4D Cone-Beam CT Image Reconstruction of Varian TrueBeam v1.6 Projection Images for Clinical Quality Assurance of Stereotactic Ablative Radiotherapy to the Lung

by

Joel Beaudry

Bachelor of Science, University of Alberta, 2010
Master of Science, McGill University, 2013

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF

Master of Science

in

THE FACULTY OF GRADUATE AND POSTDOCTORAL STUDIES
(Physics)

The University of British Columbia
(Vancouver)

April 2015

© Joel Beaudry, 2015
Abstract

On-board cone-beam computed tomography (CBCT) imaging integrated with medical linear accelerators offers a viable tool for tumor localization just prior to radiation treatment delivery. However, the exact tumor location during treatment is not well-defined due to respiratory motion. This is taken into account during treatment planning by adding margins to the visible tumor volume defining the high dose region. The respiratory motion used to optimize the treatment plan is not guaranteed to be reproducible on the day of treatment, suggesting that the high dose region may not fully contain the tumor at all points of its trajectory during treatment.

In this thesis, to image the tumor at the different portions of the breathing cycle, CBCT projections were binned by the respiratory signal at their time of acquisition. Reconstructing each bin created a 3D image depicting the tumor at one point of its trajectory. Combining the binned reconstructions added in a temporal component, defining a 4D-CBCT. 4D-CBCT reconstructions were performed on 6 stereotactic ablative radiotherapy (SABR) lung cancer patients. Imaging was performed using the Varian TrueBeam (v1.6) and respiratory information was captured with the infra-red camera-based Varian real-time position management (RPM) system. Both analytical and iterative reconstruction algorithms, and image quality metrics were used for a comparative study. Tumor motion was measured by tracking the visible tumor volume centroid from each 4D-CBCT image. The high dose regions defined during treatment planning were compared to the 4D-CBCT tumor volume during its trajectory using an overlap metric to determine if
the tumor remained confined to the treatment volume, or not.

4D-CBCTs were found to be well reconstructed using iterative methods. When viewed sequentially the 4D-CBCT images visibly show tumor motion following a sinusoidal-like behavior. Examination of the tumor motion and overlap metric verify that the margins currently used to define the high dose region fully encompass the tumor during all times of its trajectory, i.e 100% overlap within error. The results indicate the current margins used for SABR patients at the British Columbia Cancer Agency are sufficient in providing adequate tumor coverage when accounting for tumor motion and setup uncertainties.
Preface

This thesis is the work of the author, Joel Beaudry, and was completed at the British Columbia Cancer Agency (BCCA). The thesis and its results are a continuation from a previous thesis by UBC student Dr. Robert Cropp. The collection of patient data used in this thesis underwent ethics approval by the University of British Columbia and the British Columbia Cancer Agency (REB# H12-00192).
# Table of Contents

Abstract ............................................................... ii

Preface ................................................................. iv

Table of Contents ....................................................... v

List of Tables .......................................................... viii

List of Figures .......................................................... x

Acknowledgments ........................................................ xvii

1 Introduction ......................................................... 1
   1.1 Radiation Therapy ............................................... 5
   1.2 Treatment Planning .............................................. 9
   1.3 Patient Motion .................................................. 11
   1.4 Medical Imaging ............................................... 13
      1.4.1 X-ray Imaging .............................................. 14
      1.4.2 Computed Tomography ..................................... 15
      1.4.3 Cone Beam Computed Tomography (CBCT) ............... 16
   1.5 Image Reconstruction ........................................... 18
      1.5.1 CT Reconstruction ......................................... 19
      1.5.2 CBCT Reconstructions ..................................... 23
      1.5.3 Image Quality ............................................... 30
1.6 Image Registration ........................................... 32
1.7 Equipment ..................................................... 35
  1.7.1 OnBoard Imager ........................................... 35
  1.7.2 RPM ......................................................... 39

2 Methods ......................................................... 41
  2.1 Data Collection .............................................. 41
  2.2 Lung Protocol ................................................ 43
    2.2.1 Treatment Planning ................................. 43
    2.2.2 Treatment .............................................. 44
  2.3 Pre-processing ............................................. 45
    2.3.1 Scanning Procedure ................................. 45
    2.3.2 Calibrations ........................................... 46
    2.3.3 Geometry Generation ............................... 48
  2.4 Reconstructions ........................................... 50
    2.4.1 3DCBCT ................................................ 52
    2.4.2 4DCBCT ................................................ 52
    2.4.3 Binning ................................................ 53
  2.5 Dataset Naming Convention ............................. 57
  2.6 Post-processing ........................................... 58
    2.6.1 Image Calibration .................................... 58
    2.6.2 Contouring ............................................ 61
    2.6.3 Image Registration .................................. 63
  2.7 Metrics ..................................................... 64
    2.7.1 Image Quality ......................................... 64
    2.7.2 Tumor Overlap ....................................... 64
    2.7.3 Tumor Motion ......................................... 65

3 Results ......................................................... 67
  3.1 Image Quality ............................................. 67
  3.2 Image Reconstructions ................................... 71
3.2.1 3DCBCT ................................................. 71
3.2.2 4DCBCT ................................................. 73
3.3 Breathing Traces ............................................. 73
3.4 Tumor Motion ................................................ 75
  3.4.1 Tumor Centroid Motion ................................ 75
  3.4.2 Tumor Overlap Volumes ............................... 76

4 Discussions .................................................... 89
  4.1 Image Quality .............................................. 89
    4.1.1 Algorithms and Tuning ............................... 89
    4.1.2 Projections ........................................... 91
  4.2 Breathing Traces ........................................... 93
  4.3 Overlap ................................................... 94
  4.4 Tumor Motion ............................................... 95

5 Conclusion .................................................... 97

Bibliography ..................................................... 100

A Overview and General Instructions for 4DCBCT Protocol ........... 108
  A.1 Introduction .............................................. 108
  A.2 Planning CT / CT Simulation ............................. 108
  A.3 Treatment Planning ...................................... 109
  A.4 Treatment Unit .......................................... 110
    A.4.1 Patient Setup ....................................... 110
    A.4.2 RPM Setup .......................................... 111
    A.4.3 Subsequent Treatments ............................... 114
    A.4.4 Backup Procedure ................................... 115

B XML Geometry Format .......................................... 116
List of Tables

Table 1.1  CT numbers of various materials.  .............................................. 16
Table 1.2  CBCT modes and their parameters.  ........................................... 38

Table 2.1  The number of CBCTs used in the 4DCBCT study per patient  .... 42
Table 2.2  Definition of parameters used in CBCT reconstruction algo-
rithms.  ................................................................................................. 51
Table 2.3  CT numbers used for Calibration in the Catphan 504. [61]  ... 60

Table 3.1  SNR and CNR for different CBCT reconstructions of the Cat-
phan phantom.  ..................................................................................... 68
Table 3.2  SNR and CNR for different CBCT reconstructions of the QUASAR
phantom.  ................................................................................................. 68
Table 3.3  FDK reconstruction times for patient’s fraction 1 pre- and post-
treatment CBCT scans using the unmodified projections. Times
include reading and writing times. Slight variation (±10 s) for
further fractions was observed.  .............................................................. 71
Table 3.4  SART reconstruction times for patient’s fraction 1 pre- and post-
treatment CBCT scans using the unmodified projections. Slight variation (±10 s) for further fractions was observed when
recorded.  ................................................................................................. 72
Table 3.5  TV reconstruction times for patient’s fraction 1 pre- and post-
treatment CBCT scans using the 4x4 re-binned projections.
These times are all over 2 hours long.  ................................................. 73
Table 3.6 Percentage overlap with each phases GTV and iGTV (PTV) for patient 2. Taking into account contouring uncertainty and image quality issues, the error on the above % overlap values is estimated to be 2-5%. A value of 100% indicates the tumor volume remained contained within the treatment volume (e.g. PTV) 100% of the time. The average is rounded to the nearest percent.
List of Figures

Figure 1.1 The dominant interactions depending on photon energy and the atomic number of the absorber $Z$. For clinical treatment, Compton scattering is the dominant interaction. Adapted from [13]. .................................................. 7

Figure 1.2 A high dose (red) will have a high tumor control probability but also lead to a high chance of normal tissue complications. Contrarily, too low a dose will have very few complications but also leave most of the tumor undamaged. ................. 10

Figure 1.3 ICRU Tumor volume definitions. ......................... 13

Figure 1.4 The often used orange example shows how a small reduction in radius leads to a large overall reduction in area. Shown here in a 2D representation, a circle with a 10 mm radius reduced to 9mm leads to an area reduction of 19%. In larger dimensions the effect is further amplified. .......................... 14

Figure 1.5 The fan beam and cone beam geometries used in commercial CT scanners. ............................... 17

Figure 1.6 A projection, $p$, generated from a parallel beams of X-rays transversing through the object, $f(x,y)$. .................. 20

Figure 1.7 The fan beam geometry depicting the variables used in image reconstruction. .......................... 22

Figure 1.8 The cone beam geometry depicting the variables used in image reconstruction. .......................... 24
Figure 1.9  A Varian TrueBeam Linac. The On-Board Imager is highlighted by the red rectangles.  

Figure 1.10  The full-fan (top) and half-fan (bottom) scan configurations. Note the displaced detector in the half-fan scan and the larger possible FOV. The full-fan covers the majority of the object and the required rotation will be 180° plus the fan angle which may vary slightly on the geometry of the scan. In the case for the full-fan scan on a Varian TrueBeam this rotation is approximately 200°, in contrast to the 360° rotation required for the half-fan scan.  

Figure 1.11  The Varian RPM marker box (left) and infrared camera (right) used for capturing respiratory motion.  

Figure 2.1  An X-ray projection acquired from a half-fan scan with no object in the FOV, which defines the air image. Note the non-uniformity caused by the bow-tie filter and heel effect of the X-ray production.  

Figure 2.2  A hypothetical breathing trace of a patient with the amplitude read off the RPM. The red dots indicate that a projection was taken. Few projections are shown to aid in clarity. A regular thorax half-fan scan will result in 656 projections.  

Figure 2.3  The patient trace is binned by amplitude into 6 bins. Two projections can share the same amplitude and belong to different bins if one is taken during inspiration and the other expiration. Amplitude binning will often result in an uneven distribution of projections and bunching found in the max/min expiration bins. This results in poor image reconstruction quality for intermediate bins.
Figure 2.4  The patient trace is binned by phase. This representation lists the phase extracted by the RPM rather than the amplitude. Therefore a minimum in the amplitude would correspond to a 180° value in this depiction. Again, the projections are binned into 6 bins. Note in this representation there is no redundancy found as each phase corresponds to a unique bin. An advantage of phase binning is the even distribution of projections among each bin.  

Figure 2.5  The patient trace binned by phase but now represented on a unit circle, emphasizing the angular nature of the phase. The projection onto the horizontal axis represents the amplitude. The same information found in Fig. ?? is shown here. 

Figure 2.6  A patient breathing trace (p3.pre4) that exhibits good periodic behavior, making it a good candidate for both amplitude and phase binned reconstruction. The projections are well distributed. 

Figure 2.7  A patient breathing (p1.pre2) trace with poor periodic behavior. There are long pauses, bunching, and sharp peaks. The projections are not distributed evenly and the extracted phase signal has several areas of inaccuracies. In such a case, only amplitude binned reconstruction is viable.
Figure 2.8 An axial slice of the Catphan 504 phantom used for HU calibration. This image was reconstructed from a half-fan scan done on the TrueBeam unit at 120 kV with the FDK algorithm. The image is a map of the attenuation coefficient $\mu (mm^{-1})$. The phantom is 20cm in diameter. Several different material inserts are used (seen in the image as circles) are used for the calibration: air (top/bottom), Teflon (bottom right), Delrin (right), acrylic (not visible but should be top right), polystyrene (top left), low-density polyethylene (left) and polymethylpentene (bottom left).

Figure 2.9 The HU calibration fit used to convert from attenuation into CT number for the CBCT reconstructions. The slope is $6.71 \times 10^4 HU \cdot mm$ and the intercept $-1.24 \times 10^3$ HU.

Figure 2.10 2D visualization of our overlap metric. Full coverage occurs if the yellow and green areas are equal, signifying complete tumor containment.

Figure 2.11 Visualization of the tumor displacement.

Figure 3.1 The Catphan phantom reconstructed with FDK (left), SART (right), and ADMMTV (bottom) algorithms. The red and green rectangles define ROIs used for SNR and CNR calculations.

Figure 3.2 The QUASAR phantom reconstructed with FDK (left), SART (right), and ADMMTV (bottom) algorithms. The red and green rectangles define ROIs used for SNR and CNR calculations.

Figure 3.3 p2_pre1 3DCBCT images reconstructed using FDK (left), SART (middle), and ADMMTV (right). Cropped versions of the Varian reconstruction are shown at the bottom for comparison.
Figure 3.4  4DCBCT reconstruction for patient 2 (p2_pre1). Binning starts with bin 1 in the top left, corresponding with maximum expiration. ................................................................. 78

Figure 3.5  4DCBCT reconstruction for patient 5 (p5_pre1). Binning starts with bin 1 in the top left, corresponding with maximum expiration. ................................................................. 79

Figure 3.6  The CT scan for patient 2, axial (top left), sagittal (top right), coronal (bottom). The PTV (red) and IGTV (teal) are shown on top of the tumor. There are some visible motion artifacts at the diaphragm and the tumor. The image was acquired with a voltage of 120kVp, mean tube current of 80 mA, effective tube current-time of 20mAs, and a slice width of 2.5mm. . . . 80

Figure 3.7  The percentage of projections taken below the average chest amplitude reading from the RPM. A value above the blue dotted line (50%) indicates it spends more time in the lower portion of the tumor motion. A perfect breathing pattern would have a value of 50. ................................................................. 81

Figure 3.8  The percentage of projections acquired from the expiration portion of the breathing cycle. A value above the blue dotted line (50%) indicates the tumor spends more time in the expiration breathing portion than the inspiration portion. A perfect breathing pattern would have a value of 50%. ................................................................. 82

Figure 3.9  The tumor displacement at each breathing bin for patient 2. The fractions shown are the p2_pre1 (top left), p2_post (top right), and p2_pre2 (bottom). ................................................................. 83
Figure 3.10  In the first plot, the maximum tumor displacement for each component is shown: AP (blue), IS (red), LR (green). In the second plot, the total tumor displacement $D$ for the first two fractions of each patient is shown. For both plots, the patients are separated by the grey dotted line such that every two data points is a different patient. The $x$ axis defines the fraction that was used.

Figure 3.11 The tumor displacement at each breathing bin for patient 2. The fractions shown are the $p2_{\text{pre1}}$ (top left), $p2_{\text{post}}$ (top right), and $p2_{\text{pre2}}$ (bottom).

Figure 3.12 Similar to Fig. ?? but now done using the GTV registration method. Similarly, the first plot shows the maximum tumor displacement for each component: AP (blue), IS (red), LR (green). In the second plot, the total tumor displacement $D$ for the first two fractions of each patient is shown. For both plots, the patients are separated by the grey dotted line such that every two data points is a different patient. The $x$ axis defines the fraction that was used.

Figure 3.13 The average overlap for the first two fractions of each patient with the IGTV (blue) and PTV (red). The overlap with the PTV 100% within uncertainty. The IGTV overlap hovers around 90%, indicating that there are times when the 4DCBCT contour of the tumor does exceed the boundaries of the IGTV defined at planning. This may be from motion or an actual shift from the tumor that is account for the extra margins from the PTV.
Figure 3.14  Total (left) and IS (right) tumor motion plotted against the relative tumor position. A value of 0% relative tumor position was defined to be at the top of the diaphragm and 100% top of the lung. Spearman values of $\rho = -0.75$ ($\rho = -0.76$) and p-values of 0.0019 (0.0015) for the left (right) plots were found, suggesting a significant correlation.

Figure A.1  Selection of “Use Gated” checkbox in plan properties.

Figure A.2  Button to press if the configuration window didn’t automatically open up. Located on the top toolbar, near the right end.

Figure A.3  Page 1 with noted selections marked in red.

Figure A.4  Page 2 with noted selections marked in red. Uncheck the other boxes as indicated in the document.

Figure A.5  Press Next to continue.

Figure A.6  Page 4 with noted selections marked in red. Allow a few cycles for the tracking before stopping it and pressing “OK”.

Figure B.1  An example of the projection geometry stored as an XML file. The parameters for the first three projections are shown.
Acknowledgments

The help and encouragement I’ve received during my time at the BCCA has been a blessing, to which I owe many thanks. None higher than to my supervisor Alanah Bergman, for her advice, motivation, and support (doubly so during the occasional deadline rush). The entire staff at the BCCA who were always approachable and more than happy to help when I had a question. Cheryl Duzenli for giving me the opportunity to work in and explore the field of medical physics. All the radiation therapists at Unit 1, who were vital in acquiring the CBCT projections and helped troubleshoot any issues we encountered. Simon Rit and Mory Cyril for developing and maintaining an amazing (and open source!) piece of software, and Andy Shieh for helping me get past the initial hurdles.

Special mention for the guys over at MIRG: Hillgan Ma, Pedro Esquinas, and Carlos Uribe, for their help in providing some of the computer equipment used in this thesis, and their companionship during the necessary coffee breaks. Thanks to Haley Clark for sparking my interest in medical physics and for still returning my emails after many years. Finally, to Justin and Laura. For not living in Vancouver you two never felt too far away. Well it helps that one of you actually visited . . . not that it matters or anything.
Chapter 1

Introduction

Medical physics is the application of physics to the field of medicine. It can be divided into two main categories: radiation therapy and medical imaging. The former deals with using ionizing radiation to treat cancer, whereas the latter focuses on a variety of imaging modalities used for diagnosis. This thesis will stress the importance of medical imaging in radiotherapy and show that these two categories have a large overlap. A brief introduction describing the motivation and previous work will begin this section, followed by a brief overview on radiation therapy, the use of radiation and its biological effect, and treatment planning. The introduction will then move onto medical imaging, particularly computed tomography, and its use in radiation therapy. Finally, the equipment used in this thesis will be explained.

With the introduction of on-board imaging (kV scanners attached to the treatment linacs), cone beam computed tomography (CBCT) has become an important and popular tool in image-guided radiotherapy, particularly for use in exact patient positioning prior to treatment [1]. However, the objective of producing CBCT images of moving anatomical structures poses a challenge. Tumor and tissue movement primarily caused from respiratory motion can result in the reconstructed 3D images having artifacts present such as blurring or streaking [2]. These not only decrease the resolution of the produced images but can also obstruct vision of
important structures, such as tumors and organs. Over the past few years a new imaging modality, called respiratory correlated cone beam computed tomography (4D CBCT), has been developed that takes into account the breathing motion of a patient and reconstructs images that capture the trajectory of the tumor motion. During the CBCT scan (or image acquisition), the patient is fitted with a position-/motion management system that registers the patients breathing cycle by use of the marker and infrared sensors. When the scan is completed the resulting projections acquired are binned into their corresponding breath cycle phase, allowing for a CBCT image for each phase. Viewing the reconstructed images consecutively will show the tumor as it moves through the breathing cycle. 4D CBCT has shown much promise in advancing radiation treatment procedures. Being able to identify tumor motion accurately allows for comparisons to the original 4D planning CT scan and indicates if any changes are warranted prior to treatment. Ensuring that the tumor motion at treatment is the same at planning also validates the use of gated treatments, where the beam is only triggered when the tumor falls into a certain position. Finally, better positioning of the patient is achievable as the tumor’s movement can be taken into account. Visualization of the tumor trajectory can also confirm it remains in the high dose region [3].

Although 4D CBCT allows for many advances in imaging and radiation treatments, there exist tradeoffs between image quality and other less desirable effects. Since 4D CBCT is commonly obtained by the phase binning of projections, the full dataset is separated into smaller subsets. Due to the (sometimes significant) reduction in the number of projections used for a particular bin’s reconstruction, the quality of the 4D CBCT is often degraded by artifacts easily observed in the axial view. To reduce such effects, the acquisitions can be made using multiple gantry rotations or by slowing the rotation of the gantry, both of which increase the number of projections and therefore noticeably improve the 4D images [4, 5]. However, the increase in scan time make them of limited use in a clinical setting. Therefore, improving the trade-off between image quality and scan time is a key goal in making 4D CBCT a more practical clinical modality [3]. The reduction
of image dose while maintaining clinically acceptable image quality is an area of active research [6]. Modifying the 4DCBCT reconstruction algorithms is one way to improve 4DCBCT scan results (image quality) [7].

While 4D CBCT has been shown in the literature to be a well understood technique, it is currently not implemented clinically for Varian (v1.6) TrueBeam linacs. A previous student at the VCC (Dr. Robert Cropp) demonstrated with phantom studies that a 4DCBCT image can be successfully generated off-line by combining 3D CBCT projections with the breath motion data obtained from an external tracking device. His study implemented non-clinical service and development modes of the linear accelerator. The foundation for this thesis is based off of that work, the UBC MSc thesis of Dr. Cropp, “Implementation of respiratory-correlated cone-beam CT on Varian linac systems” [8]. His findings suggested that, with some proper modifications, 4DCBCT should be viable in a clinical setting. Although the particular reconstruction algorithm he used was not used in this thesis, several of his suggestions and results were implemented in this work. Some notable conclusions that were presented in his thesis:

- 4D imaging of phantoms produced reconstructions that clearly demonstrated motion of the phantom’s insert, and should be possible on patient scans.

- The strong correlation of scanning parameters on artifacts and image quality. Improvements were noted with slower gantry rotation speed, increased mAs, and increased number of projections.

- Reconstructed 4D target motion was correct to within 1mm with optimized scan parameters.

- That deformable image registration could be used to speed up semi-manual contouring on images from different breathing phases.

His thesis also suggested several corrections required for a clinical implementation of 4DCBCT imaging:
• Fixing the half-fan reconstructions artifacts, namely the discontinuity seen in the images.

• An investigation on amplitude binning as an alternative to phase binning

• The correction of ring artifacts found in the FDK reconstructions.

• Work on optimization of preprocessing and reconstruction times, including the use of GPUs.

All of these points were addressed in this thesis either by correcting the specific issue or circumventing them by using alternative methods.

CBCT has been shown to reduce setup error for patient positioning as a radiation therapist is able to verify that the tumor is found within the tumor volume margins that were defined by the planning CT [9]. However, as the CBCT pretreatment scan and planning CT are not performed at the same time, there is no guarantee that the breathing pattern on the day of scanning (the CT planning scan) will be reproduced during treatment. Therefore the set-up error motion margins in use need to be verified. This thesis hopes to investigate this issue using 4DCBCT in the case of clinical SABR treatments for non-small cell lung cancer performed at the BCCA using a Varian TrueBeam (version 1.6). Using standard fractionation (20-30 fractions), the likelihood of any part of the tumor missing an appreciable dose is reduced, as any abnormal trajectory (from any one fraction) is less common than the average motion from all fractions. Therefore, the minimum dose to the tumor should still be high enough for adequate control. However, this may not be the case for the highly dosed hypo-fractionated treatments, such as SABR (4-8 fractions), in which too few fractions are done to allow for any statistical dose averaging to occur, and makes the need for tumor motion imaging that much greater [10]. As the Volume $\propto$ Radius$^3$, a small change in margin size can result in a large change to the irradiated volume. Implementing 4DCBCT to verify intra-fractional tumor motion is an active area of research for treatment delivery verification. Determining if there is some correlation between breathing (in
terms chest expansion) and/or relative tumor location (in the superior-inferior SI direction) may help give a priori knowledge on tumor motion [11]. For example, moving tumors sufficiently far from the diaphragm may require smaller margins when defining the PTV. Finally, showing that iterative methods can be used in reconstructing images with few projections, as is required for 4DCBCT, may lead to lower doses for CBCT scanning. If sufficient image quality is demonstrated, the requirement for a high number of projections is relaxed and therefore also the patient dose. This thesis shows that with clinically used settings CBCT images can be reconstructed using iterative methods, thus verifying the usefulness of these kind of algorithms.

1.1 Radiation Therapy

The goal of radiation therapy is to use ionizing radiation to treat cancer. This is achieved by targeting tumor volumes while trying to spare normal (non-cancerous) tissues. About two-thirds of cancer patients will undergo some form of radiation therapy, with the most common being external beam therapy \(^1\) [12]. The source of the external radiation can vary, but typically photons (with energy anywhere from 4 to 25MeV) are used. Electrons and lower energy photons can also be used but are more common for more superficial treatment sites. In recent years protons (or heavy ions) have become slightly more prevalent but are used sparingly due to the complexity and cost involved. The primary delivery system for external beam treatment is the electron linear accelerator (linac), which produces either an electron beam or photon beam.\(^2\) In a linear accelerator, the photon beam is produced by steering the electron beam into a target where the electrons undergo bremsstrahlung, creating X-ray photons with an energy that is some fraction of the incident electron beam energy. Regardless of the type of particle used for radiotherapy or their method of production, the particles’ energy is absorbed by the

---

1 According to ASTRO, in 2004 external beam treated 88% of patients in the US
2 Cobalt-60 isotopes were the pioneering method for external beam but are no longer as popular and predominantly used in developing nations.
tissue. The process by which a particle deposits energy varies and depends on
the particle’s properties, such as charge, mass, and energy, and the properties of the
absorbing medium.

A charged particle, such as an electron, will deposit energy by ionizing or
exciting nearby atoms, losing energy with each interaction until it comes to rest. For
photons, an uncharged particle, the chance of interacting with atoms in an elastic
collision is less likely. Instead, the photon will interact via three main processes:
the photo electric effect, Compton scattering, and pair production. In the photo-
electric effect a photon is absorbed and the energy transferred to an atom’s bound
electron. The electron is ejected with an energy equal to the incident photon en-
ergy minus the binding energy needed to hold that electron in orbit. For Compton
scattering, the incoming photon scatters off a free electron, and imparts some of its
energy to that electron. The end result is a less energetic (longer wavelength) pho-
ton and a more energetic electron. Finally, in pair production the photon interacts
with an atom’s nucleus and splits into an electron-positron pair, thus conserving
charge and mass.\textsuperscript{3} Pair production will only occur if the photon energy is greater
than the rest mass of the $e^+e^-$ pair, 1.02 MeV. The probability of any one process
occurring depends on the energy of the photon and the material through which
the photons are passing. In every case, a charged particle (electron or positron) is
produced and it will deposit energy over some finite range past the initial photon
interaction location. The dominant interaction depending on the photon energy
and the absorber’s atomic number, $Z$, can be seen in Figure 1.1.

The quantity used to measure energy deposited in matter by ionizing radiation
is called dose (or absorbed dose), and is the amount of energy deposited per unit
mass. The SI unit for dose is the Gray (Gy), where $1\text{Gy} = 1\text{J/kg}$.

The ability to deposit energy in tissue can lead to cell damage and is the rea-
son why radiation is used in treatment of tumors. There are two main biological
mechanisms by which this occurs: direct and indirect damage. The first, direct

\textsuperscript{3}Although much less common, a photon can also undergo pair production with an electron.
The final product is three electrons and hence is called Triple production.
Figure 1.1: The dominant interactions depending on photon energy and the atomic number of the absorber Z. For clinical treatment, Compton scattering is the dominant interaction. Adapted from [13].

damage, is the direct transfer of energy to the DNA molecules leading to damage in the DNA strand. The second, indirect damage, is caused by the ionization of water creating free radicals (ionized atoms and molecules) that then react with DNA. Indirect damage is more prevalent than direct damage and accounts for approximately 70% of cell damage [14].

While radiation does not discriminate in causing cell damage to both healthy and tumor cells there are differences that make tumor cells more sensitive to radiation damage. Firstly, radiation damage occurs more often when cells are undergoing mitosis, or cell division, in particular during the G2 and M phases [15]. As tumor cells are rapidly dividing they are more often found in these sensitive phases than normal cells. Secondly, normal tissue is more efficient at repairing radiation induced DNA damage than tumor cells. Therefore not only will more damage typically occur to tumor cells but such damage is also more prone to lead to cell death.
To take further advantage of this biological difference, a treatment is spread over the course of several sessions. This spreading of the total dose is called fractionation (with each session called a fraction) and has been shown to have a positive biological effect on tumor control [16]. These effects are explained by the 4 “R’s” of radiation therapy: Repair, Redistribution, Re-population, and Re-oxygenation. Collectively, these suggest that the tumor cells are moved into a more sensitive state during subsequent fractions while normal tissue cells are able to repair/repopulate in between dose deliveries. Using different levels of dose and/or number of fractions allows for this difference in tumor and healthy cell damage to become even more evident, while also ensuring the normal tissue damage is minimized. Generally, for most cancer treatments a dose of 2Gy/fraction is prescribed.

However, some tumor sites have been shown to be positively affected by hypofractionated treatments. This relies on treating with higher doses per fraction. Exact doses per fraction will vary but can be typically 8-20 Gy/fraction. This type of treatment, that relies on high precision, is called Stereo-ablative Radiotherapy (SABR) and is most commonly used for sites such as the lung. SABR is characterized by patient immobilization, image guided treatment, tight and high dose distributions, and steep dose gradients between the tumor and surrounding normal tissue. The result is a highly localized tumor volume being treated with high dose [17]. Due to the higher precision, the tumor margins can be reduced. As the dose per fraction differs from conventional radiotherapy, comparisons between the two require calculating the biologically effective dose (BED). BED is the amount of radiation that reaches the tumor resulting in a biological effect. Conventional radiotherapy typically has a BED of 70 – 80 Gy, whereas SABR treatments can obtain a BED > 100 Gy, resulting in superior tumor cell kill [17]. The hypofractionation delivery of such high doses means that the irradiated tumor cells (as well as any normal body cells irradiated to the prescribed dose) cannot possibly repair the DNA damage resulting in tumor necrosis ensues (“overkill” of the irradiated tissues). While not effective for all tumor sites, in areas that can
tolerate such techniques, SABR offers an alternative treatment with a high BED and the ability to achieve high tumor control. For a more detailed introduction into the biology behind radiation therapy see Hall [18].

1.2 Treatment Planning

The task of sparing healthy tissue while still covering the tumor with radiation dose is a large factor in determining whether a treatment will be successful and is the goal when designing any treatment plan. In treatment planning the probability, at a given dose, for causing damage to tumor cells or normal cells is called the Tumor Control Probability (TCP) and Normal Tissue Complication Probability (NTCP), respectively. In an ideal plan, the prescribed dose is such that it has a high TCP and low NTCP, Fig 1.2. Unfortunately, producing such an idealized scenario is not a trivial task. The tumor can be surrounded and, in some cases, intertwined by healthy tissue, have a complex geometry, or cover an area as several small tumors [19]. The task becomes more challenging when organs at risk (OAR), radiation sensitive organs, are located near a tumor volume. One way to view the tradeoff that arises can be seen by looking at the two extreme cases. A high dose will lead to high tumor control but at the cost of high NTCP. While on the other hand, a low dose will spare much of the normal tissue, but equally that of the tumor, leading to poor tumor control probability. The ability to find the relevant “sweet spot” can make all the difference in a successful radiation treatment. This is shown in Fig. 1.2

The first step in successfully designing an accurate treatment plan is to acquire anatomical information. The standard imaging modality used is computed tomography (CT) scans, and when used for treatment planning, is called a planning CT. Other imaging modalities can be used in conjunction to help improve planning, such as Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), and Single Photon Emission Computed Tomography (SPECT). These images can be fused to produce better anatomical detail or to provide functional metabolic information.
**Figure 1.2:** A high dose (red) will have a high tumor control probability but also lead to a high chance of normal tissue complications. Contrarily, too low a dose will have very few complications but also leave most of the tumor undamaged.

The anatomical information will be presented as a 3D image which is input into a Treatment Planning Software (TPS). The TPS provides contouring tools to help define relevant contours of the tumor, and nearby radiation sensitive organs, as well as other important anatomical structures. It is up to the treatment planner and radiation oncologist to decide what exactly will be contoured. When contouring is complete, the type of treatment will be selected, and the plan will be optimized to try and meet specific planning goals. The optimization attempts to deliver the prescribed dose to the tumor while minimizing radiation to normal tissue. This can be done using different beam angles or modulating the beam intensity.

With advances in technology and treatment techniques the ability to localize the dose to the tumor has increased. However, there are several uncertainties that make treatment planning more difficult, the most common being patient physiological motion (eg. breathing, gas, etc).
1.3 Patient Motion

Patient motion can be split into inter-fractional, motion between treatments, and intra-fractional, motion during a single treatment. Inter-fractional motion takes place over the course of long time periods (hours, days, weeks), examples can include the growth/shrinking of a tumor, weight changes, bloating of the intestines, filling of the bladder, and repositioning of the rectum. In the event of a shift, therapists will reposition the patient based on imaging prior to delivering radiation. Occasionally, a shift may be too large or cause deformations in the treatment volume. The original treatment plan may require tweaking to adapt to these changes, this process is called adaptive radiation therapy [20].

The other motion, intra-fraction motion, deals with motion that takes place over short time periods (scale of seconds/minutes), i.e. this type of motion occurs while the treatment beam is on. The predominant example of this is respiratory motion, but can also include heart motion, and as such is approximately periodic in nature. Respiration induced displacements primarily affects lung tumors but also other abdominal organs (liver, kidneys, pancreas, diaphragm). A study of 166 lung tumors found that the percentage of tumors that moved greater than 5mm in the superior-inferior (SI), lateral (left-right), and anterior-posterior (AP) were 39.2 %, 1.8 %, and 5.4 %, respectively. The mean tumor motion was found to be less than 13.4mm, 4.0mm, and 5.9mm, respectively for the SI, LR, AP directions [21]. Another meta-study found the average lung tumor SI displacement ranged anywhere from 3 to 19mm [22]. If such motion is disregarded, the tumor may move in and out of the treatment beam, resulting in decreased tumor coverage and increased toxicity for the normal tissue.

There are several other uncertainties, aside from motion, that also need to be taken into account when creating a treatment volume. These include: microscopic tumor spread (beyond what is visible on diagnostic images), uncertainty in defining contour boundaries, and patient set-up errors. To ensure proper radiation dose coverage margins are added to the gross/visible tumor. These margins, have standard definitions, that are widespread in oncology literature. These volumes are
also depicted in Fig. 1.3. The official descriptions as defined by the ICRU 83 [23]:

- **Gross Tumor Volume:** “The GTV is the gross demonstrable extent and location of the tumor. The GTV may consist of a primary tumor, metastatic regional node(s), or distant metastasis.”

- **Internal Gross Tumor Volume:** The IGTV is defined as the GTV plus a margin to account for uncertainties in the position of the GTV due to motion.

- **Clinical Tumor Volume:** “The CTV is a volume of tissue that contains a demonstrable GTV and/or sub-clinical malignant disease with a certain probability [typically 5-10%] of occurrence considered relevant for therapy.”

- **Internal Tumor Volume:** “The ITV is defined as the CTV plus a margin taking into account uncertainties in size, shape, and position of the CTV within the patient.”  

- **Planning Target Volume:** The PTV is defined “to ensure that the prescribed absorbed dose will actually be delivered to all parts of the CTV with a clinically acceptable probability, despite geometrical uncertainties such as organ motion and setup variations. It surrounds the representation of the CTV with a margin such that the planned absorbed dose is delivered to the CTV. This margin takes into account both the internal and the setup uncertainties.”

The size of these margins determines the amount of tissue that can be spared. Ideally, one would like to have the smallest margins possible, localizing the tumor as accurately as possible, and therefore minimizing the NTCP, without compromising the TCP. Better localization will also allow for a higher dose to be administered to the CTV leading to better tumor control. To exemplify how much a

---

Note that when the CTV is 0, as is the case for SABR lung patients at the BCCA, the ITV and IGTV definitions are the same.
reduction in these margins can affect overall dose administered, consider the following scenario. A spherical tumor is first determined to have a spherical PTV of radius 10.0mm. If subsequent investigation shows the margins can be reduced by 1mm, this will correspond to a 27.1 % reduction in volume radiated. A 2D representation of this is shown in Fig. 1.4

The ability to detect and monitor patient motion has led to the development of image-guided radiation therapy (IGRT). IGRT is the use of imaging modalities to help improve the accuracy of dose delivery [24]. This can refer to several subcategories, such as better definition of the tumor volumes, measuring intra-fractional organ motion, or improving patient alignment before treatment.

1.4 Medical Imaging

CT imaging is the one of the most commonly used imaging modalities in radiation treatment. It is used, as previously mentioned, in the planning stage and also at treatment time, as a pre-treatment CT. This section intends to give a brief introduction on X-ray imaging, CT imaging, and the cone beam version that is used in treatment imaging.
Figure 1.4: The often used orange example shows how a small reduction in radius leads to a large overall reduction in area. Shown here in a 2D representation, a circle with a 10 mm radius reduced to 9mm leads to an area reduction of 19%. In larger dimensions the effect is further amplified.

1.4.1 X-ray Imaging

Photon beams are produced using X-ray tubes operating with peak photon energies from about 40-140 keV. As the X-rays transverse through the medium they interact and the beam will attenuate. At these energies, the dominant interactions are the photoelectric effect and Compton scattering. For a mono-energetic X-ray beam passing through a medium of thickness, $x$, the resulting intensity, $I$, is

$$I = I_0 e^{-\mu x}$$

(1.1)

where $\mu$ is the linear attenuation of the medium. The linear attenuation is dependent on photon energy $E$, depth in the material $x$, atomic number $Z$, mass
number $A$, Avogadro’s constant $N_A$, the electron density $\rho_e$, and the interaction cross-section $\sigma$

$$\mu = \sigma(E, Z, x) \cdot \rho(x) \cdot \frac{N_A Z}{A}. \quad (1.2)$$

$\mu$ will increase for more dense materials or if the atomic number $Z$ is increased. This is because as the number of interaction centers (electrons or nuclei) will also increase. $\mu$ is often quoted in literature as the ratio between linear attenuation and physical density, $\mu/\rho$, to characterize it as density-independent.

The use of lower KV energy photons allow the attenuation contrast between different materials to be large (bones appear white on a dark background). At higher energy ranges, $\mu$ for different materials is more similar and hence the image contrast lowers. This is why therapeutic X-ray beams (on the order of MeV energies) produce images with poor contrast. Materials that are more dense or high $Z$, like bone (calcium), will appear bright (or white) in X-ray images and objects that are low density, such as the lung, will appear dark (or black). Equation 1.1 deals with a mono-energetic beam. In reality, the X-ray beam will be poly-energetic (composed of a spectrum of energies), and the linear attenuation will be averaged over the energies. The exit intensity $I$ is given by the Lambert-Beer law:

$$I = \int_0^{E_{\text{max}}} I_0(E) \exp \left( - \int_0^d \mu(E, x) dx \right) dE \quad (1.3)$$

Where $I_0$ denotes the original intensity, $E_{\text{max}}$ the maximum x-ray energy, and $d$ the penetration depth. For planar imaging, only one projection angle is used and the resulting image will be a 2D image.

### 1.4.2 Computed Tomography

CT imaging relies on the planar imaging as described in section 14.1, but to acquire sufficient data to reconstruct a 3D image, the X-ray projections are taken at different angles around the object/patient. This usually involves the source (X-ray tube) and detector revolving around the object. A conventional CT scanner makes use of a fan beam geometry, where the beam diverges (or as the names
Table 1.1: CT numbers of various materials.

<table>
<thead>
<tr>
<th>Material</th>
<th>CT Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>-1000</td>
</tr>
<tr>
<td>Lung</td>
<td>-500</td>
</tr>
<tr>
<td>Fat</td>
<td>-100 to -50</td>
</tr>
<tr>
<td>Water</td>
<td>0</td>
</tr>
<tr>
<td>Muscle</td>
<td>+10 to +40</td>
</tr>
<tr>
<td>Grey matter</td>
<td>+37 to +45</td>
</tr>
<tr>
<td>White matter</td>
<td>+20 to +30</td>
</tr>
<tr>
<td>Liver</td>
<td>+40 to +60</td>
</tr>
<tr>
<td>Soft Tissue, Contrast</td>
<td>+100 to +300</td>
</tr>
<tr>
<td>Cancellous Bone</td>
<td>+700</td>
</tr>
<tr>
<td>Dense Bone</td>
<td>+3000</td>
</tr>
</tbody>
</table>

suggests, fans out) from the source, but is thin in the superior-inferior direction. Since the beam is thin, the patient needs to be gradually moved (scanned) in the superior-inferior direction to acquire more slices of anatomy, producing a helical scan. The geometry of a fan beam CT is shown in Fig. 1.5. The density of the medium being transversed with X-rays can be measured with CT by calculating the attenuation coefficient. To reduce the dependence on beam energy and allow for easier image interpretation, a dimensionless quantity called a CT number (measured in Hounsfield units) is used clinically. This is done by normalizing the linear attenuation to that of the linear attenuation of water as seen in 1.4.

\[
CT\ number = \frac{\mu - \mu_{\text{water}}}{\mu_{\text{water}}} \times 1000
\]  

Typical CT numbers can be seen in Table 1.1

1.4.3 Cone Beam Computed Tomography (CBCT)

The cone beam geometry is similar to the fan beam, but also fans out in the other direction, forming a cone shape. The advantage of the cone-beam CT (CBCT) is that it only requires a single (or partial) rotation around the patient to acquire a
3D image. This lowers dose to the patient, however at the cost of image quality (resolution, contrast). Since CBCT is used to verify a tumor’s location, and not for diagnosis, the need for sharp resolution is not needed. The principle of keeping radiation “as low as reasonably achievable” (ALARA) is an important concept in radiotherapy, and helps keep doses as low as possible unless a reasonable need for radiation is warranted. This will limit the energy of the X-rays, the number of projections taken, and the intensity of the beam (mAs). Another advantage for CBCT is that the system can be integrated nicely onto linac systems, eliminating the need for larger treatment rooms or separate imaging devices. Since the image acquisition and gantry rotation require at minimum one minute and are not performed during treatment, CBCT imaging is not a truly intra-fractional modality. However, as the CBCT scan is acquired immediately prior to treatment it is assumed the anatomy during treatment does not differ drastically. The geometry of CBCT is shown in Fig. 1.5.

**Figure 1.5:** The fan beam and cone beam geometries used in commercial CT scanners.
1.5 Image Reconstruction

Image reconstruction is the mathematical process that produces 3D images from 2D X-ray projections acquired around the patient. The image quality and radiation dose are both directly affected by the energy and number of X-rays used to acquire projections. There is a large variability in the effectiveness of reconstruction algorithms in terms of image quality. That is, given the same input data, reconstructions will produce images with a range of image quality. It is desirable to reconstruct images with the lowest possible dose without sacrificing image contrast and spatial resolution. Reconstructions that are able to improve image quality may translate into a reduction of radiation dose, as images of acceptable quality can be reconstructed at lower dose. There are two main categories of image reconstruction, analytical and iterative reconstruction. Analytical methods are based on filtered backprojection (FBP) are widely used in clinical environments because of their efficiency, stability, and speed. Iterative methods are considered more complex and less robust but can offer superior image quality and allow customizability not achievable in FBP methods. Furthermore, with the increase in computing power iterative techniques are becoming more popular as reconstruction times are lowered and less expensive hardware is required.

The theory of two-dimensional reconstructions of objects from their projections is well studied. Several solutions exist for such reconstruction problems, we will begin by focusing briefly on the most basic and general of these, allowing for general theory to be introduced before moving onto more complex approaches. The section will conclude with introductions to both analytical and iterative CBCT reconstruction algorithms. To obtain a more in-depth introduction to the fundamental principles of image reconstruction, refer to Kak and Slaney (in particular Chapter 3) [25].

It should be noted that the discussion in this section takes place in real space. Therefore, continuous functions and integrals will be used when introducing concepts and defining the algorithms. Projections are assumed to cover the full set of angles and the detector assumed to be a bounded but continuous 2-dimensional
space, implying an infinite amount of projections defined over continuous coordinates. This is not the case in practice and requires the additional step of discretizing the algorithms, replacing the integrals with summations, and defining coordinates as discrete pixel locations. In addition to correctly identifying the realistic restrictions on imaging these corrections also are required for the discrete data sampling, storing, and processing of data (all done electronically). This is beyond the scope of this thesis and will not be performed here.

1.5.1 CT Reconstruction

1.5.1.1 Direct Fourier Method

Let \( f(x, y) \) represent the density of a two-dimensional object being measured. The intensity from an X-ray tube is attenuated by the object along path \( L \) according to the formula

\[
I = I_0 e^{-\int_L f(x, y) dl}.
\]  

(1.5)

To obtain the line integral value of the object we take the logarithm of the relative attenuation,

\[
\int_L f(x, y) dl = -\ln \frac{I}{I_0}.
\]  

(1.6)

Therefore, X-ray measurements can be considered as line-integrals as seen in 1.6. The line can be considered to belong to a set of parallel lines constituting a projection, see Fig. 1.6. The line-integral is really the projection operator on our object, the attenuation map. Applying the projection operator, \( P \) on our object (or image) will give us a projection, \( p \), at some angle \( \theta \) and detector position \( t \).

\[
p(\theta, t) = P(f(x, y))
\]  

(1.7)

At this point we use the Fourier (central) slice theorem, which states that the 2D Fourier Transform of the image evaluated along a slice (with projection angle \( \theta \))
Figure 1.6: A projection, $p$, generated from a parallel beams of X-rays transversing through the object, $f(x,y)$.

is the same as the 1D Fourier Transform of our projection:

$$F_2(f(x,y)) = F(p(\theta,t)) \quad (1.8)$$

Taking the Fourier transforms of parallel projections over 180 degrees will span the entire two-dimensional Fourier space of the object. Hence, the object can be obtained by applying an inverse two dimensional Fourier transformation.

$$f(x,y) = F_2^{-1} F(p(\theta,t)) \quad (1.9)$$

This technique runs into practical issues as the Fourier slice theorem uses input data from a polar grid whereas the inverse Fourier transform will use a rectangular coordinate system. Since all of the slices will pass through the origin, there will be a concentration of information about the center and less further out. This is resolved by applying a filter that will emphasize data away from the center, the most commonly used is a ramp filter.
1.5.1.2 Filtered Backprojection

The most commonly used algorithm for CT reconstructions is filtered backprojection (FBP). As the name suggests, FBP consists of first filtering (again with a simple ramp filter) of the projection data followed by backprojection (BP). Rather then projecting density values of our object to a projection value, a projection value is backprojected, or smeared out, over the image points along the ray. The resulting image will be blurred out, and will need to be filtered in order to reconstruct the original object. Since the algorithm is linear, the order of operations does not matter. Therefore, the steps are to obtain the projections, apply a Fourier transform, convolve with a ramp filter, apply the inverse Fourier transform, and then back-project to obtain the reconstructed image. Note that the filtering is done before any backprojecting is performed, a consequence of the linearity of the algorithm.

The derivation is quite involved and beyond the scope of this thesis, but follows closely with the principles behind the Fourier method with an appropriate change of integration variables and moving into polar coordinates. Mathematically, FBP can be represented as follows:

\[
f(x, y) = \frac{1}{2} \int_0^{2\pi} \left[ \int_{-\infty}^{\infty} p(\theta, t) e^{-i2\pi \rho t} dt \right] |\rho| e^{i2\pi \rho (x \cos \theta - y \sin \theta)} d\rho \]  
\]

(1.10)

Where, the term in \( () \) is the Fourier transform of the projections at each angle, \(|\rho|\) is the ramp filter, the term inside \([ ]\) is the inverse Fourier transform, and the integral over \(\theta\) is the back projection operation. This mathematical statement contains the entire image reconstruction process compactly.

So far only parallel beam geometries have been used to discuss CT reconstruction. In practice, the diverging fan beam is used almost exclusively, and while the reconstruction process is similar a few minor alterations are needed. For a depiction of the parameters and geometry of a fan beam used in reconstruction, see Fig. 1.7. To distinguish between the two cases, a projection angle of \(\beta\) will refer to a fan beam configuration, compared to the projection angle of \(\theta\) used for the
parallel beam. Compared to a parallel beam, a fan beam bunches up closer to the source and the rays hitting a flat panel detector would be distributed unevenly. To account for this, weighting factors are applied. First, projections are evened out by being multiplied by a \( 1/cos \) term and the backprojections are weighted with an inverse quadratic weighting factor, \( U(x,y) \), which is a function of the distance between the source and the line parallel with the detector that intersects the image at point, \( (x,y) \). Finally, due to the geometry of a fan beam some portion of the image and will be missed and requires an additional rotation that is equal to the fan angle in order to obtain sufficient projections of the object. At this point, the regular FBP can be performed. Although FBP is widely implemented, particularly in clinical environments, it does have its disadvantages. Poor image quality is typical from artefacts (streaking, truncation) and missing data leads to poor reconstructions. However, being well understood, relatively simple, and computationally fast makes it a preferred reconstruction algorithm.

Figure 1.7: The fan beam geometry depicting the variables used in image reconstruction.
1.5.2 CBCT Reconstructions

There exists no exact reconstruction for circular cone-beam geometry, however a similar derivation, with appropriate weightings, can be performed as was done when interpolating from a parallel beam to a fan beam. If the cone angle is not too large the reconstructions image quality can be acceptable [26]. The CT algorithms discussed previously are two dimensional algorithms and reconstruct one slice of the measured object at a time. The process by which they reconstruct a volume is to perform the reconstruction slice by slice with a small movement of the object or scanner between each scan. A more efficient technique for reconstructing a volume is to use a two-dimensional detector. The photon rays will form a cone, the base at the detector and the apex at the source. Since the beam naturally forms a cone, the collimation used for fan beams is reduced. Since the need for many scans (one for each slice) is not needed, the scan time is also reduced. There were several CBCT reconstructions used in this thesis, both analytical and iterative.

The variables used in CBCT reconstruction are depicted in Fig. 1.8. The beam is defined by the cone angle $\kappa$, and fan angle $\gamma$, whereas the projection is defined by the projection angle $\beta$ and the detector coordinates $(a, b)$.

1.5.2.1 FDK

The Feldkamp, Davis, and Kress (FDK) algorithm was developed in 1984 and was the first practical algorithm for cone-beam CT [27]. Regarded as an extension of the filtered back-projection for CBCT, the algorithm finds an approximate reconstructed image $^5$ by adapting the 2D fan-beam techniques to a 3D cone-beam geometry. The speed of the reconstruction and well understood artefacts make it a well used clinical algorithm. Although it produces acceptable quality reconstructions it does have some unavoidable distortion in the non central axis, as well as a variety of image artefacts. Image quality will degrade with an increasing cone angle and image artefacts become more prominent as a function of distance from the central slice [28, 29]. Even though there has been extensive research and

$^5$Except on the midplane, where the reconstruction will be exact
progress in cone-beam algorithms, the FDK algorithm is still widely used in both its original or a slightly modified form.

The cone-beam extension, as was the case with the fan-beam configuration, requires filtering and necessary geometry factors to be applied. In this case, the geometry weighting is dependent on both the fan-angle, $\gamma$, and the cone angle, $\kappa$. Where,

$$\tan \kappa = \frac{b}{\sqrt{a^2 + R^2}}$$ (1.11)

On a planar detector with coordinates of $(a, b)$, and trajectory radius $R$, the projections are filtered by a ramp filter $g$, and a pre-weighted geometrically with two

---

6Again the order of these operations do not matter as the algorithm is linear. The reason why these are applied to the projections is a matter of convenience.
cosine factors,
\[
\tilde{p}(\beta, a, b) = \left( \cos \gamma \cos \kappa \, p(\beta, a, b) \right) \ast g. \tag{1.12}
\]

The filtered and pre-weighted projections are then back projected onto the volume of reconstruction,
\[
f_{\text{FDK}} = \int_{0}^{2\pi} \frac{R^2}{U(x,y,\beta \gamma)} \tilde{p}(\beta, a, b) \, d\beta \tag{1.13}
\]

The weighting factor \( U^2 \) is the same quadratic term that appears in the fan-beam back projection.

Several common artefacts appear in the FDK that can be reduced using additional filters. The high-pass filtering of truncated projection data will create ring artefacts. This is caused from the algorithm trying to reconstruct the sharp transition of some non-zero projections value on the edge of the projection to zero. This can be reduced by padding the projections with some small non-zero values, smoothing the transition to zero. The use of a ramp filter amplifies the high frequency components found in the back projection. So the application of FDK will also amplify the noise in the image. In order to limit this, the ramp filter can be modified to something that will still help distribute the projection data away from the central axis but without amplifying the noise too greatly. A common choice is the Hanning filter\(^7\), which is a low-pass filter defined with a tunable cut-off (critical) frequency [30]. Choosing a smaller cut off will result in less noise, and more smoothing in the reconstructed image.

### 1.5.2.2 Iterative

The other subset of reconstruction algorithms are iterative algorithms. In general, an iterative method will attempt to solve the inverse Fourier problem by expressing it in the form of a general system of linear equation, \( Ax = b \) in order to reconstruct 2D and 3D images. \( A \) is the system matrix that when applied to the image \( x \) will

\(^7\)Sometimes called the Hanning window
produce our input projections \( \mathbf{b} \). In this representation, \( \mathbf{Ax} \) represents a weighted sum over the image voxels that equal the projection data. Although computationally expensive, iterative methods offer an alternative method to analytically derived methods and offer many advantages.

Rather than attempt to reconstruct the image in a single step, iterative algorithms approach the correct solution (the original image) using multiple iteration steps. Ideally, each iteration should yield a better reconstruction eventually converging to the original (true) image. There are a variety of algorithms, some of which will be discussed later on, but the general method is the same. Each starts with an assumed image (typically a uniform image), projects the assumed image, and compares these projections with the original projection data. Based upon these differences, the algorithm attempts to modify its guess on the image and repeats this process to some level of acceptance.\(^8\)

Iterative algorithms have many advantages over analytical methods. The algorithm is more insensitive to noise, has the ability to sufficiently reconstruct images incomplete/missing data, and produces superior images when projections are not uniformly distributed. The reason for these arises from the milder assumptions that iterative methods make on missing data, and the ability to incorporate image constraints, such as image roughness, maximum values, or positivity. The model is composed of several sub-models: Forward projection model, Image representation, Statistical noise model, Inverse model, and Artifact reduction. Such advantages and customizations have made it a popular choice for imaging modalities such as PET and SPECT, and only recently due to technological improvements has it become a viable technique for CBCT, particularly for 4DCBCT [31–34].

The field of developing iterative methods for CT image reconstruction is very active. Developments on faster volume reconstructions for CBCT have been produced by reducing the system matrix size and looking for alternatives to voxels as the reconstruction functions [35]. Effort has also been put into using optimized al-

\(^8\)While the problem can be directly solved with matrix inversion, the matrix \( \mathbf{A} \) is typically not invertible unless the matrix is trivial, in which case the problem mirrors FBP
gorithms using graphics hardware, Graphic Processing Units (GPUs), rather than the less efficient Central Processing Units (CPUs) to accomplish faster reconstructions times [36].

Some criticisms against iterative algorithms are that the artefacts produced and algorithms quirks are not well understood, however, for the most part they are are well established and are beginning to appear in commercial devices.

1.5.2.2.1 Simultaneous Algebraic Reconstruction (SART) Simultaneous Algebraic Reconstruction (SART) was first developed in 1984 as a superior implementation of the current iterative algorithms in use. The following definition closely follows the one introduced by Anderson and Kak, for a more thorough derivation see [32, 37]. The main idea involved with SART is that it will forward and back project simultaneously all the rays acquired with a given angle.

The projection matrix, $A$, contains the elements $a_{ij} \geq 0$. Let the reconstructed image be denoted by $x = (x_1, \cdots, x_n)$ and the input projection data by $b = (b_1, \cdots, b_n)$. The subscripts, $i$ and $j$ are the voxel and projection indices. Subscript $k$ indicates how many iterations have occurred, such that $x_k$ will have undergone $k$ iterations. Initially, the reconstruction volume is set to some value (arbitrary), $x_0 = 0$. SART then updates the image by

$$x_{k+1} = x_k + \frac{1}{A^T \cdot I} \cdot \frac{b - A \cdot x_k}{A \cdot I}$$  \hspace{1cm} (1.14)

The correction term given on the right includes the comparison between input data (projections) and the forward projection of our guess. If the projection of our guess equals the projections that term will be zero and subsequent iterations will yield no change. The algorithm runs until the number of iterations has been performed. The SART algorithm can also be corrected to account for offset detectors and axial truncation compensation. [32]. Positivity can also be enforced to ensure no negative voxels are calculated in the reconstructed image at any iteration. There are many modifications on the SART algorithm, however the basic premise remains the same.
1.5.2.2 Total Variation Reconstruction

More recently, new iterative algorithms have been developed that are based upon compressed sensing and total variation (TV) minimization. In signal processing, the Nyquist-Shannon sampling theorem states that if the signal’s highest frequency is less than half of the sampling rate, then the signal can be perfectly reconstructed [38]. The idea is that with prior knowledge about the frequencies of the signal, fewer samples are needed for the reconstruction. However, due to the developments of compressed sensing given knowledge of the signal’s sparsity allows the signal to be reconstructed with even fewer samples than the Nyquist-Shannon theorem requires [39, 40]. That is, provided there exists some form of the image for which the corresponding coefficients of the discrete Fourier transform are sparse, the algorithm can reliably reconstruct the original object. This relaxation on the number of measurements required is useful for imaging modalities like 4DCBCT which deal with reconstructing images with few projections. The information on the signal’s sparsity comes from the total variation, which in image processing, is the integral (or summation in the discrete case) of the absolute gradient of the signal,

\[
TV(x) = \sum_{v=1}^{V} \sqrt{ [\nabla_x x(v)]^2 + [\nabla_y x(v)]^2 + [\nabla_z x(v)]^2 }
\] (1.15)

where \( v \) is the voxel position and \( V \) the number of voxels. The idea is that images with excessive detail will have a high TV. The removal of these unwanted details (such as noise), while retaining important information like preserving edges, will reduce the TV of the image and make the reconstructed image closer to the original image [41]. Conversely, minimizing the TV will denoise the image. Therefore we define a cost function that contains both a projection correction term and a term for the image’s TV. As before, let \( A \) be the projection (system) matrix, \( b \) the input projection data, \( x \) the image being reconstructed, and the cost function \( J \),

\[
J(x) = ||Ax - b||^2 + \alpha TV(x)
\] (1.16)
where $\alpha$ is a fixed parameter used to define how much the TV affects the minimization. The minimization can be solved using different techniques, for the particular algorithm used in thesis this is done using Lagrange multiplier techniques, Augmented Lagrangian (AL) and Alternating Direction Method of Multipliers (ADMM).

Because the unconstrained problem of finding $x$ that minimizes $J(x)$ is the same as the constrained problem of finding an $x$ and $y$ that minimize, the problem can be written as:

$$||Ax - b||^2 + \alpha \sum_{v=1}^{V} ||y(v)||$$

subject to the constraint, $y = \nabla x$. The Augmented Lagrangian method is used, iteratively minimizing,

$$||Ax - b||^2 + \alpha \sum_{v=1}^{V} ||y(v)|| + \beta ||\nabla x - y - d_k||^2$$

over $x$ and $y$ without constraints and updating $d_k$ (initially set as $d_0 = 0$). This is similar to 1.17 but includes an additional term which mimics the behavior of a Lagrange multiplier and accounts for the differences between $\nabla x$ and $y$. The minimization is done first by finding some $x$ that minimizes $J$ for some fixed $y$, then finding some $y$ that minimizes the cost function for some fixed $x$, alternating between the two. Therefore, for each step we have:

$$x_{k+1} = \arg\min_{x} ||Ax - b||^2 + \beta ||\nabla x - y_k - d_k||^2$$

$$y_{k+1} = \arg\min_{y} \alpha \sum_{v=1}^{V} ||y(v)||^2 + \beta ||\nabla x_{k+1} - y - d_k||^2$$

$$d_{k+1} = d_k - \nabla f_{k+1}$$

The math to derive these results is quite involved and is out of the scope for this thesis, refer to [42] for a more detailed description of the algorithm and other potential methods of minimizing the cost function. Note that the parameters, $\alpha$,
\[ \beta, \text{ and the number of iterations } k \text{ are tuneable, and the selections make can have a great impact on the image quality for the reconstruction output.} \]

### 1.5.3 Image Quality

Image quality is an important consideration that needs to be taken into account when reconstructing images. Below will briefly discuss some image metrics used to assess image quality, factors that affect CBCT image quality, and common artifacts. For much greater detail into CBCT image quality refer to [43].

#### 1.5.3.1 Noise

Noise is defined as the variations in voxel values (CT or attenuation) in a uniform image. It is the result of random processes involved in the detection and interactions of X-rays. Noise is measured using the standard deviation about the mean value of the region of interest (ROI) in the image. Noise becomes more important when looking at low contrast images, where fluctuations can largely affect measurements. One way to determine how noise is affecting an image is with the signal-to-noise ratio (SNR),

\[ SNR = \frac{\mu_{ROI}}{\sigma_{ROI}}. \quad (1.22) \]

The best example is quantum noise. Because photons hit specific detector elements in a random way, the image signal will know also contain that random distribution. There are many factors that affect noise. Increasing the number of counts or reducing attenuation both decrease noise. Attenuation can be reduced with imaging smaller objects or increasing beam energy. Photon count can be increased by increasing the number of projections, as well as increasing the tube current. Increasing the voxel/pixel size will lower noise as the statistical fluctuations are averaged with nearby voxels/pixels. Unfortunately, many of these factors will also raise the patient dose, and therefore limits the noise minimization allowed.
1.5.3.2 Contrast

Contrast refers to the mean value difference between two regions of interest (ROIs). So it represents the difference in CT number between a specific object and the surrounding area. Therefore, when dealing with objects that have a CT number close to the background, noise can mask/obscure details of the object. The contrast resolution is the smallest difference in contrast that can be detected and is strongly dependent on the image noise present. If the noise is too great, the ability to differentiate two distinct areas \((ROI_A, ROI_B)\) is diminished. The metric used to determine this is the contrast-to-noise ratio (CNR),

\[
\text{CNR} = \frac{\mu_{ROI_A} - \mu_{ROI_B}}{\sigma_{ROI_A}}.
\] (1.23)

1.5.3.3 Spatial Resolution

Spatial resolution is the ability to resolve spatial detail. It refers to the ability of an imaging system to send spatial information in an object to an image, so that tiny detail in an object is accurately displayed in the image. Spatial resolution is expressed in terms of the limiting resolution, or the smallest visible pattern, in line pairs per cm (lp/cm). When trying to distinguish between detail in an image (such as line pairs), the edges of an object must be visibly sharp meaning the contrast difference between the two is sufficiently large. This can be calculated using the modulation transfer function (MTF) which expresses spatial resolution as the contrast in the image relative to the contrast in the object and measures how well the spatial information is transferred between the two as a percentage. When the MTF\(_\%\) approaches zero (MTF\(_0\)) it indicates the limiting spatial resolution, where often a cutoff closer to 2\% (MTF\(_2\)) is used instead. The MTF offers an objective means to measure spatial resolution compared to the more subjective approach of visually assessing repeating patterns.

Like noise, there are many factors that affect spatial resolution. Increasing the number of projections (but also dose) will improve spatial resolution. However, as
dose has a clinical limit it also places a potential limit on the spatial resolution on
the reconstructed images. Increasing voxel/pixel size and the use of reconstruction
filters will both obscure fine detail and therefore lower spatial resolution. Often
changing the factors to increase spatial resolution will negatively affect noise, and
therefore obtaining good image quality involves balancing the noise and resolu-
tion trade-off. Furthermore, such factors can be involved in trade-offs in dose or
readout speed. Therefore, the task of optimizing image quality is no trivial task
and comprises an active area of research.

1.5.3.4 Artifacts

Whereas noise is stochastic, artifacts are deterministic. An artifact is an error
in the image, it represents some feature that appears in an image but not in the
original object. It is generally introduced by equipment or the technique used in
the imaging system. Some common examples include streaking, shading, ring,
and motion artifacts. Streaking occurs generally from an inconsistency in a single
projection, that is one projection (or several) have some issue, which results in the
reconstruction algorithm attempting to solve an inconsistent problem. Shading
is due to several projections deviating from the true measurement. Ring artifacts
are caused from errors in detector calibration as well as truncation at sharp edges,
such as having too small a FOV, the reconstruction algorithm cannot properly
reconstruct the sharp edges and due to the circular nature inputs the information
around the image, creating a ring. Motion artifacts arise from the CBCT scan
having a long acquisition time (1 min), allowing for organ motion during the
scan. There are many other artifacts possible and many solutions possible, for
detail on both see [43]

1.6 Image Registration

Image registration is an iterative operation with the goal of finding a geometric
transformation that will bring two images into alignment with one another. The
transformation is a mapping of points from the moving image space to the fixed
image space. This is often specified within a region of interest (ROI), but can include the entire image as well. The use in medical imaging is apparent from the ability to fuse images together or align images from different scanning procedures, including but not limited to resolution, time, space/dimension.

The two main transformation categories are linear and non-linear. A linear transformation is one that preserves the properties of addition and scalar multiplication,

\[ T(x+y) = T(x) + T(y) \]
\[ T(\alpha x) = \alpha T(x) \] (1.24) (1.25)

The most simple linear transformation is a translation displacement (a type of rigid transformation), which has 3 degrees of freedom (DOF), one for each x, y, and z displacements. The addition of rotational DOFs (another 3) results in a more robust rigid transformation. Further adding in scaling (3), and sheering (3) defines the most general case, an affine transformation, which can be expressed as a 3 \times 3 matrix \( A \) and a translation vector \( T_{\text{trans}} \).

\[ T_{\text{Affine}} = Ax + T_{\text{trans}} \] (1.26)

Linear transformations are useful when the objects being imaged have not undergone any large warping or change of shape. The simplicity of such transformations allows for fast computational time.

A non-linear transformation is one in which these properties in 1.25 are not preserved. Therefore, it allows for images to be deformed or warped. For this reason, the use of non-linear transformations is called deformable image registration. The number of DOFs in this case will depend on the algorithm used and how many parameters can be altered when performing the registration. The most commonly used, and the one used in this thesis, is the b-spline transformation. A b-spline (or basis spline) is a piecewise cubic polynomial that is used for the
image warping performed on the image grid.

Once the transformation is applied to the fixed image, the resulting image and moving image are compared. To determine how well the images match, a similarity component is calculated, and then optimized over parameter space. A cost function is typically used and minimized to find the optimal transformation. Initial conditions can help the optimization avoid local minima and also speed up the process, and oppositely slow down optimization or have it converge upon the wrong solution. Therefore, special care is required for selecting such initial conditions. The mathematical formalism is represented as

\[
\hat{T} = \arg \max_{T \in P} S(I, J, T),
\]

where \( \hat{T} \) is the registered image, \( I \) is the fixed image, \( J \) the moving image, \( T \) the transformation used, \( P \) the parameter space, \( S \) the similarity metric, and \( \arg \max \) the optimization used. For a registration to be successful it requires that the size of \( P \) not be too large, and that the solution \( \hat{T} \) can be found in \( P \).

The most common similarity metric is Mutual Information (MI). The MI between two spatially overlapping images (the moving and fixed) is obtained by regarding them as random variables, \( X \) and \( Y \), and their intensity values at a certain coordinate as the joint outcome of a random experiment. It attains its maximal value if there exists a one-to-one mapping between the values of \( X \) and \( Y \). On the other hand, it drops to zero if \( X \) and \( Y \) are statistically independent. The mathematical calculation of the MI is from the entropies of the single image and overlapping images and is beyond the scope of this work. For more information see [44, 45].

More intuitively consider any random alignment of two images, pixels from one image with certain intensities will be aligned with pixels from the other image that may have many different intensities. After matching the anatomic alignment should improve, so that similar anatomic features are matched. This implies that pixels with certain intensities should have a higher probability of being aligned
with pixels of similar intensity in the companion image (for example, bone pixels are aligned with bone pixels and lung pixels are aligned with lung pixels). In this way, MI is a search for a joint image histogram where there is a one-to-one mapping between the histograms of each image. Other common ones are sum of square differences, correlation coefficients, or feature based metrics. For a more thorough discussion on such metrics and their comparisons, see [46].

Optimizing the alignment of an image pair for matching is done with an optimizer, trying to maximize the similarity metric. The field of optimization is very vast and there is an array of popular techniques used in finding local and global max and minimums. The one used is the downhill simplex method, a simple and relatively robust method [47]. It is a commonly used numerical method for the minimization of a N-dimensional function. The algorithm uses a shape with N+1 vertices in N dimensions. The simplex moves its way up an N dimensional hill to a local maximum by means of a simple transform. Each vertex has the MI calculated, with the worst vertex then moved under contraction, expansion, or a reflection if an improvement occurs. It will continuously update it’s size and shape of the polygon under each iteration to reach the locally optimal solution as fast as possible up to the predefined convergence.

1.7 Equipment

1.7.1 OnBoard Imager

The imaging portion on the TrueBeam Linac is the On-Board Imager (OBI) which is mounted directly to the Gantry unit. The OBI is made up of an X-ray (keV) source, a flat panel detector, their respective arms, and a computer system used for reconstructing CBCT images. A Varian TrueBeam Linac, with the OBI highlighted, is shown in Figure 1.9.

The International Electrotechnical Commission (IEC) standard coordinate system used when discussing movement on the linac or its position. The gantry rotation angle increases as the gantry rotates clockwise (viewed from the foot of the
Figure 1.9: A Varian TrueBeam Linac. The On-Board Imager is highlighted by the red rectangles.

couch) and is at zero when the gantry is at it’s highest vertical position. This will be directly above the patient. The kV source and imager are mounted on robotic arms that are at $90^\circ$ and $-90^\circ$ relative to the head of the linac. The kV source is 100cm displaced from the isocenter (point of rotation), and the imager is 50cm displaced. Therefore, the source-axis distance (SAD) is 100cm and the source-detector distance (SDD) is 150cm. The kV source and imager can be displaced to other positions but these are the typical values for CBCT. Note that for half-fan scans (primarily used on thorax scans) the imager position is moved laterally (i.e. along a tangent of the circle of rotation).
The kV imager’s detector is made up of a layer of anti-scatter grid, followed by a TI-doped CsI scintillator, that sits on top of an array of amorphous silicon photo-diodes. There are $2048 \times 1536$ square pixels, with one side of a pixel being 194 $\mu$m. The total size of the detector is therefore 39.7cm lateral and 29.80cm longitudinal. The imaging mode used to capture readout is called Dynamic Gain and uses a 16-bit range to acquire signals. In Dynamic Gain the pixels are grouped in $2 \times 2$ squares, making the detector a $1024 \times 768$ array of 388 $\mu$m pixels [48]. The kV source is a rotating oil-cooled X-ray tube with a focal spot size of 1.0mm. This relatively large size is used to mediate the heat load required for consecutive projections. The tube current (mA), voltage (kVp), and pulse length (ms) can be tuned by the user depending on their needs. CBCT typically operates in the 100-125 kV range, however the X-ray tube can operate from 80-140kVp. The output from the X-ray tube can be modified by several filters and collimators before leaving the kV Source encasing. The beam is first collimated by both a primary fixed collimator and then moveable collimators blades. The moveable collimators are 3 mm thick lead, one pair moves laterally, the other longitudinally. Next, a 0.89 mm thick titanium filter is used to harden the beam by removing the low-energy component, helping to reduce patient dose. The default position of the collimators is set to have the kV Source expose the whole detector to it’s beam. Finally, there is the bowtie filter. The bowtie filter is designed to help average out the X-ray intensity laterally over the detector. It is made of aluminum and as the name suggests is shaped like a bowtie (thick at the edges, thin in the middle). A round object will attenuate the beam more at the center than at the edges, and the imager would pick up higher intensities near the edge. With a bowtie filter this higher intensity region is attenuated and improves image quality by normalizing the intensity. The bowtie filter also reduces the patient dose as low energy photons, that would contribute to dose but not image quality, are removed [49].

The Varian TrueBeam has two such filters available, a full-fan and half-fan. The full-fan is intended for head and neck imaging, with the full bowtie filter being used. As the FOV is quite large (26cm diameter, 18cm long), and most of
the object should be exposed, a short scan can be used limiting the rotation of the gantry to 200°. The scan time is 33s, and has a gantry speed of 6°/s.

The other filter, and the one used in this thesis, is for half-fan scans. These are the main scans used when imaging larger objects, such as the torso. In this mode the detector must be shifted -16cm (away from the linac head) to produce a larger FOV (46cm diameter, 16cm long). Since only a portion of the object is exposed, a full 2π rotation is necessary. With the same gantry rotation speed of 6°/s, the time needed for the scan increases to cover the full arc to 60s. Both scan configurations are depicted in Fig. 1.10. It should be noted that in TrueBeam Developer mode, a research mode, some of these parameters can be altered, however in clinical treatment mode this is not allowed. For more information on Developer mode and altering scanning parameters, see [8]. The different CBCT scan modes can be set depending on the user’s needs. They have been summarized in Table 1.2.

<table>
<thead>
<tr>
<th>Mode</th>
<th>Geometry</th>
<th>Time Pulse (ms)</th>
<th>Current (mA)</th>
<th>Voltage (kVp)</th>
<th>Rotation (deg)</th>
<th>Rotation Speed (deg/s)</th>
<th>Framerate (s⁻¹)</th>
<th>CTDIv (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thorax</td>
<td>Half-fan</td>
<td>20</td>
<td>20</td>
<td>125</td>
<td>360</td>
<td>6</td>
<td>11</td>
<td>3.48</td>
</tr>
<tr>
<td>Slow</td>
<td>Half-fan</td>
<td>20</td>
<td>20</td>
<td>125</td>
<td>360</td>
<td>4</td>
<td>7</td>
<td>3.33</td>
</tr>
<tr>
<td>Very Slow</td>
<td>Half-fan</td>
<td>20</td>
<td>20</td>
<td>125</td>
<td>360</td>
<td>3</td>
<td>7</td>
<td>4.44</td>
</tr>
<tr>
<td>Head</td>
<td>Full-Fan</td>
<td>20</td>
<td>20</td>
<td>100</td>
<td>200</td>
<td>6</td>
<td>11</td>
<td>2.85</td>
</tr>
<tr>
<td>Pelvis</td>
<td>Half-fan</td>
<td>20</td>
<td>80</td>
<td>125</td>
<td>360</td>
<td>6</td>
<td>11</td>
<td>13.94</td>
</tr>
</tbody>
</table>

Table 1.2: CBCT modes and their parameters.

Once a series of projections have been acquired, the Varian Reconstructor reconstructs the CBCT images using FDK. The reconstructor (on the Varian TrueBeam v1.6) is not able to produce 4D CBCT and in-house/modified algorithms and open source toolkits are used instead. The in-house/modified algorithms were the work and/or implementation of the author. Most scripting was done using python (or Matlab), while modifications of the reconstruction toolkit were done in C++. The topic of such reconstruction for CBCT was detailed previously.
**Figure 1.10:** The full-fan (top) and half-fan (bottom) scan configurations. Note the displaced detector in the half-fan scan and the larger possible FOV. The full-fan covers the majority of the object and the required rotation will be $180^\circ$ plus the fan angle which may vary slightly on the geometry of the scan. In the case for the full-fan scan on a Varian TrueBeam this rotation is approximately $200^\circ$, in contrast to the $360^\circ$ rotation required for the half-fan scan.

### 1.7.2 RPM

The Varian Real-time Position Management (RPM) system uses an infrared camera to track a reflective marker block placed upon a patient’s abdomen. After a period of initializing and tracking, the RPM system will output real-time amplitude and phase values approximately 30 times a second. Whenever a projection image is acquired, for either a CT or CBCT scan, the current RPM data will be stored in the header file of the respective projection image. The RPM surrogate marker is correlated to the internal motion such that the relative amplitude of the chest motion from inspiration and expiration (and hence contraction and relaxation of
the diaphragm) correlate to the motion of the internal lung motion moving down and up, respectively. An image of the RPM marker box and infrared camera are shown in Fig. 1.11 For more detail on the RPM system see the RPM reference guide described in the TrueBeam instruction manual [50].

![Image of RPM marker box and infrared camera](image.png)

**Figure 1.11:** The Varian RPM marker box (left) and infrared camera (right) used for capturing respiratory motion.

The RPM system is used in imaging for 4D capabilities in CT. The CT scan is performed with the box on the patient and records what phase the projections were taken at. Projections are binned according to their phase and reconstructed creating a 4D image. Each reconstructed phase shows the tumor in a different position, depicting the tumor trajectory over time. Imaging of the tumor motion then allows for the tumor contours to be more tightly defined reducing normal tissue complications and allowing for higher doses such as in SABR treatments.

Another use of the RPM is during treatment as the trigger for the gating of the treatment beam. Respiratory gating is the process for continuously monitoring the apparent movement of the tumor using respiratory motion (i.e. chest motion) as the surrogate. Radiation is only delivered when the tumor is in a pre-defined region. The treatment beam automatically turns off when the tumor moves outside this region. In doing so the treatment beam is only on when the tumor is in one of the phases as imaged during the 4DCT scan. Gating is one method in accounting for intra-fractional motion caused from respiratory motion.
Chapter 2

Methods

This chapter describes the collection and pre- and post-processing of data, including calibrations and projection binning, acquired from the Varian OBI. The lung protocol developed for therapists is explained and image specifications and file format descriptions are provided. Several definitions on image metrics and tools are also defined that were used in the analysis.

2.1 Data Collection

A total of 6 patients were used in this thesis with a total of 24 CBCT scans. The exact number of CBCTs that were included for each patient in the full 4DCBCT study are shown in Table 2.1. All scans were performed using the “Thorax” Mode (3°/s, 360°, 11 frames/s) on the Varian TrueBeam (version 1.6) resulting in 656 projections that were acquired over a 1 minute scanning time. There was no tuning of scanning parameters and therefore no deviation from the quoted Varian dose of CTDIw of 3.48 mGy 1.2. All patient data was anonymized using the command-line Python script (dicom-anon.py). ¹

The respiratory signal was captured using the RPM system. The RPM is ideal as it outputs both amplitude and phase information and does not require any pro-

¹The anonymization strips the files of any identifiable patient data and complies with the Basic Application Level Confidentiality Profile from the DICOM 3.15 Annex E document.
<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Number of CBCTs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>total</td>
<td>24</td>
</tr>
</tbody>
</table>

Table 2.1: The number of CBCTs used in the 4DCBCT study per patient

cessing of the breathing trace. There were no issues involved obtaining respiratory information with gantry angle near the vertical axis or from FOV limitations that appear in other methods, such as visual marker and diaphragm fluoroscopy tracking, respectively [51]. Once the RPM unit is in sync with the treatment unit/OBI the breathing information is automatically written to the header of each projection file. While the RPM does not represent ground truth it has been found to be robust and give good representation of the internal signal from an external source, in particular, showing a strong linear correlation between diaphragm motion and chest amplitude [52]. In practice this one-to-one relationship is likely to break down for very erratic breathing and will add uncertainty to our analysis.

An alternative method for extracting the breathing trace was attempted using the Amsterdam Shroud method, which does not require an external device, but rather uses image information from each projection [53]. This requires a distinct structural edge that oscillates throughout the projections, the diaphragm being the most common choice. To enhance the signal the image is horizontally averaged, cropped to focus on distinct edges, and concatenated with the other projections. This Amsterdam Shroud image is then processed to extract respiratory motion. The benefit of not requiring a tracking device is useful but the Amsterdam Shroud method was found to require high projection count and a viewable diaphragm throughout all projection angles, two criteria not always satisfied in this thesis.
This method does not provide amplitude information and therefore is only useful for obtaining the respiratory phase information. For these reasons the Amsterdam Shroud method was not used in this work, however, with some improvements such a method may be viable and warrants further investigation. Commercially, both methods are used in available 4DCBCT systems: Varian (Varian Medical Systems, Palo Alto, CA) using the former, and Elekta (Elekta Oncology Systems Ltd, UK) using the latter.

The literature has found that while the method of extracting respiratory signal (internal/external markers and projection analysis) do not produce identical respiratory motion the differences in the reconstructed images were found to be negligible. This suggests that as long as the extracted signal correctly allows binning of the projection data it should yield similar results to other extraction methods.

2.2 Lung Protocol

To determine if 4DCBCT was possible in a clinical setting as few changes as possible were made from the usual lung CBCT scanning protocol followed at the BCCA. The following discussion summarizes the protocol, particularly noting any deviations from the normal lung protocol. The full 4DCBCT lung protocol in its entirety is located in Appendix A.

2.2.1 Treatment Planning

The only change that occurs during treatment planning is to ensure that the RPM system will be activated during the scan. This is done by turning on the gating feature by checking the “Use Gated” box in the treatment plan properties window. While no gating is actually performed, activating this feature ensures that the chest amplitude and breathing phase information are captured during the CBCT acquisition.

\[^2\text{The 4DCBCT capability is not present for the Varian Linac OBI (v1.6) used in this thesis.}\]
2.2.2 Treatment

The first additional step is to place the RPM marker box on top of the patient’s chest following patient alignment and setup. The patient does not require any breath coaching and should be familiar with the RPM device from their planning CT done previously. An abdomen compression device is used to promote shallow breathing. The exact positioning of the RPM marker box is not vital as long as the treatment unit is able to detect the box and its movement. Therefore, the marker box should not be obstructed by any blankets or other devices and should be in a spot that has noticeable movement due to the patient’s breathing (i.e. not too high on the chest).

With the RPM placed on the patient, the treatment unit will automatically pop up with a RPM configuration wizard screen, creating a new tracking protocol, and require some input from the therapists. To help the system track the RPM, the therapists indicate that the motion should be amplitude gated, periodic (as opposed to a breath hold treatment) and ensure all coaching, both visual and audio, are removed. The predictive breathing filter should be set to 0% which lowers the threshold for periodicity for tracking to begin. Once tracking has begun, the system takes roughly 30s to identify the signal. This can take longer if the RPM was put in a poor location, or if the patient’s breathing is too erratic.

Once initialized, the system now permits scanning and will require the gating parameters to be set. To ensure no gating is performed, the therapists choose upper and lower bounds that are sufficiently large, i.e -5cm and 5cm. A reference curve is generated by clicking the “start” button and recording a few cycles of breathing. The breathing trace should populate the screen at which point the therapists can stop the reference curve and begin their usual CBCT scan. The radio-translucent RPM is left on during the x-ray treatment so there is no need to interrupt treatment flow for removal. Any movement to the patient, as is done during a patient alignment, will require the treatment unit to re-track the RPM marker, which is done automatically. If the initial RPM tracking was successful no problems were found to arise during treatment or any of the required re-trackings. The CBCT
scanning parameters for the first fraction are stored into memory and present for
subsequent fractions, reducing setup time.

In the event of any issues, the treatment plan can have the “gated” feature
turned off to avoid any further delays to the patient’s treatment. With all steps
included the additional time is roughly 3min or less for the first fraction, and
less than 2min for subsequent ones. There is no increase in dose from 4DCBCT
imaging.

2.3 Pre-processing

2.3.1 Scanning Procedure

Each projection (one X-ray beam pulse) is roughly 1MB in size and consists of
a header followed by a pixel data array (1024 × 768) with elements (0.388mm ×
0.388 mm) stored as unsigned 16-bit integers. The header contains X-ray tube
settings (e.g. kVp, mAs), source/detector positional values, and other scan pa-
rameters (e.g. filtration). The OBI system stores each projection in a compressed
proprietary format, .xim, accessible from only within Service mode. These files
are moved offline for pre-processing and normally collected at the end of the treat-
ment day. The OBI stores the .xim files locally for up to five days before deletion.

In order to access the pixel data the files are first run through a decompression
step using a Matlab script provided by Dr. W. Ansbacher\textsuperscript{3}, and modified by Dr.
A. Bergman\textsuperscript{4}. To avoid having to decompress the files for each reconstruction,
which would become time consuming, all the .xim files were deconstructed/de-
compressed and written in binary as two separate files, .raw and .hnd, through the
Matlab script CreateRaw.m. This step also allows the trimming of unnecessary
information, reducing file size, and for individual projections to be viewed with
no need for decompression. The .raw files were used to store pixel data and the
.hnd files stored header data only. The header information contained the neces-

\textsuperscript{3}University of Victoria
\textsuperscript{4}University of British Columbia
sary projection and geometrical data (projection angle, SAD, SSD) required for reconstruction. In order to correctly read the .raw files, each was paired with a .mhd file that supplied the required image information (height, width, pixel size, resolution, origin).

### 2.3.2 Calibrations

#### Air Normalization

The pixel data represents the detector readout but CT reconstruction requires the measured intensity \( I \) (or projection image, object in the FOV) as well as the original intensity \( I_0 \) (or air image, no object in the FOV) to create a map of the attenuation. Therefore, the pixel data undergoes air normalization calibration to correctly represent the attenuated intensity. Recall from 1.1 that the intensity is an exponential function and that the attenuation can be calculated by the dividing each projection with the un-attenuated image followed by taking the logarithm. In this way, the projections will then resemble the familiar X-ray scan, bones will appear bright, and lung/air appear dark. Some air normalization methods will assume a constant unattenuated image, typically of the maximum pixel value. This assumption, while still allowing reconstruction, will lead to improper calibration as the unattenuated image is not uniform due to the bow-tie filter and heel effect of X-rays. An example of the air image acquired through a half-fan scan is shown in Fig.2.1. A secondary correction (still classified under air-normalization) is performed to account for the difference in mAs values used for the acquisition of \( I \) and \( I_0 \). An image with higher mAs will measure higher pixel values compared to a low mAs image as the intensity of the X-ray beam is higher resulting in more photons striking the detector. Rather than measure the mAs values and scale the projection images accordingly, the scaling is done using the CT Norm Chamber (NC) value, which is found in the header of each projection. The NC value corresponds to the X-ray tube’s output for each pulse and has a linear relationship with the mAs making it a suitable replacement for scaling [8]. Although the variation
in the NC value is minor, each projection is corrected with its own NC value for better accuracy. Combining both the normalization and the mAs scaling gives the full air-normalization calibration,

$$\log(I_0) - \log(I) + \log \frac{NC_I}{NC_{I_0}}$$

(2.1)

There are two options for acquiring the air image $I_0$. The first is to take a CBCT scan with no objects in the FOV and at a relatively low mAs to avoid saturation of the detector. The second option, and the one used in this thesis, is to use the calibration .xim that is provided by Varian. It was found that the variation in both un-attenuated projections and their corresponding NC values was small and the difference in image quality when used was found to be negligible. At this point every projection should be calibrated for air-normalization and was written to disk as a .raw +.mhd +.hnd file. (ex: Proj_0034.raw + Proj_0034.mhd +

---

5Even at low mAs some pixels may oversaturate and roll-over to 0, this causes severe artefacts and is difficult to remove without applying some kind of filter.
Each projection was then down-sampled to $512 \times 384$ pixels with $0.776 \times 0.776$ mm$^2$ through a two-by-two binning process. This not only reduces the file size of each projection by a factor of 4 but also reduces noise in each projection. Using larger binning windows and alternative binning methods for down-sampling may produce better results and warrants further investigation. To avoid the requirement of looping through all the projections, the .raw files were concatenated together using `concat.sh` into one .raw file (Proj_total.raw).

**Scatter Calibration**

No scatter calibration was performed in this thesis and is left for an area of future work. In order to incorporate scatter, a model first needs to be parametrised from the comparison of pixel values and MC data. An homogeneous scatter contribution is assumed which is calculated by the volume of tissue that the X-rays must pass through. The particular choice of scatter model can vary. Two examples are the Mainegra-Hing model or the Boellaard model [56]. The latter is currently being implemented into RTK, in terms of a scatter-to-primary ratio. Another technique to help reduce noise produced from scatter would be to use a median filter across the projection data. This step would need to be implemented prior to down-sampling, to eliminate the scatter from propagating during the re-binning step.

### 2.3.3 Geometry Generation

Another requirement for reconstruction is the geometry of the scan. The projections are run through a modified toolkit script `rtkvariationgeometry` that generates the correct geometry of the treatment unit and output this as a single .xml file.

The 3D geometry is based on the international standard IEC 61217, which was designed for cone-beam imagers for use on linac systems [57]. The fixed coordinate system $(x, y, z)$ is defined as the Varian coordinate in real space with an isocenter at the origin $(0, 0, 0)$, as described in section 1.7. The default units
used in the geometry are degrees (0-360°) for angles, and the millimeter (mm) for any distance and/or spacing. Projection images are converted from voxel indices into physical space from their header information (image origin, spacing, direction). The projection geometry is defined from the set of 2D projection images, as acquired along a circular trajectory (about the y axis) from the flat panel detector. The position of the source and detector (i.e the moving coordinate system) is defined by 9 parameters from each projection.

The first 3 parameters are the rotation angles used to define the detector orientation. The subscript for each angle denotes the axis by which the angle rotates: The gantry angle $\phi_y$, The out-of-plane angle $\phi_x$, and the in-plane angle $\phi_z$. The latter two angles are normally 0, reducing the rotation matrix to

$$M_R = \begin{pmatrix}
\cos(-\phi) & 0 & \sin(-\phi) & 1 \\
0 & 1 & 0 & 0 \\
-\sin(-\phi) & 0 & \cos(-\phi) & 0 \\
0 & 0 & 0 & 1
\end{pmatrix}$$

The setup is defined such that if the rotation parameters are 0 the detector will be normal to the z-axis.

The remaining 6 parameters define the source and detector position. The position of the detector is defined from the detector displacements or offsets $\vec{DO} = (DO_x, DO_y, DO_z)$. Likewise for the position of the source, $\vec{SO} = (SO_x, SO_y, SO_z)$. The offsets are defined with the isocenter as the reference point. The required information is normally expressed in terms of the projection offset ($\vec{PO} = \vec{DO} - \vec{SO}$). The source and projection offset in z are the called the Source-Axial-Distance (SAD) and Source-to-Detector-Distance (SDD), respectively.  

---

6The ZXY convention of Euler angles is followed.

7In IEC 61217 the SDD is called SID. Not to be confused this with SSD, the source-to-skin distance used in radiotherapy.
the parameters results in the final matrix that fully defines the geometry,

\[ M_{\text{final}} = \begin{pmatrix} 1 & 0 & PO_X \\ 0 & 1 & PO_Y \\ 0 & 0 & 1 \end{pmatrix} \times \begin{pmatrix} -SDD & 0 & 0 & 0 \\ 0 & -SDD & 0 & 0 \\ 0 & 0 & 1 & -SAD \end{pmatrix} \times \begin{pmatrix} 1 & 0 & 0 & -SO_X \\ 0 & 1 & 0 & -SO_Y \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \times M_R. \] (2.2)

All of the above information is saved and later accessible from the generated XML file (PatientGeo.xml). Only parameters that differ from the defaults are saved. In the event they are not the defaults but are the same for all projections they will be recorded once, otherwise it will be required for each projection. The geometry matrix 2.2 is saved for each projection. Any modifications to the parameters will also require the matrix to be recalculated, and therefore manual edits are discouraged. An example of the format for the XML file is provided in Appendix B.

### 2.4 Reconstructions

To perform the CBCT reconstruction the inputs, Proj_total.raw, Proj_total.mhd, and PatientGeo.xml were fed into the user-chosen RTK reconstruction algorithm [58]. The user also chooses the size and pixel dimensions as well as other reconstruction-specific parameters shown in table 2.2. The size of the generated 3D image varies strongly on the inputs chosen. For a 512x240x512 (0.88mm³ voxel) reconstructed image, the file size was 251.7MB.

All reconstructions were run on a dedicated machine that was constructed with relatively dated computer parts, aside from the GPU, which was used to perform the bulk of tasks needed for the reconstructions. The reconstructions were run on a Nvidia (Santa Clara, CA, USA) Tesla C1060 GPU, a high performance com-
<table>
<thead>
<tr>
<th>Algorithm</th>
<th>Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>(d) Dimension (default = “256”)</td>
</tr>
<tr>
<td></td>
<td>(s) Spacing (default = “1”)</td>
</tr>
<tr>
<td></td>
<td>(o) Origin (default = “centered”)</td>
</tr>
<tr>
<td></td>
<td>(d) Dimension (default = “256”)</td>
</tr>
<tr>
<td>RTK</td>
<td>(hann) Cutoff frequency for hann filter</td>
</tr>
<tr>
<td></td>
<td>(pad) Data padding value for truncation</td>
</tr>
<tr>
<td>SART</td>
<td>(f) b</td>
</tr>
<tr>
<td></td>
<td>(n) Number of iterations (default = “1”)</td>
</tr>
<tr>
<td></td>
<td>(\lambda) Convergence factor (default = “0.3”)</td>
</tr>
<tr>
<td></td>
<td>(p) Positivity (default = “off”)</td>
</tr>
<tr>
<td>AADMTV</td>
<td>(n) Number of iterations (default = “1”)</td>
</tr>
<tr>
<td></td>
<td>(\alpha) Regularization parameter (default = “0.1”)</td>
</tr>
<tr>
<td></td>
<td>(\beta) Augmented Lagrangian constraint multiplier (“1”)</td>
</tr>
<tr>
<td></td>
<td>(n_{CG}) Number of nested iterations (default = “5”)</td>
</tr>
</tbody>
</table>

**Table 2.2:** Definition of parameters used in CBCT reconstruction algorithms.

A computing device with a high floating point performance, 4GB of dedicated memory, 800MHz memory speed, and a 512-bit GDDR3 memory interface [59]. The use of a GPU allowed for the reconstructions to be implemented to run using the Nvidia Compute Unified Device Architecture (CUDA). CUDA is a parallel computing platform that can be implemented into GPUs, allowing for parallel computing, greatly decreasing computing time required for reconstruction compared to CPUs.[60] Performance improvements for the reconstruction algorithms could occur with upgrades to the CPU, hard drives, GPU, or RAM (DDR2 was used which is a rather old architecture).

Although the storage of the files was a concern, especially at high resolution, it was found that file storage was less of an issue than RAM requirements used during reconstruction. The largest memory requirement was for the input projection data which was directly proportional to the number of projections. However,
even at high resolution (512 × 512 × 512, 0.88mm/pixel), the FBP methods encountered no issues. The same didn’t hold for iterative methods as they required more memory to store the assumed image and even more to allow for interactions to take place. In particular, TV minimization techniques were found to require high memory to perform high iterations at high resolution. FBP methods were able to be performed solely on a CPU, whereas without a GPU the iterative reconstruction algorithms would take too long and not feasible. Once the GPU/CUDA reconstructions were implemented CPU reconstructions were never attempted.

2.4.1 3DCBCT

3D CBCT reconstructions were run using FDK, SART, and ADMMTV algorithms, using the entire projection dataset. Parameters for each are described in table 2.2. The required inputs were the geometry file, “PatientGeo.xml”, and total set of projections, “Proj_total.mhd + Proj_total.raw”. Reconstruction times and the resulting images are shown in the next chapter.

2.4.2 4DCBCT

As defined in section 1.5.3, 4DCBCT uses the same algorithms as used in the 3D CBCT reconstructions but with the additional step of binning the set of projections by either amplitude or phase. The files are regrouped by moving the appropriate files into their own directory (phase1, phase2, … phase_n and amp1, amp2, … amp_n). The binning process is explained in detail in the following section. Once binned the same procedure used for 3DCBCT (concatenation, geometry generation, and running the reconstruction algorithm) is then applied to each binned set of projections. Due to the limited the number of projections, as a result of binning, the FDK algorithm does not produce adequate images and therefore is not used in 4DCBCT image reconstruction. Instead, the iterative TV minimization algorithm is used. The issues with memory are reduced as the input Proj_total.raw file is smaller. The entire process is handled through one script (pre4DCBCT.sh).
2.4.3 Binning

Binning grouped the projections by some characteristic such that the projections in one bin all imaged a similar anatomy. In terms of respiratory motion this meant that for projections to belong to the same bin they must have been taken at the same point in (or within some range of) the breathing cycle. The two criteria used in this thesis are amplitude and phase.

The amplitude in amplitude binning refers to the relative chest amplitude as measured by the RPM, with the idea being that RPM measurements near a certain height should represent a similar patient anatomy. When the RPM is at its maximum (minimum) height the patient breathing cycle is at its max inspiration (expiration). For phase binning, the phase is extracted from the respiratory trace by assuming it follows a pseudo-sinusoidal shape. The phase is extracted automatically from the RPM system, however, the specifics on how this is done is not publicly documented by Varian. The similar patient anatomy should appear periodically, as any arbitrary point should be repeated after an integer number of cycles \( n \times 360^\circ \). The value of the phase is arbitrary depending on the reference point chosen. In this thesis, \( 0^\circ \) \( (180^\circ) \) is defined to correspond to maximum inspiration (expiration). Binning by the extracted phase is called phase binning. A hypothetical breathing trace is is shown in Fig 2.2. The red dots indicate a projection.

The amplitude binning algorithm follows [55] and is described below and executed with the Matlab script (amplitude.m).

1. Find the local amplitude maxima and minima of the phase trace.
2. Find the median values of each and define that as the upper and lower boundary.
3. Divide the projections between the two median values into equal sized bins.
4. Excluding the max and min bins, the remaining bins are classified as mid-inspiration(expiration) depending on the gradient.
Figure 2.2: A hypothetical breathing trace of a patient with the amplitude read off the RPM. The red dots indicate that a projection was taken. Few projections are shown to aid in clarity. A regular thorax half-fan scan will result in 656 projections.

5. Outliers projections that are beyond the upper (lower) boundary are appended onto max (min) bin.

Median peaks and troughs are used as reference points to remove large spikes (ex: one deep breath) that would alter the binning intervals. Instead, any outliers are added to either the max expiration or max inspiration bin instead. Noise in the trace can also produce local minima and minima that are incorrect and not a proper peak or trough. To correct for this a peak finding algorithm was used that only triggered on “true” extrema. The classification of a particular projection belonging to the expiration or inspiration portion of the breath cycle was done by examining nearby projections. An example of amplitude binning of the hypothetical breathing trace is shown in Fig. 2.3. Note the uneven distribution of projections in each bin. The max expiration and inspiration contain the most projections, while the bins between the two extremes suffer from less projections. This will lead to poor reconstruction for inner bins.

The phase binning algorithm is easier as the phase identifies inspiration/expiration and does not have the redundancy found in amplitude binning. The extracted phase is bounded from 0 to 360° and divided into $n$ equal bins. An example
Figure 2.3: The patient trace is binned by amplitude into 6 bins. Two projections can share the same amplitude and belong to different bins if one is taken during inspiration and the other expiration. Amplitude binning will often result in an uneven distribution of projections and bunching found in the max/min expiration bins. This results in poor image reconstruction quality for intermediate bins.

of phase binning of our hypothetical projection is shown in Fig. 2.4., again with 6 bins being used. Another figure, and one that further emphasizes the angular representation is shown in Fig. 2.5.

The decision on how many bins the binning algorithm should have depends on finding the correct trade off between image quality and tumor motion. Image quality will suffer with less projections (more binning), and vice versa. However, fewer bins cause the loss of the temporal component of the reconstructed images and more motion blurring will occur. Therefore the number of bins should be as high as possible without losing satisfactory image quality. Typically this is around 8-10 bins, however, there are a few cases in which 6 bins have been used. The largest factor in predicting the amount of bins required for sufficient image quality is the total number of projections. The number of bins used in this study and how this was determined will be discussed in the image quality section in the following section.

Each binning algorithm has its advantages and disadvantages. Phase binning
Figure 2.4: The patient trace is binned by phase. This representation lists the phase extracted by the RPM rather than the amplitude. Therefore a minimum in the amplitude would correspond to a $180^\circ$ value in this depiction. Again, the projections are binned into 6 bins. Note in this representation there is no redundancy found as each phase corresponds to a unique bin. An advantage of phase binning is the even distribution of projections among each bin.

Figure 2.5: The patient trace binned by phase but now represented on a unit circle, emphasizing the angular nature of the phase. The projection onto the horizontal axis represents the amplitude. The same information found in Fig. 2.4 is shown here.
often will have the majority of organ motion occurring in only a few bins, similar to how a swinging pendulum (or spring) has most motion occur away from the minimum and maximum. Therefore, reconstructing of these bins will contain the majority of the motion blurring. For this reason, the most stable image will reconstructed for the max/min expiration bins. This effect will limit the benefit of 4D imaging, as the visualization of the moving organ becomes more difficult to see. Amplitude binning spreads the motion equally across its bins, subsequently, the reconstructions for these bins will all have a similar amount of motion blurring. However, amplitude binning does not bin the projections as uniformly as phase binning, and some bins will contain significantly less projection than other bins. This leads to reconstructions of these bins being quite poor in image quality. The phase method also requires extracting the phase from the breathing trace and adds another factor that may lead to inaccuracy. This issue is more common when the patient’s trace suffers from lack of periodicity. Regardless of what method is used, the signal acquired has been shown to be quite robust and give a close approximation to the internal signal [52].

An example of a patient’s breathing trace that exhibits good periodic behavior is shown in Fig. 2.6. Another that does not share such traits is shown in Fig. 2.7. Both traces are binned with 8 bins.

### 2.5 Dataset Naming Convention

Datasets are defined by the patient number and the fraction in which the scan took place. Each dataset is labelled with a format of “\textit{pn}_m”, where \textit{n} is the patient number and \textit{m} is a string that contains the fraction. That is, \textit{m} will state if it is a pre- or post-treatment CBCT, and in the case of the former what fraction it took place on. Therefore all datasets will be have elements \textit{n} and \textit{m} such that:

\begin{align*}
    n & \in \{1, 2, 3, 4, 5, 6\} \quad (2.3) \\
    m & \in \{\text{post}, \text{pre1}, \text{pre2}, \text{pre3}, \text{pre4}\} \quad (2.4)
\end{align*}

57
Figure 2.6: A patient breathing trace (p3_pre4) that exhibits good periodic behavior, making it a good candidate for both amplitude and phase binned reconstruction. The projections are well distributed.

As an example, the dataset of patient 3 from his/her 4th fraction pre-treatment CBCT would be “p3_pre4”, the dataset from patient 1 from his/her post-treatment CBCT would be “p1_post”. The reconstruction algorithms will be labelled by their acronyms: FDK, SART, ADTVMM. Binning will define the bin used but also binning algorithm used, either phase or amplitude. Any other additional information will be included in it’s entirety and vary on a case by case basis.

2.6 Post-processing

2.6.1 Image Calibration

Following the successful reconstruction of a patient dataset into a CBCT image the values represent the $\mu$ mapping of our object. They require conversion to Hounsfield units (CT numbers) for more meaningful representation. This can be
Figure 2.7: A patient breathing (p1_pre2) trace with poor periodic behavior. There are long pauses, bunching, and sharp peaks. The projections are not distributed evenly and the extracted phase signal has several areas of inaccuracies. In such a case, only amplitude binned reconstruction is viable.

performed from eq.1.4, however a more convenient method is to perform calibration by fitting the values to a CT-numbers to $\mu$ values calibration curve. The calibration is done using a the CT404 module of the Catphan 504 phantom [61]. The phantom contains inserts of different materials each with a known CT number, which are listed in table 2.3. To perform the calibration, a CBCT scan is taken with the same kV value and filter choice as the patient CBCTs. The projections are reconstructed into a 3D CBCT and the pixel values of the inserts are measured from a particular axial slice that contains all the inserts. The pixel value average of each insert is calculated, reducing the effect of noise, and represents the uncalibrated $\mu$ value for that particular insert. The slice used for the calibration is shown in Fig. 2.8. The $\mu$ values are then compared to the known CT numbers and plotted. A linear fit provides the slope, $m$, and y-intercept $b$, for the conversion
<table>
<thead>
<tr>
<th>Material</th>
<th>CT number (HU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air</td>
<td>-1000</td>
</tr>
<tr>
<td>PMP (polymethylpentene)</td>
<td>-200</td>
</tr>
<tr>
<td>LDPE (low-density polyethylene)</td>
<td>-100</td>
</tr>
<tr>
<td>Polystyrene</td>
<td>-35</td>
</tr>
<tr>
<td>Acrylic</td>
<td>120</td>
</tr>
<tr>
<td>Delrin</td>
<td>240</td>
</tr>
<tr>
<td>Teflon</td>
<td>990</td>
</tr>
</tbody>
</table>

**Table 2.3:** CT numbers used for Calibration in the Catphan 504. [61]

**Figure 2.8:** An axial slice of the Catphan 504 phantom used for HU calibration. This image was reconstructed from a half-fan scan done on the TrueBeam unit at 120 kV with the FDK algorithm. The image is a map of the attenuation coefficient $\mu$ (mm$^{-1}$). The phantom is 20cm in diameter. Several different material inserts are used (seen in the image as circles) are used for the calibration: air (top/bottom), Teflon (bottom right), Delrin (right), acrylic (not visible but should be top right), polystyrene (top left), low-density polyethylene (left) and polymethylpentene (bottom left).
between the two,

\[ \text{CT number} = m\mu + b. \]  

(2.5)

The linear fit used for the FDK HU calibration is shown in Fig. 2.9. The parameters are stored in a text file and can then be applied to the patient CBCTs to convert them from \( mu \) values to CT numbers. After calibration, areas of air and bone are closer to their typical values of -1000 and \( > 1000 \), respectively. It is not expected to get exact CT numbers as they are better defined for CT scans rather than CBCTs and in the latter's case are better considered as an approximation. Regardless, it is still a common calibration performed on CBCT images. This calibration was done for each reconstruction algorithm used in this thesis.

![Figure 2.9](image)

**Figure 2.9:** The HU calibration fit used to convert from attenuation into CT number for the CBCT reconstructions. The slope is \( 6.71 \times 10^4 \text{HU} \cdot \text{mm} \) and the intercept \(-1.24 \times 10^3 \text{HU} \).

### 2.6.2 Contouring

Contouring was necessary so that the gross tumor volume was identifiable in each 4DCBCT image and could be compared to other tumor volumes contoured on the patient’s treatment CT. All contouring was done using ITKsnap, using an semi-automatic contouring algorithm [62]. The algorithm uses a gradient threshold...
limit on the contrast of the image to segment the tumor. As the 4DCBCT images suffer from poor image quality this also require manual touch ups on to ensure proper tumor contouring. Contouring was not performed by an oncologist and therefore introduces potential error into the contouring, however the original GTV’s contoured in the treatment CT were used as reference. The volumes of all 4DCBCT GTV contours were within \( \pm 5\% \) of the oncologist contoured GTV on the CT image. Although it is possible to perform tighter or more defined contours, the limiting factor is the image quality and more time spent on contouring will yield little improvement. Each phase requires contouring and as such can require a large amount of time. To help speed up the process, a b-spline pseudo-automatic contour algorithm was developed. All bins were registered with b-spline registration with the first bin, producing a series of deformable transformations, \( T_1, T_2, \ldots, T_n \). The first bin had the GTV contoured, producing \( GTV_1 \). Subsequent bins were contoured by applying the deformable transformations onto \( GTV_1 \), such that,

\[
T_{ln}(GTV_1) = GTV_n
\]

This process speeds up the contouring process, but each contour still requires manual corrections, as the image quality of 4DCBCT was not sufficient enough to permit fully automated algorithms.

It was later determined that contouring of the 4DCBCT images lead to inaccurate contours and difficulty in comparing them to the CT contours, primarily for two reasons. First, the low image quality caused the tumor volume to appear blurry and made it difficult in distinguishing tumor from normal lung tissue. This led to a \( GTV_i \) contour that overestimated the size of the actual tumor. Secondly, the decision to use a deformable registration, while allowing the visible tumor to be well covered, was not a realistic representation of the actual tumor movement. Lung tumor deformation is considered negligible and motion consists of primarily only translational movement [63]. Therefore another method using image registration was used for tumor identification. The starting contour was the GTV from the planning CT. This contour was then rigidly registered to each 4DCBCT im-
age, allowing the translational transform to be extracted and be used as the tumor motion for that phase.

### 2.6.3 Image Registration

In order to make comparisons the images are aligned so that the CBCT images are in the same coordinate space as the CT image. The registration is performed using plastimatch and/or Slicer 3D [64, 65]. The optimization criteria is mutual information using downhill simplex as the optimizer. These were chosen to have a matching algorithm that will perform similarly to the Varian algorithm in use on the treatment unit [50]. The CBCT-CT matching was done using rigid transformation, aligning the two images upon one another. After the registration, contours from CT properly align on top of the anatomy in the CBCT images. The times to perform the registration typically take less than 30s. In some events, the registration fails and requires a second registration. This can most likely be fixed with correct setting of initial conditions.

In order to compare the contours from the CBCT and CT images, the following steps are first performed.

1. Extract tumor volume contours PTV, IGTV, and GTV from planning CT structure dicom file
2. Perform CBCT-CT registration and acquire the transformation $T$
3. Apply the transformation to the 4DCBCT images, $T(4DCBCT_{CBCT}) = 4DCBCT_{CT}$
4. The extracted CT contours can now be compared to the reconstructed 4DCBCT images.

The tumor volume is identified on the 4DCBCT images by using rigid registration. The GTV is registered to the visible tumor volume for each phase, producing contours $GTV_1, GTV_2, \ldots GTV_n$. The centroid of each volume can be calculated and used to show relative tumor motion.
2.7 Metrics

2.7.1 Image Quality

Two commonly used metrics were used to quantify image quality, and aid in the comparison of reconstruction methods. The signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) are defined for a region of interest (ROI) as:

\[
SNR = \frac{\mu_A}{\sigma_A} \quad (2.7)
\]

\[
CNR = \frac{|\mu_A - \mu_B|}{\sigma_A} \quad (2.8)
\]

Where \(\mu_A(\mu_B)\) is the average of the ROI \(_A(ROI_B)\), and \(\sigma_A\) the standard deviation of ROI\(_A\). Both metrics can be used to determine image quality. A high SNR indicates that the ROI has a high intensity relative to the noise, while a high CNR indicates a higher contrast between two ROIs compared to the background. While SNR is a good indicator for image quality it suffers from a bias such as a systematic error that adds a uniform value to the full image. The features of the image will be washed out but the image may still have high intensity and if the error is noiseless it will result in a high SNR. However, as this washing effect will lower the contrast of the image the CNR will remain sensitive to its effect. The combination of the two results in a useful tool for image comparison.

2.7.2 Tumor Overlap

To quantify tumor motion a metric based upon volume (or set) overlaps was used. Consider two volumes, A and B, that ideally have some level of overlap. The first metric used to quantify if volume A is fully encompassed by the other, volume B. In other words, this metric determines the amount of containment between the two. 100\% indicates full coverage, anything less will indicate that volume A has moved outside of volume B. Higher values indicate more of the volume has escaped and therefore results in less overlapping between the two volumes. In this

64
thesis such volumes represent the treatment planning contours (ITV or PTV), and the 4DCBCT tumor volumes ($GTV_i$). A depiction of this is shown in Fig. 2.10

$$\% \text{Overlap} = \frac{(V_{\text{tumour}} \cap V_{\text{contour}})}{V_{\text{tumour}}} \times 100 \quad (2.9)$$

Figure 2.10: 2D visualization of our overlap metric. Full coverage occurs if the yellow and green areas are equal, signifying complete tumor containment.

### 2.7.3 Tumor Motion

Tumor motion was calculated after the contouring of the tumor volume (either manually or by registration). Once the contour was defined for each phase, the centroid $\vec{C}$ of each bin was calculated via the center of mass and saved as $\vec{C}_{bin} = (LR_{bin}, AP_{bin}, IS_{bin})$. The displacement of each bin was calculated relative to the first bin. That is, $\vec{D}_{phase} = \vec{C}_{phase} - \vec{C}_1$, where each component labels the displacement in the LR, AP, and IS direction. The total displacement of the tumor motion was calculated as the Euclidean distance with the maximum displacement for each
component,

$$D_{total} = \sqrt{\Delta(AP)_{max}^2 + \Delta(LR)_{max}^2 + \Delta(IS)_{max}^2}.$$  \hspace{1cm} (2.10)

An example of the measuring the tumor displacement after several bins is shown in shown in Fig. 2.11.

**Figure 2.11:** Visualization of the tumor displacement.
Chapter 3

Results

CBCT images were reconstructed using RTK with the FDK, SART, and AD-MMTV algorithm on the QUASAR respiratory motion phantom (Modus Medical Devices), Catphan 504 phantom, and patient data. [66]. The QUASAR phantom projections scans were run using the “Thorax Very Slow” mode, for a total of 836 projections, all others were run using “Thorax” mode for 656 projections, see 1.2. The output pixel dimensions of each reconstruction, unless otherwise stated, was $512 \times 512 \times 240$ in the LR, AP, and then IS direction, respectively. GPU computing greatly reduced the reconstructions times on both iterative and analytic algorithms and was used in all reconstructions.

3.1 Image Quality

Image quality was performed on the Catphan and a QUASAR respiratory motion phantom to quantify the effectiveness of each algorithm when dealing with full projection datasets (3DCBCT). The QUASAR phantom is comprised of an oval shaped body ($30cm \times 20cm \times 12cm$) and moveable cedar lung cylinder, containing a spherical tumor insert (3cm diameter), controlled by a drive unit. Motion was programmed to be in the SI direction with a maximal displacement of 2cm from peak to trough. The breathing period was 15s (4 breaths per minute). The choice
of 15s was motivated by having the slowest possible motion and determining if the binning procedure yielded a sufficient number of projections per bin for 4D imaging. To be more clinically relevant, a more suitable value would be a breathing period of 3-5s. The Catphan phantom projection data already used for HU calibration for each algorithm (see section 2.7.1), was now used to compliment the values obtained from the QUASAR. Fig 3.1 depicts the coronal and sagittal slice from each algorithm’s CBCT reconstructed Catphan image. The regions of interest (ROIs) used to calculate the signal-to-noise (SNR) and contrast-to-noise (CNR) ratios are shown as red and green rectangles, respectively. Fig 3.2 shows the same but for the moving QUASAR phantom. The values of the SNR and CNR for the Catphan and QUASAR phantoms are listed in Table 3.1 and 3.2, respectively. The SNR is depicted as negative since the ROI measured was a negative value.

<table>
<thead>
<tr>
<th></th>
<th>Coronal</th>
<th></th>
<th>Sagittal</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SNR</td>
<td>CNR</td>
<td>SNR</td>
<td>CNR</td>
</tr>
<tr>
<td>FDK</td>
<td>-36.5</td>
<td>38.8</td>
<td>-36.5</td>
<td>40.5</td>
</tr>
<tr>
<td>SART</td>
<td>-27.0</td>
<td>29.5</td>
<td>-32.6</td>
<td>36.8</td>
</tr>
<tr>
<td>ADMMTV</td>
<td>-55.5</td>
<td>62.2</td>
<td>-56.7</td>
<td>61.8</td>
</tr>
</tbody>
</table>

Table 3.1: SNR and CNR for different CBCT reconstructions of the Catphan phantom.

<table>
<thead>
<tr>
<th></th>
<th>Coronal</th>
<th></th>
<th>Sagittal</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SNR</td>
<td>CNR</td>
<td>SNR</td>
<td>CNR</td>
</tr>
<tr>
<td>FDK</td>
<td>-6.5</td>
<td>11.1</td>
<td>-4.5</td>
<td>9.4</td>
</tr>
<tr>
<td>SART</td>
<td>-5.1</td>
<td>9.3</td>
<td>-3.7</td>
<td>8.3</td>
</tr>
<tr>
<td>ADMMTV</td>
<td>-6.2</td>
<td>10.9</td>
<td>-4.6</td>
<td>9.3</td>
</tr>
</tbody>
</table>

Table 3.2: SNR and CNR for different CBCT reconstructions of the QUASAR phantom.
Figure 3.1: The Catphan phantom reconstructed with FDK (left), SART (right), and ADMMTV (bottom) algorithms. The red and green rectangles define ROIs used for SNR and CNR calculations.
Figure 3.2: The QUASAR phantom reconstructed with FDK (left), SART (right), and ADMMTV (bottom) algorithms. The red and green rectangles define ROIs used for SNR and CNR calculations.
3.2 Image Reconstructions

3.2.1 3DCBCT

3.2.1.1 FDK

FDK reconstructions were run with a Hanning filter, \( w(n) \) of 0.5, and a padding filter, \( p \) of 0.1, when reconstructing images from the unmodified projections (pixel size of 0.388mm\(^2\)). If the projections were rebinned (2 by 2 or 4 by 4), the Hanning filter was disabled. Listed in table 3.3 are the reconstruction times for the first fraction CBCT for both the pre- and post-treatment CBCTs for each patient with no projection rebinning. Subsequent scan times were found to be similar to those listed. Rebinning of the input projection data lowered the FDK reconstruction times to around 30s or less.

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Time (s) Pre</th>
<th>Time (s) Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>118.5</td>
<td>118.0</td>
</tr>
<tr>
<td>2</td>
<td>119.4</td>
<td>123.6</td>
</tr>
<tr>
<td>3</td>
<td>122.6</td>
<td>119.7</td>
</tr>
<tr>
<td>4</td>
<td>121.0</td>
<td>121.7</td>
</tr>
<tr>
<td>5</td>
<td>118.5</td>
<td>117.6</td>
</tr>
<tr>
<td>6</td>
<td>117.7</td>
<td>119.4</td>
</tr>
</tbody>
</table>

Table 3.3: FDK reconstruction times for patient’s fraction 1 pre- and post-treatment CBCT scans using the unmodified projections. Times include reading and writing times. Slight variation (±10 s) for further fractions was observed.

The left column in Figure 3.3 contains the 3DCBCT images for the 1st fraction CBCT pre-treatment for one patient (p2_pre1). The particular slices shown intersect the tumor.
3.2.1.2 SART

SART reconstructions were run with 5 iterations \((n = 5)\) and a convergence factor \(\lambda\) of 0.3. Listed in table 3.4 are the reconstruction times for the first fraction CBCT for both the pre- and post-treatment CBCTs for each patient. A positivity constraint was optional and not used in the reconstructions\(^1\). The 3DCBCT

<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
</tr>
<tr>
<td>1</td>
<td>604.5</td>
</tr>
<tr>
<td>2</td>
<td>604.6</td>
</tr>
<tr>
<td>3</td>
<td>608.1</td>
</tr>
<tr>
<td>4</td>
<td>607.9</td>
</tr>
<tr>
<td>5</td>
<td>614.5</td>
</tr>
<tr>
<td>6</td>
<td>611.2</td>
</tr>
</tbody>
</table>

Table 3.4: SART reconstruction times for patient’s fraction 1 pre- and post-treatment CBCT scans using the unmodified projections. Slight variation \((\pm 10 \text{ s})\) for further fractions was observed when recorded.

SART reconstructed images for patient p2.pre1 are shown in the second column of Figure 3.3.

3.2.1.3 ADMMTV

Due to memory requirements ADMMTV reconstructions required rebinning \((4 \times 4)\) of the input projections. The images were reconstructed using parameters of \(\alpha = 0.1, \beta = 1000, n = 10, CGint = 5\). Listed in table 3.5 are the reconstruction times for the first fraction CBCT for both the pre- and post-treatment CBCTs for each patient. An example of these reconstructed images is shown in Figure 3.3 in the far right column.

\(^1\)If positivity was enforced the image quality became marginally better but at a 4x the reconstruction time

72
<table>
<thead>
<tr>
<th>Patient Number</th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8135.2</td>
<td>8140.1</td>
</tr>
<tr>
<td>2</td>
<td>8182.4</td>
<td>8413.6</td>
</tr>
<tr>
<td>3</td>
<td>8337.7</td>
<td>8300.4</td>
</tr>
<tr>
<td>4</td>
<td>7992.6</td>
<td>8130.5</td>
</tr>
<tr>
<td>5</td>
<td>7949.9</td>
<td>7980.6</td>
</tr>
<tr>
<td>6</td>
<td>8289.1</td>
<td>8214.6</td>
</tr>
</tbody>
</table>

Table 3.5: TV reconstruction times for patient’s fraction 1 pre- and post-treatment CBCT scans using the 4x4 re-binned projections. These times are all over 2 hours long.

### 3.2.2 4DCBCT

The FDK algorithm was found to produce images with insufficient image quality and so all 4DCBCT images were reconstructed with iterative algorithms, in particular the ADMMTV algorithm. Binning was done by both amplitude and phase binning with 8 bins. The parameters used for the ADMMTV algorithm were the same listed in the 3DCBCT case. Such parameters were not always the most ideal and require fine-tuning on a case-by-case basis. Figs 3.4 and 3.5 display visible tumor motion in both the coronal and sagittal view. The top left image is bin 1, which, in our model corresponds to max expiration, subsequent images 2-8 follow. For brevity only two 4DCBCT images, p2.pre1 and p5.pre1 fraction, are shown. The motion is also viewable as a movie if preferred. The CT scan for patient 2 with the PTV (in red) and IGTV (in teal) is shown in Fig. 3.6, these will be used later to calculate the tumor overlap. The PTV margins for all patients were 5mm isotropically added onto the IGTV margin.

### 3.3 Breathing Traces

The RPM system recorded the breathing traces for each CBCT scan. Each projection was identified as being either below/above the average chest amplitude and
**Figure 3.3:** p2.pre1 3DCBCT images reconstructed using FDK (left), SART (middle), and ADMMTV (right). Cropped versions of the Varian reconstruction are shown at the bottom for comparison.

either in the inspiration/expiration breathing phase. Fig. 3.7 plots the percentage of projections found below the average amplitude for each breathing trace. Projections are taken at a fixed rate and therefore are directly proportional to time. Fig. 3.8 depicts how many projections were acquired during expiration compared to inspiration.
3.4 Tumor Motion

Tumor motion was calculated as explained in 2.8.3, which was first done by manually contouring the visible tumor from each 4DCBCT image. Following input from radiation oncologists, the method was then changed to use the planning CT GTV contour as the starting basis. As such, the results in this section are divided using both starting points.

3.4.1 Tumor Centroid Motion

3.4.1.1 Manual Contouring

The relative tumor motion for patient 2 (pre1, post, pre2) are shown in Fig. 3.9. The displacement is relative to bin 1 and therefore the bin 1 position is defined to have no displacement. The IS (red), AP (blue), and LR (green) motion for each bin is shown. Two fractions from every patient were analyzed with this method. The maximum displacement found in the IS, AP, and LR axis were recorded and are shown in the first plot in Fig. 3.10. The total tumor motion, D, as define as summation of each vector component (see section 2.8.3) is shown as the second plot in Fig. 3.10. As described in the methods section, the manual contouring for each phase was oversized due to the tendency to over-estimate the GTV volume due to image quality issues.

3.4.1.2 GTV Registration

The same analysis was performed but on a smaller subset of the data due to registration inaccuracies from poor image quality and oversized GTV contour. Image quality is being improved and several suggestions are being worked on to allow for better registration and completion of the full dataset, but is not included in this thesis. This restricted the analysis to three patients: p2, p4, and p5. The relative

\[ IS = \text{inferior/superior}, \ AP = \text{anterior/posterior}, \ LR = \text{left/right} \]
tumor motion, again with bin 1 used as the reference point, but now showing patient 4 (pre1, post, pre2) is shown in Fig. 3.11. Two fractions from the reduced dataset were analyzed and the maximum displacement found in the IS, AP, and LR axis. This is shown in Fig. 3.12

3.4.2 Tumor Overlap Volumes

The overlap of the 4DCBCT tumor volumes with the treatment planning IGTV and PTV is shown in Table 3.6. The contours for each bin were done using the manual contouring method. The average overlap for the first two fractions for each patient are shown in Fig. 3.13

Finally, IS tumor motion and total tumor motion were plotted against the relative tumor location within the lung, shown in Fig. 3.14, as plot 1 and 2, respectively. Correlation calculations found a Spearman value of $\rho = -0.75$

<table>
<thead>
<tr>
<th>Bin</th>
<th>IGTV %</th>
<th></th>
<th>PTV %</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pre1</td>
<td>post</td>
<td>pre2</td>
<td>pre3</td>
</tr>
<tr>
<td>1</td>
<td>92</td>
<td>92</td>
<td>90</td>
<td>91</td>
</tr>
<tr>
<td>2</td>
<td>94</td>
<td>93</td>
<td>93</td>
<td>92</td>
</tr>
<tr>
<td>3</td>
<td>92</td>
<td>97</td>
<td>92</td>
<td>93</td>
</tr>
<tr>
<td>4</td>
<td>96</td>
<td>97</td>
<td>95</td>
<td>96</td>
</tr>
<tr>
<td>5</td>
<td>96</td>
<td>92</td>
<td>93</td>
<td>94</td>
</tr>
<tr>
<td>6</td>
<td>91</td>
<td>94</td>
<td>93</td>
<td>93</td>
</tr>
<tr>
<td>7</td>
<td>91</td>
<td>93</td>
<td>90</td>
<td>93</td>
</tr>
<tr>
<td>8</td>
<td>89</td>
<td>94</td>
<td>91</td>
<td>93</td>
</tr>
<tr>
<td>Average</td>
<td>93</td>
<td>94</td>
<td>92</td>
<td>93</td>
</tr>
</tbody>
</table>

Table 3.6: Percentage overlap with each phases GTV and iGTV (PTV) for patient 2. Taking into account contouring uncertainty and image quality issues, the error on the above % overlap values is estimated to be 2-5%. A value of 100% indicates the tumor volume remained contained within the treatment volume (e.g. PTV) 100% of the time. The average is rounded to the nearest percent.
(\rho = -0.76) and p-values of 0.0019 (0.0015) for the total tumor motion (IS tumor motion) plots. A value of 0\% relative tumor position indicates the tumor is touching the diaphragm, 100\% would mean at the top of the lung. This finding is not unexpected as tumors close to the diaphragm tend to exhibit more motion compared to tumors in the upper lobe of the lung.
Figure 3.4: 4DCBCT reconstruction for patient 2 (p2_pre1). Binning starts with bin 1 in the top left, corresponding with maximum expiration.
Figure 3.5: 4DCBCT reconstruction for patient 5 (p5_pre1). Binning starts with bin 1 in the top left, corresponding with maximum expiration.
Figure 3.6: The CT scan for patient 2, axial (top left), sagittal (top right), coronal (bottom). The PTV (red) and IGTV (teal) are shown on top of the tumor. There are some visible motion artifacts at the diaphragm and the tumor. The image was acquired with a voltage of 120kVp, mean tube current of 80 mA, effective tube current-time of 20mAs, and a slice width of 2.5mm.
Figure 3.7: The percentage of projections taken below the average chest amplitude reading from the RPM. A value above the blue dotted line (50%) indicates it spends more time in the lower portion of the tumor motion. A perfect breathing pattern would have a value of 50.
Figure 3.8: The percentage of projections acquired from the expiration portion of the breathing cycle. A value above the blue dotted line (50%) indicates the tumor spends more time in the expiration breathing portion than the inspiration portion. A perfect breathing pattern would have a value of 50%.
Figure 3.9: The tumor displacement at each breathing bin for patient 2. The fractions shown are the p2_pre1 (top left), p2_post (top right), and p2_pre2 (bottom).
**Figure 3.10:** In the first plot, the maximum tumor displacement for each component is shown: AP (blue), IS (red), LR (green). In the second plot, the total tumor displacement $D$ for the first two fractions of each patient is shown. For both plots, the patients are separated by the grey dotted line such that every two data points is a different patient. The x axis defines the fraction that was used.
Figure 3.11: The tumor displacement at each breathing bin for patient 2. The fractions shown are the p2_pre1 (top left), p2_post (top right), and p2_pre2 (bottom).
Figure 3.12: Similar to Fig. 3.10 but now done using the GTV registration method. Similarly, the first plot shows the maximum tumor displacement for each component: AP (blue), IS (red), LR (green). In the second plot, the total tumor displacement $D$ for the first two fractions of each patient is shown. For both plots, the patients are separated by the grey dotted line such that every two data points is a different patient. The x axis defines the fraction that was used.
Figure 3.13: The average overlap for the first two fractions of each patient with the IGTV (blue) and PTV (red). The overlap with the PTV 100% within uncertainty. The IGTV overlap hovers around 90%, indicating that there are times when the 4DCBCT contour of the tumor does exceed the boundaries of the IGTV defined at planning. This may be from motion or an actual shift from the tumor that is account for the extra margins from the PTV.
Figure 3.14: Total (left) and IS (right) tumor motion plotted against the relative tumor position. A value of 0% relative tumor position was defined to be at the top of the diaphragm and 100% top of the lung. Spearman values of $\rho = -0.75$ ($\rho = -0.76$) and p-values of 0.0019 (0.0015) for the left (right) plots were found, suggesting a significant correlation.
Chapter 4

Discussions

4.1 Image Quality

The quality of the reconstructed images (both 3D and 4D) rely on many variables. These include the algorithm used, the algorithm parameters, the number of projections, the type of binning, the pre-processing of projections, the breathing pattern, and the projections themselves.

4.1.1 Algorithms and Tuning

The three algorithms tested all were successfully able to perform 3DCBCT reconstruction on the moving QUASAR phantom and static Catphan phantom. The SNR and CNR were calculated for each algorithm using both phantoms and the results indicate that overall the ADMMTV algorithm performed the best, followed by the FDK algorithm, and lastly the SART algorithm. While individually the results from SNR or CNR can be misleading, the combination of the two makes a useful metric when comparing image quality between images. It is not very surprising that the algorithms performed well using the full dataset (836 projections for the QUASAR, 656 projections for the Catphan). This is particularly true for the FDK algorithm, whose performance is more strongly dependent on the num-
ber of projections that iterative algorithms [27, 33], and can be seen as the FDK algorithm performs particularly well on the QUASAR phantom, on par with the ADMMTV algorithm 3.2. One metric that was not used but demonstrates an advantage of using total variation minimization algorithms (such as ADMMTV) is edge detection. In image reconstruction the ability to keep defined edges sharp rather than smoothing them out is very desirable [55].

The complexity of the algorithms increases from FDK to SART and even more so when moving to the ADMMTV algorithm. This can be demonstrated by the tuning parameters available for each (Table 2.2). The particular set of variables used were chosen by iteratively looping over a range of possible parameters (and holding all other parameters constant) and viewing the output reconstruction image. When that particular parameter was sufficient, the next parameter was looped, and so forth, until all parameters were found. This time-consuming procedure was not performed on each image but rather a suitable set of parameters were found for each algorithm and used for the entirety of the thesis. It should be noted that these parameters are not guaranteed to be optimal and, in fact, the optimal set will change on a case-by-case basis. There is no ability to know a priori what parameters will perform best and as such one of the easiest ways to improve image quality would be to uniquely fine tune all parameters for each reconstruction image. With the additional complexity also comes additional computational requirements. While the FDK and SART algorithms can be run on CPU (although not ideal), the ADMMTV algorithm must be run on a GPU to keep the times to something manageable. This is further magnified when performing 4DCBCT and each patient has 8 volumetric images being reconstructed. The 3DCBCT images were used for registration (CT-CBCT) and as shown all algorithms produced high quality CBCT images. For simplicity, speed, and image quality, the FDK algorithm was used as the default for the 3DCBCT images.
4.1.2 Projections

The number of projections was the largest factor in determining image quality. This is first exemplified by the fact that only the ADMMTV algorithm produced adequate 4DCBCT images, as there are not enough projections for adequate FDK reconstruction. The binning procedure, either by amplitude or phase, reduces the number of projections to some fraction of the total amount. The more bins used, the fewer the projections, and the worse the image quality, but the motion is theoretically more defined. The idea is to get the most bins possible while still maintaining sufficient image quality to extract the tumor position in each bin. In this thesis 8 bins were chosen and seemed to be a good balance between the two factors. In literature this number varies and depends on the scan parameters used and number of projections being acquired.

The exact binning method, as defined in section 2.4.3, uses either phase or amplitude as its criterion for binning. Amplitude binning enforces an equal distribution of motion per bin but an unequal distribution of projections, while phase binning does the opposite. Therefore in terms of accuracy, amplitude binning is better as each bin has the same amount of motion, and given enough projections should mean less motion blur per bin. However, due to the way in which projections get bunched in the max/min expiration phase, it is often only these two phases that are produced with adequate image quality. The other bins are reconstructed with too many artifacts, rendering the “accuracy” argument for using amplitude null. Therefore phase binning was chosen as the primary mode of binning and on average offered good image reconstruction per bin. In an ideal case, a large amount of projections binned by amplitude or a large amount of projections binned into many phase bins would produce equally impressive 4DCBCT images. Provided there are enough projections per bin, the motion found from either method was the same [55]. One problem that affects both binning methods is the bunching of projections by projection angle. That is, projections of the same anatomy tend to be taken near similar angles (or complimenting), essentially oversampling that phase space and undersampling everywhere else. An approach
to remedy this was performed by [5], where the projections were spread out more evenly and resulted in better image quality. Finally, an increase in the total number of projections by altering the scan time or other scanning parameters would have a very large effect [8]. It seems that many studies use projection counts of 1200 or 2000 (2-4 minute scans), a great deal more than the 656 used in this thesis. However, this comes at a cost as the increased number of projections will result in a higher patient dose.

The reason the ADMMTV algorithm performs well with low statistics is due to the principles of compressed sensing and the regularization that takes place in the algorithm. If no regularization is performed the information embedded in a given projection ends up in the Fourier transform of their reconstructed volume, with each projection roughly related to a particular Fourier coefficient. If a projection is missing in the reconstruction process, its corresponding coefficient is not modified. If too many projections are missing, so too are the corresponding frequencies in the Fourier transform and the image cannot be fully reconstructed (Nyquist sampling rate). However, regularization is able to correct the Fourier coefficients that correspond to missing projections by “spreading out” information from other projections and partially compensate for the missing information. This requirement allows for the image to be reconstructed (even under the Nyquist sampling rate), provided some additional information is known, such as the number of non-zero voxels. This is useful for 4DCBCT where there is substantial undersampling.

The method by which the raw projection data is read into the algorithm can also have consequences. The pixel dimensions from the CBCT projections are 1024 × 768 (0.388mm²). Knowing the geometry of the OBI, the reconstructed voxel size at isocenter can be smaller than the size at the detector, by the factor of $SDD/SAD = 1.5$. The pixel dimensions for the reconstructed volume were chosen to be 512 × 512 × 240 (0.88mm²). If the detector data is rebinned (4 × 4) the dimensions that are used during the reconstruction of the CBCT image are 256 × 192 (1.556mm²). To find the ideal voxel size the geometry is taken into
account, $1.556\text{mm}/1.5 = 1.037\text{mm}$. Selecting a voxel size above this value will undersample the data and is to be avoided. The value of $1.037\text{mm}$ is known to be the ideal voxel size at the isocenter. To allow for some deviation away from the isocenter $0.88\text{mm}$ was chosen as the final voxel size.

This re-binning of the raw projection data leads to a number of positive consequences: the projection data is reduced by a factor of 16 ($4 \times 4$), the read input times decreases, and the reconstruction algorithms ran quicker. It also has an effect on the image quality. Applying a re-binning algorithm essentially acts like a low-pass filter. In doing so it helps reduce scatter while increasing contrast. This is the reason why the Hanning filter is turned off for the FDK algorithm if re-binning is used, there is no need to apply another low-pass filter. For more detailed explanation on the relationship between CBCT reconstruction, image quality, and scan parameters, see [43].

### 4.2 Breathing Traces

The frame rate at which projections are acquired is fixed. This means that the number of projections taken is proportional to time, see 1.2. Therefore the number of projections provides information about how long a tumor stays in a particular portion of a breathing phase. In the patient data analyzed in this thesis, it was found that all tumors spent more time in the expiration portion of the breathing cycle. The other indicator, which varied for each patient, was the fraction of time the tumor is in the lower half of the breathing cycle. While, these results are very preliminary it suggests that careful monitoring of patient breathing may be used to weight the 4DCBCT bins differently. For example in patient one, the fraction of time spent in the lower portion of the breathing phase (averaged over the 4 scans) is 75%. This indicates that even though the tumor does stay within the high dose region it does so by spending a majority of its time in the lower portion of the breathing cycle. Perhaps this upper half region may be receiving more dose than necessary. It should be noted that this patient was the outlier of the group, with all other patients falling within 40% to 60%.
Finally, observing trends in the breathing traces may indicate whether or not 4DCBCT will be successful prior to reconstructing. One suggestion would be to look at the periodicity or reproducibility of the signal by using a recurrence plot or some quantification of the Fourier transform. The shape of the breathing trace directly affects the binning (both amplitude or phase). In the event of erratic breathing, the phase trace will be unreliable and noisy, but the amplitude data will still provide a functional binning method. The main effect on amplitude are the occasional deep inspiration or expiration breath which will act as outliers but as long as they remain infrequent should not have too large an effect.

Such variety in the breathing traces motivate the need for 4DCBCT imaging (or preferably real time imaging), if the patient’s breathing can vary from fraction to fraction, or pre1 to post, it seems reasonable that so too would the breathing trace during the planning CT and treatment days change.

4.3 Overlap

The overlap metric verified that the tumor remains fully contained in the high dose region. A value of 0% would indicate the tumor was fully outside the high dose region, while a value of 100% would indicate full overlap (containment). Using it as a verification tool for PTV overlap any value that significantly dipped under 1 (not within error) may warrant an investigation. For IGTV overlap, the restriction could be relaxed slightly perhaps to something closer to 90%. The reason being that the PTV margin takes into account shifts and uncertainties in the both the IGTV and Gross Tumor Volume for one phase (pGTV). If the 4D CBCT GTV was contained 100% of the time by the IGTV, one might argue that the margins could be reduced.

One of the biggest challenges of this project was to define the pGTV on the 4DCBCT images. This was initially done by manually contouring the contour using ITKsnap [62]. The planning GTV contour’s volume was used as reference for contouring on the 4DCBCT. This helped to mitigate the “overcontouring” problem caused by the blurriness in the CBCT images. However, recall that the GTV
is defined as the visible tumor volume from the CT scan. It does not relate to one particular phase but instead may include many (assuming the tumor moves). Therefore it is too large and also does not accurately represent the true pGTV.

The correct procedure would be to get an oncologist to contour one phase of the 4DCT tumor volume (pGTV - phase GTV) and use that as the initial volume contour. The 50% pGTV would be the most ideal, as the tumor in that location was found to be the closest in size in a breath hold CT study, i.e. it’s closest to the size of the tumor at stand still (the real size). [67] However, the fact that even with the over-generous manual contours the overlap with the PTV was 100% was encouraging.

4.4 Tumor Motion

The tumor motion values followed the expected sinusoidal shape to some degree. Inferior/superior (IS) motion was found to have the largest displacement, followed by anterior/posterior (AP) motion, and then left/right (LR). Significant correlation between tumor motion and position of the tumor in the lung was demonstrated (i.e close to the diaphragm vs apex). Generally, tumors closer to the diaphragm will experience more total displacement due to respiratory motion. However, this is not always true and the fact exceptions or outliers exist, limit the predictive capabilities of such a correlation [68]. Finally, the total motion within error was found to be under 1cm of maximum tumor displacement for the majority (86%) of the patient cases.

The best way to reduce uncertainty is to increase the motion resolution, increase image quality, and/or begin with a better initial contour for CBCT tumor tracking. A few ways to achieve this without altering the clinical settings:

- Reduce scatter (Boellard method)
- Quality permitting, increase bin number (up to 10? more?)
- Apply a median filter to projections (this needs to be done before any rebinning)
• Is linear interpolation the best re-binning method or will others provide better performance (bi-linear, tri-linear, bi-cubic).

• Make use of prior image information such as the 3DCBCT, provided our regularization is strong enough to correct it. (the PICCS algorithm is a popular choice) [69]

• Find better performing algorithm parameters (specific to each image)

• Test Amsterdam Shroud phase extraction for potentially better binning
Chapter 5

Conclusion

In conclusion, 4DCBCT image reconstruction was shown to be possible on the Varian TrueBeam (v1.6) in a clinical environment. The moving lung tumor volumes for 6 SABR patients were shown to be fully enclosed within the high dose region (PTV) as visualized on the pre-treatment and post-treatment verification 4DCBCT. The ability to conclude that the tumor volume, in all phases, remained within the PTV 100% of the time provides treatment staff with confidence that the lung treatments are being accurately delivered.

The thesis was roughly divided into three main sections: an introduction, method, and results of the 4DCBCT imaging modality. An introduction to 4DCBCT with necessary background information was provided in Chapter 1. Patient motion and the problems that arise from it were used as motivation for implementing 4DCBCT. The relevant theory as well as equipment used were provided in this section.

Chapter 2 described the process of reconstructing 4DCBCT images, from image acquisition to tuning algorithm parameters, or from start to finish, respectively. A 4DCBCT lung protocol was developed, with input from radiation therapists, and is described briefly. This protocol was used for all scans in this thesis. The pre-processing, in particular the re-binning (or down-sampling), of projections had a noticeable effect on the reconstructions. It lowered the memory storage for
each set of projections by a factor of 16, which due to the large volume of data was important for data handling and long term storage. Subsequently, it also allowed for faster reconstruction times for all algorithms. It also improved the contrast in the reconstructed images by acting like a low-pass filter. The re-binning/down-sampling was chosen to be $4 \times 4$, by both geometrical and pixel size arguments. The reconstruction algorithms used (FDK, SART, and ADMMTV) demonstrated that both old and new methods can reliably reconstruct 3DCBCT images. For 4DCBCT only the ADMMTV algorithm sufficiently reconstructed the images and therefore was the only algorithm used to reconstruct the patient 4DCBCTs. It was found that amplitude and phase binning while describing similar anatomy do not produce the same image quality across each 4DCBCT bin. This is due to the distribution of projections and how amplitude binning results in the max and min expiration bin holding a majority of them, leaving the other bins severely undersampled.

Chapter 3 revealed the results from the analysis on relative tumor motion and tumor overlap. In both, the main challenge was the initial step of defining the visible tumor volume in each 4DCBCT phase (pGTV). The first method, manual contouring, successfully covered the pGTV but due to deformation and over-estimating the contour suggested instead to use the GTV from the planning CT as the initial contour and register it to the 4DCBCT tumor volume for each phase. As the GTV does not represent any one phase (pGTV), it too was deemed to be imprecise. Regardless, once the contour of the pGTV was defined (with uncertainty from the over-estimation), the centroid of the contour was used to determine the relative tumor motion and the volume of each was used to calculate the overlap with the IGTV and PTV contours.

Due to the time involved for image reconstruction, the 4DCBCT method used in this thesis would not be suitable for real-time clinical use. However, it does serve a useful offline tool for verifying the tumor remains in the high dose region. In order to make it more clinically viable the time needed for reconstruction would need to be drastically reduced. This would mean relying on the FDK algorithm, or
some modified version that would be capable of producing high quality images. With the current clinical settings, and hence low projection count, the author is not sure it is possible.

Some ideas for future work include:

- Testing of different algorithms with optimized parameter tuning.
- Using the TrueBeam mode Thorax Slow would spread the projections out and also provide more overall projections (180 more) helping to improve image quality, with only a small increase in the imaging dose to the patient.
- Improvements to image quality will allow for less dose (fewer projections) and the same tumor tracking capabilities, or better tumor tracking with finer motion resolution.
- Determine the effect of changing scanning parameters with iterative algorithms.
- With a signal extracted from either cardiac or liver motion, 4DCBCT should be viable for such sites. Cardiac-correlated 4DCBCT could work with an electrocardiogram (ECG), liver motion may involve tracking a fiducial marker.
Bibliography


Appendix A

Overview and General Instructions for 4DCBCT Protocol

A.1 Introduction
This overview lists the various steps that need to be taken in order for the acquisition of 4D CBCT images of patients. The steps do not deviate too much from normal clinical imaging protocols, but we have highlighted the areas in which an additional step is needed. Contained in this document are the necessary extra steps in all phases of the patient’s treatment cycle: planning CT, treatment planning, and then patient CBCT imaging and treatment at the unit.

A.2 Planning CT / CT Simulation

- Refer to CT simulation procedure SBRT lung, and follow the same procedure.
  H:\RADTXGRP\Planning\CTsimulator\CT Sim procedures\Stereotactic\SBRT Lung CT Sim Procedure.doc

- The only additional step is to add documentation of location of RPM box (general anatomic region) in the patient’s set-up notes, so that it can be
reproduced on the treatment unit.

A.3 Treatment Planning

Ensure that the following is completed in addition to regular protocol:

- Turn on the “Use Gated” checkbox (refer to Fig.1)

![Figure A.1: Selection of “Use Gated” checkbox in plan properties](image)
• Location: Right click on plan name, open properties window, under general tab, midway down the page

• Set the Imaging Vert set to 50cm (This needs to be confirmed, it may already by the normal procedure)

• Check with planning on the tolerance table - OBI – appears to be VC standard? (Also needs confirmation)

• Currently for CBCTs, the Thorax mode is used, if many of the projections are invalid Thorax Slow mode may be selected.

• Indicate in the Technical Notes that this is a 4DCBCT/RPM plan.

• The naming convention follows the standard procedure. (ex: LungFIN)

A.4 Treatment Unit

The extra time required pre-CBCT to go through the following procedure (going through the Breathing Trace Acquisition windows that the TB will pop up) takes approximately 3 min.

A.4.1 Patient Setup

• Refer to SBRT lung treatment process and follow similar procedure.
  (The location of this file is on the POD VCC radiation team site, under RT techniques, subfolder SBRT)

• Patient education: The patient should already be familiar with the setup from their planning CT.

• After the SSD has been verified and the patient has been set up, place the RPM as noted by CT sim staff (see set-up notes).
• The patient should be breathing shallowly, at which point go set up the RPM.

• Mode up CBCT per normal

A.4.2 RPM Setup

When the patient is opened up on the unit, the computer will automatically start the RPM configuration wizard. (See Fig.3) Follow the steps below and refer to the diagrams to see what buttons should or should not be selected.

NOTE: If the RPM configuration page doesn’t load it may have been since the couch needed to be centered or some other event needed to happen first. In this case, you will need to select the play/pause button at the top of the page when you are ready for the RPM. (See Fig. 2) If it loaded automatically, skip this step.

Figure A.2: Button to press if the configuration window didn’t automatically open up. Located on the top toolbar, near the right end.

1. On the first page ensure that the following are selected:
   • “Create a new Tracking Protocol using default values”
   • “amplitude gating”

2. Click Next

3. On the following page (See Fig.4) ensure the following are (un)selected on the second page:
   • select “periodic breathing technique”
Figure A.3: Page 1 with noted selections marked in red.

Figure A.4: Page 2 with noted selections marked in red. Uncheck the other boxes as indicated in the document.

- **unselect** “enable visual patient motion monitoring”
- **unselect** “enable audio coaching instructions”
- **unselect** “enable visual coaching instructions”
- Enter 0 for the “Breathing Predictive Filter [%]”

4. Click Next

5. Click Next (Fig.5)
6. At this point, the system will begin tracking. It takes a few moments (roughly 30s, maybe slightly more) to begin.

7. On this page (see Fig.6), ensure the following are performed:
   - Open the gating window thresholds to 5.0cm and -5.0 cm (wide open)
   - Record the reference curve by clicking “Start”

8. Allow the system to record the patient’s breathing for several cycles.

9. Press the “Stop” button and then the “OK” button.

At this point all the necessary steps have been completed and you may continue in your normal proceedings to acquire the CBCT.

Some final notes:
   - To acquire kVp images, you will need to change the trigger option to “no trigger”, in order for the kVp imager to take a projection.
Figure A.6: Page 4 with noted selections marked in red. Allow a few cycles for the tracking before stopping it and pressing “OK”.

- Once the CBCT is acquired and the 3D/3D match is performed, the RPM box may remain on the patient during treatment (no need to enter the room and remove it).

- Finally the SABR treatment can proceed as normal.

- Post CBCTs (when performed) will also require the tracking of the RPM.

### A.4.3 Subsequent Treatments

Since the plan is gated, this means that the RPM breathing trace will have to be acquired for every one of the 4 fractions (TB will require it). After the first fraction, the gating parameters are stored in memory and the initial set-up windows will not appear (saving time on the unit). The breathing trace acquisition should take only 1-2 minutes instead of 3 minutes (estimated time for the 1st fraction).
A.4.4 Backup Procedure

As we want as little interference in both the therapist’s workload and patient treatment, in the event of an error/issues, a backup procedure was created. Follow the scenario that applies on when the RTTs/RO decide not to do 4DCBCT.

A.4.4.1 Scenario 1: Before 1st Treatment

- Physicist unapproves plan
- Physicist turns “off” check box
- Physicist removes reference to RPM box placement in set-up notes and/or technical notes and/or planning aim and narrative.
- Physicist “plan approves”
- RTT “treatment approves”
- Continue without 4DCBCT

A.4.4.2 Scenario 2: After 1st Treatment

- Physicist creates “plan revision”, this retires RPM plan and creates a new copy called LlungFIN:1 which is unapproved.
- Physicist turns “off” check box
- Physicist removes reference to RPM box placement in set-up notes and/or technical notes and/or planning aim and narrative.
- Physicist “plan approves”
- RTT “treatment approves”
- Modified plan will have correct number of remaining fractions
Appendix B

XML Geometry Format

Shown below is an example of the CBCT projection geometry stored for each patient scan as an XML file as was described in Section 2.3.3. The projection angle can be found by adding 90° to the gantry angle. Shown are the first three projections acquired during a CBCT. The file will have similar listing for the other 653 projections. The angle increases by 0.5° for each projection shown but does deviate slightly throughout the scan. The angles are measured in degrees, all other values have units of mm.
Figure B.1: An example of the projection geometry stored as an XML file.
The parameters for the first three projections are shown.