Comparing target volumes used in radiotherapy planning based on CT and PET/CT lung scans with and without respiratory gating applied

by

Tamarisk du Plessis

Submitted in fulfillment as part of the requirements for the degree of Master of Science Medical Physics in the Faculty of Health Sciences

University of Pretoria

Student number: 04404874

Supervisor: Prof A. Janse van Rensburg

June 2012

Declaration

I, Tamarisk du Plessis, hereby declare that this dissertation, submitted in fulfillment as part of the requirements for the degree of Master of Science Medical Physics, in the Faculty of Health Sciences, at the University of Pretoria, is entirely my own work unless otherwise referenced or acknowledged. This document has not been submitted for qualifications at any other academic institution.

Signed: _____ Date: _____

Acknowledgements

First and above all I would like to thank God, my heavenly father, for the talents, gifts and opportunities He has given me to accomplish this study. Secondly, I would like to thank my husband Greg, for his continuous support, encouragement and belief in me.

I want to extend a special thank you to my supervisor Prof Ado, for his encouragement, his suggestions, and especially for his help with some of the technical aspects of this study.

I am very thankful to all radiation workers who contributed to this study in their field of expertise. To the four oncologists, Dr. Bassa, Dr. Hocepied, Dr. Soares and Dr. Westerink, for invaluable advice and for delineating multiple target volumes. To the planning radiographers, Juanita, Stephne, Cecile and Katinka, for taking the time to train me on the treatment planning system, for scanning the lung patients and for assisting me in creating treatment plans. And to all the nuclear radiographers for assisting me with gated lung scans on the PET/CT scanner.

Lastly, I would like to thank all the patients who volunteered to participate in this study for without them this study would not have been possible.

Contents

List of tables

List of figures

List of abbreviations

3D	Three Dimensional
4D	Four Dimensional
ARC	American College of Radiology
CRT	Conformal Radiation Therapy
CT	Computed Tomography
CTV	Clinical Target Volume
DICOM	Digital Imaging and Communication in Medicine
DSC	Data Sufficiency Condition
DVH	Dose Volume Histogram
^{18}F-FDG	Fluorine-18 Fluorodeoxyglucose
GTV	Gross Tumor Volume
ICRU	International Commission on Radiation Units and Measurements
IMRT	Intensity Modulated Radiation Therapy
LSO	Lutetium Oxyorthosilicate
NEMA	National Electrical Manufacturers Association
OAR	Organ at Risk
PACS	Picture Archiving and Communications System
PC	Personal Computer
PET	Positron Emission Tomography
PTV	Planned Target Volume
QUANTEC	Quantitative Analysis of Normal Tissue Effects in the Clinic
RCCT	Respiration Correlated Computed Tomography
RT	Radiation Therapy / Radiotherapy
SRS	Stereotactic radiosurgery
SUV	Standard Uptake Value
TPS	Treatment Planning System
WB	Whole Body

CHAPTER I – INTRODUCTION

The human lungs move three dimensionally during normal respiration.[8] If a thoracic tumor is present, it will automatically follow lung movement. Typically, tumors can move between 1 and 3 centimeters during respiration.[24]

When a lesion in the lung is the object of interest during a CT or PET/CT scan, it will appear larger, more widely spread and with a lower calculated SUV in PET than it actually is, due to respiratory motion.[19] Respiratory motion also often causes spatial misalignment between the PET and CT data on a PET/CT scan, since it is acquired in different time frames.[20] Physicians are therefore limited by these subjective images, which may result in less accurate localization.

Also, the accurate delineation of a target to be treated in radiotherapy is crucial in determining the outcome. If a part of the tumor is not treated, a local recurrence can occur while morbidity is increased if too much normal tissue falls within the treated field. Therefore, it follows that an improved imaging modality will result in more accurate delineation and improved treatment.

When acquiring CT scans, patients can be asked to hold their breath for the few seconds it takes to acquire the image (breath-hold technique). Since it takes several minutes to acquire a PET scan (up to 30 minutes for a whole-body scan) or to receive radiotherapy treatment, this will be impossible for the patient. Therefore while acquiring a PET/CT scan or receiving radiotherapy, patients continue with their normal breathing cycle, which may include uneven breathing or even coughing due to poor lung function.

Except for the disadvantages regarding the lesion size, position and SUV (in PET only) in diagnosis, respiratory movement may also degrade the resolution, contrast and reproducibility of CT and PET/CT scans and cause image artifacts.[19]

A well researched and accepted solution for improving image quality, diagnostic accuracy and the effectiveness of radiotherapy for patients with lung lesions is to apply respiratory

gating to CT and PET/CT scans.[20,26] All these studies on 4D respiratory gating was however done abroad and not in the South African public health sector.

Steve Biko Academic hospital has respiratory gating equipment associated with the PET component of the Siemens Biograph True Point PET/CT scanner at its disposal. Gating can also be simulated on the CT component of the PET/CT scanner and on a radiotherapy CT scanner by applying the breath-hold technique.

The aim of this study was to compare the differences between delineated clinical target volumes of respiratory gated and ungated CT lung scans. The primary objective was to acquire gated CT and PET/CT scans and to measure and compare the clinical target volumes. The secondary objective was to analyze the influence that gated studies will have on the way patients receive radiotherapy treatment and to determine whether it will be meaningful to purchase and implement respiratory gating systems on CT and PET/CT scanners in the South African health sector (radiation oncology departments).

Previous research studies done in other countries showed a decrease in the clinical target volume of up to 34% and also a significant improvement in localization, when gating was applied to CT and PET/CT lung scans.[19] Gated radiation therapy treatment has also been introduced and successfully implemented on selected patients in various countries. The patient parameters required to successfully implement gated radiation therapy are a periodic and reproducible respiratory cycle which can be maintained during treatment.[26]

When a centre claims to be 4D, it must include the whole spectrum of four dimensional techniques, which include; 4D simulation/imaging, 4D planning and evaluation, 4D set-up, 4D quality assurance and 4D treatment.[14] Chester Ramsey also made an important statement: “Before respiratory gated radiotherapy can be implemented clinically, the efficacy of the procedure must be justified. The magnitude of dosimetric and geometric uncertainties associated with respiratory motion must be identified to determine if gating can provide an advantage over conventional treatment techniques”.[24] This study can therefore be considered as the first step of 4D implementation in the South African public health sector.

Ungated CT thoracic and PET/CT whole-body scans are currently acquired at Steve Biko Academic hospital to diagnose patients with lung lesions. After diagnoses, patients will

receive a second CT scan on a CT radiotherapy couch, from which planning for radiation therapy treatment is done. These RT CT scans are acquired without using any respiratory motion reduction technique.

This study consists of three sections. In the first section, four-dimensional respiratory gated CT images were obtained and delineated with 4D software. The full-inspiration and full-expiration phases of the gated scans were then fused to obtain ungated scans which were also delineated. The gross target volumes of the gated phases were compared to the ungated GTVs to determine the primary objective of this study. Apart from demonstrating the effectiveness of the 4D delineation software, yet another aim was to determine the influence that 4D imaging will have on radiotherapy treatment planning. One of the 4D study sets was therefore imported to the treatment planning system. IMRT treatment plans were created on both the gated and ungated scan and clinical parameters such as dose-volume-histograms were used to evaluate the plans.

In the second section of this study, respiratory gated CT scans were simulated by applying the breath-hold technique to patients with lung cancer. The technique was applied during full-inspiration, which in essence represents the maximum peak of the sinusoidal respiration waveform. An ungated scan was also acquired during normal respiration. The clinical target volumes were identified and compared to the clinical target volumes of the gated scans. The principal aim of this chapter was to quantitatively determine the influence simulated respiratory gating will have on the clinical target volumes of lung cancer patients.

For the third section of the study, respiratory gated PET scans were acquired on a PET/CT scanner to evaluate external, non-technical parameters that influence respiratory gating.

All three sections' results were considered to determine whether it will be meaningful to permanently implement a 4D respiratory gating system on CT scanners in the South African public health sector (radiation oncology departments) and to use these images for target delineation in radiotherapy planning.

CHAPTER II – LITERATURE OVERVIEW

1. Introduction

Two types of movement occur in the human body during scanning or radiotherapy treatment; inter-fractional and intra-fractional motion. Inter-fractional motion occurs over a longer period of time (few hours or days) and might change during the course of radiotherapy treatment. For example, a bladder filling could change the positions of organs on a daily basis. Intra-fractional motion occurs over a short period of time and during a single treatment, for example the movement in the thorax due to respiration.[10]

Inter-fractional motion can be manually controlled, for example by emptying the bladder before each treatment, but intra-fractional motion is more difficult to manage. This is because when, for example, a lung lesion is the object of interest during a CT or PET/CT scan, it will appear larger and more widely spread than it actually is due to intra-fractional respiratory motion.[19]

There are various respiratory motion managing methods currently available such as added margins in treatment planning, mechanical compression devices, active breathing control, motion tracking and respiratory gating. A team in the USA is at present busy to develop the concept of 4D dynamic-virtual-patient-modeling which might be the next step in improving movement management.[14] In South Africa however, gating is still the latest solution for respiratory movement.

Respiratory gating can be applied to CT and to PET scanners and both these modalities were discussed in this chapter. It has been regarded as two separate modalities, even though it can be combined to form a dual modality scanner. Only CT scans are used for radiation therapy treatment planning, since anatomical detail and relative electron density information is required and not necessarily metabolic information.

2. Respiratory gating

Various motion reduction techniques have been developed to improve image quality degraded by respiratory motion in CT and PET scans. The simplest is the breath-hold technique used during CT acquisition. It is however not always successful in patients with lung lesions due to poor lung function. Other, more sophisticated techniques used in CT are Respiratory-correlated CT, 4D-CT and 4D-CT with respiratory gating. Two methods have been introduced to correct for respiratory motion artifacts in PET; Respiratory correlated dynamic PET and Gated PET.[20]

The term "gating acquisition" refers to data being acquired and arranged into segments according to signals received. Ungated scans provide stationary images taken at a specific moment in time, but with gating applied to images, lesion and other organ movement can be followed with time. Consequently when 3D volumes are acquired with respect to time it results in 4D scanning for which a 4D imaging modality is essential.

Three different respiratory trigger devices are currently available; a pressure sensor, an optical device and a look-down video camera.[12] The pressure sensor, or load cell, is placed inside a pocket of an elastic belt and positioned around the patient's diaphragm. This detects the pressure changes caused by lung expansion and reduction during inspiration and expiration. A study has proved that the elastic respiratory belt and pressure device provide an adequate trigger, even though optical devises are most often used for gating.[18] The optical device consists of an infrared camera mounted at the end of the CT or PET/CT couch. The camera tracks the vertical displacement of two infrared markers mounted on a plastic block which is placed on the patients' abdomen.[20] Another less popular technique is to mount a look-down video camera to the gantry of the scanner. The respiratory cycle is then obtained through segmented video analysis of the thorax movement.[12]

The number of gates used in previous respiratory gated studies varies significantly across the globe, from 2 to 20 gates. In 2009 a mathematical function was developed to calculate the optimal number of gates required to obtain motion free images as a function of lesion size and motion displacement.[4] A recent study simplified this complicated calculation and proved that the optimal number of gates to use for time based studies is six, and for amplitude based studies, eight.[9]

CT and PET gating techniques differ significantly. Nonetheless, it is possible to gate both scans on a PET/CT scanner, since they are acquired and reconstructed independently. Both scanners' gating techniques are discussed below.

2.1 CT respiratory gating technique

Computed tomography respiratory gating can either be prospective or retrospective. Prospective gating refers to the data acquisition triggered by specific events in the respiratory cycle such as end-inspiration, end-expiration and the transition point between inspiration and expiration. Image data is then sorted into the correct segments. Retrospective gating refers to the acquisition of data through all phases of respiration. Correlation and registration of the respiratory cycle with the CT images are then only performed after acquisition.[22]

Most of the recent generation computed tomography scanners commonly use helical protocols with continuous image acquisition to acquire 3D scans. A single 3D helical scan (ungated) however does not provide any respiratory information since it is merely a snapshot in time.[1] A 4D CT scanner, where 3D images are obtained with respect to time, is therefore essential to acquire respiratory gated scans.

Two acquisition modes are available for 4D CT imaging; helical- and cine-acquisition. A helical scan acquires data while the table translates at a constant speed programmed by the pitch factor (the relationship between the table motion, distance and the rotation speed of the CT gantry). A cine scan acquires data continuously at the same table position and uses a step-and-shoot method of table translation.

2.1.1 Helical mode acquisition

Single- and multi-slice scanners can be used for respiratory gated image acquisition, but it was proven that gated 4D CT single-slice scans with helical acquisition result in image gaps between images of the same phase.[21] When 4D CT multi-slice helical scans are used instead, the helical pitch can be significantly reduced. This prevents the image gaps and meets the data sufficiency condition (DSC) introduced by Tinsu Pan.[22]

The DSC concept states that for each CT table position data has to be acquired for one full respiratory cycle plus the duration of data acquisition for helical image reconstruction. When the DSC is satisfied, all scans will provide complete coverage of the image volume without any gaps between the slices.[22]

The pitch factor *p* should obey equation 2.1, where T_g is the gantry rotation time and T_b is the breathing cycle time, for full scan reconstruction to ensure that no image gaps exist and the DSC is satisfied.[22]

$$p \leq \frac{T_g}{T_b + T_g} \qquad [2.1]$$

When half-scan reconstruction is used, the pitch factor should satisfy equation 2.2.[22]

$$p \leq \frac{T_g}{T_b + \frac{2}{3}T_g} \qquad [2.2]$$

To compare image quality, it is necessary to mention that the pitch factor for CT scans with the breath-hold technique is usually between 0.75 and 1.5.[22]

2.1.2 Cine mode acquisition

Cine mode acquisition protocols are available on some modern scanners and offer an alternative to acquire gated CT scans. The cine acquisition mode collects multiple low dose slices of the same anatomical region over time.[1] The x-ray beam is only on during a specific couch position and switched off when the couch translates from one position to the next.[21] A step-and-shoot acquisition technique is therefore used in conjunction with the cine mode protocol.

A number of images will be reconstructed at each CT couch position, depending on the number of slices on the multi-slice CT. The scan time for each step has to be equal to or greater than the average respiratory cycle plus the duration of data acquisition for image reconstruction to avoid image gaps.[21]
To obey the DSC, the time for each table step T_t, should satisfy equation 2.3 for full scan reconstruction and 2.4 for half scan reconstruction.[21,22]

$$T_t \geq T_b + T_g \qquad [2.3]$$

$$T_t \geq T_b + \frac{2}{3}T_g \qquad [2.4]$$

Figure 2.1 is a schematic indication of gated cine acquisition on a 4-slice CT scanner. For a more detailed explanation of cine mode acquisition, please refer to reference 21.

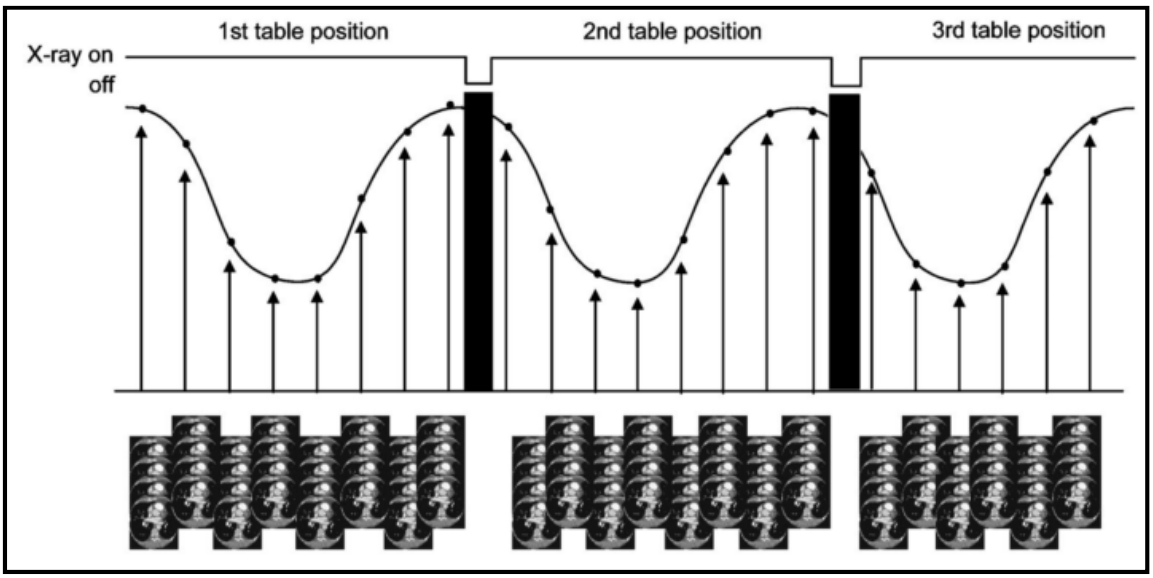

Figure 2.1: Schematic graph of gated cine CT indicating 3 table positions with each position longer than one respiratory cycle plus the duration for image reconstruction. Each dot represents four image reconstructions on a 4-slice CT scanner. Eight phases are acquired in each respiratory cycle. The x-ray beam is off during table translation. (21. Pan, et. al. (2004))

2.1.3 Helical versus Cine acquisition

Helical acquisition is faster than cine 4D CT for large acquisition areas, but for small areas the cine CT acquisition time will be less. This is because cine CT needs time between two steps for table translation, while helical CT needs one extra breathing cycle at the end of data acquisition to ensure gap free images.[22]

Helical mode is more flexible as it allows data reconstruction at any position in the volume of data acquisition, where cine mode allows reconstruction only at the positions of data acquisition. Cine mode uses data from a single respiratory cycle only to reconstruct images, while helical mode may use data from one or two breathing cycles for reconstruction.[22] Dose efficiency in respiratory gating can be defined as the duration of x-rays used for the image reconstruction to the total x-ray time for the data acquisition. The dose efficiency for cine mode is 100%, since the beam is switched off during table translation. For helical mode the efficiency will always be less than 100% because of the additional breathing cycle required to reconstruct gap free images.[22]

Cine 4D CT is superior to identify irregular breathing patterns. The location of the irregular breathing cycle can easily be identified and the dose can be kept a minimum when only the specific locations are rescanned.[22]

It is suggested that for current systems prospective gating with end-expiration as trigger, be used with helical 4D CT and retrospective gating with cine 4D CT. Prospective gating is however recommended for all future studies. The only set back is that some systems cannot yet accurately identify the end-expiration phase, and care has to be taken to identify the correct phases before reconstruction.[22]

2.1.4 Respiration-correlated computed tomography

There are various techniques as mentioned before, to obtain CT data at a specific position in the respiratory cycle. 4D respiratory gated scans require a trigger signal to acquire images at specific phases during the respiratory cycle. Another method worth discussing is the respiration-correlated-CT (RCCT) technique where 3D image data sets are acquired at multiple respiratory phases with a spiral scan.

The principle behind RCCT is that a respiratory wave form is recorded concurrently with the spiral CT scan acquisition. The CT data is then categorized together with the respiratory wave form. CT slices are retrospectively reconstructed at several phases of the respiratory cycle, imitating four dimensional imaging.[13] Figure 2.2 provides a schematic illustration of aligning the spiral CT scan with specific positions in the respiratory cycle. In this illustration the scan was categorized with the end-expiration, 50% expiration and end-inspiration phases, but any other phase positions can also be selected after acquisition.

The respiratory cycle can be recorded with a block emitting infrared light which is placed on the patients' abdomen and recorded with an infrared sensitive camera. This is similar to the optical device used for gated CT, but no trigger is sent from the respiratory monitoring system to the CT scanner.

During reconstruction, only specific phases of the respiratory cycle will be considered. As much data as is possible should be obtained to ensure sufficient data for good quality images

without gaps. A very small pitch factor will cause the table to translate slowly and the smallest possible slice thickness should be selected. Faster gantry rotations will cause better temporal resolution but might cause larger gaps. A smaller pitch factor will however decrease the gaps but will not influence the temporal resolution.[13]

The advantage of RCCT over gated CT scans is that it is much faster and only 3D software is required. The disadvantage is that the total dose to the patient is approximately three times more than with gated CT. The image acquisition time on some scanners is also restricted due to heating of the x-ray tube. The RCCT technique is particularly useful to determine the specific respiratory phase for which lesion motion is minimal, that can be used for gated treatment planning.[13]

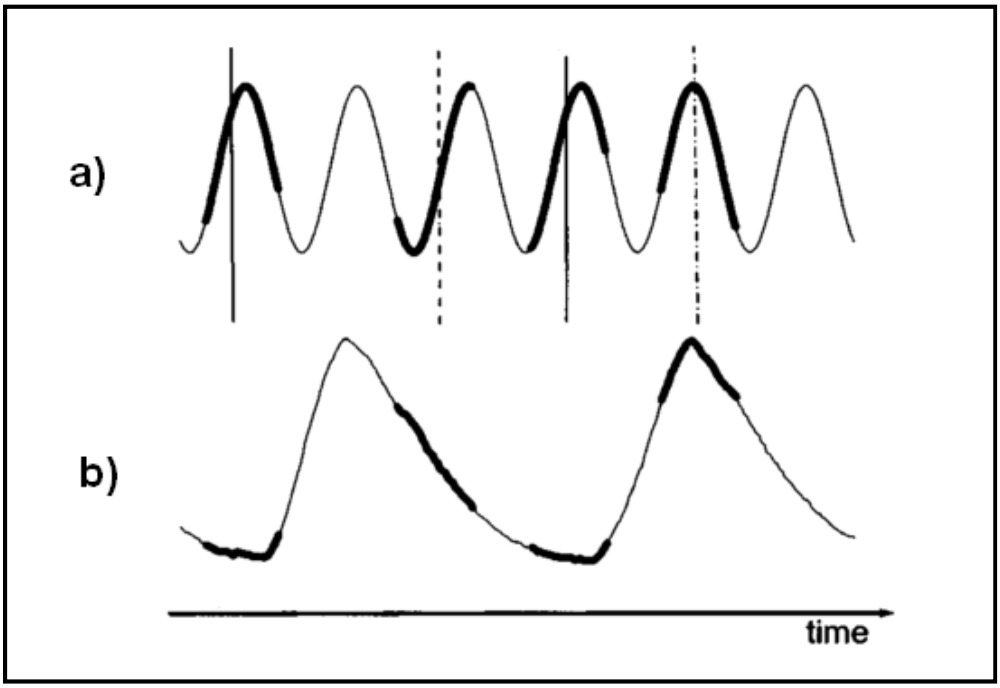

Figure 2.2: Schematic illustration of categorizing the spiral CT (a) with the recorded respiratory wave form (b) using the RCCT technique (13. Ford (2003))

2.2 PET respiratory gating technique

Positron Emission Tomography gating is based on the same principles as ungated PET imaging. Only the acquisition and reconstruction protocols will differ from those of ungated scans.

List mode image acquisition is used for gated PET studies so that data can be sorted and reconstruction can be done after acquisition. This is in comparison to frame mode acquisition generally used for ungated studies. In frame mode acquisition all interactions with the detector are accumulated to form a pixel. When a certain limit (e.g. time frame) is reached, the acquisition is stored and the next frame will begin to accumulate interactions. In list mode all interaction positions are stored in a list with periodic time markers. Only once the acquisition is completed can data be sorted and reconstructed.[7]

Respiratory gated reconstruction can be done with one of two principle methods; amplitude-based gating or time-based gating. Figure 2.3 is an illustration of time- versus amplitude-based gated respiratory curves. In time-based studies each respiratory cycle is divided into an equal number of gates. The gates in each respiratory cycle have identical time increments, but the gate width amongst each respiratory cycle might differ, depending on the total time of the cycle. Amplitude-based gating divides each respiratory cycle in an equal number of gates with fixed gating positions, depending on the amplitude of the respiratory signal. The time difference between each gate may therefore differ, because of uneven respiration. The number of events in each gate remains equal, for both time- and amplitude gating, but accurate motion detection can only be guaranteed in amplitude-based gating.[9]

Various variations of the two principle methods for reconstructing list mode data are used for gated scans. Seven of the most popular methods were compared in a study and the variable-amplitude-based gating method was found to be the most effective.[8] This is based on the criteria that it captures the respiratory motion best while the noise levels are kept constant amongst all respiratory phases.

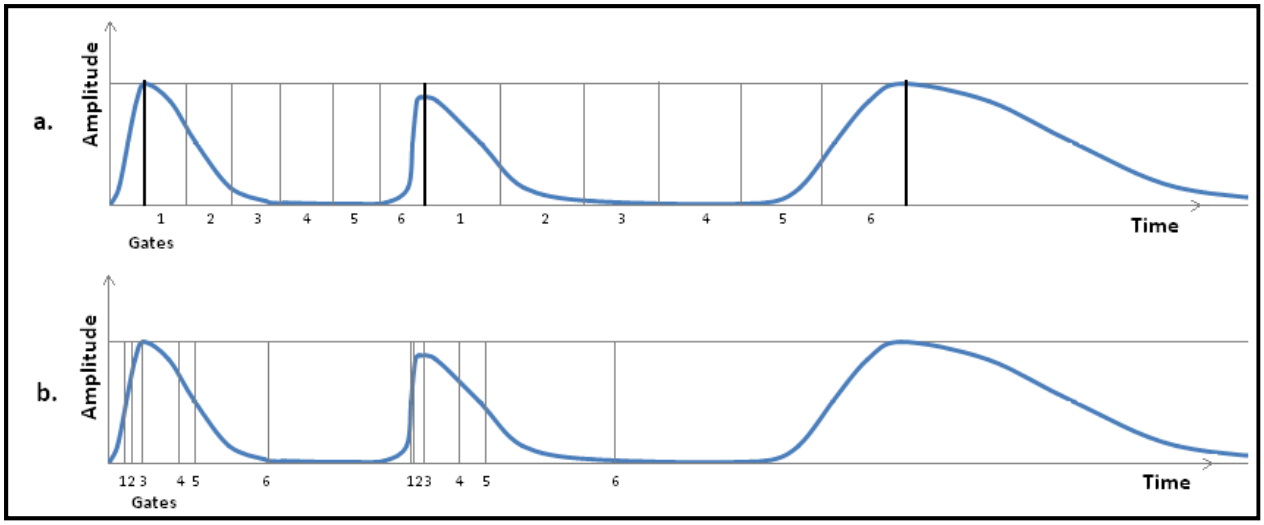

Figure 2.3: a.) Time based respiratory graph with 6 gates of equal width within each respiratory cycle. b.) Amplitude based respiratory graph with 6 gates positioned at 50%, 75% and 100% inspiration and expiration respectively. The gating positions in each cycle are equal and predetermined.

Gated PET imaging was proved to have many advantages above ungated imaging and some of the most important ones include;[19]

- Improved image quality (contrast, resolution and noise)
- Less image artifacts
- More accurate lesion position and size
- Increased Standardize-uptake-value (SUV)

When assessing PET scans, the Standard-uptake-value (SUV) is considered to be a useful, but not definite tool to evaluate the lesion status. When a SUV of more than 2.5 (measured with a filtered back projection reconstruction algorithm) is measured, it indicates a higher probability of malignancy.[19] By applying respiratory gating, the SUV is increased to a more reliable value which allows physicians to more accurately identify the tumor staging.[19]

2.3 Respiratory gating system

The function of the gating system is to detect the respiratory signal, interpret and display the signal and to export the signal to the imaging modality. The scanner software will then interpret the signal and acquire information accordingly.

A commonly used gating system for CT and PET/CT scanners is the Anzai respiratory system. The Anzai AZ-733V system was also installed with the PET/CT scanner at Steve Biko Academic hospital and its specialized hardware and software is described in Chapter V, section 2.1.

The system software has various changeable parameters that will influence the quality of the gated scans. It can manually be adjusted by the user for each individual patient:[2]

1. Sweep point: The estimated first point of each respiratory cycle.
2. Estimated respiratory waveform: This enables the system to draw estimated waveforms from sweep point to sweep point.
3. Moving average: This is to calculate and to draw the respiratory waveform. Smaller values will result in steeper waveforms, while bigger values have smoother waveforms.
4. Range of normal respiratory level: When the waveform is out of this range, gating will be terminated.
5. Range of normal respiratory rate: When the respiratory rate is out of this range, the gating will be terminated.

The Anzai system can be used for respiratory as well as cardiac gating and has five different gating modes to choose from.[2]

- Gating MODE 1: This allows outputting a gate signal at each peak (inspiration or expiration) of the respiratory wave form. A maximum of two gates can therefore be acquired at each respiration cycle. (Figure 2.4)
- Gating MODE 2: This allows outputting a single gate signal at an optional phase position and level of the respiratory waveform. (Figure 2.5)
- Gating MODE 3: This allows outputting a gate signal at an optional starting and ending point of the respiratory waveform. The gate width is therefore determined by the start and end points rather than by a preset time. (Figure 2.6)

- Gating MODE 4: This allows outputting a gate signal at maximum 10 points of optional phases and levels within one cycle of the respiratory waveform. This mode was applied to all patients in this study. (Figure 2.7)
- Gating MODE 5: This allows for outputting a gate signal without using the respiratory waveform information, but only E.C.G. signals. (Figure 2.8)

The width of each gate can manually be selected in each of the above modes. Mode 1, 2 and 3 can also be used in conjunction with an E.C.G signal for cardiac gating should it be required.

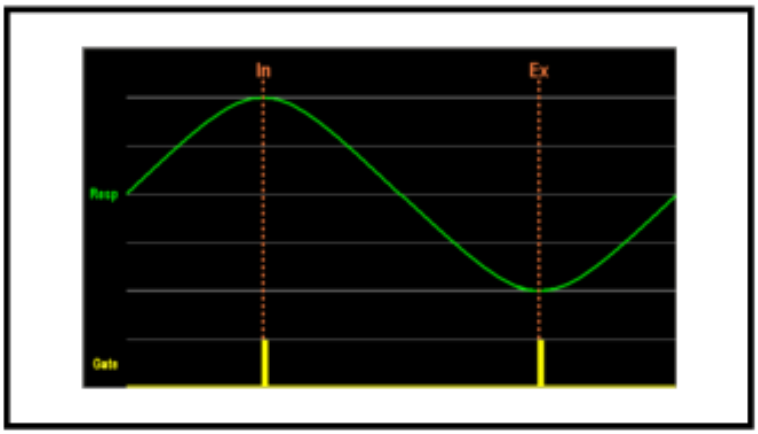

Figure 2.4: Anzai gating MODE 1

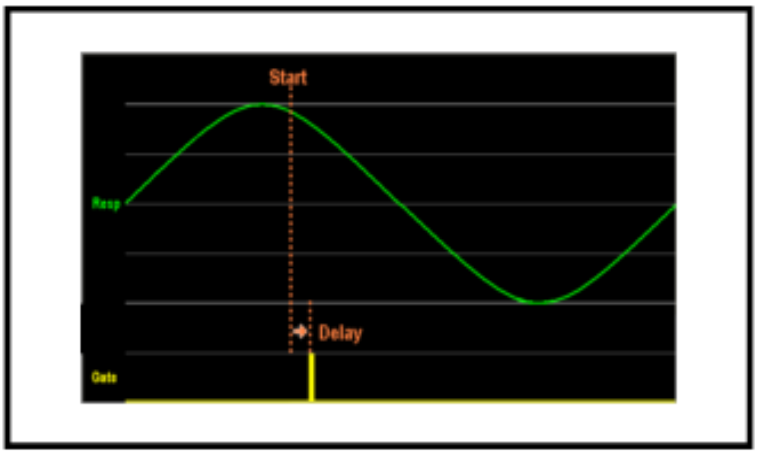

Figure 2.5: Anzai gating MODE 2

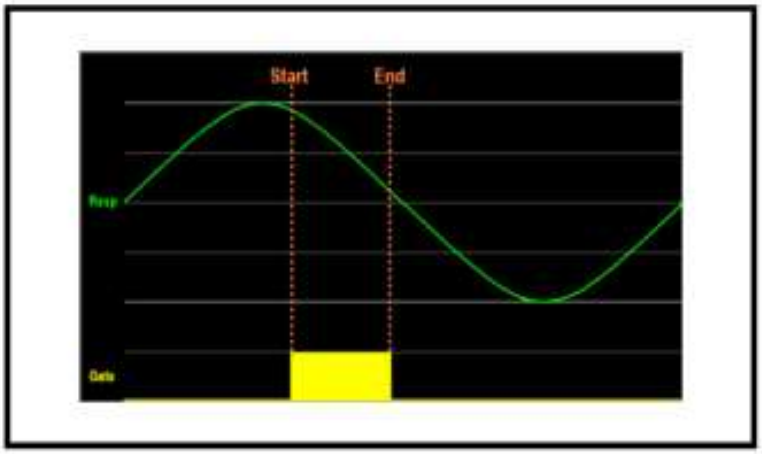

Figure 2.6: Anzai gating MODE 3

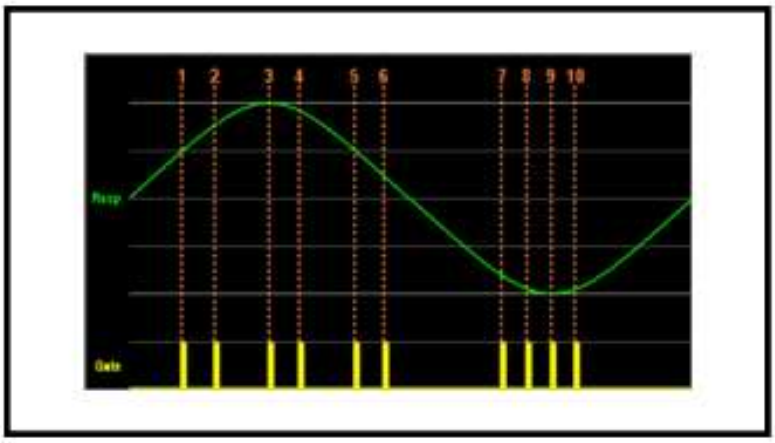

Figure 2.7: Anzai gating MODE 4

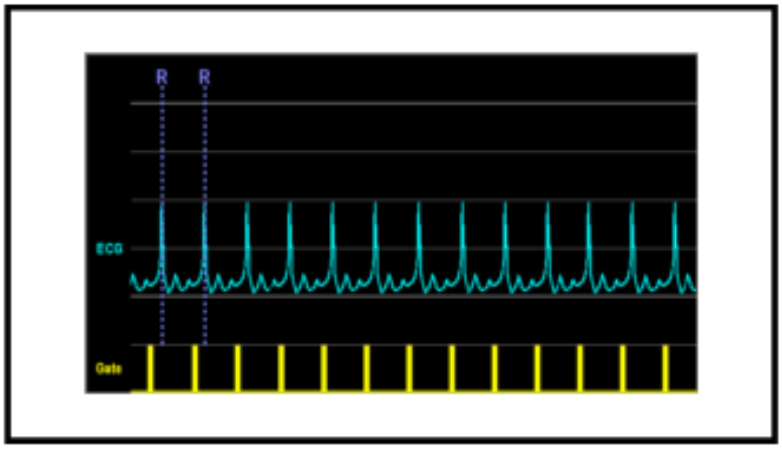

Figure 2.8: Anzai gating MODE 5

3. Radiotherapy treatment planning

3.1 Imaging

Data from the CT and PET/CT scanners is stored in DICOM (Digital Imaging and Communication in Medicine) format. DICOM is an international standard for handling, transmitting, storing and printing information in medical imaging.

In 1982 the ARC and NEMA developed standards for interconnection of digital imaging devices. Shortly after this in 1985, the first version, Version 1.0 was published. It specified a hardware inter-phase which only allowed point-to-point image transmissions. It also designed a data dictionary (set of rules for encoding information) and created a set of commands (SEND, GET, MOVE, etc.) to initiate transactions. These commands were linked to three kinds of data sets: image, text and graphics. By 1988 an upgraded Version 2.0 emerged where semantic rules by which messages are organized were included. In 1992 Version 3.0, which is known as the ARC-NEMA DICOM standards, was released. The first DICOM standards encouraged open system interconnection of imaging equipment over standard networks, but maintained compatibility with point-to-point networks. An important addition to Version 3.0 is that it focused on the problem of conformance which eliminated incompatibility between different systems. It included the concept of object oriented design and it developed and implemented the picture-archiving-and-communication system (PACS).[3,5] The DICOM standards were established with Version3.0 and only updated from then onwards. The latest DICOM version, Version 2009, was published in January 2010.

DICOM differs from other digital data formats in that it saves information into data sets which ensures that important patient information cannot be separated from the data. A DICOM data object can contain multiple attributes (e.g. patient name, ID, etc.), but hold only one attribute containing pixel data. Each one of these pixel data attributes can consist of multiple ‘frames’ for multi-dimensional, multi-frame images such as PET/CT images.[3] Three- or four-dimensional data can be compressed using various standards such as JPEG.

The ARC-NEMA DICOM standards (Version 2009) consist of 18 related parts described independently. Table 2.1 gives a layout of the different DICOM parts and a short description of each part.

Table 2.1: Summary and description of the 18 ACR-NEMA DICOM standard parts[3]

Part	Title	Description or Scope
Part 1	Introduction and overview	Describes the overall structure of the standard.
Part 2	Conformance	Specifies the general requirements which must be met by implementations claiming conformance.
Part 3	Information object definitions	Specifies a number of Information Object Classes which provides an abstract definition of real-world entities applicable of communication to digital medical images and related information.
Part 4	Service class specification	Describes how a conformance statement to an individual service class is structured and defines the characteristics shared by all service classes. Some of these services classes include image storage, retrieval and printing [(a)].
Part 5	Data structures and encoding	Specifies the construction and encoding of the data set information resulting from the use of information objects (Part 3) and service classes (Part 4).
Part 6	Data dictionary	Centralized registry which defines the collection of all DICOM data elements available to represent information.
Part 7	Message exchange	Specifies the operations and protocol used to exchange messages over the communication support services defined in Part 8.
Part 8	Network communication support for message exchange	Specifies the communication services and upper layer protocols necessary to support communication between DICOM applications as specified in Parts 3, 4, 5, 6 and 7.
Part 9	Point-to-point communication support for message exchange	RETIRED – Depreciated in the latest implementations in favor of those alternatives remaining in the standard.
Part 10	Message storage and file format for media interchange	Specifies a general model for the storage of medical imaging information on removable media.
Part 11	Media storage application profiles	Specifies specific subsets of the DICOM standards to which an implementation may claim conformance.
Part 12	Media formats and physical media for media interchange	Facilitates the interchange of information between digital imaging computer systems in the medical environment.
Part 13	Print management point-to-point communication support	RETIRED – Depreciated in the latest implementations in favor of those alternatives remaining in the standard.

Part	Title	Description or Scope
Part 14	Grayscale standard display function	Specifies a standardized display function for display of grayscale images.
Part 15	Security and system management profiles	Specifies security and system management profiles to which implementations may claim conformance.
Part 16	Content mapping resource	Defines the templates and context groups used elsewhere in the standards.
Part 17	Explanatory information	Consists of informative and normative annexures containing explanatory information.
Part 18	Web access to DICOM persistent objects (WADO)	Specifies a web based service for accessing and presenting DICOM persistent objects.

[(a)] DICOM consists of many different service classes which include; Storage, Storage commitment, Query/Retrieve, Modality work-list, Modality performance procedure step, Printing and Off-Line Media.

3.2 Treatment planning techniques

Relative electron density information is essential for radiation therapy treatment planning, but it was proved that fused PET/CT scans provide more accurate information than CT images alone.[6] Specialized treatment planning software is however required to use PET data for planning.

Ungated CT scans are generally used in South African hospitals to do treatment planning from but gated CT scans can possibly improve the treatment planning results. It can either be used to track the movement of the tumor throughout the respiratory cycle so that tighter planning margins can be applied, or to do gated radiation treatment planning from.

Gated radiotherapy treatment is especially favorable to patients receiving treatment in the thorax and abdomen region which are both greatly influenced by respiratory motion. Gated treatment is mostly planned at end-inspiration or end-expiration phases depending on the diagnosis, but it is known that anatomic positions are more reproducible at end-expiration.[13]

3.2.1. Contouring

In 1978 the ICRU developed a universal dose specification protocol (Report no. 29) to define various volumes in treatment planning.[16] Reports no. 50, 62, 71 and 78 followed (1993, 1999, 2004 and 2007) with the latest publication, Report no. 83 which includes IMRT planning, in June 2010.[15] The planning target volume (PTV) consists of the gross tumor volume (GTV), the clinical target volume (CTV) and an extra margin for planning. The internal target volume (ITV) was introduced in Report no. 62 and can be defined as the CTV plus a margin taking into account the uncertainties of size, shape and position of the CTV.

Once an image is acquired and reconstructed, a radiation oncologist will delineate the clinical target volume ensuring that the gross target volume is completely covered. This process is called contouring. A planning radiographer will then add another margin when designing the treatment plan so that finally the PTV will be treated with radiation. The derivation of CTV to PTV margins is normally based on an institutional protocol.

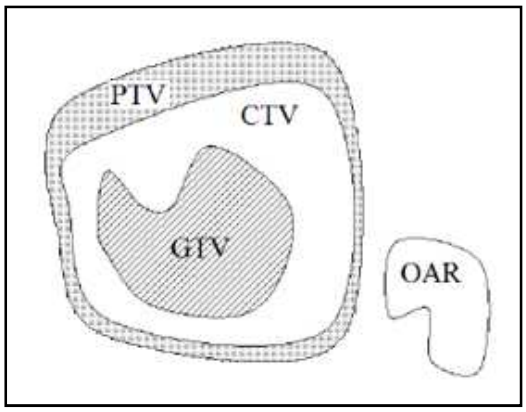

Figure 2.9: Schematic illustration of the various volumes used in radiation treatment planning

Because of the uncertainty of the exact tumor position and tumor volume in the lung due to respiratory movement, treatment planners have to add a large margin around the CTV to obtain a confident PTV. A 1.5 – 2.0 cm margin in the upper lobe and a 2.5 – 3.0 cm margin in the lower lobe are added on average for both 3D conformal and for IMRT ungated planning. When respiratory gated techniques are applied, this margin can be significantly reduced to 0.5 cm.[25] However, at Steve Biko Academic hospital, CTVs are only delineated for radical treatment of lung lesions. Should the patient be palliative, a simple 2-field opposing plan will be created from 2D films without spending time on contouring.

3.2.2. 3D conformal radiation therapy and IMRT

To generate treatment plans for radical treatment of lung tumors, either 3D conformal planning or Intensity Modulated Radiation Therapy (IMRT) can be used. 3D conformal techniques will mainly be used to plan ungated radiotherapy treatment from ungated scans. In exceptional cases where the tumor is attached to a stationary anatomical structure such as the chest-wall, IMRT planning might be used for ungated therapy. IMRT planning is however always recommended for gated radiation therapy planned from gated scans. This is because non-uniformed fluences are optimized to deliver a high dose to the PTV and an acceptable low dose to the surrounding tissue.

3D conformal radiation therapy (CRT) is based on three dimensional anatomic information with a dose distribution that conforms as closely as possible to the target volume and ensures minimum dose to normal tissue. Forward treatment planning is used for 3D-CRT in conjunction with one of two model-based dose computation algorithms; Convolution-

superposition method or Direct Monte Carlo method. A variety of parameters such as beam direction, beam weighting, number of fields and intensity modifiers can be used by the treatment planner to optimize the dose distribution in 3D-CRT.[16]

Intensity Modulated Radiation Therapy is primarily used for patients receiving gated radiation therapy for lung tumors. With this treatment technique, non-uniform fluences can be delivered to the patient from any given position of the treatment beam to optimize the composite dose distribution.[16] IMRT planning relies on automated, iterative optimization techniques. The optimization process takes into account the absorbed-dose constraints and weights the importance of the PTV and the organs at risk (OARs). Inverse planning techniques are used for IMRT, where iterative algorithms calculate the optimal dose distribution from pre-defined constrain parameters.[15]

3.2.3. Dose limits

For many years oncologists had to rely on their clinical experience and intuition to select field sizes and doses for radiation therapy, but in 1991 a group of physicians summarized their experiences in an article called the “Emami Paper”. In 2010 the QUANTEC (Quantitative Analysis of Normal Tissue Effects in the Clinic) articles were released which is an updated version of the Emami papers.[17]

Many critical organs are in close vicinity of the lung. Organs at risk to consider during treatment planning for lung tumors will be the normal lung tissue, the heart, the spinal cord and at some hospitals the oesophagus is also considered. Table 2.2 is a summary of the dose limits for these organs as indicated by QUANTEC.

Table 2.2: Dose limits for critical organs during radiation therapy treatment (QUANTEC)[17]

OAR	Volume segment	Irradiation type[(b)]	Dose (Gy) OR Dose/Volume parameters	Notes on D/V parameters
Lungs (Normal tissue, excluding PTV)	Whole organ	3D - CRT	V20 < 30%	For combined lung. Gradual dose response.
	Whole organ	3D – CRT	Mean dose = 7 Gy	Excludes purposeful whole lung radiation.
	Whole organ	3D – CRT	Mean dose = 13 Gy	
	Whole organ	3D – CRT	Mean dose = 20 Gy	
	Whole organ	3D – CRT	Mean dose = 24 Gy	
	Whole organ	3D – CRT	Mean dose = 27 Gy	
Heart	Pericardium	3D – CRT	Mean dose < 6 Gy	Based on a single study.
	Pericardium	3D – CRT	V30 < 46%	
	Whole organ	3D – CRT	V25 < 10%	Based on model predictions.
Spinal cord	Partial organ	3D – CRT	Dmax = 50 Gy	Including full cord cross section.
	Partial organ	3D – CRT	Dmax = 60 Gy	
	Partial organ	3D – CRT	Dmax = 69 Gy	
	Partial organ	SRS	Dmax = 13 Gy	Partial cross section irradiated.
	Partial organ	SRS	Dmax = 20 Gy	
Oesophagus	Whole organ	3D – CRT	Mean dose < 34 Gy	Based on RTOG[(c)] and several studies
	Whole organ	3D – CRT	V35 < 50%	A variety of altered threshold doses have been implicated.
	Whole organ	3D – CRT	V50 < 40%	
	Whole organ	3D – CRT	V70 < 20%	

[(b)] 3D – CRT = Three dimensional conformal radiotherapy

SRS = Stereotactic radiosurgery

[(c)] RTOG = Radiation therapy oncology group

3.3 Treatment plan evaluation

Dose volume histograms (DVHs) were developed in the late 1970's to evaluate 3D conformal, IMRT, electron and heavier particle treatment plans.[15] Differential and cumulative DVHs are available but cumulative DVHs are most commonly used and will also be the DVH of choice in this study.

A cumulative DVH is a plot of a volume of a given structure (V) receiving a certain absorbed dose (D) as a function of dose. Each point on a relative cumulated DVH can be described by equation 2.5 where D_{max} is the maximum dose in the structure.[15]

$$DVH_{rel\ cum}(D) = 1 - \frac{1}{V}\int_0^{D_{max}} \frac{dV(D)}{dD} dD \qquad [2.5]$$

An absolute cumulative DVH can easily be obtained by multiplying equation 2.5 with the total volume of the structure.

DVHs are widely used and allow for direct comparison between different plans of a patient.[15] It is important to mention that DVHs are not an ideal representation of 3D doses since they ignore all organ specific information and do not provide biological data. In other words it assumes that all regions are of equal functional importance and do not account for anatomic variation during therapy.[17]

Another accepted evaluation method is to calculate the absorbed dose at the ICRU reference point. However, the fundamental reason for the use of dose-volume reporting in IMRT is that the coverage of the PTV by a specific absorbed dose can be better controlled through optimized planning.[15] Dose volume reporting is therefore also preferred for 3D-conformal planning for similar reasons and also to maintain constant practice.

Dose-volume constraints should be used for each defined volume to obtain more accurate planning aims. The dose at 95% of the volume (D_{V95}) is mainly used at Steve Biko Academic hospital for evaluating the PTVs.

CHAPTER III – 4D RESPIRATORY GATED CT

1. Introduction

Four dimensional respiratory gated imaging has been introduced to improve the visualization of moving tumors. These 4D scans can also be used for target volume delineation which cause treatment plans to conform closer to the lesion of interest because tighter margins can be applied. In addition gated radiotherapy can also be applied from 4D scans. Various CT vendors have a gating option available on the scanner.

The aim of this chapter was to determine the difference in the GTVs of 4D gated scans to ungated scans in order to demonstrate the effectiveness of 4D delineation software. Another objective was to determine the influence that 4D imaging has on radiotherapy treatment planning.

4D planning can either be done on individual phases or on maximum intensity projections (MIP).[14] For the purpose of this chapter, delineation was done on individual phases only. By delineating each phase individually, one could determine whether the target volume changes (increase or decrease) with respiration. Radiation oncologists at Steve Biko Academic hospital assumed that the target volumes do not change in size due to respiration but that only the location changes.

2. Methodology

2.1 Equipment

2.1.1 CT scanners

4D gated CT scans were acquired on four different 4D CT scanners at various institutions. The four scanners were all from different vendors and included a Toshiba, a Phillips, a GE and a Siemens CT scanner. It was assumed for the purpose of this study that the type of scanner would have no influence on the target volumes since the same gating technique was used on all four scanners.

The gated 4D study sets were obtained and imported from abroad by ELEKTA, CMS since 4D CT scanners have not yet been implemented in any South African training hospital.

2.1.2 Focal 4D

To delineate and calculate all respiratory gated GTVs, Focal4D Version 4.62.00 (ELEKTA, CMS® Inc, Missouri, USA) was used.

Focal4D allows the import of 4D image sets and also provides tools for intuitive and easy visualization and contouring. Apart from the standard viewing options available, this 4D version includes multiple robust toolsets such as cine view, variable window formats and an automated process for creation of internal target volumes. This software also allows for respiratory phases to be fused for contouring or plan reviewing, although only a single respiratory phase can be exported to the XIO treatment planning system.

2.1.3 Treatment planning system

XIO® Release 4.3.1 (CMS, Inc., St. Louise, Missouri, USA) software was used for treatment planning of the 4D gated scans.

XIO 4.3.1 is a 3D conformal therapy and IMRT planning system with real time visualization of patient anatomy and beam parameters for both photons and electrons. It has multiple

available algorithms for dose calculations such as FFT/Convolution, Clarkson, Multi-Grid Superposition and Fast Superposition. Multi-modality (CT, MRI and/or PET) fusion is also possible on this software should it be required.

2.2 Patient selection and preparation

Four patients were included in this part of the study. All four patients' 4D datasets were obtained from ELEKTA, the company providing the 4D software. There was therefore no control over or record of patient selection and preparation.

All patients included in this study gave consent that their scans may be used anonymously for research purposes. Standard 4D scan procedures and protocols were followed at each scan institution.

2.3 Data acquisition

Cine acquisition mode was used to acquire the respiratory gated CT images. According to the vendor company it was discovered that more consistent images can be obtained with this acquisition mode than with helical gated imaging.

Four individual patients were scanned with CT scanners, each on a CT scanner from a different vendor; Toshiba, Phillips, GE and Siemens. A respiratory gated scan with 10 phases was acquired for each patient. Phases 0 and 5 were the extreme positions (full-inspiration and full-expiration) in the breathing cycle of each patient.

2.4 Data processing

2.4.1 Data transport

Since all study sets were acquired on different CT scanners, the easiest was to import the acquired data from CDs. It was important that these data sets complied with the latest DICOM standards which included Part 10. This part specifies a general model for the storage of medical imaging information on removable media which ensured that the gated images were imported in the correct order.

After target and critical organ delineation, one patient's gated and ungated study sets were transported to the XIO treatment planning computers for planning. The delineated study sets were imported to the TPS via a CD, even though a network connection exists between the Focal 4D and the TPS. This tedious process was necessary because a new directory needed to be created on the XIO TPS for each individual CT scanner and this had not yet been done for the specific CT scanner.

2.4.2 CT target volume delineation

Gross tumor volumes (GTVs) were delineated on the 4D gated scans, instead of the clinical target volumes (CTVs) as would normally be done for treatment planning, because a more objective volume is achievable. The margin added to the GTV to obtain the CTV is a self-determined decision of the oncologist and will likely differ from one gated phase to another and also from patient to patient. One aim of this chapter was to compare the target volumes of one phase to another and it is therefore crucial to delineate the target volumes as accurately as possible with minimal space for errors.

External oncologists delineated the GTVs of three of the patients; Patient 1, Patient 2 and Patient 3. An experienced oncologist from Steve Biko Academic hospital was then asked to delineate the GTVs of the remaining patient, Patient 4.

GTVs were identified separately on all 10 gated phases of each study set. This was to improve the accuracy of the average GTV that will be used for comparison with the ungated

volumes. Delineating all 10 phases was also necessary to determine whether the target volumes changed during respiration.

To obtain the ungated GVTs, the images of phases 0 and 5 were fused. These two phases are the extreme positions in the respiratory cycle and therefore it could be accurately assumed that realistic ungated images were obtained.[26] This fusion was necessary because no ungated scans for these patients were acquired. The ungated GTVs were then delineated on the fused images and saved.

Critical organs such as the normal right and left lung tissue, the heart, the oesophagus and the spinal cord, were identified.

2.4.3 Treatment planning

Treatment planning was done for one of the four patients. Patient 2 was selected because this patient had a percentage difference between the gated and the ungated GTV, closest to the average percentage difference of the four patients.

An oncologist prescribed an IMRT radiation treatment dose of between 60 and 66 Gy in 30 fractions for Patient 2. For the gated treatment plan, a 0.5 cm planning margin was added to the GTV to obtain the PTV and for the ungated plan a 1.2 cm margin was added. These isotropic margins are according to the margins used for IMRT planning in the apex area of the thorax at Steve Biko Academic hospital. Even though the margins have non-uniform movement from one phase to the next, it was decided to follow standard protocol for each individual phase.

Phase 5 of the gated scans was selected to perform gated treatment planning. A four field plan was created on the gated scan and saved as a template. The template was then copied to the ungated scan and some adjustments were made to conform to the bigger, ungated PTV. Both plans were designed with the planning aim that GTVs receive the prescribed dose of 66 Gy and that the PTVs receive a dose of 60 Gy at 95% of the volumes.

2.5 Data evaluation

The Focal software automatically calculated the GTVs of each of the 10 gated phases for each patient respectively. The average volume (in cubic centimeters) of the 10 phases was calculated to obtain the most accurate gated GTV for each patient. The GTVs of the ungated scans were also calculated by the software. The average gated GTV and the ungated GTV was compared for each patient using equation 3.1, where V_g and V_u are the gated and ungated volumes respectively.

$$\%\,difference = \frac{V_u - V_g}{V_u + V_g} \times 100\% \qquad \text{[Eq. 3.1]}$$

After IMRT treatment planning was done on one of the patients, dose volume histograms were calculated. The doses received by all the critical structures (heart, left and right lung normal tissue, oesophagus and spinal cord) were recorded from the DVHs of both the gated and ungated plans. The dose at 95% of the target volumes was used to evaluate the planning aims. Again the percentage differences between the gated and the ungated values were calculated.

3. Results

3.1 Target volumes

Four individual patients were scanned on the four different 4D CT scanners and the patients were numbered 1 to 4. Patient 1 was scanned on a Toshiba scanner, Patient 2 on a Phillips scanner, Patient 3 on a GE scanner and Patient 4 on a Siemens scanner.

Three of the four patients only had one lesion present in the lung, but patient 3 had two lung lesions. These two lesions were delineated separately and named 3a and 3b respectively.

Table 3.1: The gated gross tumor volumes of 10 respiratory phases with a calculated average of the 10 phases

CT Phase	Gated GTV (cc)				
	Patient 1	Patient 2	Patient 3a	Patient 3b	Patient 4
0	30.2	108.7	14.8	46.2	45.9
1	30.8	107.2	17.1	46.2	45.6
2	30.2	104.7	18.4	46.1	46.4
3	28.4	99.0	17.3	46.3	46.8
4	28.3	101.7	16.9	46.0	46.3
5	29.0	101.2	17.7	45.9	47.8
6	30.5	101.9	17.6	45.8	47.7
7	29.8	101.0	17.5	45.7	47.9
8	31.5	104.6	16.2	45.6	47.8
9	31.7	110.6	15.2	45.4	47.7
Average	30.0	104.1	16.87	45.9	47.0

Table 3.2: The ungated gross tumor volumes determined from fused respiratory phase scans

CT Phases fused	Ungated GTV (cc)				
	Patient 1	Patient 2	Patient 3a	Patient 3b	Patient 4
0 and 5	51.6	132.3	20.4	46.2	58.3

3.2 4D Respiratory gated scans

The GTV of respiratory phase 5 was copied on top of phase 0 to indicate the movement of the lesion in the lungs during respiration. Phases 0 and 5 are the two extreme positions, full-inspiration and full-expiration during breathing. The scans are shown in figures 3.1 to 3.8.

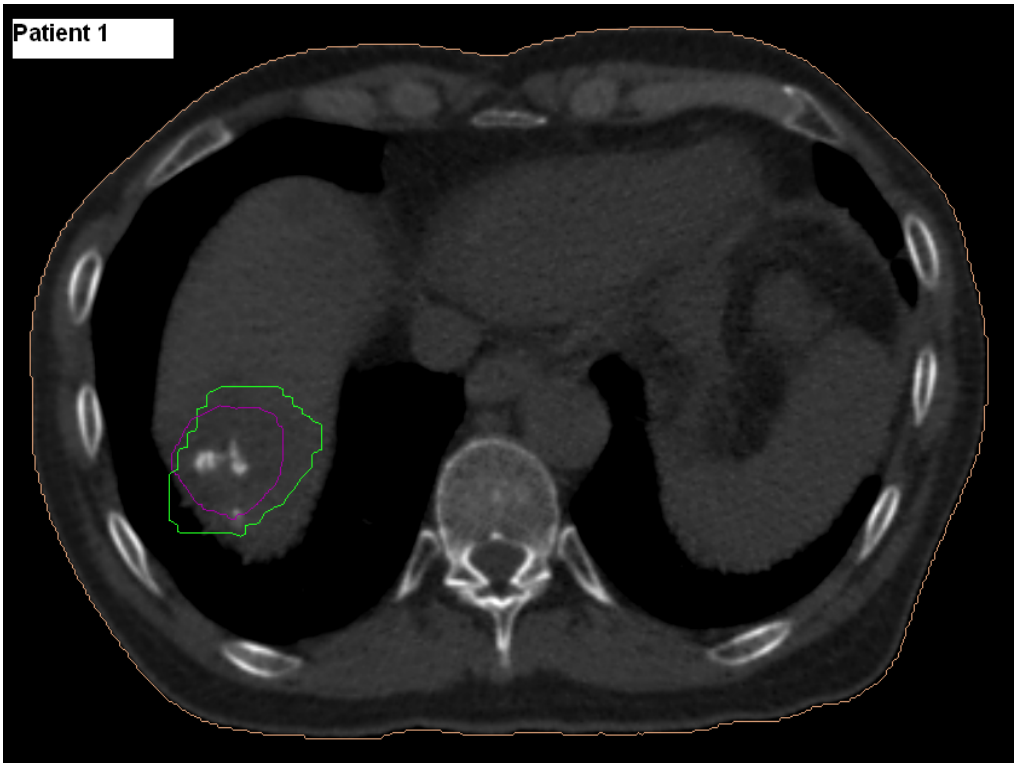

Figure 3.1: GTVs of phases 0 and 5 on a transaxial view of Patient 1

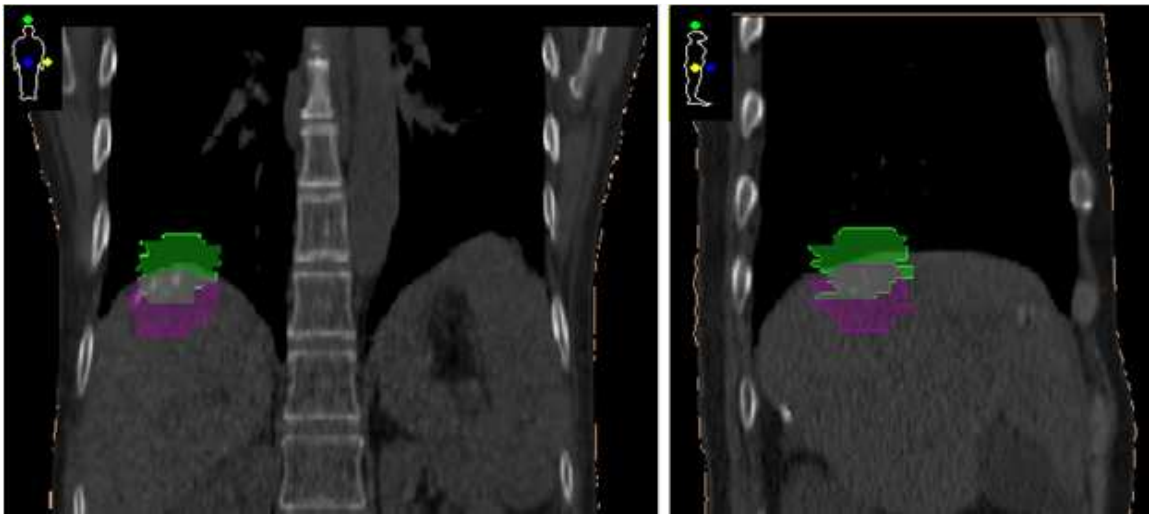

Figure 3.2: GTVs of phases 0 and 5 on the coronal and sagital view of Patient 1

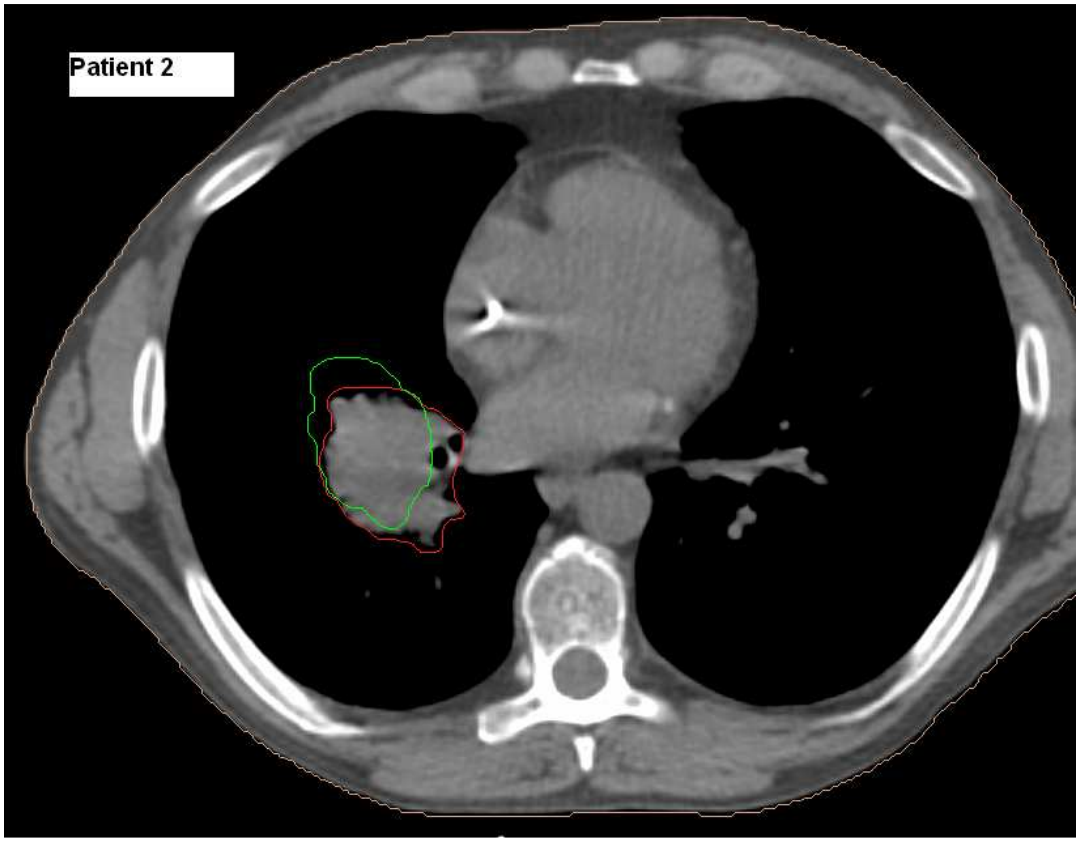

Figure 3.3: GTVs of phases 0 and 5 on a transaxial view of Patient 2

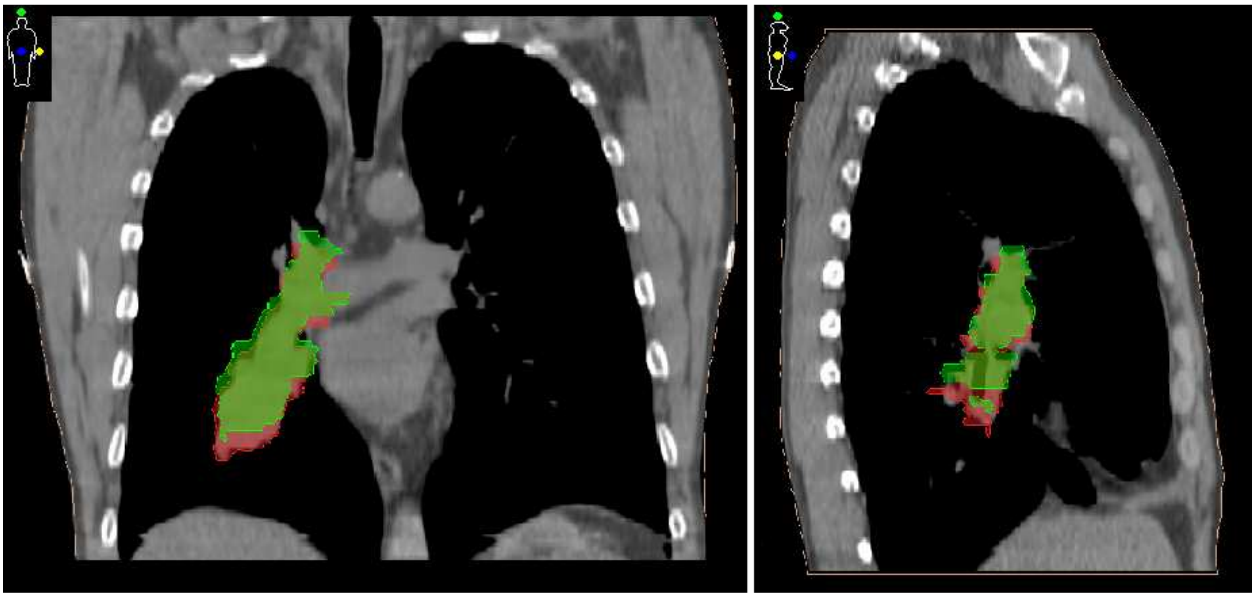

Figure 3.4: GTVs of phases 0 and 5 on the coronal and sagital view of Patient 2

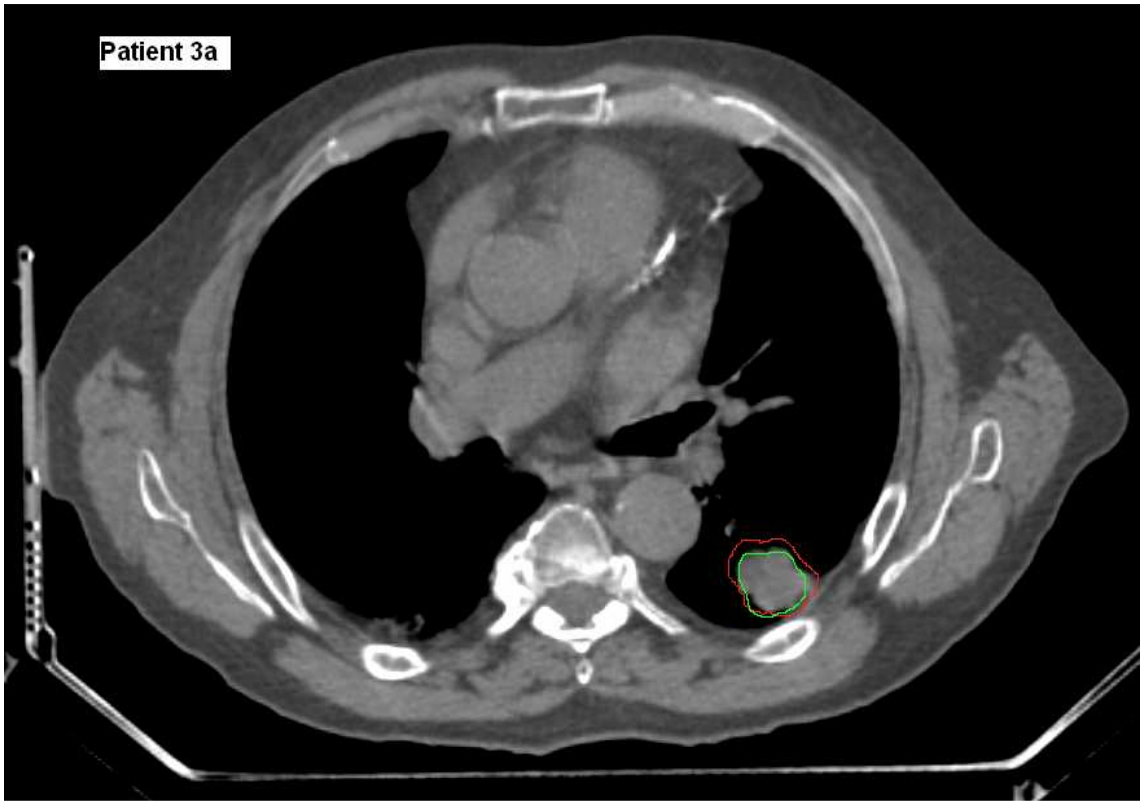

Figure 3.5: GTVs of phases 0 and 5 on a transaxial view of Patient 3, indicating lesion 3a

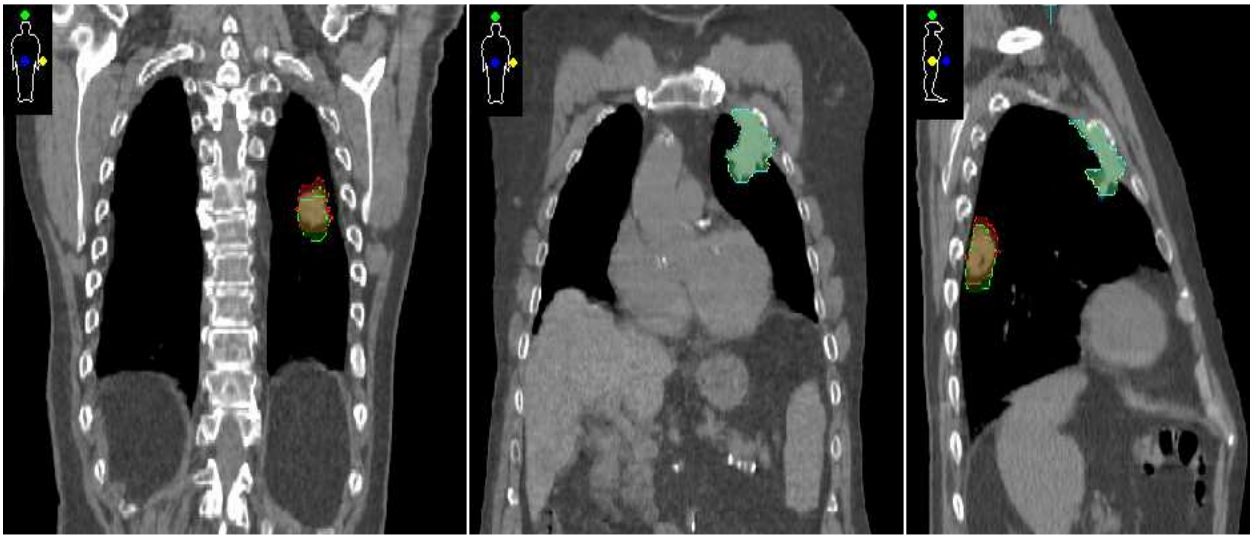

Figure 3.6: GTVs of phases 0 and 5 on the coronal and sagital view of Patient 3. The first coronal view indicates lesion 3a, and the second coronal view lesion 3b.

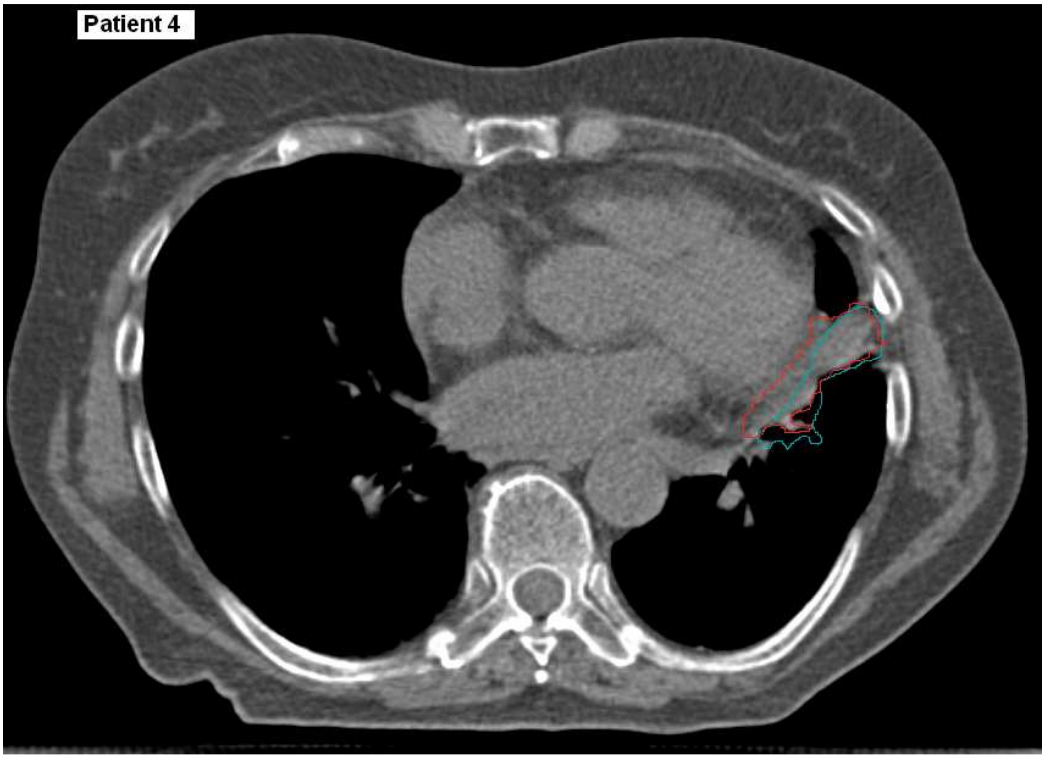

Figure 3.7: GTVs of phases 0 and 5 on a transaxial view of Patient 4

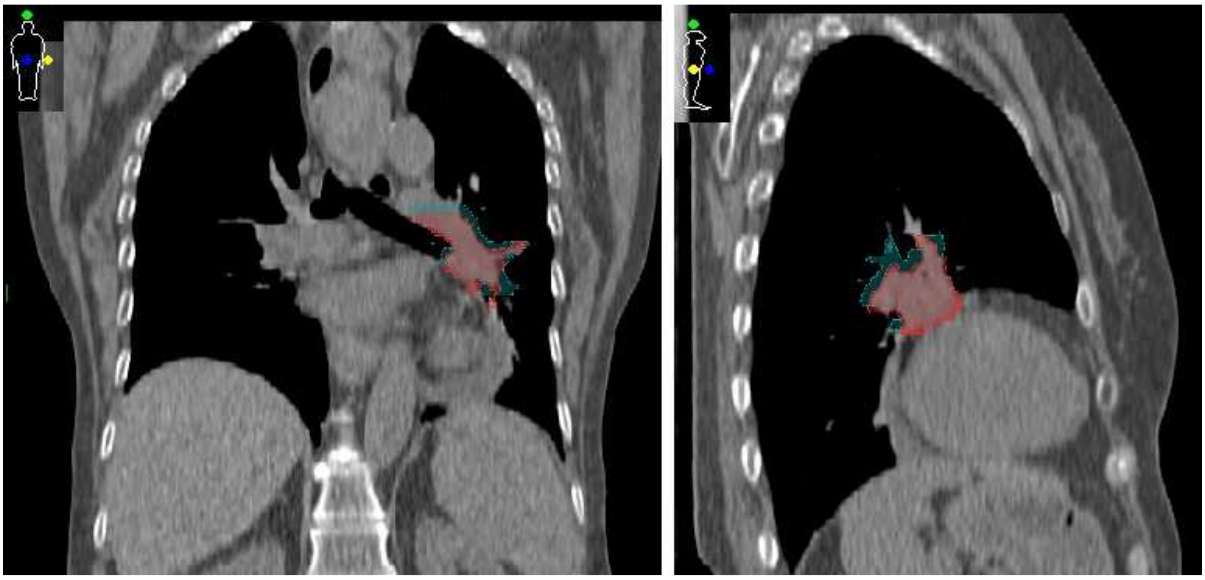

Figure 3.8: GTVs of phases 0 and 5 on the coronal and sagital view of Patient 4.

The 4D cine view videos of all four patients can be viewed on the attached CD. It gives a clear indication of the influence of respiratory movement on the lesion.

3.3 Treatment planning

A four field IMRT treatment plan was created on the gated scan and then copied to the ungated scan with some alterations made. Tight restrictions to the lung doses received top priority. The two plans, the DVHs and the dose values obtained from the DVHs and treatment plan reports are displayed below. Snapshots of the DVHs of the target volumes and most of the OARs, as well as snapshots of the two treatment plans are available on the attached CD.

Table 3.3: Percentage volumes and dose values, obtained from the DVHs and the treatment plan reports, for the gated and the ungated GTVs, PTVs and all OARs

Structure	Description	Gated	Ungated
GTV	D_{V100} (Gy)	61.18	64.19
	D_{V95} (Gy)	65.23	66.17
	V_{D100} (%)	87.32	95.86
	V_{D95} (%)	99.92	100.00
PTV	D_{V100} (Gy)	51.22	49.32
	D_{V95} (Gy)	59.55	58.78
	V_{D100} (%)	55.78	60.84
	V_{D95} (%)	82.98	82.00
Right Lung	D_{V30} (Gy)	28.58	35.80
Left Lung	D_{V30} (Gy)	4.27	8.41
Lungs (without PTV)	D_{V30} (Gy)	11.83	16.86
Heart	D_{V25} (Gy)	20.27	27.48
	D_{max} (Gy)	65.94	70.30
	D_{mean} (Gy)	15.24	21.34
Oesophagus	D_{max} (Gy)	37.87	45.79
	D_{mean} (Gy)	8.57	12.97
Spinal Cord	D_{max} (Gy)	22.52	25.14
	D_{mean} (Gy)	7.76	10.26

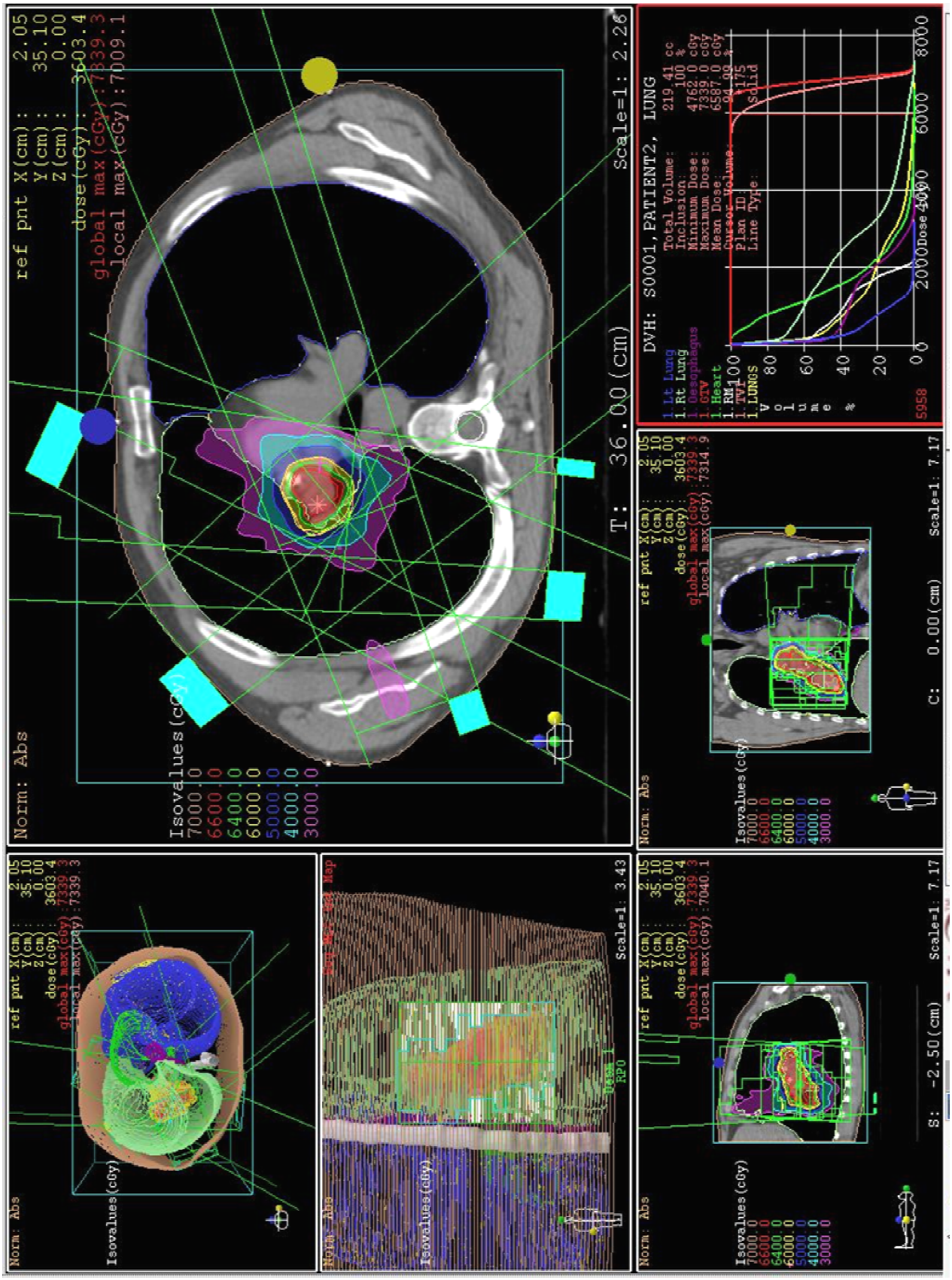

Figure 3.9: IMRT treatment plan done on the gated scan of Patient 2 with a 0.5 cm planning margin around the GTV

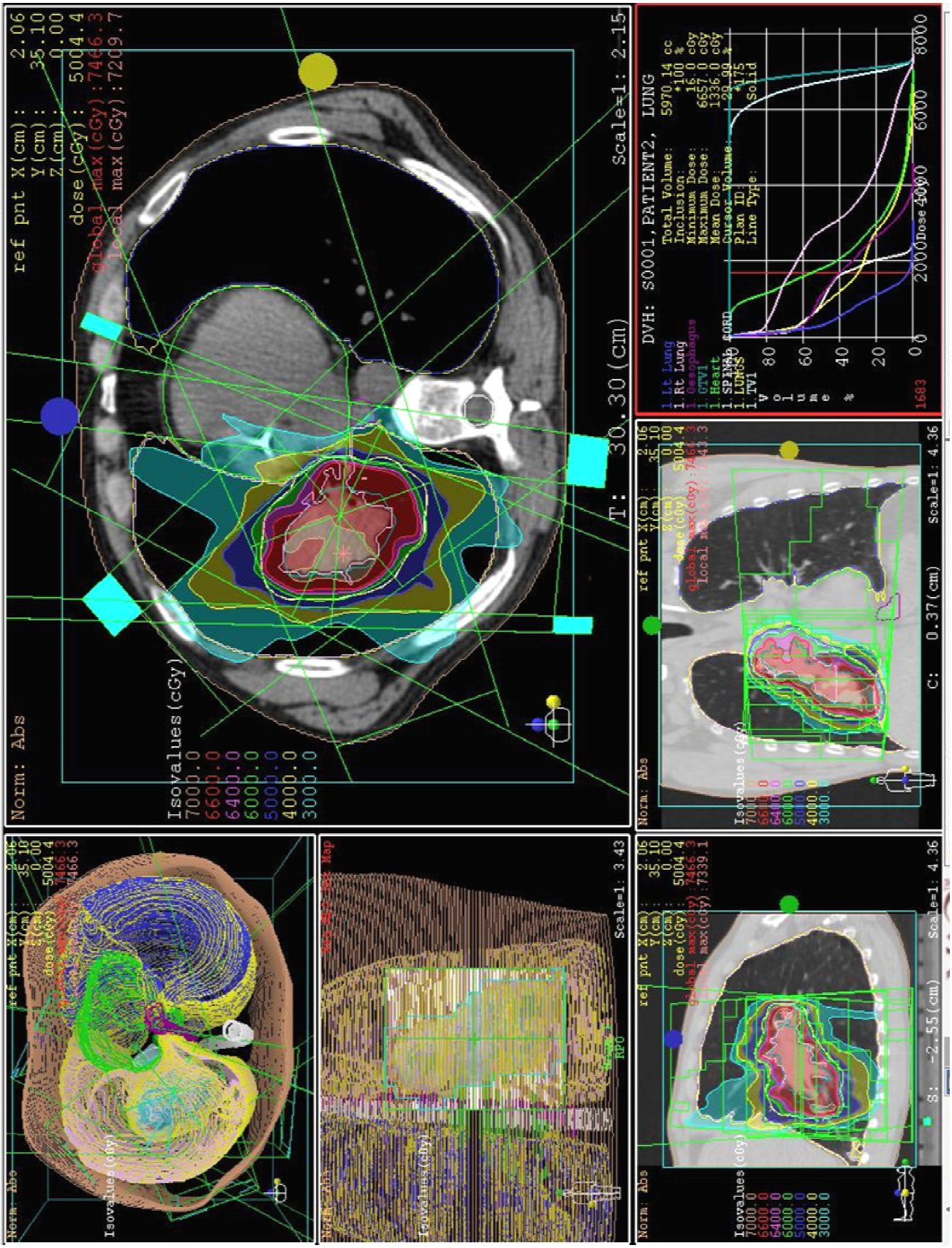

Figure 3.10: IMRT treatment plan done on the ungated scan of Patient 2 with a 1.2 cm planning margin around the GTV

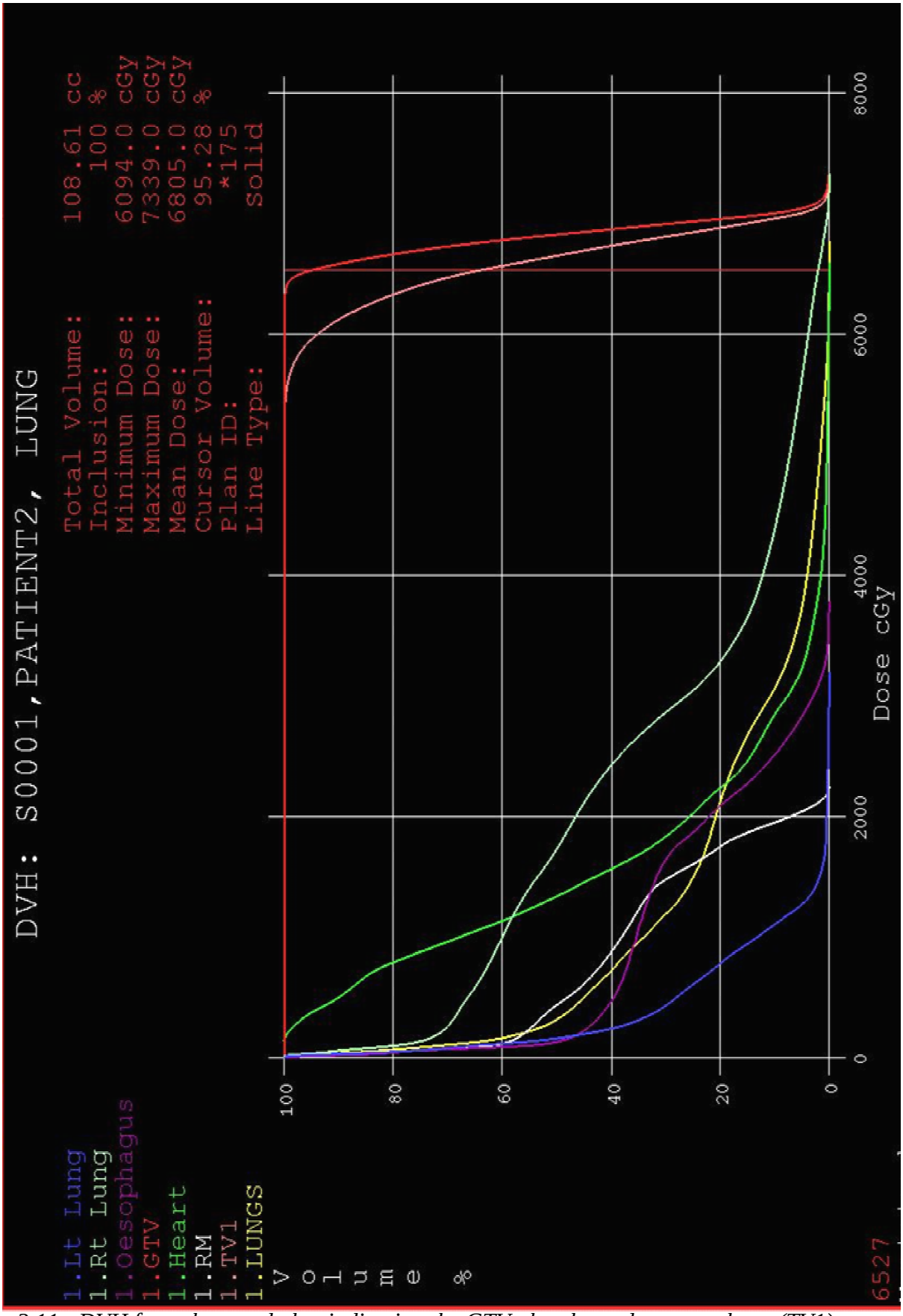

Figure 3.11: DVH from the gated plan indicating the GTV, the planned target volume (TV1) and all the critical organs

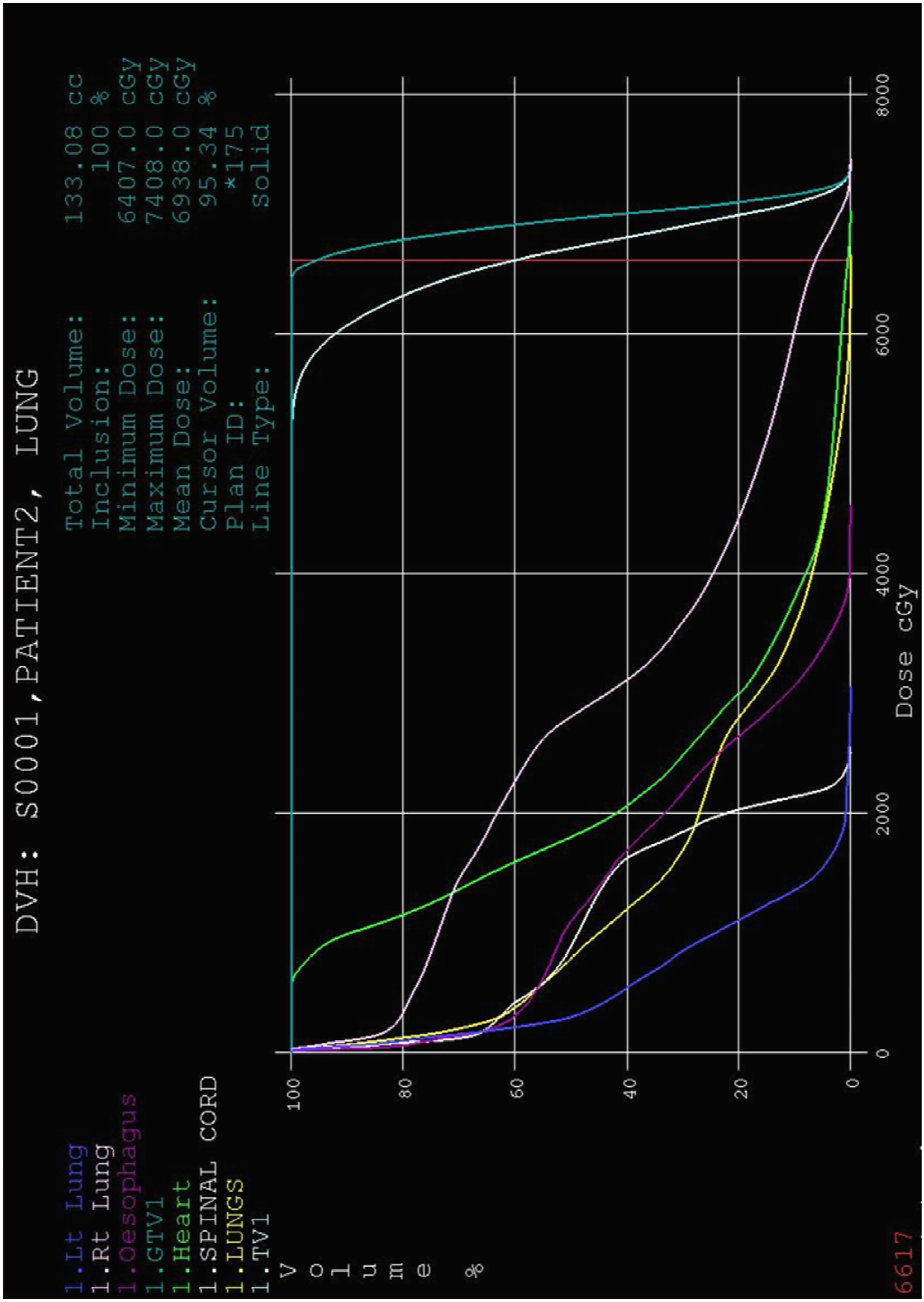

Figure 3.12: DVH from the ungated plan indicating the GTV, the planned target volume (TV1) and all the critical organs

4. Analysis

4.1 Comparison of respiratory gated to ungated GTVs

The average gated and the ungated GTVs of each patient were compared and the percentage difference calculated. (See figure 3.13 and table 3.4)

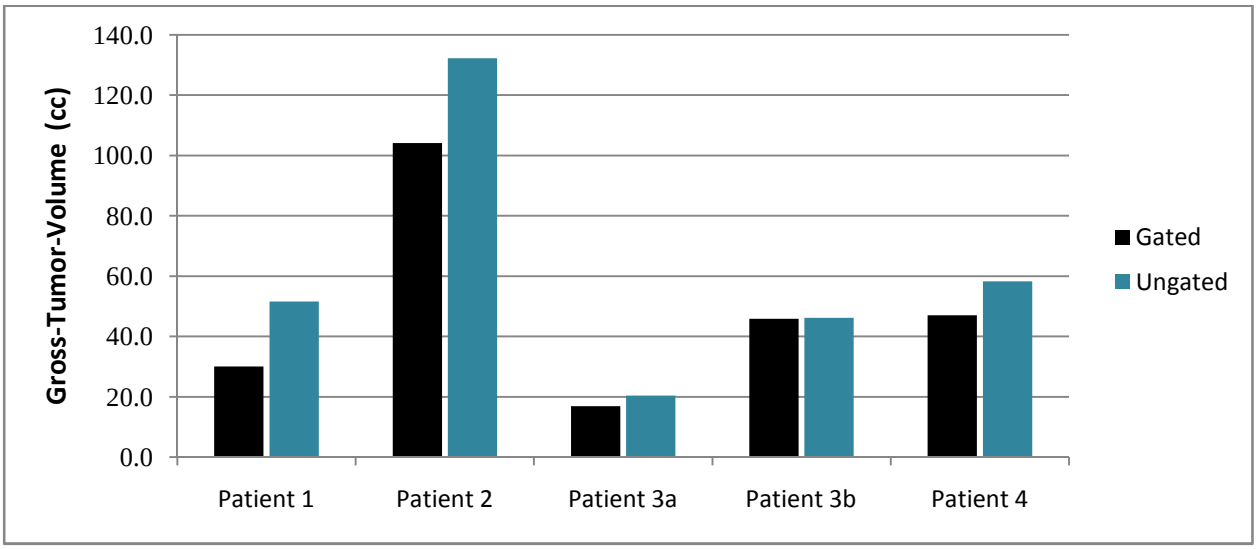

Figure 3.13: Graphical comparison between lesion volumes in gated and ungated respiratory 4D CT scans

Table 3.4: Calculated percentage differences between the gated and the ungated GTVs

	Gated GTV (cc)	Ungated GVT (cc)	% reduction in GTV
Patient 1	30.0	51.6	26.47%
Patient 2	104.1	132.3	11.93%
Patient 3a	16.9	20.4	9.38%
Patient 3b	45.9	46.2	0.33%
Patient 4	47.0	58.3	10.73%

A very small percentage difference of less than 1% between the gated and ungated GTV was observed in lesion b of Patient 3. This can be expected since the lesion is attached to the anterior chest wall of the upper lobe. See figure 3.6. It proves that the current technique used at Steve Biko Academic hospital where IMRT planning is done from ungated scans for lesions attached to the chest wall, is satisfactory. Since this lesion can be treated without using gating techniques, it will be ignored for the rest of the analysis.

The average percentage difference in the GTV between the gated and ungated CT scans was 14.63% with a standard deviation of 7.96%. Since the sample size of 4 is very small, the median which has a value of 11.33% will give a more accurate indication of the difference between the gated an ungated GTVs.

4.2 Gross target volume analysis

Oncologists at Steve Biko Academic hospital suspected that the tumor volume in each phase of the gated CT scans will remain constant since the tumor will only move with respiration and not increase in size. The calculated standard deviation over the 10 phases of the gated scans is a good indication that this prediction is true.

Table 3.5: The calculated average of all ten gated phases with the maximum and minimum GVTs of the ten phases and the calculated standard deviation

	Ave GTV (cc)	Max GTV (cc)	Min GTV (cc)	Standard Deviation (cc)
Patient 1	30.0	31.7	28.3	1.18
Patient 2	104.1	108.7	99.0	3.77
Patient 3a	16.9	18.4	15.2	1.14
Patient 3b	45.9	46.3	45.4	0.29
Patient 4	47.0	47.9	45.6	0.89

The standard deviation was the biggest in Patient 2, but this is due to the large GTV of this patient. Since the GTVs differ significantly across the 4 patients, a more accurate comparison can be made when the standard deviation is expressed as a percentage of the average GTV.

Table 3.6: The standard deviation expressed as a percentage of the average GTVs calculated in table 3.1

	Ave GTV (cc)	Standard Deviation (cc)	Standard Dev (% of the Ave GTV)
Patient 1	30.0	1.18	3.93%
Patient 2	104.1	3.77	3.62%
Patient 3a	16.9	1.14	6.75%
Patient 3b	45.9	0.29	0.63%
Patient 4	47.0	0.89	1.89%

Table 3.6 indicates that the GTV of each phase differs by less than 7% from the average GTV for a specific patient.

4.3 Influence of gating on treatment planning

Treatment planning was done on one of the four 4D CT scans. Patient 2 was selected since this patient's percentage reduction in the GTV was the closest to the average percentage reduction of 14.63%. Values that can be used for plan evaluation were recorded in table 3.3 from the DVHs and the treatment plan reports for the gated and ungated plans. The values that will be used for evaluation in this study were included in table 3.7 and the percentage differences between the gated and the ungated values calculated.

Table 3.7: Calculated percentage differences between the gated and the ungated values that will be used for plan evaluation

Structure	Description	Gated	Ungated	% difference
GTV	D_{V95} (Gy)	65.23	66.17	0.72%
PTV	D_{V95} (Gy)	59.55	58.78	-0.65%
Right Lung	D_{V30} (Gy)	28.58	35.80	11.21%
Left Lung	D_{V30} (Gy)	4.27	8.41	32.65%
Lungs (without PTV)	D_{V30} (Gy)	11.83	16.86	17.53%
Heart (Pericardium)	D_{V30} (Gy)	20.27	27.48	15.10%
Oesophagus	D_{mean} (Gy)	8.57	12.97	20.43%
Spinal Cord	D_{max} (Gy)	22.52	25.14	5.50%

The GTVs for the gated and the ungated plans were 108.61 cc and 133.08 cc respectively. A 0.5 cm planning margin was added to the gated GTV and a 1.2 cm margin to the ungated GTV to obtain the PTVs. The PTVs were then 219.41 cc for the gated plan and 467.37 cc for the ungated plan. The GTVs differ therefore by 10.12% while the PTVs differ by an enormous 36.10%.

To evaluate a treatment plan, the target volume coverage should be discussed first. The planning aim used for lung treatment at Steve Biko Academic hospital is that 95% of the target volume should receive within ±3% of the prescribed dose. Therefore D_{V95} should be 66 Gy ±3% for the GTV and 60 Gy ±3% for the PTV respectively.

The GTV dose was 0.65% under 66 Gy for the gated plan and 0.13% over 66 Gy for the ungated plan. The PTV dose was 0.38% under 60 Gy for the gated plan and 1.03% under 60 Gy for the ungated plan.

The organs at risks should be evaluated next. The following limits are used at Steve Biko Academic hospital (also see table 2.2):

- V(30%) of the lungs should receive less than 20 Gy,
- V(46%) of the heart should receive less than 30 Gy,
- D_{mean} of the oesophagus should receive less than 34 Gy, and
- D_{max} of the spinal cord should receive less than 50 Gy.

The reason for the exceptional high dose in the right lung is because it was delineated in such a manner that it included the target volume. Even though the tumor dose can be subtracted from the normal tissue dose, it is preferred to include the tumor dose because it gives a better indication of total lung morbidity. Right lung doses were therefore not considered for dose restrictions. The left lung and the combined lungs for both plans were below the limit of 20 Gy. There was however a significant reduction of 32.65% in the left lung dose and also 17.53% in the combined lung dose for the gated plan compared to the ungated plan.

The dose to 46% of the heart (Pericardium) volume was also below the limit of 30 Gy. The dose to the heart was however 15.10% lower in the gated plan than in the ungated plan.

The mean dose to the oesophagus was less than the 34 Gy limit and the maximum dose to the spinal cord was also less than the 50 Gy limit in both the gated and the ungated plans. The dose to the oesophagus was reduced by 20.43% and to the spinal cord by 5.50% in the gated plan.

5. Discussions

Multiple studies have been done in other countries to indicate the improvement of target volumes in gated scans. A similar study was repeated in this chapter where the gross tumor volumes of 4 patients were delineated on all ten phases of respiratory gated scans. The scans were imported from countries familiar with gated imaging to ensure that the scans were accurate. The average percentage difference in the GTV between the gated and ungated CT scans was 14.63%. This confirms the results of previous studies and also proves that the 4D delineation software was successfully applied without extensive training.

Oncologists at Steve Biko Academic hospital suspected that the tumor will only move with respiration and not increase in size. To confirm this, the standard deviation between the ten phases of each scan was calculated and expressed as a percentage of the average GTV. A deviation of less than 7% for all four patients confirmed that the tumor volume in each phase of the gated CT scans will remain constant with respiration.

The gated and the ungated IMRT treatment plans were in general very successful since all the requirements and limitations were met. The PTV coverage differed by less than 1% between the gated and the ungated plans, but significant dose reductions to the OARs of up to 32.65% for the contralateral lung were recorded on the gated plan. This indicates that the dose delivered to the normal tissue might significantly be reduced by using gated scans to do radiotherapy planning from.

CHAPTER IV – SIMULATED RESPIRATORY GATED CT

1. Introduction

The aim of this chapter was to determine the percentage differences between delineated target volumes when simulated respiratory gating is applied to target volumes of non-gated scans. Although respiratory gated CT acquisition is a well researched topic, no studies have been done in South Africa to indicate its relevance in South African public health sector (radiation oncology departments). The results of this chapter were considered to determine whether it will be meaningful to purchase and implement a respiratory gating system on CT scanners in South African hospitals and to use these images for target delineation in radiotherapy planning.

Steve Biko Academic hospital has no access to 4D respiratory gating software for CT scanners. Respiratory gating was therefore simulated to research the primary objective of this study. The easiest and less expensive way to simulate gating is by applying the breath-hold technique to patients with lung lesions. Full-inspiration and full-expiration phases can be considered as the two extreme positions in the respiratory cycle. This might be somewhat of an exaggeration because patients will not necessarily inhale and exhale as deeply during normal respiration as during breath-hold. The lesions present in the lung will therefore follow this additional movement and move to more extreme positions during breath-hold. This will however not influence the results of this chapter because only the volume of the lesion is considered during respiration and not its position. The ungated scans were acquired during normal respiration, so the lesion size will be true to the actual ungated size and not be exaggerated by fusing the two extreme positions.

2. Methodology

2.1 Equipment

2.1.1 CT scanner

CT data was acquired with a Siemens SOMATOM Sensation 4 scanner (Siemens AG Medical Solutions, Erlangen, Germany), which is a 4-slice spiral CT scanner. This is a 3D scanner only and was installed at Steve Biko Academic hospital in 2002.

It has variable slice thicknesses ranging between 1.0 mm and 10 mm and a maximum transverse field of view of 50 cm. The tube current is variable between 28 and 500 mAs with tube voltages of 80, 120 and 140 kV. Eight detector rows are positioned in the gantry consisting of a total of 5376 elements. The reconstruction time is up to 1.5 images per second for a matrix of 512 x 512 pixels. The spiral rotation times can either be 0.5, 0.75, 1.0 or 1.5 seconds and the scanner has a pitch-factor between 0.5 and 2.0.

2.1.2 Treatment planning system

XIO® Release 4.3.1 (CMS, Inc., St. Louise, Missouri, USA) software was used together with FocalPro Release 4.3.1 (CMS, Inc.) for target volume delineation.

XIO 4.3.1 is a 3D conformal therapy and IMRT planning system. Please see the previous chapter on 4D respiratory gating, section 2.1.3 where it has already been discussed.

FocalPro is a contour and plan review system and includes DICOM support. It also has an auto fusion option which allows fusion of CT, PET and MRI images. At Steve Biko Academic hospital the FocalPro software is mainly used by oncologists for contouring and seldom for plan reviewing.

2.2 Patient selection and preparation

2.2.1 CT patient selection

Six patients were included in this part of the study. All patients who reported for a RT CT scan of the thorax between July and September 2011 were considered for this study. However, only patients with good communication skills who were able and willing to participate were included. Only one of the seven patients referred for a lung scan during this period could not participate due to very poor lung function and a recent surgery.

2.2.2 CT patient preparation

The scan procedure was thoroughly explained to the patients and they received an informed consent form before participating. Before the scan, the participating patients also had the opportunity to train to hold their breath at full-inspiration for the duration of the scan. This was to ensure the patients that the time of the breath-hold was easily achievable so that they could relax during the scan.

The patients were made comfortable on the RT CT couch in a supine position with their arms and legs in the position it would be during radiotherapy treatment; either in cradle position above their head, or next to their sides.

2.3 Data acquisition

To simulate respiratory gating on a CT scanner, two scans were acquired for each patient; an ungated scan during normal respiration and a gated scan using the breath-hold technique during full-inspiration. The full-inspiration scan represents the maximum gating peak of the sinusoidal respiratory curve.

End-inspiration phases were used for the breath-hold scans even though the lung position is more reproducible during the end-expiration phase. Mentally it is easier for patients, especially patients with poor lung function, to hold their breath during inspiration.[26]

Minimizing the radiation doses received by patients from the CT scans were a priority even though the dose received from the two scans was insignificant compared to the dose levels patients would receive during radiotherapy treatment. The average dose given to a patient during a chest CT is approximately 5.8 mSv (±0.0058 Gy) while a typical treatment dose of the thorax will be between 46 and 50 Gy.[27]

The CT data was acquired with continuous helical acquisition using the same procedure required to do a normal RT CT scan. A topogram was done on the patient to determine the scan length. A CT scan of the thorax was then acquired during normal respiration with either a standard emergency CT protocol or a routine pelvic protocol, depending on whether the patient was palliative or would receive radical radiotherapy. The normal respiration scans acquired were also used for the prescribed radiotherapy treatment planning to minimize the doses received by the patients. This is the reason for using two different protocols for this study.

The emergency CT protocol was used for acquiring images of palliative patients. The vast majority of patients with lung lesions admitted at Steve Biko Academic hospital for radiation therapy are however palliative. This protocol acquired images with a 178 mAs effective tube current, a 120 kV voltage and the slice thickness is 10.0 mm. The scan had a 4 second delay and a scan time of less than 10 seconds. These scans were automatically reconstructed with a filtered back projection algorithm using a B30f medium smooth kernel.

The routine pelvic protocol was used to acquire images of patients who will receive radical radiotherapy. This protocol also acquires images with a 178 mAs effective tube current, a 120 kV output but a slice thickness of 5.0 mm. The scan delay was 4 seconds with an average scan time of about 10 seconds. Again these scans were automatically reconstructed with a filtered back projection algorithm using a B30f medium smooth kernel.

After the first ungated scan was done, the patients were instructed to inhale and hold their breath while the same scan was repeated and the patients remained in the same scan position. The normal respiration scan was acquired first so that the ungated scan would not be influenced by uneven breathing of patients still trying to normalize their breathing pattern after breath-hold.

2.4 Data processing

2.4.1 Data transport

The RT CT scanner and the treatment planning computers are located in the Radiation Oncology department and most computers in this department are connected via an internal network. DICOM images were therefore directly imported from the scanner to the XIO planning software and saved as two study sets for each patient; study-set 1 was the normal breathing/ungated scan and study-set 2 was the inspiration scan. This was repeated three times so that the three oncologists who delineated the target volumes each had their own study sets to work on.

Patient information (name and identity number) was changed at the CT scanner before exporting it to the TPS, which conforms to the DICOM standards, to maintain patient confidentiality.

2.4.2 Target volume delineation

The patients' body and lungs were identified on both scans, the normal breathing and full-inspiration scan, at the XIO TPS before exporting it to the FocalPro computer where target volume delineation was done by oncologists.

Three experienced radiation oncologists (Oncologist A, B and C) were asked to contour the clinical target volumes of the visible tumors on both the gated and the ungated scans. Contouring of the CTV did account for the tumor's residual motion and setup uncertainty and allowed for deviation from the expected respiratory cycle during breathing.[26] The gated CTVs were delineated with a conservative margin because it was assumed that gated treatment planning would be done from these scans. The ungated scans received a more generous margin which accounted for respiratory movement during ungated therapy.

There was a time delay of minimum one day between contouring the gated and the ungated scans to avoid any possible bias from the oncologists due to familiarity with the specific patient's anatomy.

2.5 Data evaluation

The FocalPro software automatically calculated the volumes (in cubic centimeters) of the delineated target volumes. The CTVs for both the simulated gated and ungated scans from all three oncologists were recorded and the average CTV was determined. The average delineated volumes were used for data analysis because contouring is fairly objective, especially on palliative patients where oncologists are not very cautious to spare normal tissue. By using the averages of three oncologists instead of only one oncologist's interpretation of the CTV, a more reliable result could be obtained.

The percentage differences between the gated and the ungated averages were then calculated using a simple mathematical equation (see equation 3.1).

2.6 Log book evaluation

The log books of the radiotherapy CT scanner in the Radiation Oncology department were consulted to evaluate the population of patients that will be influenced by this study. The log books were analyzed from January 2010 to September 2011 and the number of patients whom received a RT lung scan was recorded.

3. Results

3.1 Patient data

Table 4.1 is a summary of all the patients who participated in this study. Only one of the six patients received radical treatment, the rest were all palliative.

Table 4.1: Summary of patient data

Patient	Sex	Age (yrs)	Diagnosis	Palliative/ Radical
1	Male	51	NSCLC - Right Lung	Palliative
2	Female	45	Lung Cancer – Mediastinum	Palliative
3	Female	44	Lung Cancer - Left main bronchus	Palliative
4	Male	55	Adenoid Cancer - Right lung	Palliative
5	Female	57	Small Cell Cancer - Superior Mediastinum	Radical
6	Male	57	NSCLC - Right Lung	Palliative

3.2 Clinical target volumes

Table 4.2: Clinical target volumes of six patients delineated by three different oncologists (Oncologist A, B and C) from ungated and gated scans, with the average CTVs calculated

Patient	Gated / Ungated	Clinical Target Volumes (cc)			Average CTV (cc)	Standard Deviation
		Oncologist 1	Oncologist 2	Oncologist 3		
1	Ungated	550.6	550.2	739.8	613.5	109.4
	Gated	506.3	380.9	242.2	376.5	132.1
2	Ungated	527.5	622.6	554.5	568.2	49.0
	Gated	416.7	621.8	301.9	446.8	162.1
3	Ungated	359.5	473.1	388.1	406.9	59.1
	Gated	243.5	469.8	315.4	342.9	115.6
4	Ungated	1084.1	1019.1	1150.5	1084.6	65.7
	Gated	1004.9	731.8	1104.9	947.2	193.1
5	Ungated	482.6	386.5	755.6	541.6	191.5
	Gated	384.7	305.1	639.3	443.0	174.6
6	Ungated	1027.7	1046.3	1576.6	1216.9	311.7
	Gated	630.8	698.8	871.8	733.8	124.3

Snapshots of the 3D CTVs of Oncologist A are available on the attached CD.

3.3 Log book results

The number of patients whom received a RT CT scan for lung therapy was counted from the recorded log books at the CT scanner in the Radiation Oncology department.

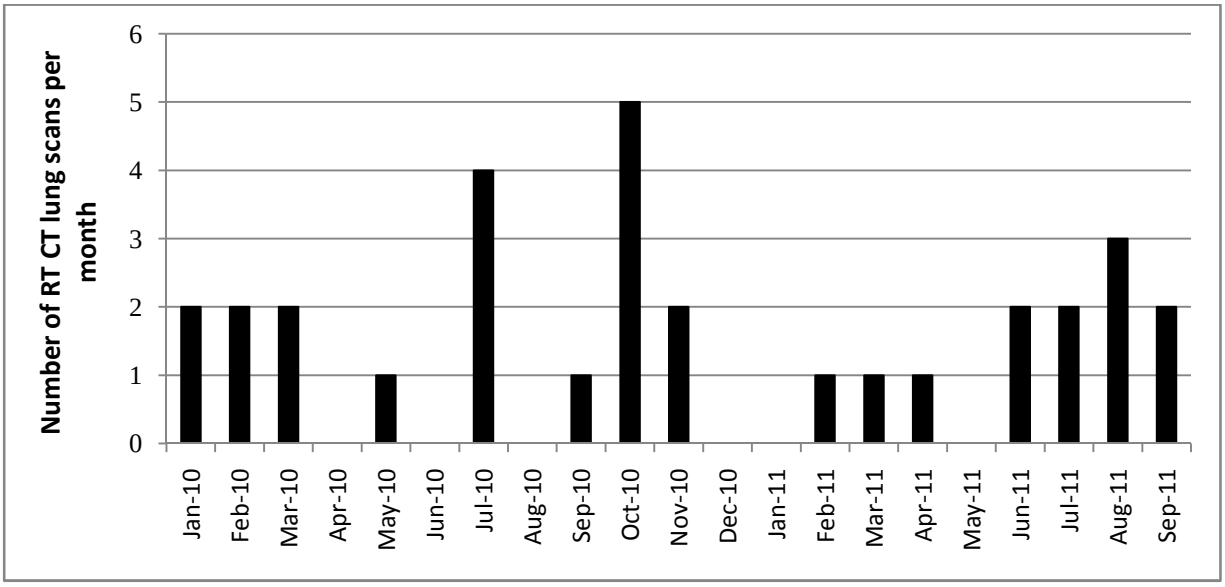

Figure 4.1: Graphical indication of the number of patients referred to the Radiation Oncology department per month (from January 2010 to September 2011) for a radiotherapy planning lung scan

4. Analysis

4.1 Target volume analysis

The aim of this chapter was to determine the percentage differences between the ungated and simulated gated target volumes of lung patients. These percentage differences were calculated in table 4.3 by using the average CTVs of the three oncologists as calculated in table 4.2. The average CTVs were used to obtain a more reliable result.

Table 4.3: The percentage differences calculated between the average ungated and the gated CTVs

Patient	Gated / Ungated	Average CTV	% difference
1	Ungated	613.5	23.95%
	Gated	376.5	
2	Ungated	568.2	11.96%
	Gated	446.8	
3	Ungated	406.9	8.54%
	Gated	342.9	
4	Ungated	1084.6	6.76%
	Gated	947.2	
5	Ungated	541.6	10.01%
	Gated	443.0	
6	Ungated	1216.9	24.76%
	Gated	733.8	

Figure 4.2 is a graphical presentation of table 4.3 and clearly indicates that the CTVs decreased for all six patients when simulated gating was applied. The largest and smallest differences are seen in Patient 6 and Patient 4 respectively, where the target volumes decreased by 24.76% and 6.76% respectively, when the breath-hold technique was used. The average percentage difference between the ungated and the gated CTVs of all six patients was 14.33% and the median was 10.98%.

The target volumes of Patient 4 and 6 were also the biggest amongst the six patients. This is an indication that the size of the lesion does not have an influence on the percentage difference between the ungated and the gated scans since Patient 4 had the smallest percentage difference and Patient 6 the largest.

According to standard practice at Steve Biko Academic hospital, only CTVs of radical patients are delineated. Only one of the six patients included in this study was radical, namely Patient 5 and the percentage difference between the gated and the ungated scan was 10.01%.

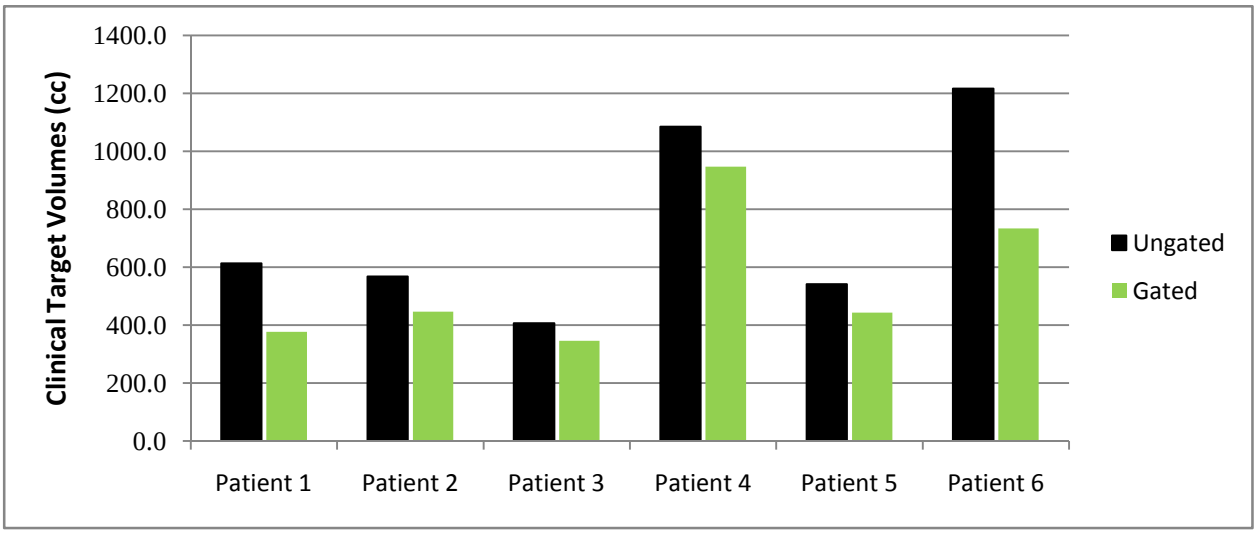

Figure 4.2: Graphical comparison between the CTVs of ungated and simulated gated CT scans

4.2 Log book analysis

Figure 4.1 indicates the number of patients referred to the Radiation Oncology department for a lung scan between January 2010 and September 2011. Only 29 patients were referred in 21 months which is an average of 1.4 patients per month and the vast majority of these patients were palliative. Lung patients are a very small percentage of the total number of patients whom receive a RT planning scan monthly at Steve Biko Academic hospital. When assumed that about 132 patients receive a RT planning scan per month (6 per day), then the lung patients are a mere 1.06% of the RT scans patient population.

5. Discussions

Five of the six patients whom participated in this study were palliative patients. At Steve Biko Academic hospital, palliative lung patients are treated with two simple parallel opposing fields. This treatment is not even done from the 3D CT images, but from a 2D coronal view film. Oncologists will identify a rectangular treatment field size on the film which will then be treated with the dose and fractions prescribed. These fields are determined with a broad margin to ensure complete tumor coverage and critical organs are not so much considered.

Even though the CTVs, done from 3D CT scans, decreased significantly by an average of 14.33% it is very unlikely that the parallel opposing field sizes will differ. It can therefore be concluded that only radical patients referred to the Radiation Oncology department will benefit by applying respiratory gating or any motion-reduction technique.

Since only one radical lung patient was scanned in three months (July to September) it can be estimated that approximately 4 radical lung patients will be scanned annually which is merely 0.03% of the total radiation therapy patient population.

CHAPTER V – RESPIRATORY GATED PET/CT

1. Introduction

A positron-emission-tomography/computed-tomography (PET/CT) scanner is a dual modality scanner which allows the examiner to perform both imaging studies simultaneously. The scans are however not acquired concurrently. The CT scan is acquired first and then the PET scan immediately afterwards while the patient remains in the same position on the couch.

The CT and PET images are reconstructed independently and the two separate images are then fused with a process called co-registration.[23] CT gating and PET gating techniques differ significantly, but because of separate acquisition and reconstruction, both modalities can be gated in a dual modality scanner.

It has been proven that the combined scan provides a more accurate diagnosis than the two scans performed separately, since the CT scan provides anatomical information while the PET scan shows metabolic detail.[6] A single modality CT scan is adequate to use for radiation therapy treatment planning, since only relative electron density information is required.

Steve Biko Academic hospital has respiratory gating equipment associated only with the PET component of the Siemens Biograph True Point PET/CT scanner at its disposal. Since relative electron density information is required for target volume delineation, these gated PET scans could not have been used for the primary objective of this study. The respiratory gated PET data was however used to evaluate other non-technical parameters influenced by gating such as time of procedure, patient participation, effectiveness of the system and the gated results.

2. Methodology

2.1 Equipment

2.1.1 PET/CT scanner

All gated PET data was acquired with a dual modality Siemens Biograph 40 True Point PET/CT scanner (Siemens AG Medical Solutions, Erlangen, Germany). This is a whole body scanner with an axial field for view of 162 mm. This scanner has 3D, static, dynamic, whole body, gated 4D respiratory and/or cardiac acquisition possibilities.

The PET component of this scanner consists of 39 detector rings with each photo-multiplier-tube consisting of 42 LSO crystals. The typical dwell time per bed position is 2 to 3 minutes and the reconstruction time is less than 1 minute per bed. Prospective and retrospective respiratory gating options are available on the Biograph 40 PET scanner.

The CT component of the tomograph is a 40-slice spiral CT. It has a variable slice thickness of 0.6 mm to 24 mm and a maximum transverse field of view of 50 cm. The scanner's tube current ranges between 28 and 580 mAs and it has tube voltages of 80, 100, 120 and 140 kV. It can reconstruct 20 images per second for a reconstruction matrix of 512 x 512 pixels. It maintains an image resolution of 0.33 mm regardless of the pitch.

2.1.2 Anzai respiratory gating system

The Anzai AZ-733V gating system (Anzai Medical Co Ltd, Shinagawa-ku Tokyo, Japan) was used in conjunction with the PET/CT scanner to acquire gated PET images. The system consists of various specialized hardware and software components described below.

2.1.2.1 Anzai gating hardware

The hardware related to the Anzai system is; respiratory sensors, a sensor-port, a wave-deck and a personal computer (PC). A respiratory phantom is also available for quality assurance and system checks.

Two types of sensors/load cells namely HIGH and LOW (with dimensions: 30 mm in diameter, 9.5 mm in thickness) are available. The HIGH load cell has low sensitivity because it has a large gauge range between 0 and 1 kg. The LOW load cell has high sensitivity because of its low gauge range of 0 to 0.5 kg. The HIGH load cell should therefore be used for patients with weak abdominal respiration, while the LOW load cell should be used for patients with strong abdominal respiration.[2]

The sensor-port amplifies the analog signals received by the sensor and transmits the signals to the wave-deck. The wave-deck converts the analog signals into digital signals. These signals are then transmitted to the PC which displays the respiratory signal input and outputs the gating signals to the scanner.[2]

A respiratory phantom which simulates the human breathing cycle has an adjustable respiratory rate and respiratory level. The phantom was used after setup for familiarization on the system, for quality assurance and for system evaluation. The phantom's results are also included in this chapter.

2.1.2.2 Anzai gating software

Two sets of software are essential for acquiring gated scans. The first is a gating license installed by the scanner vendor on the control computer which reacts to digital signals received from the hardware. The second is the Anzai application software on the PC.

The application software allows creating and storing of each patient's data separately. The main window on the PC will display all patient information, gating information, the gating time and the average respiration rate (see figures 5.8 to 5.12 in section 3.2). The following graphs will also be displayed:

- The main sine graph indicating the real time recorded respiratory waveform,
- "Resp." indicating the pre-selected gating positions and
- "Gate" indicating the gating signal sent to the scanner.

Figure 5.1: Anzai load cells

Figure 5.2: Anzai sensor port

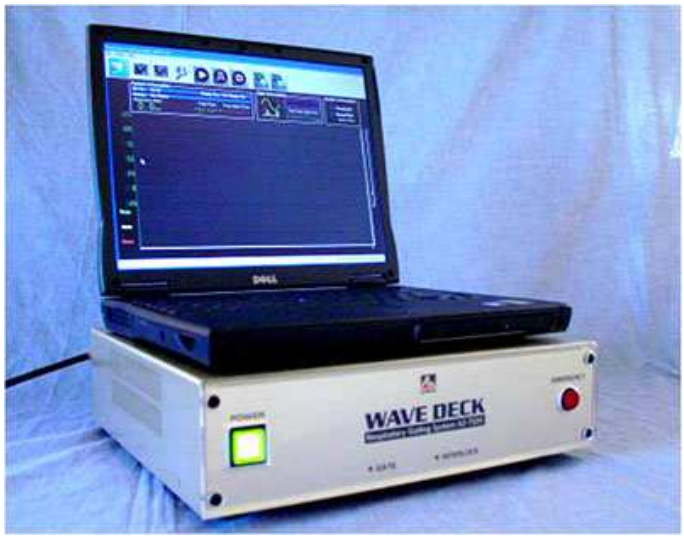

Figure 5.3: Anzai wave deck and personal computer

Figure 5.4: Respiratory phantom associated with the Anzai system

2.2 Patient selection and preparation

2.2.1 PET/CT patient selection

Three patients were included in this study. All patients referred to the Nuclear Medicine department for an ungated whole-body (WB) PET/CT scan of the lungs from July 2011 to October 2011 were considered, but only patients whom did not have a repeat scan prescribed by their physician were included. The reason for this was to minimize radiation received by the patient from the CT scan. Since these patients will most likely not receive radiotherapy treatment, the CT doses cannot be justified and considered insignificant compared to the radiation treatment doses. Another reason was also to minimize discomfort to the patient due to long periods on the couch in the uncomfortable scanning position.

2.2.2 PET/CT patient preparation

The patients once again received an informed consent form explaining the procedure. The patients were trained to hold their breath at full-inspiration for the CT scan acquisition and to continue even breathing during the PET scan acquisition.

The greater part of the patient preparation procedure was identical as for the prescribed ungated WB scan. Patients were not allowed to eat any carbohydrates 24 hours prior to the scan and should have been in a fasting state 12 hours before the scan. The three patients were injected intravenously with between 10.3 - 12.8 mCi Fluorine-18 Fluorodeoxyglucose (^{18}F-FDG) approximately 90 minutes before the WB scan was acquired. This was according to the departmental protocol where all patients should receive ungated WB scans 90 minutes after radiopharmaceutical injections so that physicians can compare the SUVs. The gated scans were acquired either immediately after the WB scan, or just before.

Take note that no additional radiopharmaceuticals or increased activity was admitted to the patient for the purpose of this study. The patients received only the ^{18}F-FDG prescribed for their WB scan.

An elastic strap which contained the pressure sensor was placed around the patients' diaphragms. The patients were then setup in a supine position on the PET/CT couch with

their arms in a cradle position above their heads. The pressure sensor was then inserted into the pocket of the elastic strap. The strap was adjusted so that the sensor position was in line with a rib bone which ensured ample pressure to the sensor during respiration.

2.3 Respiratory gating system setup

The respiratory gating system was obtained together with the scanner installation to improve image quality and misalignment between the CT and PET images for patients with thoracic tumors. This function was however not implemented before this study. Therefore the system had to be implemented and tested before data acquisition could be done.

This was done by systematically following the Anzai gating system manual. Various scans were acquired using the respiratory phantom to ensure correct setup, parameter selection and functionality. The pressure sensors also require annual calibration. For more information regarding the implementation procedure, please refer to reference 2 (the Anzai gating system manual) and section 2.1.2.1 of this chapter.

A short scanning protocol with step-by-step instructions was developed for the nuclear radiographers who had never before been trained on acquiring respiratory gated scans. Figure 5.5 is a copy of the summarized instructions given to the radiographers.

All hardware and as much as possible software associated with the respiratory gating system was set-up before the patient arrived at the scanning room.

2.3.1 Respiratory gating hardware setup

The PC and the wave-deck were located in the control room where the PET/CT scanner was operated from. This was for easy access to the gating software during acquisition. The wave-deck was connected to the sensor-port and the gantry which were both inside the scan room. The correct load cell, depending on the strength of the patient's respiration, was connected to the sensor port inside the scan room. See figure 5.6 for a schematic layout of the gating hardware setup.

Procedure to scan patient with respiratory gating
(Radiographers)

The physicist will connect all the hardware and create a patient file on the laptop. (Before the patient enters the room)

1. Place the respiratory strap around the patient's diaphragm before positioning the patient on the bed.
2. Secure the load cell in the pocket of the strap around the patient's waist.
3. Make sure the pressure on the load cell is correct (the light on the wave deck should be green at all times). The belt should be adjusted until the correct pressure is attained.
4. Ensure the patient is in a stable scanning position.
5. The physicist will normalize the respiratory wave and do the gating setup.
6. On the laptop, click the **"Gate Out ON/OFF"** button to initiate the gating signal to the scanner.
7. Now do a **PETCT_Lung_LM** scan with the following parameters:
   - ROUTINE: Scan duration = 8 - 10 min/bed
   - SCAN: Scan output = List mode
   - SCAN: Input trigger = Respiratory
   - RECON: Output image type = No recon
8. After acquisition, click the **"Gate Out ON/OFF"** button again to stop the gating signal to the scanner.
9. Remove the load cell and the strap form around the patient.

The physicist will save the waveform, reconstruct, fuse and save the respiratory scan. The physicist should also disconnect all the respiratory hardware.

Figure 5.5: Copy of the summarized instructions for nuclear radiographers on how to acquire a gated scan with the respiratory gating protocol

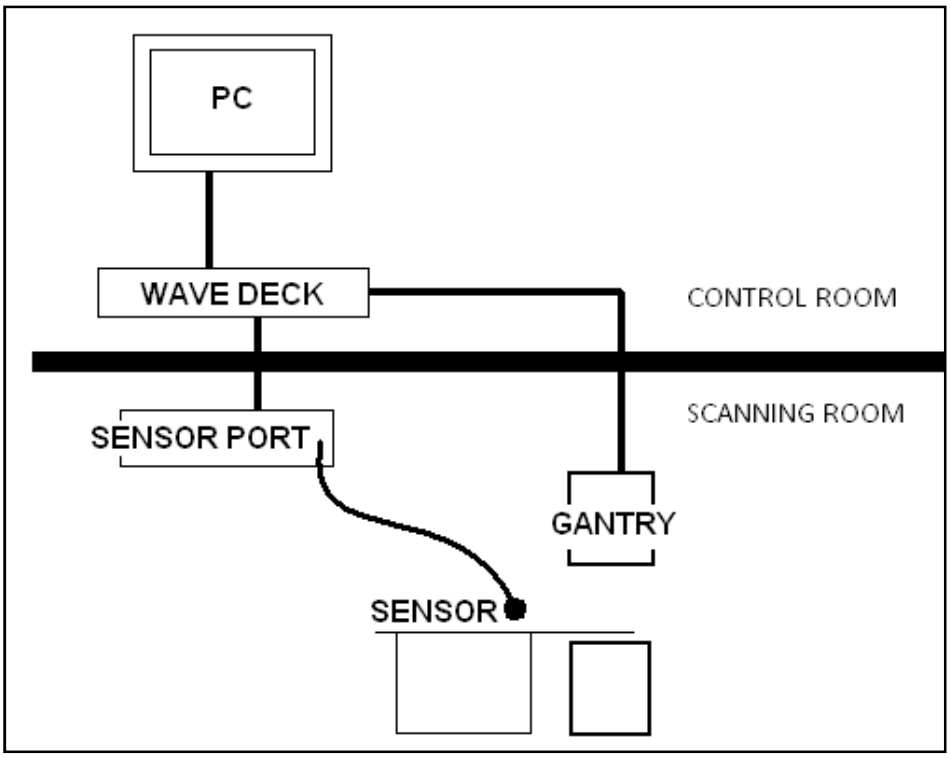

Figure 5.6: Schematic diagram of the Anzai gating hardware setup

2.3.2 Respiratory gating software setup

A complete system setup should be done before registering each patient. All system parameters were selected after consulting a nuclear physician whom is familiar with the human respiratory cycle. A wide margin was added to the parameters to ensure multiple counts to be acquired, and in some instances the default settings were used. Please see figure 5.7 for a copy of the specific system parameters selected for all three patients.

A new patient was then created on the PC. The patient's personal details were entered and saved before the waveform setup could be done. The software can automatically normalize (adjust the position and amplitude) the patient's respiration cycle with the waveform setup function. If this however is unsuccessful, a manual normalization mode is also available.

The gate mode setup was selected next. MODE 4, which is an amplitude-based technique, was used for all patients with 8 gates selected on 20%, 50%, 80% and 100% inspiration and also on 20%, 50%, 80% and 100% expiration. (See Chapter II – Section 2.3 for a full description of the different modes.) Eight gates were used since it was proved to be the optimal number of gates to use with amplitude based reconstruction studies.[9]

After all the settings were saved, the 'Start' button initiated the recording of the respiratory wave form. The gating signal will only be sent to the scanner during the PET acquisition since the CT and PET parts of the scanner operate as two separate modalities.

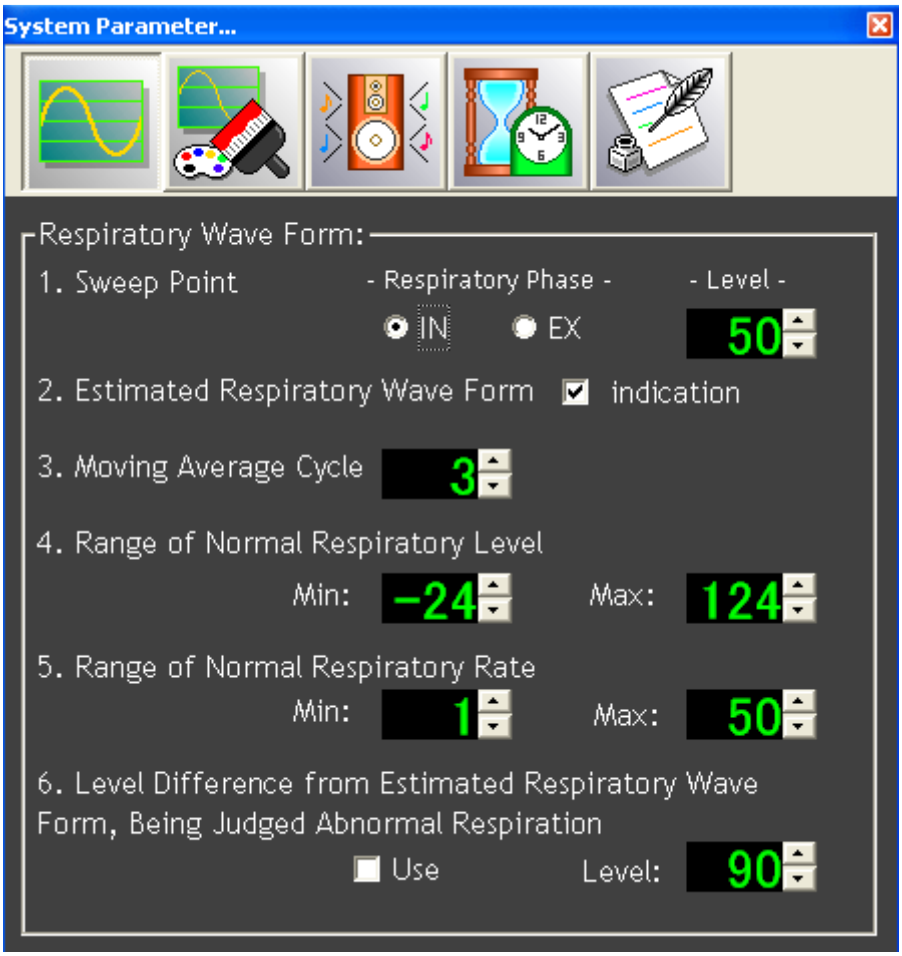

Figure 5.7: The system parameters selected for the phantom and all three patients

2.4 Data acquisition

For gated PET/CT acquisition a PET/CT lung list mode protocol was used. The following scan parameters were selected for the gated PET scan:

- Scan duration – 8 minutes per bed (this protocol has a limit of only one bed per study)
- Scan output – List mode
- Input trigger – Respiratory
- Output image type – No reconstruction

A topogram was acquired first to determine the position of the scan followed by a CT scan acquired during full-inspiration with the breath-hold technique. The settings were 120 mAs, 120 kV and the 'Care Dose' 4D option was selected. The total scan time for all patients was between 5 and 7 seconds with a delay of 4 seconds. The selected slice thickness was 5.0 mm with a pitch-factor of 1.4. All scans were automatically reconstructed using a B31f very smooth kernel with filtered back projection algorithms.

The reconstructed CT scan was then used to determine the position of the single PET bed. Since the protocol used for respiratory gating has only one bed, it is important to ensure the bed is positioned over the center of the lesion. The gated PET scan was then acquired in list mode (32-bit).

The raw list mode PET data was manually reconstructed at a later time using an iterative reconstruction algorithm with a Gaussian filter. The default registration matrix available on the system was used. The replay settings were selected in such a manner that the maximum number of counts would be used for reconstruction;

- The lower and upper trigger rejection threshold: 10 to 300
- The number of triggers to skip after a bad trigger: 5
- The delay (in seconds) to be skipped in the list mode data before gating: 0
- The duration (in seconds) of the list mode data to gate: Total scan duration
- Sinogram mode: Net trues

2.5 Data processing

2.5.1 Data transport

The reconstructed gated PET and breath-hold CT images were saved on a CD in an uncompressed DICOM format in the Nuclear Medicine department and then imported from the CD to a computer in the Radiation Oncology department. The data was opened and analyzed with a DICOM reader, DicomWorks 1.3.5 (© 2002 Philippe PUECH – Loïc BOUSSEL).

2.5.2 Non-technical data recording and analysis

Some of the non-technical data of importance for this chapter, such as time and effectiveness of the system, was manually recorded on the result sheets during or immediately after the gated scan acquisition. These result sheets were copied to the results section of this chapter.

2.6 Data evaluation

The PET/CT scans were used to evaluate external, non-technical, but crucial parameters when considering respiratory gating implementation. These parameters were recorded during and after each scan acquisition and included; time, patient participation, effectiveness of the gating system, effectiveness of gated scans and gated results. The results were tabulated with a short explanation next to each result.

2.7 Log book evaluation

The log books in the Nuclear Medicine department were consulted to determine the number of lung patients admitted for a PET/CT scan from January 2010 to September 2011.

3. Results

The recorded respiratory waveforms, PET/CT images and recorded result sheets are shown for the respiratory phantom and for all three patients whom participated in this study.

3.1 Patient data

Table 5.1: Summary of the patient data

Patient no.	Sex	Age (yrs)	Activity FDG (mCi)	Time of FDG admission	Time of ungated WB scan	Time of gated lung scan
1	Male	72	12.8	9h45	11h10	11h50
2	Female	55	10.3	11h30	13h00	13h50
3	Male	39	10.5	8h30	10h00	9h40

3.2 Respiratory waveforms

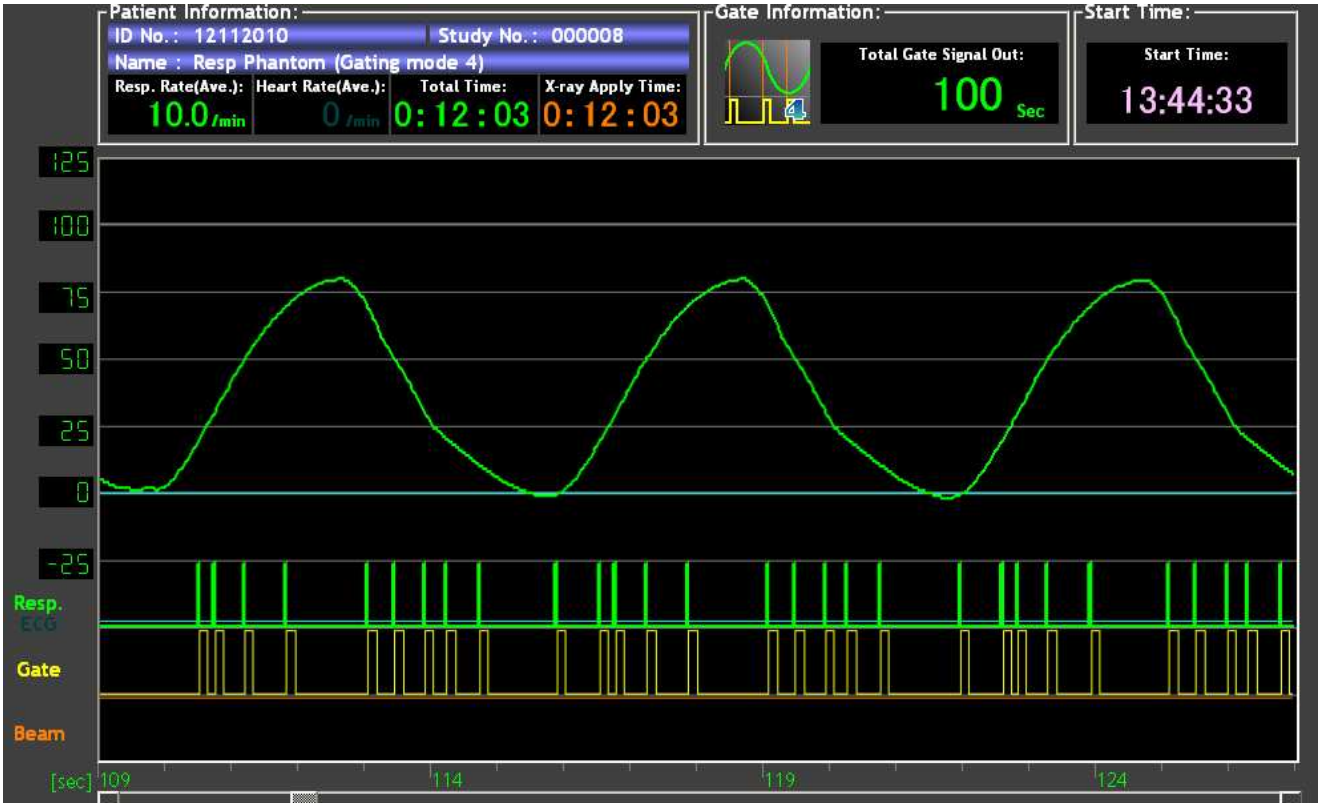

Figure 5.8: Recorded respiratory waveform of the respiratory phantom

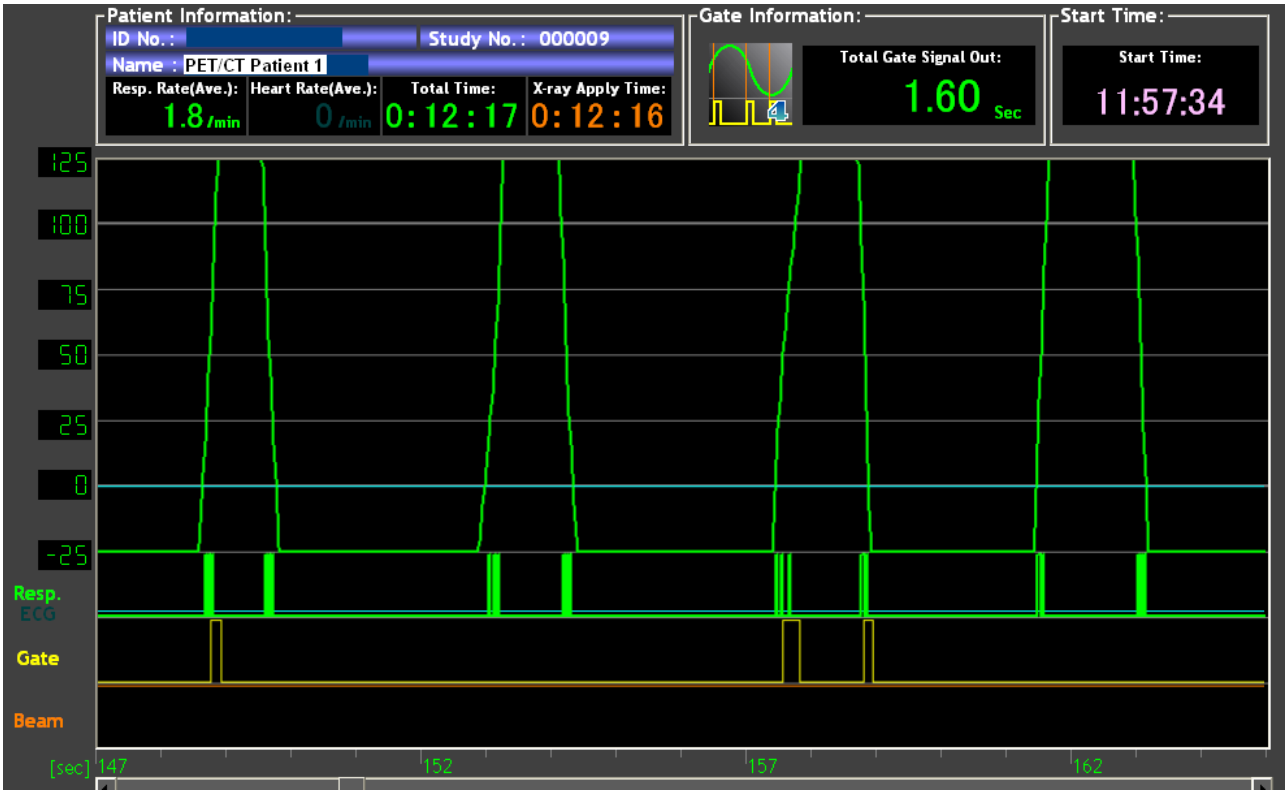

Figure 5.9: Recorded respiratory waveform of Patient 1

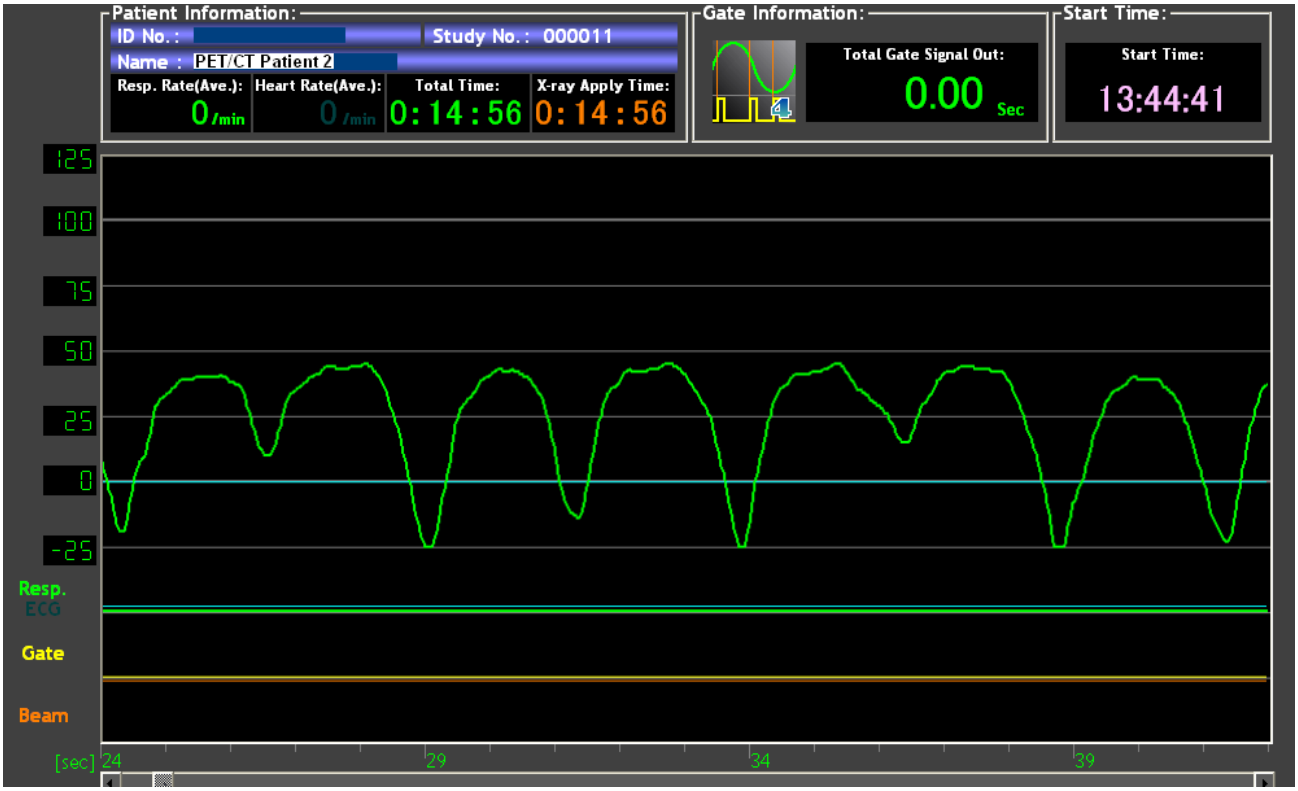

Figure 5.10: Recorded respiratory waveform of Patient 2

Figure 5.11: Recorded respiratory waveform of Patient 3

Figure 5.12: Enlarged recorded respiratory waveform of Patient 3

3.3 Gated PET/CT scans

The acquired CT and PET images are separately displayed below. The fused images are however not presented because they are very vague and somewhat blurred.

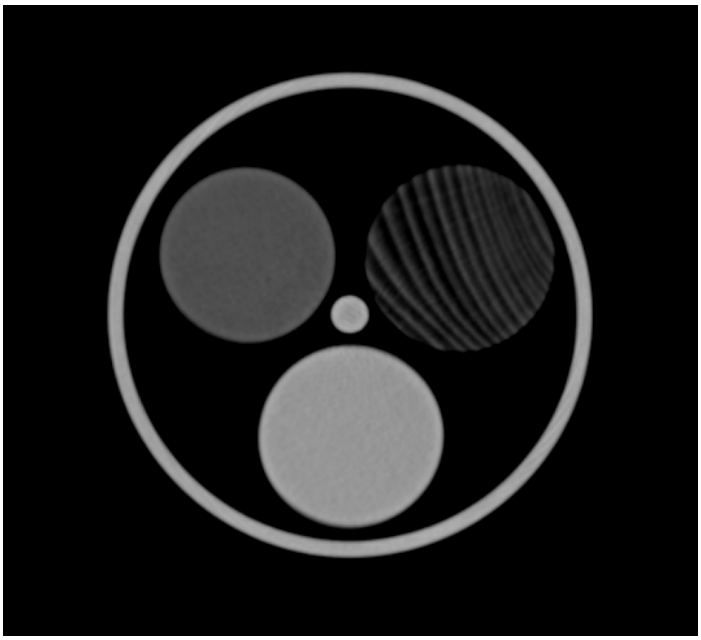

Figure 5.13: CT scan of the phantom

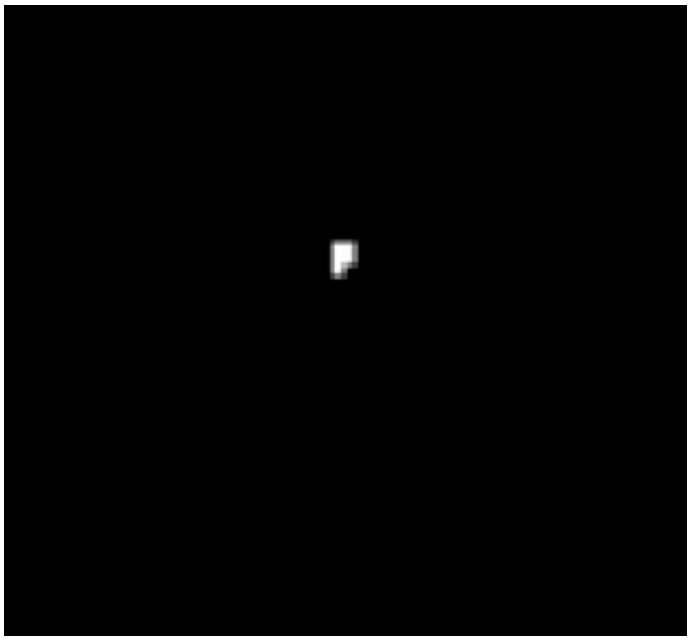

Figure 5.14: Gated PET scan of the phantom

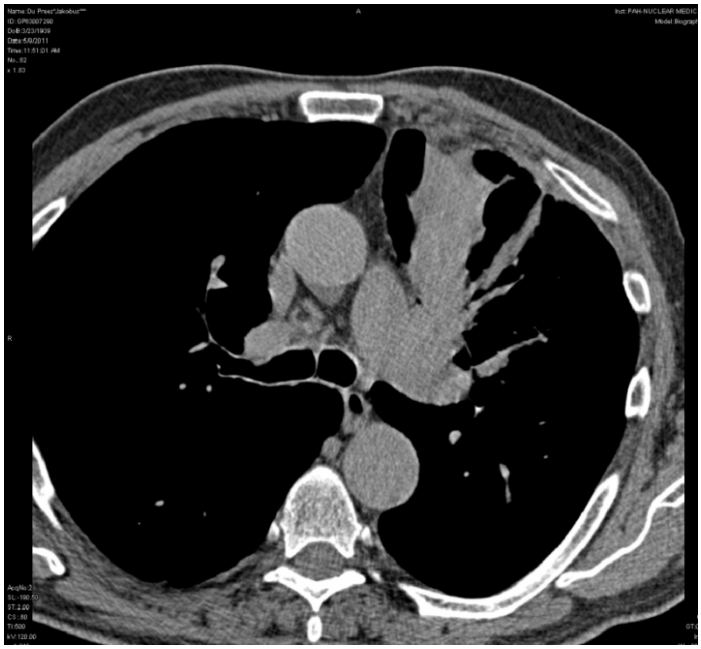

Figure 5.15: Breath-hold CT of Patient 1

Figure 5.16: Gated PET scan of Patient 1

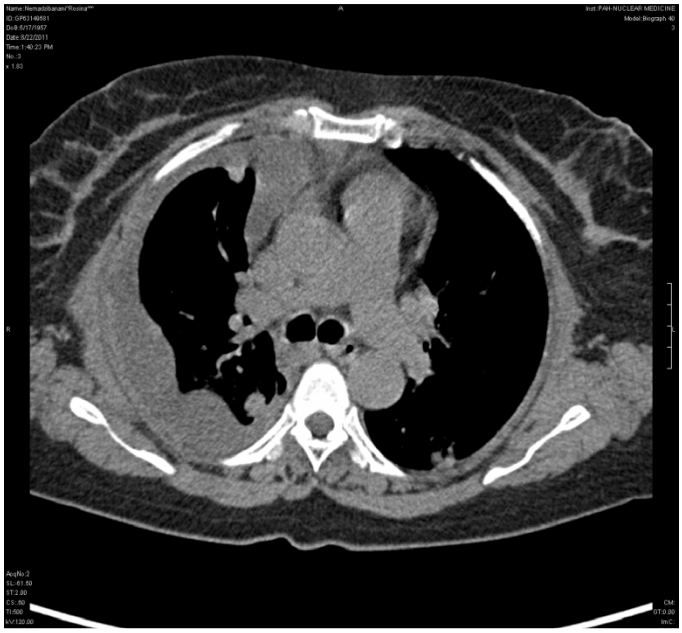

Figure 5.17: CT scan of Patient 2

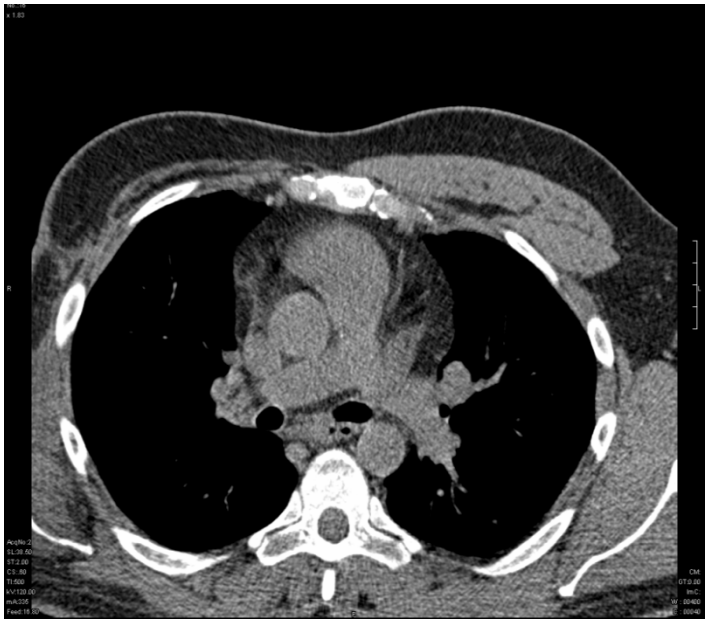

Figure 5.18: Breath-hold CT of Patient 3

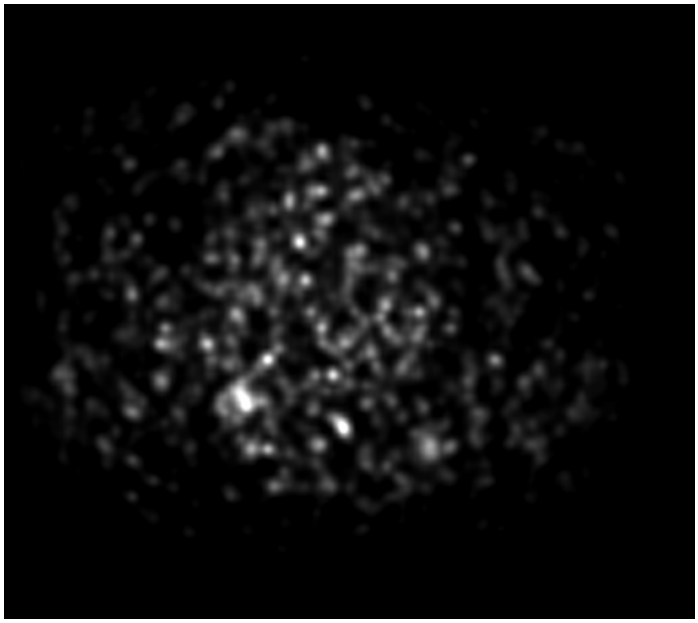

Figure 5.19: Gated PET scan of Patient 3

3.4 Recorded result sheets

Table 5.2: Non-technical parameters result sheet for a gated PET/CT scan of the respiratory phantom

Respiratory Phantom			
			NOTES
Time	**Hardware and Software Setup time**	75 minutes	Initial set-up
	Additional patient preparation time	n/a	
	Total PET/CT scan time	9 minutes	30 seconds CT + 8 minutes per PET bed
	Hardware and Software Pack-up time	20 minutes	First time disconnection and pack-up
	Manual reconstruction time	40 minutes	Instructions had to be studied and followed promptly since it was the first time for manual reconstruction
Patient participation	**Breath-hold CT scan (inspiration)**	n/a	
	Gated PET scan	n/a	
Effectiveness of gating system	**Load cell positioning**	Correct	The phantom has an stationary pocket for the load cell
	Respiratory waveform normalized	Successful	
	Waveform continually recorded	Successful	
	Software recorded preset trigger signals	Successful	
	Output gating signal to the scanner	Successful	
Success of gated scans	**Breath-hold CT scan acquisition**	n/a	A normal CT was acquired of the phantom
	Gated PET scan acquisition	Successful	
	Gated PET scan reconstruction	Successful	
	Fuse CT and PET images	Successful	
Gated results	**CT scan**	Successful	A small volume of activity was attached to the phantom which was clearly seen on all the phases of the gated scan
	Gated PET scan	Successful	
	Improved alignment between CT and PET	Unsure	The small volume could not be associated to any CT structure

Table 5.3: Non-technical parameters result sheet for a gated PET/CT scan of PET/CT Patient 1

Patient 1 - Male			
			NOTES
Time	**Hardware and Software Setup time**	13 minutes	Not skilled yet in setup
	Additional patient preparation time	5 minutes	Load strap attachment & tuning
	Total PET/CT scan time	9 minutes	30 seconds CT + 8 minutes per PET bed
	Hardware and Software Pack-up time	2 minutes	To save waveform and disconnect all hardware
	Manual reconstruction time	15 minutes	The save reconstruction parameters from the previous reconstruction was used
Patient participation	**Breath-hold CT scan (inspiration)**	Yes	Patient had good communication skills and lung function
	Gated PET scan	No	Patient moved his arms from the correct setup and placed it on top of the pressure sensor
Effectiveness of gating system	**Load cell positioning**	Moved	Position was initially correct until it was moved by the patient's hand that rested on it
	Respiratory waveform normalized	Unsuccessful	
	Waveform continually recorded	Interrupted	Interrupted after 182 seconds when patient placed arm on sensor
	Software recorded preset trigger signals	Successful	
	Output gating signal to the scanner	Interrupted	Terminated when patient placed arm on top of load cell
Success of gated scans	**Breath-hold CT scan acquisition**	Successful	Patient participated
	Gated PET scan acquisition	Unsuccessful	Due to interrupted acquisition
	Gated PET scan reconstruction	Successful	
	Fuse CT and PET images	Successful	Very low number of recorded counts and multiple artifacts
Gated results	**CT scan**	Successful	
	PET scan	Unsuccessful	Multiple artifacts cause PET images to be useless
	Improved alignment between CT and PET	n/a	Due to bad PET images

Table 5.4: Non-technical parameters result sheet for a gated PET/CT scan of PET/CT Patient 2

Patient 2 - Female			
			NOTES
Time	**Hardware and Software Setup time**	6 minutes	
	Additional patient preparation time	12 minutes	Patient had uneven breathing and was overweight. Normalization of waveform was difficult.
	Total PET/CT scan time	9 minutes	30 seconds CT + 8 minutes per PET bed
	Hardware and Software Pack-up time	1 minute	To save waveform and disconnect all hardware
	Manual reconstruction time	n/a	Unable to do reconstruction
Patient participation	**Breath-hold CT scan (inspiration)**	No	Patient had weak lung function and could not hold breath
	Gated PET scan	Yes	Patient lay still and tried to breath evenly
Effectiveness of gating system	**Load cell positioning**	Correct	
	Respiratory waveform normalized	Unsuccessful	Weak lung function and being overweight
	Waveform continually recorded	Successful	
	Software recorded preset trigger signals	Unsuccessful	No preset signals displayed
	Output gating signal to the scanner	Unsuccessful	No preset signals to send to scanner
Success of gated scans	**Breath-hold CT scan acquisition**	Successful	An ungated CT was acquired due to poor lung function
	Gated PET scan acquisition	Unsuccessful	Gating signals were not sent for acquisition
	Gated PET scan reconstruction	Unsuccessful	Software was unable to do reconstruction
	Fuse CT and PET images	n/a	Unusable PET images
Gated results	**CT scan**	Successful	
	PET scan	n/a	Result is inconclusive because the reconstruction was unsuccessful
	Improved alignment between CT and PET	n/a	No reconstructed PET images

Table 5.5: Non-technical parameters result sheet for a gated PET/CT scan of PET/CT Patient 3

Patient 3 - Male			
			NOTES
Time	**Hardware and Software Setup time**	5 minutes	
	Additional patient preparation time	3 minutes	Patient had good lung function and even breathing
	Total PET/CT scan time	9 minutes	30 seconds CT + 8 minutes per PET bed
	Hardware and Software Pack-up time	1 minute	To save waveform and disconnect all hardware
	Manual reconstruction time	5 minutes	The same reconstruction parameters from the previous reconstruction was used, and it could be done without consulting a manual
Patient participation	**Breath-hold CT scan (inspiration)**	Yes	Patient was eager to participate
	Gated PET scan	Yes	Patient had even and strong breathing and lay still
Effectiveness of gating system	**Load cell positioning**	Correct	
	Respiratory waveform normalized	Successful	Even respiration level and rate
	Waveform continually recorded	Successful	
	Software recorded preset trigger signals	Successful	
	Output gating signal to the scanner	Interrupted	Only interrupted twice, so normal gating continued after a few seconds when signal was regained
Success of gated scans	**Breath-hold CT scan acquisition**	Successful	Patient participated
	Gated PET scan acquisition	Successful	
	Gated PET scan reconstruction	Successful	
	Fuse CT and PET images	Successful	Vague because of multiple PET artifacts
Gated results	**CT scan**	Successful	
	PET scan	Unsuccessful	Multiple artifacts caused PET images to be useless
	Improved alignment between CT and PET	n/a	Due to awful PET images

3.5 Log book results

All patients who receive a PET/CT scan in the Nuclear Medicine department are recorded in a log book together with the provisional diagnosis (made from previous scans such as CT or MRI) and activity and contrast received. The number of patients who received a PET/CT scan for lung lesions between January 2010 and September 2011 was counted from these log books and recorded in figure 5.20.

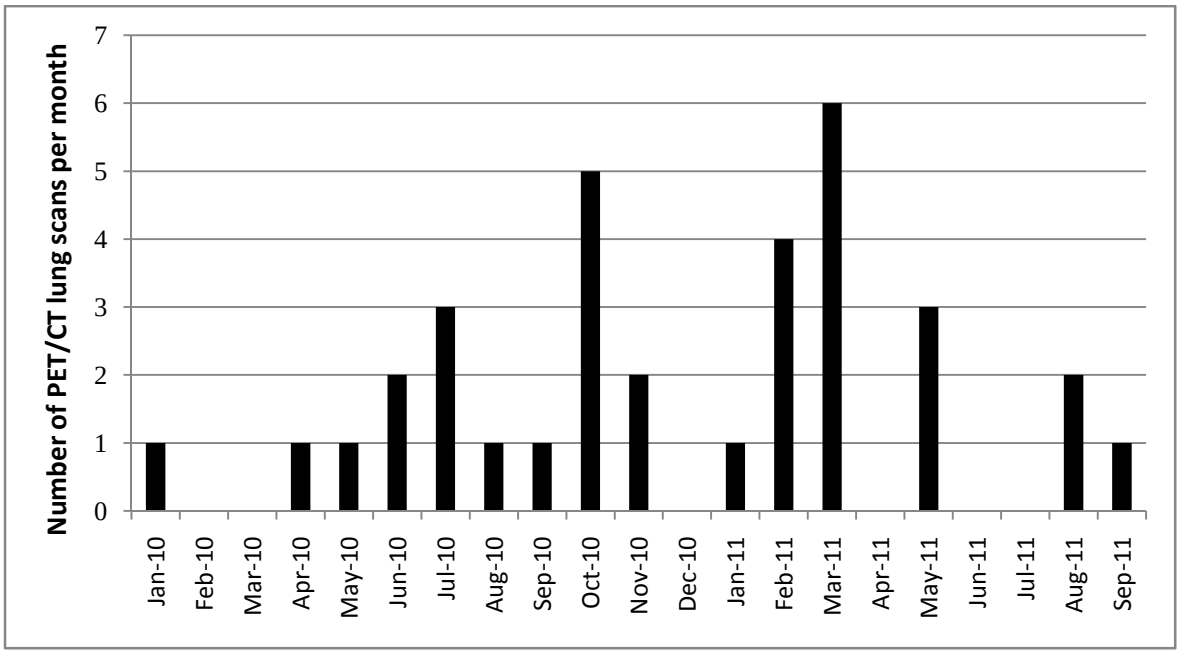

Figure 5.20: Graphical indication of the number of patients referred to the Nuclear Medicine department per month (from January 2010 to September 2011) for a PET/CT lung scan

4. Analysis

4.1 Data analysis

The aim of this chapter was to evaluate external, non-technical parameters that influence respiratory gating such as time, patient participation, effectiveness of the gating system, success of the gated scans and the gated results. These parameters can be analyzed using the recorded waveforms and the result sheets.

Table 5.6: Summary of the result sheets for the phantom and all three patients

		Phantom	Patient 1	Patient 2	Patient 3
Time	**Hardware and Software Setup time**	75 minutes	13 minutes	6 minutes	5 minutes
	Additional patient preparation time	n/a	5 minutes	12 minutes	3 minutes
	Total PET/CT scan time	9 minutes	9 minutes	9 minutes	9 minutes
	Hardware and Software pack-up time	20 minutes	2 minutes	1 minute	1 minute
	Manual reconstruction time	40 minutes	15 minutes	n/a	5 minutes
Patient participation	**Breath-hold CT scan (inspiration)**	n/a	Yes	No	Yes
	Gated PET scan	n/a	No	Yes	Yes
Effectiveness of gating system	**Load cell positioning**	Correct	Moved	Correct	Correct
	Respiratory wave form normalized	Successful	Unsuccessful	Unsuccessful	Successful
	Waveform continually recorded	Successful	Interrupted	Successful	Successful
	Software recorded preset trigger signals	Successful	Successful	Unsuccessful	Successful
	Output trigger signal to the scanner	Successful	Interrupted	Unsuccessful	Interrupted
Success of gated scans	**Breath-hold CT scan acquisition**	n/a	Successful	Successful	Successful
	Gated PET scan acquisition	Successful	Unsuccessful	Unsuccessful	Successful
	Gated PET scan reconstruction	Successful	Successful	Unsuccessful	Successful
	Fuse CT and PET images	Successful	Successful	n/a	Successful
Gated results	**CT scan**	Successful	Successful	Successful	Successful
	PET scan	Successful	Unsuccessful	n/a	Unsuccessful
	Improved alignment between CT and PET	Unsure	n/a	n/a	n/a

4.1.1 Time

The results of the phantom were not analyzed in this part of the study because it can be considered as training on the system.

The result sheets indicate that the setup time of the gating system improved from 13 minutes to 5 minutes. It can be expected that repetition of this procedure will drastically improve setup time since it will become a simple routine task. The same accounts for pack-up time.

Patient preparation time varied between 3 and 12 minutes depending on patients' participation. Repetition will again speed up the patient preparation process to less than 5 minutes on average when radiographers become familiar with the positioning of the sensor strap and instructions to be given to the patient.

The total PET/CT scan time was 9 minutes for all patients. This will not improve since the acquisition rate of 8 minutes/bed cannot be shortened if adequate counts ought to be recorded. This is almost three times the rate of ungated scans which is 3 minutes/bed.

For ungated scans, reconstruction is done automatically by the software. The manual reconstruction time for gated scans improved from 15 minutes to 5 minutes as indicated. However, if the radiation workers are trained in reconstructing the images, it is expected to generally take 5 minutes. Faster times will not be achieved because the limiting factor is the processing speed of the software.

4.1.2 Patient participation

Two of the three patients participated with the breath-hold CT scan while two other patients participated with the PET scan. When the patients have poor lung function it is difficult for them to hold their breath for the few seconds to acquire the CT scan. Participation in a gated PET scan does not require any additional effort from the patient compared to an ungated scan.

4.1.3 Effectiveness of the gating system

Every aspect of the gating system functioned successfully with the respiratory phantom due to it having a perfectly even respiratory level and respiratory rate. This is an indication that the system is functioning well when the human factor is not considered.

The load cell positioning was accurate for all three patients until one patient moved his sensor. The respiratory waveform normalization was however successful in only one of the three patients. Even though the waveforms were initially normalized in all the patients, the system merely did not adjust the respiratory level of the two patients, Patient 1 and 2, with uneven breathing levels. Automatic normalization before acquisition also failed on patient 2, so it was done manually.

The waveforms were successfully recorded for all three patients even thought they were not normalized. The waveform of Patient 1 was lost after 182 seconds because he moved the sensor when he removed his hand from the cradle position.

It can be seen from the waveforms that the software only displayed the pre-selected gating positions of Patients 1 and 3. A possible reason for the loss of signal for Patient 2 is that the "Gate out ON/OFF" button, which initiates the gating signal to the scanner, was clicked "OFF" without any warning from the software.

The gating signal received by the scanner from the PC was interrupted for both Patients 1 and 3 where the pre-selected gating positions were sent to the scanner. The signals were however retrieved again and gating acquisition could continue. This implies however that a radiographer should monitor the PC continually during acquisition and click the "CONTINUE ACQUISITION" button when the "SIGNAL INTERRUPTION" message is displayed.

From figures 5.12 and 5.13 it appears that the gated signal was not sent to the scanner, but that specific snapshot of the figure (between 403 and 431 seconds) was simply a period during signal interruption.

4.1.4 Success of the gated scans

A CT scan was successfully acquired of all three patients even though the breath-hold technique was applied to only two of them (see figures 5.15, 5.17 and 5.18). PET scans were successfully acquired for two patients where gating signals were sent to the scanner and both scans were also successfully reconstructed. Very few counts were however acquired for Patient 1 since the signal was interrupted after 182 seconds (3 minutes) of acquisition.

The PET scan of Patient 2 could not be reconstructed since no gating signals were sent to the scanner and therefore no counts could have been acquired. In the cases where PET images were successfully reconstructed, the different phases could be separately fused with the CT image. This however caused blurred images due to the multiple artifacts on the PET scans and definitely did not improve misalignment compared to ungated scans.

4.1.5 Gated results

Even though the PET scans of Patient 1 and 3 were successfully acquired are they not viable due to multiple artifacts. The artifacts could be accounted for by the limited counts recorded due to trigger loss.

The position of the bed should be selected over the center of the lesion since the respiratory gating list mode protocol only has one available bed. Due to the multiple artifacts it cannot be verified whether the correct bed position was indeed selected.

4.2 Log book analysis

Very few patients are annually referred to the Nuclear Medicine department for a PET/CT scan of the lungs. Figure 5.20 is an indication of the number of patients who received a PET/CT scan for lung lesions from January 2010 to September 2011. A total of 32 cases were recorded with an average of 1.4 and 1.9 patients per month for 2010 and 2011 respectively. On average 88 patients are scanned on the PET/CT scanner per month (4 patients daily) and therefore only approximately 2% of the total PET/CT patient population are lung patients.

It is important to regard these statistics when considering purchasing and implementing the respiratory gating system.

5. Discussions

Non-technical parameters that have an influence on acquiring respiratory gated scans were considered in this chapter. The specific parameters focused on were; time of procedure, patient participation, effectiveness of the system and the gated results.

Even when respiratory gating is a routine protocol at an institution, it is expected to take longer than ungated scanning because of additional setup time, longer acquisition times to record an adequate number of counts and also for patient preparation. When an estimated 5 minutes are planned for setup, 1 minute for pack-up, 5 minutes for patient preparation, 9 minutes to acquire a gated PET/CT scan and 5 minutes for reconstruction, the total scan time will be approximately 25 minutes.

Most patients admitted to public institutions for a PET/CT scan have adequate communication skills and the intellectual ability to understand and participate in gated scans. Sometimes and unfortunately, in moments of unfamiliarity and loss of concentration they forget to follow instructions. However when gating software is obtained for the CT modality of the PET/CT scanner, patients would not have to hold their breath for the scan. This will cause the patient participation for a gated scan to be equal to that of an ungated PET/CT scan, currently acquired at Steve Biko Academic hospital.

It was relatively easy to find the correct position on the patients' diaphragm to position the pressure sensor. However, in the case where the patient was overweight, it was more difficult to identify a rib bone where adequate pressure could be applied to the sensor.

The gating system's hardware seems to be efficient but some software problems did occur. The hardware was successful in recording the patients' waveform but normalization failed in most cases. Initial normalization was successful, but when the patients' respiratory level changed during the scan the software did not automatically readjust the normalization. This caused some of the respiratory gating phases to not be displayed and acquired. Also, the system did not display any warning messages when the pre-determined respiratory signal was acknowledged but not sent to the scanner.

The output gating signal was interrupted several times. By clicking on the "CONTINUE ACQUISITION" message, the signal could be retrieved and acquisition could continue. But during the time of signal lost some counts were missed. Incorrect normalization also caused many gates, especially at the extreme respiratory positions, to have a very low number of counts recorded.

The simplest solution to the low number of acquired counts would be to increase the acquisition time of the bed. 10 minutes is unfortunately the maximum acquisition time for this specific list mode protocol and the extra 2 minutes will doubtfully have a notable influence. Another solution will be to increase the dose ^{18}F-FDG admitted to the patient. This however will cause the patient to receive a higher dose than which is acceptable by the international standards.

The quality of the images is the biggest concern for gated scanning. Gated acquisition can only be considered after a solution to the software interruptions and multiple artifacts is found. Professional training on how to operate the gating hardware and software and also to understand and solve these problems should they continue to occur will be beneficial.

Another major software limitation to the system is the size of the anatomical area where gating is allowed. The position of the single available PET bed is determined from the CT scan, but what if the lesion position is uncertain, or if more than one lesion is present in the lung?

Furthermore when the logbook statistics are considered, only 2% of all patients admitted to the Nuclear Medicine department received a lung scan.

CHAPTER VI – CONCLUSIONS

Respiratory gating for CT and PET/CT scanners is a well-researched and accepted solution for improving image quality, diagnostic accuracy and the effectiveness of radiotherapy for patients with lung tumors. However all these studies on 4D respiratory gating was done abroad and not in the local public health sector.

The aim of this study was to compare the differences in delineated target volumes between respiratory gated and ungated CT lung scans. The primary objective was to acquire gated CT and PET/CT scans and to measure and compare the target volumes. The secondary objective was to analyze the influence that gated studies will have on the way patients receive radiotherapy treatment and to determine whether it will be meaningful to purchase and implement respiratory gating systems on CT and PET/CT scanners in South African hospitals.

In the first section of this study, 4D respiratory gated CT scans were imported from first world countries and delineated using 4D software. In the second section gating was simulated with the breath-hold technique in a South African academic hospital since the hospital had no access to respiratory gating software. The target volumes decreased in both sections for all patients, without exception, when gating was applied. An average decrease of 14.93% in the GTVs was detected in the 4D gated scans and when gating was simulated, the average decrease in the CTVs was 14.33%. This is coincidental that the two values are so close to each other because great standard deviations were calculated in each case. This reduction indicates that almost 15% of the area treated with ungated radiotherapy is actually normal tissue, most likely heart or lung tissue since it is in close proximity of the lesion.

The above results proved that respiratory gating will have just as big influence on the target volumes of South African patients as it has on patients in other countries. The biggest difference however to consider between South Africa and first world countries is the patient population. It was shown in Chapter IV that the vast majority of lung patients admitted to Steve Biko public hospital for lung cancer are palliative.

A possible explanation for the majority palliative patients in this study is because the patients in the South African public health sector wait until symptoms are unbearable before consulting a doctor or after no traditional healer could find a cure. By that time the cancer has spread to a palliative state. In the South African private sector, the tendency might be that patients are diagnosed with lung cancer at a less advanced stage.

During the time period of this study only 0.03% of the total radiation therapy patient population was radical lung cancer patients. It was discussed at the end of chapter IV that only radical lung cancer patients will benefit from respiratory gating since palliative patients are treated with two simple parallel opposing fields which will not be influenced by gating or any motion-reduction technique.

To evaluate the influence that gating will have on treatment planning, IMRT plans were created on a 4D gated and an ungated scan of a lung patient and compared. The target volume coverage differed by less than 1% between the gated and the ungated plans, but significant dose reductions to all the OARs of up to 32.65% for the contralateral lung were recorded on the gated plan compared to the ungated plan. This indicates that using gated scans to do planning will have a significant influence on the dose delivered to normal tissue during radiation therapy.

The third section of this study was used to evaluate external but crucial parameters influenced by gating, such as time of procedure, patient participation, effectiveness of the system, and also the gated results. It was noted that gated scanning takes much longer than normal/ungated scanning, but in the South African public health sector this will not be a limiting factor when good time management is applied. Patients are also willing and able to participate in the studies. The biggest concerns however were the software limitations and the quality of the images.

Multiple artifacts were detected on all PET images due to an inadequate amount of counts detected. The only way to improve the image quality will be to increase the acquisition time per bed or to increase the ^{18}F-FDG dose admitted to the patient, but this will not solve the problem. Other major concerns were the software limitations, the area of acquisition (only a single PET bed is available) and the signal interruptions during acquisition. Automatic normalization was also seldom successful.

Professional training can be recommended to solve most of the external parameter problems detected. The training should include effective setup methods, operation of the gating hardware and software and also problem solving should these problems continue to occur. Different gating systems with other trigger devices might also be more successful, as was proved in multiple studies done abroad.

It was proved that respiratory gating causes a significant reduction in the target volume and also has a positive influence on the doses delivered to normal tissue during radiation therapy treatment. However, the patient population that will benefit from this technique is very small and the financial implications to obtain, install and train the radiation workers will be massive. It can therefore be concluded, considering all of the above, that it will not be meaningful to purchase and implement respiratory gating systems on CT and PET/CT scanners in the South African public health sector.

CHAPTER VII - REFERENCES

1. Alessio, A.M., et al. (2007). Cine CT for Attenuation Correction in Cardiac PET/CT. *Eur J Nucl Med,* 48(5): 794 – 801.

2. Anzai Medical. (2007). AZ-733V User's Manual, Respiratory Gating System. Version 2.5.

3. ARC/NEMA Standards Publications no PS 3. (2009). *Digital Imaging and Communication in Medicine (DICOM).* Virginia, USA: National Electrical Manufacturers Association. Parts 1 – 18.

4. Bettinardi, V., Rapisarda, E., Gilardi, M.C. (2009). Number of partitions (gates) needed to obtain motion free images in a Respiratory gated 4D-PET/CT study as a function of the lesion size and the motion displacement. *Med. Phys.*, 36 (12): 5547 – 5558.

5. Bidgood, W.D., Horii, S.C. (1992). PACS Mini refresher course: Introduction to the ARC-NEMA DICOM standard. *RadioGraphics,* 12(2): 345 – 355.

6. Branstetter, B.F., et al. (May 2005). Head and Neck malignancy: Is PET/CT more accurate than PET or CT alone? *Radiology* (4th Ed), 235(2): 580-586.

7. Bushberg, J.T., et al. (2002). *The essential physics of medical imaging.* (2nd Edition). Philadelphia: Lippincott Williams & Wilkens.

8. Dawood, M., et al. (2007). Respiratory gating schemes in PET: A quantitative comparison. *Med. Phys*., 34(7): 3067 – 3076.

9. Dawood, M., et al. (2009). Optimal number of respiratory gates in positron emission tomography: A cardiac patient study. *Med. Phys*., 36(5): 1775 – 1784.

10. ELEKTA (April 2011). Focal4D Training Guide. Version 4.62.00.

11. Ellis, H., Logan, B., Dixon, A. (1991). *Human Cross-Sectional Anatomy: Atlas of body sections and CT images.* (1st Edition). Oxford, UK: Butterworth Heinemann Ltd.

12. Faasse, T., Shreve, P. (2010). Patient and Image Data Management in Positron Emission Tomography-Computed Tomography for Radiation Therapy and Therapy Response Assessment. *Seminars in UNTRASOUND CT and MRI,* 31(6): 480 – 489.

13. Ford, E.C. (2003). Respiration-Correlated spiral CT: A method of measuring respiratory induced anatomic motion for radiation treatment planning. *Med. Phys.,* 30(1): 88 – 97.

14. Guo, B., Xu, X.G., Shi, C. (2011). Real time 4D IMRT Treatment Planning Based on a Dynamic Virtual Patient Model: Proof of Concept. *Med. Phys.,* 38(5): 2639 – 2650.

15. International Commission on Radiation Units and Measurements (2010). Report 83. *Journal of the ICRU.* 10(1): 7 – 61.

16. Kahn, F.M. (2003). *The physics of radiation therapy.* (3rd Edition). Philadelphia: Lippincott Williams & Wilkins.

17. Marks, L.B., et al. (2010). Use of normal tissue complication probability models in the clinic. *Int. J. Radiation Oncology Biology and Physics,* 76(3): 10 – 19.

18. Martinez-Möller, A., et.al. (2007). Dual cardiac-respiratory gated PET: implementation and results from a feasibility study. *Eur J Nucl Med Mol imaging,* 34: 1447 – 1454.

19. Nehmeh, S.A., et al, (July 2002). Effect of respiratory gating on quantifying PET images of lung cancer. *The journal of Nuclear medicine,* 43(7): 876 – 881.

20. Nehmeh, S.A., Erdi, Y.E., et al. (2004). Quantitation of respiratory motion during 4D-PET/CT acquisition. *Med. Phys.,* 31(6): 1333 – 1338.

21. Pan, T., et al. (2004). 4D-CT imaging of a volume influenced by respiratory motion on multi-slice CT. *Med. Phys.*, 31(2): 333 – 340.

22. Pan, T. (2005). Comparison of helical and cine acquisitions for 4D-CT imaging with multislice CT. *Med. Phys.*, 32(2): 627 – 634.

23. Radiological Society of North America (RSNA) and American College of Radiology (ACR). "Positron Emission Tomography – Computed Tomography" http://www.radiologyinfo.org/en/info.cfm?pg=PET

24. Ramsey, C.R., Scaperoth, D., Arwood, D., Oliver, A.L. (1999). Clinical efficacy of respiratory gated conformal radiation therapy. *Med. Dosim.*, 24(2). 115 – 119.

25. Saito, T., Sakamoto, T., Oya, N. (2010). Predictive factors for lung dose reduction by respiratory gating at radiotherapy for lung cancer. *J Radiat Res.*, 51(6): 691 – 698.

26. Saw, C.B., et. al. (2007). A review of the clinical implementation of respiratory-gated radiation therapy. *Biomed Imaging Interv. Journal*, 3(1):e40. 1 – 8.

27. Shrimpton, P.C., Miller, H.C., Lewis, M.A., Dunn, M. (2005). *Doses from Computed Tomography (CT) examinations in the UK.* Oxon, UK: National Radiology Protection Board (NRPB).

Annexures

500 Word summary

Ethics clearance certificate

CD

SUMMARY

A study was done at Steve Biko Academic hospital to determine the influence that respiratory gating will have on target volumes used in radiotherapy treatment planning. The primary objective was to compare target volumes of respiratory gated scans to ungated scans and to determine whether it will be meaningful to permanently implement a 4D respiratory gating system on CT scanners in the South African public health sector and to use these images for target volume delineation in radiotherapy planning.

The study consisted of three sections. In the first section, 4D respiratory gated CT images were obtained and delineated with 4D software. The full-inspiration and full-expiration phases of the gated scans were then fused to obtain ungated images which were also delineated. The gross tumor volumes (GTVs) of the gated phases were compared to the ungated GTVs, and found that on average the volumes decreased by 14.63% with a standard deviation of 7.96% when gating was applied.

Yet another aim was to determine the influence that 4D imaging will have on radiotherapy treatment planning. One of the 4D study sets was imported to the XIO treatment planning system where IMRT treatment plans were created on both the gated and ungated scans. The plans conformed to the treatment aims and restrictions when clinical parameters such as DVHs were used to evaluate it. The planned target volume coverage differed by less than 1% between the gated and the ungated plans, but significant dose reductions to the OARs of up to 32.65% to the contralateral lung were recorded on the gated plan.

In the second section of this study, respiratory gated CT scans were simulated by applying the breath-hold technique to lung cancer patients. The technique was applied during full-inspiration which fundamentally represents the maximum peak of the sinusoidal respiratory waveform. An ungated scan was also acquired during normal respiration. The clinical target volumes (CTVs) were identified on both scans by three oncologists and the average CTVs were compared. It was found that the CTVs decreased significantly by an average of 14.33%.

Palliative patients receive parallel opposing field therapy which is planned from 2D films. It is very unlikely that these opposing field sizes will differ when gating is applied. It was therefore concluded that only radical lung patients, which was estimated to be a mere 0.03% of the total radiation therapy patient population, will benefit by implementing respiratory gating or any motion-reduction technique.

For the third section of the study, respiratory gated PET scans were acquired on a PET/CT scanner to evaluate external, non-technical parameters that will influence respiratory gating. The results indicated that time and patient participation were not limiting factors. The biggest concerns however were the effectiveness of the gating system, software limitations and the gated results. These problems might be minimized with thorough training on the system.

All three sections as well as the financial implications were considered to conclude that it will not be meaningful to implement 4D respiratory gating techniques in the South African public health sector.

(499 words)

Key words: Respiratory, Gating, CT, PET/CT, Breath-hold, Four-dimensional (4D), Radiotherapy, Radiation Therapy, Gated, Ungated