The fluence \( (\Phi) \) received by each point is then determined by multiplying the radiation exposure time \( (\Delta t) \) by the fluence rate \( (\phi) \). The fluence rate is assumed to be constant in this study:

\[
\Phi(y) = \phi \cdot \Delta t(y), \quad \phi = \text{constant}
\] (5)

In the absence of tumour motion, \( T_g / p \) is the time required for the couch to travel a distance equal to one fan beam thickness \( (b) \). This means the trailing beam edge position reaches its corresponding leading beam edge position after the elapsed time of \( T_g / p \):

\[
y_L(t_i) = y_T(t_i + T_g / p)
\] (6)

In the presence of tumour motion, the above Condition (6) is reproduced under a synchronous interplay condition \( (\beta = \text{integer}) \) as Condition (7), shown as the following:
\[
y_L(t) = \frac{p \cdot b}{T_g} t_i + A \sin \frac{2\pi}{T_r} t_i - \frac{D}{2} + \frac{b}{2}
\]
\[
y_T\left( t_i + \frac{T_g}{p} \right) = \frac{p \cdot b}{T_g} \left( t_i + \frac{T_g}{p} \right) + A \sin \frac{2\pi}{T_r} \left( t_i + \frac{T_g}{p} \right) - \frac{D}{2} - \frac{b}{2}
\]
\[
= \frac{p \cdot b}{T_g} t_i + b + A \sin \left( \frac{2\pi}{T_r} t_i + \frac{2\pi T_g}{p \cdot T_r} \right) - \frac{D}{2} - \frac{b}{2}
\]
\[
= \frac{p \cdot b}{T_g} t_i + \beta \left( 2\pi \right) - \frac{D}{2} + \frac{b}{2}
\]
\[
= \frac{p \cdot b}{T_g} t_i + A \sin \left( \frac{2\pi}{T_r} t_i + \beta \left( 2\pi \right) \right) - \frac{D}{2} + \frac{b}{2}
\]

Since \( \beta = \text{integer} \), \( A \sin \left( \frac{2\pi}{T_r} t_i + \beta \left( 2\pi \right) \right) = A \sin \frac{2\pi}{T_r} t_i
\]
\[
\therefore y_T\left( t_i + \frac{T_g}{p} \right) = \frac{p \cdot b}{T_g} t_i + A \sin \frac{2\pi}{T_r} t_i - \frac{D}{2} + \frac{b}{2} = y_L(t_i)
\]
\]

Going back to Equation (5) and substituting Equation (4) into (5),
\[
\Phi(y) = \phi \cdot \Delta t(y)
\]
\[
= \phi \int_{t=0}^{R_T} \left( H(y - y_T(t)) - H(y - y_L(t)) \right) dt
\]
\[
= \phi \left( \int_{t=0}^{R_T} H(y - y_T(t)) dt - \int_{t=0}^{R_T} H(y - y_L(t)) dt \right)
\]

Substituting Condition (7),
\[
\Phi(y) = \phi \left( \int_{t=0}^{R_T} H(y - y_T(t)) dt - \int_{t=0}^{R_T} H\left( y - y_T\left( t + \frac{T_g}{p} \right) \right) dt \right)
\]
\[
= \phi \left( \int_{t=0}^{R_T} H(y - y_T(t)) dt - \int_{T_g/\pi}^{(RT_E+T_g)/\pi} H(y - y_T(t)) dt \right)
\]
\[
= \phi \left( \int_{t=0}^{R_T} H(y - y_T(t)) dt - \left( \int_{T_g/\pi}^{(RT_E+T_g)/\pi} H(y - y_T(t)) dt + \int_{R_T}^{(RT_E+T_g)/\pi} H(y - y_T(t)) dt \right) \right)
\]
Since $0 \leq t \leq R \cdot T_g$, 
$$
\Phi(y) = \phi \int_{T_g}^{RT_g} H(y - y_T(t)) \, dt = 0,
$$

(8) 

\[ \Phi(y) = \phi \left( \int_{t=0}^{RT_g} H(y - y_T(t)) \, dt - \int_{t=RT_g/p}^{RT_g} H(y - y_T(t)) \, dt \right) = \phi \int_{t=0}^{RT_g/p} H(y - y_T(t)) \, dt \]

For $0 \leq t \leq \frac{T_g}{p}$ and $\beta = \text{integer},$

\[ y_T(0) = \frac{p \cdot b}{T_g}(0) + A \sin \frac{2\pi}{T_r}(0) - \frac{D}{2} - \frac{b}{2} = -\frac{D}{2} - \frac{b}{2} \]

\[ y_T \left( \frac{T_g}{p} \right) = \frac{p \cdot b}{T_g} \left( \frac{T_g}{p} \right) + A \sin \frac{2\pi}{T_r} \left( \frac{T_g}{p} \right) - \frac{D}{2} - \frac{b}{2} = b + A \sin 2\pi \beta - \frac{D}{2} - \frac{b}{2} = -\frac{D}{2} + \frac{b}{2} \]

\[ \therefore -\frac{D}{2} - \frac{b}{2} \leq y_T(t) \leq -\frac{D}{2} + \frac{b}{2} \text{ for } 0 \leq t \leq \frac{T_g}{p} \]

Since the target region is positioned between $-\frac{D}{2} + \frac{b}{2} \leq y \leq \frac{D}{2} - \frac{b}{2},$

\[ \therefore y \geq y_T(t) \text{ for } 0 \leq t \leq \frac{T_g}{p} \]

\[ \therefore H(y - y_T(t)) = 1 \text{ for } 0 \leq t \leq \frac{T_g}{p} \]

Back to Equation (8),

\[ \Phi(y) = \phi \int_{t=0}^{T_g/p} H(y - y_T(t)) \, dt = \phi \cdot \left( \frac{T_g}{p} \right) \]

Therefore, under a synchronous interplay condition ($\beta = \text{integer}$), the fluence inside the target region remains constant, thus leading to the absence of dose rippling.
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# Curriculum Vitae

**Name:** Bryan Kim  

**Post-secondary Education and Degrees:**  
McMaster University  
Hamilton, Ontario, Canada  
1996-2001 B.A.  

The University of Western Ontario  
London, Ontario, Canada  
2001-2011 Ph.D.  

**Honours and Awards:**  
Chancellors’ Entrance Scholarship  
1996  

Dean’s Honour List  
1996-2001  

Special University Scholarship (SUS)  
2001-2004  

Canadian Institute of Health Research (CHIR) Strategic Training  
2004-2010  

**Related Work Experience**  
Clinical Physics Assistant  
Cancer Centre of Southeastern Ontario  
1999  

Research Assistant  
Princess Margaret Hospital  
1999  

Technical Writer  
Canberra Canada  
2000  

Harold E Johns Summer Student  
Odette Cancer Centre  
2001  

Teaching Assistant  
The University of Western Ontario  
2003-2004
Publications:


