Four-Dimensional Imaging of Respiratory Motion in the Radiotherapy Treatment Room Using a Gantry Mounted Flat Panel Imaging Device

by

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James Bowsher, Ph.D.

Nicole Larrier, M.D.

Dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Medical Physics Program in the Graduate School of Duke University

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ABSTRACT

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Abstract

Imaging respiratory induced tumor motion in the radiation therapy treatment room could eliminate the necessity for large motion encompassing margins that result in excessive irradiation of healthy tissues. Currently available image guidance technologies are ill-suited for this task. Two-dimensional fluoroscopic images are acquired with sufficient speed to image respiratory motion. However, volume information is not present, and soft tissue structures are often not visible because a large volume is projected onto a single plane. Currently available volumetric imaging modalities are not acquired with sufficient speed to capture full motion trajectory information. Four-dimensional cone-beam computed tomography (4D CBCT) using a gantry mounted 2D flat panel imaging device has been proposed but has been limited by high doses, long scan times and severe under-sampling artifacts. The focus of the work completed in this thesis was to find ways to improve 4D imaging using a gantry mounted 2D kV imaging system. Specifically, the goals were to investigate methods for minimizing imaging dose and scan time while achieving consistent, controllable, high quality 4D images.

First, we introduced four-dimensional digital tomosynthesis (4D DTS) and characterized its potential for 3D motion analysis using a motion phantom. The motion phantom was programmed to exhibit motion profiles with various known amplitudes in
all three dimensions and scanned using a 2D kV imaging system mounted on a linear accelerator. Two arcs of projection data centered about the anterior-posterior and lateral axes were used to reconstruct phase resolved DTS coronal and sagittal images. Respiratory signals were obtained by analyzing projection data, and these signals were used to derive phases for each of the projection images. Projection images were sorted according to phase, and DTS phase images were reconstructed for each phase bin. 4D DTS target location accuracies for peak inhalation and peak exhalation in all three dimensions were limited only by the 0.5 mm pixel resolution for all DTS scan angles. The average localization errors for all phases of an assymetric motion profile with a 2 cm peak-to-peak amplitude were 0.68, 0.67 and 1.85 mm for 60° 4D DTS, 360° CBCT and 4DCT, respectively. Motion artifacts for 4D DTS were found to be substantially less than those seen in 4DCT, which is the current clinical standard in 4D imaging.

We then developed a comprehensive framework for relating patient respiratory parameters with acquisition and reconstruction parameters for slow gantry rotation 4D DTS and 4D CBCT imaging. This framework was validated and optimized with phantom and lung patient studies. The framework facilitates calculation of optimal frame rates and gantry rotation speeds based on patient specific respiratory parameters and required temporal resolution (task dependent). We also conducted lung patient studies to investigate required scan angles for 4D DTS and achievable dose and scan times for 4D DTS and 4D CBCT using the optimized framework. This explicit and
comprehensive framework of relationships allowed us to demonstrate that under-sampling artifacts can be controlled, and 4D CBCT images can be acquired using lower doses than previously reported. We reconstructed 4D CBCT images of three patients with accumulated doses of 4.8 to 5.7 cGy. These doses are three times less than the doses used for the only previously reported 4D CBCT investigation that did not report images characterized by severe under-sampling artifacts.

We found that scan times for 200° 4D CBCT imaging using acquisition sequences optimized for reduction of imaging dose and under-sampling artifacts were necessarily between 4 and 7 minutes (depending on patient respiration). The results from lung patient studies concluded that scan times could be reduced using 4D DTS. Patient 4D DTS studies demonstrated that tumor visibility for the lung patients we studied could be achieved using 30° scan angles for coronal views. Scan times for those cases were between 41 and 50 seconds. Additional dose reductions were also demonstrated. Image doses were between 1.56 and 2.13 cGy. These doses are well below doses for standard CBCT scans. The techniques developed and reported in this thesis demonstrate how respiratory motion can be imaged in the radiotherapy treatment room using clinically feasible imaging doses and scan times.
Dedication

This work is dedicated to my mother, Jody, who inspired and motivated me with her enthusiasm and encouragement. This work is also dedicated to my father, Douglas, who taught me the importance of being practical, using common sense, paying attention to details and taking pride in one’s work. I thank my parents for the numerous ways in which they have influenced and supported me.
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<td>AI</td>
<td>Angular Interval</td>
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<tr>
<td>AP</td>
<td>Anterior-Posterior</td>
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<tr>
<td>CT</td>
<td>Computed Tomography</td>
</tr>
<tr>
<td>CBCT</td>
<td>Cone-Beam Computed Tomography</td>
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<tr>
<td>CNR</td>
<td>Contrast-to-Noise Ratio</td>
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<td>DTS</td>
<td>Digital Tomosynthesis</td>
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<tr>
<td>fps</td>
<td>Frames Per Second</td>
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<td>FR</td>
<td>Frame Rate</td>
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<td>GRS</td>
<td>Gantry Rotation Speed</td>
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<td>ITV</td>
<td>Internal Target Volume</td>
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<td>LR</td>
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1 Introduction

1.1 Clinical Motivation and Background

1.1.1 Prevalent Thoracic and Abdominal Cancers and Indications for Radiotherapy

In the United States, cancer is the second leading cause of death for both males and females. Lung cancer is the second most commonly diagnosed cancer for both men and women and is responsible for more deaths than any other cancer.\textsuperscript{1,2} It is estimated that lung cancer was responsible for about 30\% of cancer-related deaths in males and 26\% in females in both 2008 and 2009. Cancers of the pancreas and liver are also among the ten leading causes of cancer deaths for both men and women.\textsuperscript{1,2}

Lung cancers are categorized into two main categories: small cell lung cancer (SCLC) and non-SCLC (NSCLC), with SCLC and NSCLC accounting for approximately 20\% and 80\% of lung cancers, respectively.\textsuperscript{3} Standard management of SCLC usually includes combined chemotherapy and radiation therapy. Management of NSCLC may include surgery, chemotherapy and/or radiation therapy. When possible, NSCLC should be treated by surgical resection. While survival rates are relatively high for patients treated surgically, there are many contraindications to surgical treatment, and only about 20\% of patients are good candidates for curative surgery. Definitive radiation therapy is prescribed for about 40\% of these patients, and definitive chemoradiation is prescribed for other patients with NSCLC.\textsuperscript{4}
For patients with cancer of the pancreas, surgical resection in combination with chemotherapy and/or radiation is the only potentially curative management strategy. Local failure after resection occurs in the majority of patients. Thus, strong indications exist for adjuvant radiation therapy. Studies have shown that adjuvant radiation therapy reduces local failure rates and increases both 2 and 5 year survival rates. Unresectable pancreatic cancers are usually managed with combination chemotherapy and radiation. Various studies show that the best short term survival rates are achieved when both chemotherapy and radiation are used as opposed to using either alone.5

Hepatocellular carcinoma (HCC) is the most common primary liver cancer. If resectable, local control is best achieved by surgical resection. Conformal radiation therapy may be used as part of a multi-modality approach with surgery or a number of other procedures used to treat liver cancer.6

In addition to primary lung, pancreas and liver cancers, these organs may be the sites of metastatic disease from other primary cancers. Radiation therapy is indicated for treatment of many metastatic lesions in abdominal and thoracic regions.

1.1.2 Volume Definitions in Radiotherapy

The currently used language and methodology for defining radiotherapy treatment volumes was standardized by the International Commission on Radiation Units and Measurements (ICRU) Reports 50 and 62.7,8 ICRU Report 50 was published in 1993 and specifies volumes as follows. The visible tumor is referred to as the gross
tumor volume (GTV). The gross tumor volume plus the region that may contain microscopic spread of the disease is called the clinical target volume (CTV), and the planning target volume (PTV) is the CTV plus a margin that accounts for geometric uncertainties. As the name would suggest, the PTV is the volume to which the dose delivery is planned. The GTV and CTV are volumes that are defined by a physician based on clinical information such as images, pathology and patient history. The PTV includes a margin that accounts for inaccuracies in patient setup, organ motion or any other uncertainties.

Between 1993 and 1999 there were considerable advancements in imaging capabilities (positron emission tomography and magnetic resonance imaging) and in delivery capabilities such as the advent of intensity modulated radiation therapy (IMRT). These technologies resulted in an enhanced ability to delineate tumor volumes and the ability to deliver more conformal dose distributions. This prompted the ICRU to provide a more detailed methodology for defining the PTV. In 1999 the ICRU published Report 62 as a supplement to Report 50. The primary addition was the concept of the internal margin (IM) to delineate between the uncertainties due to organ motion (respiration, bladder or rectum filling, etc.) and the uncertainties due to setup errors. Thus, the internal target volume (ITV) is the CTV plus the IM, and the PTV is the ITV plus a setup margin (SM). These volumes are illustrated in Figure 1.1.
1.1.3 Summary of Observed Patient Respiratory Motion Characteristics

Respiration induces motion in most thoracic and abdominal organs including the lungs, liver, pancreas and kidneys. Important characteristics that define respiratory patterns include amplitude, period, regularity and baseline. Studies show that correlations between these parameters and tumor location, tumor size or pulmonary function do not exist and must be determined on an individual basis.9,10

Respiratory period varies from patient to patient. It also varies from day to day and even during a period of observation for a single patient. Average respiratory periods for healthy individuals typically range from 3.4 s to 6 s. For patients with lung cancer, average respiratory periods range from 3.2 s to 7.5 s.11 In the absence of coaching, breathing patterns are irregular in frequency and exhibit baseline drifts for both healthy individuals and cancer patients. Audio-visual coaching has been shown to eliminate baseline drifts and help improve regularity.11
Amplitudes of respiration induced tumor motion can be relatively large for tumors in abdominal and thoracic regions. Observed lung tumor motion displacement data from 14 previous studies was summarized by the American Association of Physicists in Medicine Task Group 76 (AAPM TG-76) in their report on the management of respiratory motion in radiation oncology. The data are shown in millimeters in Table 1.1. Superior-inferior (SI) displacements up to 50 mm have been observed, and lateral (LR) and anterior-posterior (AP) displacements up to 16 and 24 mm have also been seen. Data for motion of the pancreas, liver and kidneys were also presented in this report. For shallow breathing, SI displacements up to 4 cm were observed, and for deep breathing, up to 8 cm displacements were observed.
1.1.4 The Increasing Need for Motion Management

While current standard doses and fractionation schedules improve local control and often survival rates, normal tissue toxicity usually limits dose and therefore efficacy of radiation therapy. To give a specific example, basic radiobiology principles indicate that doses of 80 – 100 Gy are needed to eliminate common lung tumors. Current standard doses of 60 – 66 Gy result in local recurrence rates of 33% - 52%. As systemic therapies continue to improve, the role of radiation therapy in achieving local control is...
becoming more important in the management of lung cancer patients. There are various methods under investigation which aim to increase local control while controlling toxicities. For all therapies involving radiation therapy, reducing the volume of normal tissue irradiated helps to control toxicities. One substantial opportunity for margin reduction for thoracic and abdominal radiation therapy is the reduction of the internal margin (IM), or the margin which is applied to account for intra-fractional motion. For tumors located in abdominal and thoracic regions, respiratory motion is often the primary constituent of intra-fractional motion.

Various dosimetric parameters such as mean dose to an organ and organ volume receiving a specified dose or greater have been consistently correlated with incidence of toxicities in abdominal and thoracic organs including but not limited to the lungs, liver, and small bowels. Technologies of the past mandated extensive field sizes. Thus, high doses were delivered to large volumes of normal tissue. Resulting toxicities have been prohibitive to dose escalation.

Advances in immobilization devices and on-board image guidance as well as advanced radiation delivery technologies such as conformal radiation therapy (CRT) and intensity modulated radiation therapy (IMRT) have begun to address this issue. Immobilization devices and on-board image guidance help to reduce uncertainties in errors due to setup and intra-fractional patient movement. CRT and IMRT make it
possible to achieve conformal dose distributions and at least partially avoid dose accumulation in critical structures.

Since the advent of these technologies, dose-escalation for definitive radiotherapy has been investigated by various phase I and II trials. Many studies have reported positive responses to dose-escalation, but for very high doses, there are some disagreements regarding safety and efficacy. For example, analyses of a trial conducted by the Radiation Therapy Oncology Group (RTOG 93-11) reported that doses of 90.3 Gy to inoperable NSCLC did not improve outcomes compared to lower doses and were too toxic.26, 27 A similar trial conducted in the Netherlands reported that dose-escalation to 94.5 Gy was both safe and beneficial in terms of outcome.28 Both trials studied dose-escalation to NSCLC using CRT and typical fractionation schedules. Both studies also assigned individuals to risk groups and administered higher doses to the lower risk groups. Differences in patient selection and factors used to assign individuals to risk groups may be responsible for the different conclusions. Dose-escalation is still in its infancy. It is very important in this endeavor that treated volumes are minimized to reduce the risks of toxicity and facilitate the delivery of doses that are adequate to control disease. Respiratory motion can have large effects on treatment volumes if not accounted for and should be managed for optimal results of dose-escalation trials.

While dose-escalation investigations for standard fractionated schedules continue, hypofractionated schedules are also being investigated. Full prescription
doses may be delivered in a single fraction; this is called stereotactic radiosurgery (SRS). The doses may also be delivered in a few fractions. This is known as stereotactic radiotherapy (SRT) or stereotactic body radiotherapy (SBRT). Most studies have demonstrated phenomenal improvements in local control over conventional fractionated deliveries for both lung \textsuperscript{29-32} and liver\textsuperscript{29, 33, 34}. Many of these studies report one and two year local control rates that are greater than 90\% for NSCLC. In 2008 Gunven et al. reported long term survival of patients treated for liver cancer with SRT.\textsuperscript{35} These are the first ever long term survivors of inoperable liver cancer. Local control was better for higher doses, but there is still concern about toxicities for these treatments.\textsuperscript{36}

Reducing the treated volumes for SRS and SRT/SBRT procedures is important for the same reasons as for standard fractionated treatments, and volume reduction is even more important due to the risk of late term effects associated with hypofractionation. Respiratory management is almost always a part of lung and liver SRT and SRS treatments. Many investigators are developing new methods for better controlling and accounting for respiratory motion for SRT.\textsuperscript{37-39} The precision of respiratory motion management is exceedingly more critical for SRT and SRS than for conventionally fractionated deliveries. Errors during a single fraction may cause severe under-dosage of a malignancy and/or severe over-dosage of normal tissue.

Concurrent chemotherapy and radiation regimens are already considered standard clinical practice\textsuperscript{4}, but there are various new combination treatment regimens
being investigated and surely more to come. Investigators are studying new chemotherapy regimens\textsuperscript{40, 41} as well as dose-escalation.\textsuperscript{42, 43} Reducing normal tissue irradiation is especially important for these treatments because the chemotherapy agents increase tissue sensitivity to radiation, therefore drastically increasing radiation toxicity. Many combination chemo-radiation regimens are associated with high rates of toxicity.\textsuperscript{4} Respiratory motion management should play a role in reducing normal tissue irradiation and therefore toxicity for existing standard treatments and while new regimens are being developed and tested.

Proton irradiation is another area of recent development in radiation oncology. The dosimetric advantages (sharp lateral penumbra and finite penetration range) potentially provide increased normal tissue sparing over photon irradiation.\textsuperscript{45, 46} Several centers have already investigated the use of protons for treating sites in the thorax including liver\textsuperscript{47} and lung\textsuperscript{48-51} cancers with some reports indicating improved local control and survival over conventional photon therapies. Treating cancers that move due to respiration is complicated because the radiologic path lengths of protons are sensitive to changes in density. This phenomenon may result in distortions of the intended dose distribution and/or geometric miss. Treatment planning in the absence of breath-hold or gated techniques requires complicated considerations.\textsuperscript{52, 53} Accurate and precise motion management techniques should be employed for treating abdominal and thoracic malignancies with protons.
While there is special motivation to reduce normal tissue dose for new treatment methods that are potentially more dangerous than the standard methods, it is nevertheless important to do so whenever possible. Standard radiation therapies, while acceptably safe, still carry risks of toxicity, and some patients do suffer from radiation induced injuries. Respiratory motion management should be used to reduce normal tissue irradiation whenever large respiratory induced tumor motion is observed.

1.2 Contemporary Motion Management Techniques and Limitations

Motion management techniques must be applied separately to all stages of the RT process. During the simulation process, if motion is a potential clinical concern it must be directly quantified via imaging. This may be accomplished via fluoroscopy but with some limitations. Fluoroscopically acquired 2D images can capture motion information but often do not provide adequate target visibility since all of the anatomy is projected onto a single plane. The third dimension of motion is missing, and volumetric information is not available. Four-dimensional computed tomography (4DCT) is now available on many CT simulators and may be used to acquire volumetric motion information. This technology is thoroughly discussed in the next section.

If respiration induced motion is minor, a small internal margin may be added to the PTV to compensate for the motion. This method results in the blurring of a static dose distribution as the anatomy moves with respiration. As long as the PTV covers the entire range of motion, tumor coverage is adequate, but normal tissues also move in and
out of the high dose region. For small motion margins, this effect may be negligible, but for sites that exhibit large motion due to respiration, PTV expansion to cover the entire range results in excessive dose to normal tissues.

Various methods including breath-hold and respiratory gating are used to reduce ITVs. Dosimetric evaluations of these techniques have shown that volumes of normal tissue and mean dose to normal tissues can be greatly reduced. Hanely et al. demonstrated a 30% reduction in lung volume irradiated using deep-inspiration breath-hold (DIBH) and an 18% reduction for gating. Another study by Barnes and coworkers reported a 32.5% decrease for DIBH. Harsolia and colleagues reported a 44% reduction in PTV, and 31% reductions in both volume of normal lung irradiated and mean lung dose. A study using gating for liver cancer patients achieved 21% decreases in liver volume irradiated and enabled patients who would have otherwise been unsuitable for radiation therapy to have the treatment.

Breath-hold treatments involve simulation and treatment delivery while the patient is holding his or her breath. Normal lung dose is decreased not only because respiratory motion is eliminated but also because lung density is decreased during inspiration. Many institutions have implemented breath-hold motion management techniques. The techniques vary among institutions. Self-directed breath-hold has been determined adequately reproducible. Another approach is to monitor the position of a surrogate and treat only when the surrogate position indicates that the patient is in the
correct breath-hold state. Surrogates include thoracic belts with pressure sensors,\textsuperscript{61} external optical markers\textsuperscript{62} and spirometers.\textsuperscript{54, 63, 64} Regardless of the breath-hold technique applied, the ITV is defined to incorporate any residual motion that might be expected to occur.

Breath hold is quicker, easier to implement and more reproducible than interval gated treatments, but there are patients who are unable to comply with the procedure.\textsuperscript{65} For those patients interval gating is an appropriate management technique. During gated radiotherapy, the patient is allowed to breathe freely, and delivery occurs only during a specific phase of the respiratory cycle. The ITV is defined to include the volume within which the tumor moves during a particular window of the respiration. The first clinically implemented respiratory gating application was in 1991 in Japan for use with proton therapy.\textsuperscript{66, 67} In the past decade, dozens of studies have investigated benefits, potential benefits and appropriate techniques of window based respiratory gating,\textsuperscript{57, 68–75} and a few institutions have reported on clinical implementations of window gating.\textsuperscript{76, 77} The same surrogates used for monitoring breath-hold delivery are typically used to trigger beam-on when the surrogate is within the selected window. The primary limitations of respiratory gating are the associated uncertainties and safety risks. There are concerns that the limitations of gating are not well understood, and that implementation is unsafe in the absence of robust on-board setup and dose verification technologies.\textsuperscript{78} Accurate methods for imaging motion during both simulation and
treatment delivery have yet to be developed. This is discussed more thoroughly in the following subsection. The focus of this thesis is to develop fast, low dose 4D imaging techniques that can be used in the treatment room for verification of any delivery involving motion management but particularly for the improvement in gating.

1.3 Imaging for Motion Managed Radiotherapy

The development of 4D computed tomography (4DCT) has made it possible to obtain volumetric kinetic information for tumors that are subject to respiratory motion.\textsuperscript{57} \textsuperscript{79-82} 4DCT generates three-dimensional (3D) images for different phases of the respiratory cycle. It is also possible to obtain a CT image of a single phase window by prospectively gating the acquisition. This technology facilitates analysis of anatomical motion and may be used for delineating an ITV or planning respiratory gated radiation therapy (RGRT).\textsuperscript{12, 57, 76, 83} 4DCT is available on CT simulators and may be implemented in the few treatment rooms that have a CT system integrated with the treatment system.\textsuperscript{84-87} In-room CT scanners are not typically available, and thus, 4DCT is generally only available for ITV and motion analyses during simulation.

The most commonly used on-board localization techniques currently include two-dimensional (2D) kV and MV projection imaging and 3D cone-beam computed tomography (CBCT).\textsuperscript{88, 89} Although 2D images acquired in fluoroscopic mode are acquired with sufficient speed to capture motion information, the use of these images for 3D localization is not ideal. kV fluoroscopy, MV electronic portal imaging (EPI),
implanted surrogate monitoring and hybrids of these techniques have been proposed.\textsuperscript{73, 75, 83, 90} Surrogate monitoring is not ideal, because it requires an invasive surgical procedure before radiotherapy. Direct monitoring of the tumor is difficult or impossible for small or low contrast tumors that are not visible on 2D images. CBCT is used for 3D soft tissue localization, but CBCT images are not acquired with sufficient speed to obtain kinetic information. Gantry rotation speed is limited by the international electrotechnical commission (IEC) to about 60 seconds per rotation. Thus, one complete CBCT acquisition contains motion blur from many respiratory cycles.

Planning, setup and verification should ideally be performed using imaging techniques which render 3D motion information without the use of implanted markers. Scan time and imaging dose should be kept as low as possible.

\subsection*{1.3.1 4D Computed Tomography}

Respiratory motion artifacts in computed tomography (CT) scans introduce uncertainties during the process of tumor and structure delineation for radiotherapy planning.\textsuperscript{91, 92} Four dimensional computed tomography (4DCT) is an imaging technology that has been available for several years for imaging motion on a CT simulator. This imaging technique produces respiratory correlated phase images. In other words, several CT volumes are reconstructed, each representing a specific phase of the respiratory cycle, where phase refers to the percentage of the respiratory cycle that has passed since the last peak inhalation.
Several groups have described implementations of 4DCT on axial CT scanners.\(^{79-82,93}\) Axial 4DCT scans are conducted by scanning the patient at a single couch position for the entire duration of the patient’s breathing cycle. Since the longest breathing cycle is not known, a clinician will observe the patient’s respiration and estimate what the longest cycle may be. This is referred to at the ciné duration. After scanning at one couch position for an entire ciné duration, the couch moves to the next position and scans there for another ciné duration.

Axial images are reconstructed at intervals referred to as the ciné time. The ciné time should be such that at least one image is reconstructed for every phase for which a CT volume is desired. This is determined according to the phase window (or the width of the phase bin). For example if the respiratory cycle were 3 s, and the phase window were 10%, then an axial image would need to be reconstructed every 0.3 s or less, so that for every couch position there was an image for every phase bin.

During the image acquisition, the respiratory signal is monitored by an external surrogate, typically an infrared marker attached to a patient’s abdomen and tracked by an infrared camera or a pressure sensing belt worn around the patient’s abdomen. The x-ray ON signal and the surrogate signal are recorded together to temporally correlate the signal and axial image correlation. Respiratory phases are calculated for each of the time points in the respiratory signal, and the time-stamped axial images are then assigned phases. For each couch position in each desired phase CT image, the axial
image closest to that phase will be selected. If the ciné time is set correctly, there exists at least one axial image for each respiratory phase within the desired phase window. If the patient exhibited shorter respiratory cycles than expected, the ciné time may not have been set low enough such that all the couch positions have phase images at every phase within the desired phase window. If that happens, the two options are to have missing axial images in some phase images or to expand the phase window. The latter decreases the temporal accuracy of the scan.

4DCT is used to find the mean tumor positions, range of tumor motions and to determine appropriate motion management techniques based on target specific motion information. 4DCT has also been used to conduct studies for quantification of tumor motion,94-96 to evaluate standard motion margins for various clinical sites97 and to determine patient specific ITVs.98, 99 The technology has been used in many research studies such as for determining correlations between tumor and diaphragm motions100 and for characterizing intra- and inter-fractional motion variations.101-104

As the first commercially available technique for imaging respiratory motion, 4DCT has been widely utilized, but it does have its limitations. Axial images are reconstructed from data acquired over source rotations that are typically 0.5 to 1 s. Thus, each axial image contains a substantial portion of the respiratory motion. This is particularly problematic for short respiratory cycles, as the source rotation occurs over a large portion of the respiratory cycle. There are errors associated with correlating the
surrogate respiratory signals with the projection acquisitions and phase assignment errors. These things result in blurring artifacts, inaccurate volume rendering (under and overestimations), banding artifacts, variations in CT numbers and errors in localization in phase images.\(^\text{105-109}\) One further limitation is that it is typically not available in the treatment room for on-board verification for treatments involving motion management techniques that require specific and current knowledge of motion information. 4DCT may be implemented in treatment rooms equip with linac integrated CT scanners, but these are not available in most treatment rooms. Even with in-room CT scanners, there are errors due to the necessity of moving the couch (and patient) between imaging and treatment.

1.3.2 4D Imaging Using an On-Board 2D kV Imaging System: Review of Previously Proposed Techniques

To date there are no commercially available 4D imaging technologies that can be used in the treatment room in the absence of a CT scanner. Shortly before the work for this thesis began, there were a handful of studies proposing 4D cone-beam CT (4D CBCT) using gantry mounted 2D flat-panel kV imaging devices.\(^\text{110-114}\) Several additional 4D CBCT and 4D DTS studies have since been published.\(^\text{115-121}\) While these studies vary widely in technique and feasibility in terms of image quality, dose and scan time, they are all focused on the development of 4D imaging techniques using a gantry mounted 2D imaging system such as the on-board kV imaging system (OBI) (Varian Medical Systems, Palo Alto, CA). These imaging systems are composed of a kV x-ray tube (or
source) and an opposing 2D flat panel detector. The specifics of one such system were described in a report on quality assurance for on-board imagers by Yoo et al.\textsuperscript{122} An example of such a system is shown in Figure 1.6.

The following paragraphs will briefly explain a general procedure for 4D imaging with a flat panel detector and describe the methods, findings and limitations of the studies that have been done in this area. While the techniques and the results vary substantially, the general procedure for 4D imaging using 2D projection images involves the following steps: 1) projection acquisition, 2) respiratory signal acquisition (sometimes), 3) phase or amplitude assignments of projection images 4) sorting images into bins, and 5) reconstruction of phase or amplitude images. The procedures for phase and amplitude projection assignment are different. Figure 1.2 illustrates a phase based 4D imaging technique.
In the above illustration, the first step is to acquire a series of 2D projection images. Each projection must then be assigned an appropriate phase. In the above schematic, phases are assigned in the following manner. The projection images are inspected in sequence in order to determine peak inspiration phases (0%). An interpolation is then performed to assign phases to the projection images between consecutive 0% phases. After all of the projections have been assigned phases, the projections are sorted into phase bins. The range of phases included in a phase bin is determined by the phase window. Images are then reconstructed for each phase bin, and the set of reconstructed phase images is the 4D data set.
There are various other techniques that can be used for sorting the projection images. Instead of manual acquisition of 0% phase images, a respiratory signal may be acquired by monitoring the motion of a surrogate marker that is externally attached to the patient’s thorax or abdomen. The signal might also be generated by retrospectively using mathematical algorithms designed to analyze the projection data. These respiratory signals may be used for phase or amplitude based sorting. The most commonly used method for clinical 4DCT imaging is to use a respiratory signal that is generated by monitoring an externally applied surrogate marker. The signal is then analyzed to determine 0% phase images. This is followed by a linear interpolation to determine phases for the other images.

The first 4D CBCT studies were proof-of-concept studies conducted in 2005-2006 by Sonke et. al, Dietrich et. al, and Kriminski et. al. 4D images were reconstructed after sorting projections that were acquired for standard CBCT images using conventional imaging protocols. At the time CBCT imaging protocols utilized slower gantry rotations and lower frame rates than are used for conventional CBCT protocols today. In the study by Sonke et. al, projections were acquired over 200° rotations using 0.8°/s gantry rotation speeds and 2.7 fps frame rates. The imaging dose was approximately 1.9 cGy, but the scan time was 4 minutes, which is considered longer than desired for a radiotherapy localization imaging procedure. Patients become uncomfortable during these procedures and may move or exhibit organ motion during
the scanning procedure, which compromises the potential for accuracy in the delivery. Furthermore, the long scan times reduce patient throughput in the clinic. The images in this study were characterized by severe streaking artifacts caused by the gaps between projection images in phase bins. The artifacts were the worst for patients with longer respiratory cycles.

At about the same time, Kriminski et. al.\textsuperscript{111} conducted a study using a similar procedure (0.6\textdegree/s gantry rotation speed and 3.3 fps frame rate over 200\textdegree gantry rotations). This study proposed a methodology that was primarily aimed at imaging for gating studies (as opposed to general 4D imaging), and rather than studies with patient data, Kriminski et. al, conducted phantom studies to characterize the residual motion blur in phase images as a function of total overall peak-to-peak motion amplitudes and ‘gating windows.’ The study concluded that motion blurring is greater for motion profiles with larger peak-to-peak amplitudes and also that larger gating windows reduce reconstruction artifacts with a tradeoff in residual motion blur in the gated images. This study made no attempts to characterize a methodology for patient scans.

One year later, Dietrich et. al.\textsuperscript{111} published their first results for investigations of 4D CBCT imaging. The primary focus of the work conducted by Dietrich et. al was to investigate the correlation between diaphragm motion and the motion of surrogate respiratory signal, but the publication also included a 4D CBCT feasibility study. Similar to the studies by Kriminski et. al and Sonke et al., the projections were acquired
using conventional CBCT imaging protocols. The projections were sorted according to respiratory phase, and the phase bins contained very few, irregularly spaced projection images. The reconstructed 4D CBCT images contained severe streaking artifacts as a result.

Recognizing that 4D CBCT imaging studies to date were providing images with severe reconstruction artifacts, Li et al.\textsuperscript{112} conducted a study using reduced mAs per projection and multiple gantry rotations to increase the projection density in 4D CBCT phase bins. The gantry rotation speed was 6\textdegree/s, and projections were acquired at intervals of about 0.53\textdegree. Phantom studies were conducted to determine the optimal number of gantry rotations/mAs per projection combination while the imaging dose was kept constant. The investigators found that 4D image quality increased with gantry rotation number. The highest number of gantry rotations used was 8, and image quality was the best for this, though the scan time was impractically long. As a compromise, one patient was scanned using 4 rotations and 32 mAs per projection. The scan time was about 5 minutes which is longer than ideal, and the artifacts due to reduced projection numbers in phase bins were not entirely alleviated. The patient scanned in this study had an average respiratory cycle of 4.2 s, and the study did not address how variations in respiratory cycle would affect the images.

A second study was published by the same group a year later investigating slow gantry rotation rather than multiple gantry rotations.\textsuperscript{119} As the name suggests, a slow
gantry scan is conducted by slowing the gantry down to acquire more projections per revolution. This study compared using multiple gantry rotations to using a single slow gantry rotation scan. Phantom studies were conducted using various respiratory cycles and gantry rotation speeds ranging from 1 to 8 °/s. The investigators found that the images were the best for the slowest gantry rotation speed and the shortest respiratory cycle. They also concluded that a single, slow gantry rotation scan was superior to multiple gantry rotations. The only problem associated with the slow gantry rotation scan was the extensive scan time. The study was limited in that it did not investigate lower gantry rotation speeds, and while various respiratory cycles were scanned, no explicit relationships between gantry rotation and respiratory cycle were derived or investigated. Patient studies were not conducted, and thus, conclusions about doses could not be made.

The most comprehensive 4D CBCT study prior to the completion of the work for this thesis was published by Lu et. al in 2007. This slow gantry rotation study adjusted the gantry rotation speed and frame rate according to the patient’s average respiratory cycle. The gantry rotation speed was adjusted, so the gantry would not move more than about 3° per average patient respiratory cycle, and the frame rate was set to give at least 20 frames during a patient’s average cycle. While this technique resulted in excellent 4D CBCT images, the doses were high, and the scan times were very long. Scan times were between 4.5 and 7 minutes, and doses ranged from 10.4 to 14.2 cGy. These doses are
double to triple the doses used for conventional CBCT scan, which are already a concern and cannot be easily accounted for since kV imaging dose is thought to have a different radiobiological effect and cannot simply be added to a treatment dose distribution.\textsuperscript{123} The study reports that the doses were half as large; however, we have communicated with the authors of the publication, and there was an error in the calculations.

To summarize, 4D CBCT studies to date at the time we began this work resulted in either 1) poorly sampled phase images characterized by severe streaking artifacts or 2) very long scan times and high imaging doses. Most of the studies did not consider any of the relationships between the respiratory cycle and the imaging parameters. The study by Lu et al did make a general consideration of the relationships between frame rate and average respiratory cycle and between gantry rotation speed and average respiratory cycle, but there were no considerations for the irregularities typical of patient respiration, and no recommendations were made as far as how to optimally set parameters for patient studies. The focus of the work completed in this thesis was to find ways to improve 4D imaging using a gantry mounted 2D kV imaging system. Specifically, the goals were to investigate methods for minimizing imaging dose and scan time and to develop and investigate methods for achieving consistent, controllable, high quality 4D images.
1.4 Digital Tomosynthesis

Tomosynthesis was developed decades ago and was used clinically in the 1970’s and 1980’s.\textsuperscript{124-129} Before the development of digital detectors, radiographic images were reduced and re-projected using the acquisition geometry. The position of the screen onto which the radiographs were projected could be adjusted to view different tomosynthesis planes within the imaged object.\textsuperscript{127} New techniques were developed for easier viewing of tomosynthesis planes using computers when digital detectors became available, and digital tomosynthesis (DTS) has since become widely used for diagnostic mammography and chest radiology.\textsuperscript{130-137} Studies investigating the use of DTS for surgical guidance\textsuperscript{138, 139} and seed localization in brachytherapy\textsuperscript{140} have also been conducted, and there has been substantial interest in using DTS for localization in radiation therapy\textsuperscript{141-147}.

Digital tomosynthesis may be thought of as a hybrid between 2D radiographic and fully volumetric tomographically reconstructed images. Three dimensional visualization is not possible with 2D radiographic images, since the entire volume is projected onto a single plane. In other words, depth resolution is lost. CBCT images are three-dimensional images reconstructed from projection images acquired over scan angles of at least 180° plus fan-angle. This scan angle requirement gives complete sampling of the 3D volume. Stacks of 2D images are reconstructed, and these images can be sliced in any dimension to give accurate renditions of anatomy in other planes.
Stacks of 2D images may also be reconstructed using digital tomosynthesis, which involves projection acquisitions over limited scan angles (typically less than 60°). The images have good spatial resolution in planes that are perpendicular to the axis about which the projections are centered but compromised resolution in other planes. The acquisition trajectories are illustrated in Figure 1.3.

<table>
<thead>
<tr>
<th>Radiograph</th>
<th>CBCT</th>
<th>DTS</th>
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<tbody>
<tr>
<td><strong>Source</strong></td>
<td></td>
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<tr>
<td><strong>Detector</strong></td>
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<tr>
<td><strong>Single projection image</strong></td>
<td><strong>Projections acquired over 180° plus fan angle Volume Image</strong></td>
<td><strong>Limited Arc of Projections Pseudo-volume Image</strong></td>
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</tbody>
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Figure 1.3  Illustration of projection, volumetric and tomosynthesis image acquisition techniques using the circular orbit characteristic of DTS use in radiotherapy.

Due to the ‘out-of-plane’ blurring, DTS images are often referred to as pseudo-volumetric. The degree to which the out-of-plane blurring exists depends on the scan angle (smaller scan angles result in more blurring). Another way to think about this is that the apparent slice thickness increases with decreasing scan angle. The effects of scan angle on spatial resolution, contrast sensitivity, apparent slice thickness and
distortion have been characterized by Badea et. al\textsuperscript{148} for the isocentric geometry used for on-board imaging with a gantry mounted 2D kV image device.

Figure 1.4 shows a 2D image acquired using such a system (top left), DTS images reconstructed using various scan angles and the full CBCT (bottom right). These are coronal image slices, and the DTS spatial resolution is good in this plane because the projections were centered about the anterior-posterior (AP) axis (perpendicular to the coronal plane). Note that the ribs which contribute to anatomic noise in the projection image do not exist in the DTS images. Note also the small structure pointed out using arrows in the 20, 40, 60 and 80° images. The structure appears to have a high contrast in the DTS image but is barely visible in CBCT image. This low contrast structure spans several slices in the CBCT images, but due to the increased slice profile in the DTS images, the structure appears to have a higher contrast.

Figure 1.4 Single 2D projection and reconstructed images at various scan angles.
Figure 1.5 illustrates the geometric distortions and loss of spatial resolution in the planes other than those perpendicular to the acquisition axis for various DTS scan angles compared with a fully sampled image (360°). The images in this figure are of a circular ball with a small channel in through the center.

![Figure 1.5 Illustration of DTS image data for various scan angles. The projections for this scan were acquired about the AP axis.](image)

The previous two sections have already mentioned that the commonly used on-board imaging techniques are 2D kV and MV imaging and CBCT. 2D images are typically used to align the patient by matching bony anatomy in the planning images with bony anatomy in images acquired with the patient in the treatment position. Matching bony anatomy provides enough certainty in positioning for some cases, but for many cases it is ideal to match soft tissue targets, because bony anatomy may be matched while the soft tissue structures have moved due to internal organ motion or...
anatomical changes in the patient (weight loss/gain). 2D images may be used to match
very high contrast soft tissue structures, but often 3D soft tissue matching is difficult or
impossible using 2D images. The main advantages of using 2D imaging techniques are
low dose and negligible scan time. The short scan time is particularly advantageous for
radiotherapy localization for a number of reasons. First, the patient is required to lie
motionless in the treatment position for the duration of the scan. Short imaging times
reduce the likelihood that a patient will move due to discomfort from having to lie in the
treatment position for extended periods of time. Short imaging times are advantageous
for clinical workflow and patient throughput, and they are fast enough to use for
patients that must be imaged under breath-hold. While CBCT has excellent soft tissue
contrast, imaging doses and scan times are much greater. As discussed in the last sub-
section, dose and scan time are particularly problematic in the context of 4D CBCT
imaging, as more projections are needed to sample the image volume at different phases
of respiration.

Digital tomosynthesis applications in a radiotherapy treatment room most
commonly utilize a gantry mounted imaging device that consists of a kV or MV imaging
source and a flat panel detector as using shown in Figure 1.6.
Figure 1.6  Linear accelerator with a gantry mounted 2D flat panel detector imaging device. This particular system is the on-board imager (OBI) (Varian Medical Systems, Palo Alto, CA) mounted on a Varian 21EX Clinac.

The above figure shows a Varian 21EX Clinac with a gantry mounted on-board imager (OBI) (Varian Medical Systems, Palo Alto, CA). While there are other commercially available systems, all gantry mounted systems have the circular rotational geometry. The two opposing arms of the OBI system are retractable. The third arm shown in this figure is a second flat panel detector for generating MV images with the same source used to deliver therapeutic radiation. While there is more interest in kV DTS due to the soft tissue contrast advantage, MV DTS has also been proposed.149, 150 DTS images are typically reconstructed using a modified cone-beam filtered back projection technique.142
1.5 Scope and Specific Aims

4D imaging in the treatment room would facilitate better motion management for patients needing radiotherapy to sites that are affected by respiratory motion. While there has been substantial interest in the development of in-room 4D imaging technologies, this area is under-developed. Widespread integration of CT systems in treatment rooms would be expensive and technically demanding. Furthermore, the temporal accuracy of 4D CT is currently limited by source rotation times. Several studies have investigated techniques for 4D imaging using on-board kV flat panel detector imaging devices commonly used for CBCT imaging. The proposed techniques result in inconsistent (and often very poor) image quality or unreasonably high imaging doses and long scan times. The scope of this work was to investigate novel techniques for 4D imaging using on-board kV imagers. This work aims to achieve consistent, reliable image quality while pushing imaging doses and scan times as low as possible.

The following were the specific aims of this thesis:

1. Develop four-dimensional digital tomosynthesis (4D DTS). Define an acquisition procedure for obtaining 3D motion information using limited scan angles and characterize the accuracy with which the technique can be used to assess motion. Compare motion information with that achieved using 4DCT. (Chapter 2)
2. Develop and experimentally validate a framework that will comprehensively establish relationships between patient respiratory parameters and acquisition and reconstruction parameters for 4D imaging using a 2D kV imaging device for use in optimizing both 4D DTS and 4D CBCT imaging acquisition protocols. (Chapter 3)

3. Optimize slow gantry rotation 4D imaging for lung based on the developed framework, phantom studies and lung simulation studies. Assess the feasibility in terms of scan times and imaging doses. (Chapters 3 and 4)

4. Conduct slow gantry rotation 4D CBCT and DTS lung patient studies using the optimized framework to determine 1) required scan angles for 4D DTS, 2) required frame rates, 3) required gantry rotation speeds 4) required phase windows, 5) image artifacts compared with those achieved using previously reported acquisition techniques and 6) doses and scan times compared with those achieved using previously reported 4D CBCT acquisition techniques. (Chapter 5)

5. Quantitatively compare the range of image quality variations between phase images (due to dose fluctuations resulting from variations in projection numbers) with image quality variations as the dose per projection (mAs) is varied. (Chapter 6)
2 4D DTS Theory and Benchmark Characterization

2.1 Introduction

As described in Section 1.3, the primary limitation of 2D imaging is that subject anatomies are often obscured due to all of the anatomy being projected onto a single plane, and scan times and imaging doses are the primary limitations of the previously proposed 4D CBCT techniques. DTS has been used in the past to achieve better target visibility than 2D imaging techniques with lower doses and scan times than CBCT.\textsuperscript{132-134, 137, 141, 142, 146, 147, 151-155} The purpose of this study was to develop 4D DTS and obtain a benchmark characterization of the technique’s precision in motion identification. The proposed method utilized two sets of projections acquired over limited scan angles centered about the anterior-posterior (AP) and lateral (LR) axes to construct phase resolved coronal and sagittal DTS images of a motion phantom. Projections were binned, sorted and reconstructed according to phase. Coronal images provided superior-inferior (SI) and LR motion information, and sagittal images provided SI and AP motion information. The anatomic simplicity of the phantom and its inherently high contrast allowed us to study the baseline motion analysis potential of the technique.

The majority of the content in this chapter was first published in Medical Physics.\textsuperscript{156} The journal has granted permission for the reproduction of this work in this thesis.
2.2 Methods and Materials

2.2.1 Imaging Device and Motion Phantom

Kilovoltage projection images were acquired using an on-board imager (OBI) (Varian Medical Systems, Palo Alto, CA) mounted on a Varian 21EX Clinac. This system is shown in Figure 1.6. This imaging system consists of a kV X-ray tube and a flat panel detector mounted on a linear accelerator. The kV beam axis was orthogonal to the treatment beam axis, and the isocenters of the two beams were calibrated to the same position. The imaging field of view was 26.5 cm in diameter, and the cranial-caudal coverage was larger than 15 cm. The physical size of the detector was 30 × 40-cm², and the image acquisition matrix was 1024 × 768 pixels with a 0.26 mm pixel pitch at the isocenter. Projections were acquired with a full-fan bowtie filter to modulate x-ray exposure to allow more radiation to pass through the central, thicker part of the object. Exposure parameters were 125-kVp, 40-mA and 10-ms per projection. Projections were down-sampled to 512 × 384 pixels before processing in part to reduce reconstruction time and required data storage space and also because there was no need to use the full resolution projection images. The final reconstructions had a pixel size of approximately 0.5 mm.

A CIRS Model 008 Dynamic Thorax Phantom (CIRS Inc., Norfolk, VA), as shown in Figure 2.1, was used for imaging. Spherical targets of various diameters were
inserted into a removable cylindrical rod which was attached to the motion actuator. The rod and one of the inserts are shown in the lower left corner the figure.

**Figure 2.1 CIRS Model 008 Dynamic Thorax Phantom (CIRS Inc., Norfolk, VA).**

Three-dimensional motion of the tumor was achieved as the rod in the phantom body underwent simultaneous translation and rotation while mounted obliquely as shown in Figure 2.1. The rod was mounted horizontally and set to undergo translation only to simulate simple SI motion with no AP or LR components. A small gold marker was attached to the end of the rod for use in respiratory signal acquisition as discussed in the following section. The density of the soft tissue target was 1.04-g/cc, and its electron density relative to water was 1.003. The density and electron density relative to water for the surrounding lung material were 0.21-g/cc and 0.207, respectively.

**2.2.2 Projection Data Acquisition and Respiratory Phase Assignment**

Acquisition of projections for 4D DTS requires a special protocol to obtain projection sets at similar phases over a DTS arc. A protocol for acquisition using slow
gantry rotation is discussed in Section 3. Because it was not possible at the time of this study to modify the acquisition sequence of our clinical OBI system to enable slow gantry rotation at the time of the initial feasibility study, multiple CBCT scans were acquired consecutively, and sets of projections were extracted to simulate 4D DTS projection acquisition. Projection images were acquired at approximately every 0.54° over consecutive 364° rotations. Each gantry rotation took about one minute. Depending on the motion profile, projections were acquired over 16 - 24 gantry rotations. The number of gantry rotations used for each case in our study was determined such that we were able to extract sets of projections similar to what would be acquired using the slow gantry method discussed in Section. Excessive numbers of projections were acquired using this method, so it is not feasible for clinical use.

4D DTS image formation requires that projections be sorted according to respiratory phase. For this study, a radiopaque marker was attached to the free end of the moving rod, as shown in Figure 2.1. The trajectory of the marker was extracted from the projections and later used for assigning respiratory phases to each projection. A “successive searching” method developed by Li et al. was employed to locate the marker in each projection.112 This method was implemented as described by Li et al., with the only difference being that the marker position in the first projection was manually identified. After manual identification of the marker in the first projection, a region-of-interest (ROI) was applied with the marker position at the center. This ROI
was applied to the next projection, and a minimum intensity search was conducted to find the marker location. The location of the marker in the second projection was then set as the center of the ROI applied to the third projection. This method was used to identify the position of the marker in each projection.

As the OBI rotates during acquisition, the projected position of the marker on the detector is affected by magnification to varying degrees. Thus, marker location could not be directly used for sorting projections. Instead, marker location was used to determine respiratory phases for each of the projections. We implemented a method developed by Lu et al. to automatically detect peaks and valleys of a respiratory signal. This technique involved calculating a moving average at every point in the waveform. For our study the respiratory signal was comprised of marker locations extracted from the projections. The moving average curve intersected the respiratory signals twice during each respiratory period: one time during expiration and one time during inspiration. Searches were conducted between intersections for minima and maxima corresponding to peaks and valleys. Phases were labeled in units of percent with 0% corresponding to peak inspiration. Linear interpolation was performed to determine phases for the projections in between consecutive peaks and valleys. This phase assignment strategy is consistent with what is currently used in 4DCT protocols.
2.2.3 Sorting, Binning and Reconstruction

Following respiratory phase assignment, projections were sorted into bins corresponding to selected respiratory phases. The range of phases assigned to each bin is called the phase window. For example, if the selected respiratory phase is 50% of the respiratory cycle and the phase window is 10%, then the range of phases in the 50% bin spans from 45 to 55% of the respiratory cycle.

After compiling bins of projections sorted according to phase, the DTS scan angle and spacing between projections were chosen. For every angle along the arc for which a projection was needed, the projection closest to that angle was chosen for each phase. We define the projection spacing resolution limit (PRL) as the maximum allowable difference between a desired projection angle and the nearest projection angle for which there is an available projection for any phase. Thus, for a PRL of 1.0°, there will exist in each phase bin at least one projection within 1.0° of any angle. For each of the 4D DTS reconstructions in this study, a PRL of 1.0° was achieved using projections acquired from multiple CBCT acquisitions as described in Section 2.2.2. Note that the PRL parameter was defined specifically for this experimental study in which 4D DTS projection sets are extracted from multiple CBCT acquisitions. The analogous parameter for the case of slow gantry rotation acquisition technique is the maximum angular interval between projections ($A_{\text{MAX}}$). That parameter is explained in Section 3.
Images were reconstructed using an in-house, Feldkamp-type reconstruction program developed and implemented by Godfrey et al. The algorithm is as follows, with axes defined as shown in Figure 2.2.

**Equation 2.1**

\[
f(x, z/y) = \int_{\beta=\min\beta}^{\max\beta} \int_{-\infty}^{\infty} \frac{d^2}{(d-s)^2} \frac{d}{\sqrt{d^2 + p^2 + \zeta^2}} \times R(\beta, p, \zeta) h\left(\frac{d \cdot t}{d - s} - p\right) dp d\beta
\]

**Figure 2.2: Reconstruction geometry.**

In Equation 2.1, \( f(x, z/y) \) is the reconstructed \((x, z)\) plane at a depth \( y \). \( \beta \) is the angle of the projection, relative to the \( y \) axis; \( d \) is the source-to-isocenter distance; \( s \) is the distance between a voxel and the detector plane. The detector axes are \( p \) and \( \zeta \). \( \zeta \) is parallel to the axis of rotation. A one dimensional ramp filter with a Hamming window, \( h(t) \), is applied along the axis \( p \), with \( t = x \cos \beta + y \cos \beta \). This technique is analogous to Feldkamp CBCT reconstruction but reconstructs a single plane at a specified depth \( y \) and
takes projections over a limited arc. Volume images were reconstructed by solving for planes at various depths.

The DTS reconstruction volumes were 512 x 320 x 301 with an in-plane pixel size of 0.507 mm². Spacing between reconstructed planes was set at 0.507 mm. Coronal DTS slices were reconstructed from projections centered about the AP axis, and sagittal DTS slices were reconstructed from projections centered about the LR axis.

2.2.4 4D DTS and 4DCT Comparisons

For 4DCT reconstructions, axial CT data were acquired in ciné mode on a 4-slice CT scanner (Lightspeed QX/i, General Electric, Milwaukee, WI). Ciné time and ciné duration were 0.5 sec and 6.5 sec, respectively, and the slice width was 1.25 mm. An infrared marker was fixed to a chest plate mounted on the anterior surface of the phantom. The chest plate is coupled to the motor system such that it moves in synchrony with the target. Motion was monitored using a real-time position management (RPM) respiratory gating system (Varian Medical System, Palo Alto, CA) by tracking the infrared marker. Axial images were retrospectively sorted according to phase as tracked by the RPM system. 3D-CT images were reconstructed for motion phases using GE Advantage4D software. Volume images were constructed for the same 10 phases as were DTS images (0% through 90% at 10% intervals with a phase window of 10% for each). For more details pertaining to 4DCT image formation, see Rietzel et
al. We hypothesized that, due to the nature of both imaging modalities, 4D DTS images would contain far fewer motion artifacts than 4DCT images.

2.2.5 Scan Angle

Depending on the goal of motion imaging, DTS may be used to image the range of anatomical motion, also known as the internal target volume (ITV), or to obtain images of the anatomy at selected phases of respiration. For the case of estimating the range of motion, volumetric images of the moving target were reconstructed using projections from scan angles of 20, 40, 60, 120 and 360°. For each of the scan angles, the projections were centered about the AP axis. Projections were spaced approximately 1.0° apart, so the number of projections for each reconstructed image was equal to the scan angle. Coronal, sagittal and axial slices are shown for each scan angle. The motion profile was sinusoidal with a 6 s period and motion in three dimensions. Peak-to-peak motion amplitudes were 20 mm SI, 10 mm LR and 2 mm AP.

Phase correlated images with suppressed motion artifacts were constructed according to the phase assignment and sorting methods described in Sections 2.2.2 and 2.2.3. 3D reconstructions for 20, 40, 60, 120 and 360° of projection data centered about the AP axis were reconstructed for selected respiratory phases using a 10% phase window. Again, projections were spaced approximately 1.0° apart, and the number of projections was equal to the scan angle. Coronal, sagittal and axial slices are shown for each scan angle.
2.2.6 Motion Analysis

Because DTS images retain geometric integrity in the plane perpendicular to the axis about which the projections are acquired, two sets of projections centered about the AP and LR axes were used to reconstruct coronal and sagittal DTS images for motion analysis. Phase resolved coronal images were used to obtain SI and LR motion information, and sagittal images were used to obtain SI and AP motion information.

Two sets of experiments were conducted to demonstrate how 3D motion can be analyzed using this technique. The motion profile used for the first set of experiments was sinusoidal with peak-to-peak motion amplitudes of 20 mm in the SI dimension, 10 mm in the LR dimension and 2 mm in the AP dimension. The objective was to measure AP and LR motions. Phase resolved coronal and sagittal DTS images were constructed from sets of projections acquired over 60° scan angles centered about AP and LR axes. Projections were spaced approximately 1.0° apart, so each image was reconstructed from 60 projections. Ten sets of images corresponding to phases 0 – 90% at 10% intervals were reconstructed using a 10% phase window for each. Normalized, horizontal signal profiles through the center of the target in coronal images were obtained and used to determine LR motion. All signal profiles in this study were normalized such that the minimum value was equal to 0 and the maximum value was equal to 1. An easily identifiable landmark in the profile was chosen, and the position of the landmark in each phase image was manually identified. The positions of the landmark in the phase
images were compared with the true positions according to the lateral component of the motion profile programmed into the dynamic phantom. The same procedure was used to determine AP motion from the sagittal phase images.

A second experiment was performed to analyze the motion in the SI dimension for an asymmetric motion profile. The motion profile had a peak-to-peak SI amplitude of 20 mm and no motion in either the AP or LR dimensions. The duration of inhalation was 3.4 s, and the duration of exhalation was 2.6 s. The motion profile is shown in Figure 2.3. The positions of the target at each of the 10 reconstructed phases were calculated based on the phase assignment strategy detailed in Section 2.2.2. They are shown in this figure.

![Asymmetric Respiratory Profile](image)

**Figure 2.3** Asymmetric profile. Expected target positions for phases 0 - 90 % are marked on the curve.

Coronal images were constructed from projections acquired over 60° scan angles at approximately 1.0° intervals for 10 phases using a 10% phase window. Vertical,
normalized signal profiles were obtained through the target for each phase. The SI center of the target at each phase was determined by manually locating the edges of the peak and calculating the position midway between the two edges. The edges were taken as the points where the profile signal dropped to the background level. Because the edges of the peaks in the profiles were clearly visible, we estimated that the accuracy of this measurement technique was 0.5 mm. For comparison, the same procedure was applied to analyze motion using 360° cone-beam and 4DCT images. Errors in measured positions were calculated for each phase for 60° and 360° 4D DTS images as well and for 4DCT.

Images were also reconstructed using 10, 20 and 30% phase windows in order to determine whether phase window affected the ability to delineate target locations at peak inhale and exhale. These images were reconstructed using subsets of the data acquired for the sinusoidal motion profile with 2 cm peak-to-peak superior-inferior motion amplitude. Both the centers of the target and the outermost edges of the targets were located for inspiration and expiration phases to determine the measured extent of motion. The outer edges were determined visually, and the target centers were determined using the method described in the previous paragraph. The accuracies for each phase window were determined by computing the differences between programmed and measured excursions.
2.3 Results

2.3.1 4D DTS and 4DCT comparisons

Coronal 4D DTS and 4DCT images of the target at selected respiratory phases for the sinusoidal 3D motion profile are shown in Figure 2.4. Motion artifacts are substantially less in 4D DTS images than in 4DCT images as hypothesized. This is largely due to the differences in data acquisition and phase assignment techniques between the two modalities. For 4DCT data acquisition, axial slices are reconstructed using raw data acquired over 1 s. It is these slices which are assigned respiratory phases. Reconstructed axial images may be reconstructed at intervals less than 1 s apart with some overlapping projection data, but the axial images themselves contain 1 s of motion blur. Thus, the ability of 4DCT to suppress motion artifacts is inherently lower than for 4D DTS which assigns phases directly to projections acquired in 10 ms.

![Coronal 4D DTS and 4DCT images](image)

Figure 2.4 Coronal 4D DTS and 4DCT images of the target at various respiratory phases. All phase windows are 10%.
The other consideration is that 4D DTS projections were assigned phases based on a retrospective analysis of the position of a marker in projection space. The axial slices used for the 4DCT image reconstructions were assigned phases by monitoring an infrared marker attached to the chest plate of the phantom and correlating this motion with acquisition of the data used to reconstruct the axial slices. This method is less direct than the one used for 4D DTS phase assignment and is known to introduce errors in phase assignment. While this effect was minimal in this phantom study, larger discrepancies between the two phase assignment strategies would be present in patient applications, as relationships between internal targets and externally attached surrogate markers are known to be transient. Since the phase assignment errors are minimal in this study, the differences in motion artifacts between these two imaging techniques are primarily a result of the differences in the acquisition times for a single projection (4D DTS) vs. the acquisition times for axial images (1 s).

2.3.2 Scan Angle

Figure 2.5 shows reconstructed coronal DTS images for the 3D sinusoidal motion profile using 20, 40, 60, 120 and 360° of projection data centered about the AP axis. The extent of SI and LR motion is evident in coronal slices for scan angles of 40° and larger. Since the respiratory period was 6 s, and approximately 6 degrees of projection data were acquired per second, it was necessary to have about 36° of projection data to visualize the full extent of the motion in the coronal view. For limited
scan angles, reconstruction artifacts in the axial and sagittal planes as shown in Figure 2.5 are prohibitive to obtaining AP motion information. The distortions in these planes are reduced with increasing scan angle but not adequately within the range of scan angles used for DTS imaging. As an alternative to a full CBCT acquisition, which would require a scan of 180° plus fan angle, AP motion information can be achieved by acquiring a second subset of projection data about the LR axis to construct geometrically accurate sagittal images. Thus, two sets of projection data acquired about AP and LR axes over at least one respiratory cycle each will provide images that show the extent of motion in 3D. Figure 2.6 shows 0% and 30% phase images for the same motion profile for scan angles of 20, 40, 60, 120 and 360°. The 0% phase images incorporate very little motion. Thus, the artifacts are predominantly reconstruction artifacts. Substantial motion occurs within the 30% phase window, so these images contain notable motion artifacts as well as reconstruction artifacts similar to those in the 0% phase images.
Figure 2.5  Coronal, axial and sagittal slices of the motion phantom. Images are reconstructed using projections acquired over various total scan angles, centered about the AP axis. Projections are spaced approximately 1.0° apart.

Figure 2.6  a. (right): Coronal, axial and sagittal slices from peak expiration (0 % phase) 4D DTS images, reconstructed using various scan angles. b. (left): mid-inspiration (30 % phase).
2.3.3 Motion Analysis

Figure 2.7 shows phase resolved coronal and sagittal DTS images of the 3D sinusoidal motion profile for selected respiratory phases. Coronal images were reconstructed using projections centered about the AP axis, and sagittal images were reconstructed using projections centered about a LR axis. SI and LR motions were obtained from coronal images, while the SI and AP motion were obtained from the sagittal images.

![Coronal and sagittal images](image)

**Figure 2.7** Coronal and sagittal images reconstructed for various respiratory phases using 60° of projections centered about AP and LR axes. The lines drawn on the 0 and 50% phase images correspond to the signal profiles shown in Figure 2.7 and Figure 2.8.

Figure 2.8 shows normalized signal profiles across the center of the target in coronal images for 0 and 50% phases. The dashed lines drawn on the coronal images in Figure 2.7 correspond to the locations of these profiles. The profiles from the 0 and 50% phase images were shifted by 10 mm in the LR dimension. This was consistent with the expected 10 mm displacement based on the LR component of the programmed motion.
profile. The accuracy of this measurement was limited by the pixel width, which was approximately 0.5 mm.

Figure 2.8 Normalized signal profiles across the center of the target for the 0 and 50% coronal phase images shown in Figure 2.7 illustrating LR motion analysis potential.

Figure 2.9 shows profiles across the center of the target from the 0 and 50% sagittal images. The dashed lines drawn on the sagittal images in Figure 2.7 correspond to these profiles. The 2 mm shift determined by comparing the relative positions of the profiles was consistent with the expected 2 mm AP shift. This measurement was also within the accuracy limitations of the pixel size.
Figure 2.9 Normalized signal profiles across the center of the target for the 0 and 50 % sagittal phase images shown in Figure 2.7, illustrating AP motion analysis potential.

Figure 2.10 shows coronal images from a 60° 4D DTS scan of the asymmetric motion profile. Figure 2.3 shows the motion profile and the expected positions of the target at different phases. Based on the information in Figure 2.3, it is expected that the 10 and 70% phases will exhibit the most motion blur. The results shown in Figure 2.10 are consistent with this expectation.

Figure 2.10 Coronal images reconstructed for various respiratory phases using 60° of projections centered about the AP axis. The lines drawn on the 0, 10, 20 and 50 % phase images correspond to the signal profiles.

Vertical, normalized signal profiles through the target are shown for phases 0, 10, 20 and 50% in Figure 2.11. The relative displacements of the peaks show the positional
differences in the SI dimension between phases. The rounding and widening of the peaks indicate the extent of the motion, and the asymmetry indicates inconsistent velocity throughout the phase window.

Figure 2.11 Normalized signal profiles through the target from the 0, 10, 20 and 50 % phase images shown in Figure 2.10, illustrating SI motion analysis potential.

Figure 2.12 shows the measured positions of the center of the target for the 60° DTS scan, the 360° scan, and the 4DCT scan compared with the true positions for each phase. The averages of the absolute values of the errors were 0.68, 0.67 and 1.85 mm for the 60° DTS, 360° CBCT, and 4DCT images, respectively. The errors for the 10% phase were the highest for each of the images.
Figure 2.12 Measured target positions obtained from 60° DTS, 360° CBCT and 4DCT images compared with the true motion curve.

The errors are greater for this phase because it contains the most motion over the phase window. The measured positions are all shifted towards the portion of the motion curve which exhibits higher velocity and thus more motion blurring. For reasons described in the paragraph below, the 4DCT errors are substantially larger. The results from the 60° and 360° images are nearly identical. The effect of decreased scan angle is an increase in apparent slice thickness. Due to the simplicity of this phantom, the effect is minor. The magnitude of the effect is specific to the anatomy being imaged.
Reconstruction of 4D DTS images requires a predetermined phase window. The number of projections required is inversely proportional to the phase window, so it is best to use the largest phase window which will give adequate motion artifact suppression for the task at hand. Figure 2.13 shows reconstructions of our target moving according to the 3D motion profile for phase windows of 10, 20 and 30%. Figure 2.14 shows normalized signal profiles parallel to the direction of motion in the coronal plane. As the phase window is increased, the profile width increases. The profile also becomes less symmetric, indicating that the target velocity changes across the phase window. The peak of each profile corresponds to the target’s center of mass for the phase window.
Figure 2.14 Normalized signal profiles parallel to the direction of motion from the coronal images shown in Figure 2.13 using 10, 20 and 30% phase windows.

The extent of motion in a phase bin increases with increasing phase window (as shown in Figure 2.14). The following results demonstrate how this may affect the baseline ability to determine overall tumor excursion. Peak inspiration and expiration phases exhibit less motion than other respiratory phases (as shown in Figure 2.13) due to the slowing, stopping and reversing direction of motion. We estimated the phase window effect on the ability to delineate the entire duration of motion by analyzing peak inspiration and peak expiration images. When we measured the center of the target in peak inspiration and peak expiration phase images for 10, 20 and 30% phase windows, we found that motion accuracy was limited only by pixel resolution for the 10 and 20% phase windows, but we measured a 1.5 mm error for the 30% phase window. When we looked at only the most superior edge of the target in the peak expiration phase images and the most inferior edge of the target in the inspiration phase images,
we found that the range of motion was estimated similarly in 10, 20 and 30% phase windows. The limiting factor was the spatial resolution at 0.5 mm.

2.4 Discussion

While very accurate results were obtained in this phantom study, there are several considerations to be aware of for patient applications. The phase assignment technique employed for this study was nearly error free, as we were working with a rigid phantom and using a marker in projection space to determine phase. There are additional complications for assigning phases to images for patients. We refer to what we know about phase assignment for 4DCT, as the same issues will apply to phase assignment for 4D DTS. The current method used clinically to reconstruct 4DCT images requires correlating a signal from an infrared marker placed on the patient’s abdomen to the target motion. The accuracy of this technique depends on the accuracy of the temporal correlation between the signal and projection acquisition. It also assumes a reliable and consistent correlation between abdominal and target motions. Errors in the temporal correlation between signal and target motion or violations of the aforementioned assumption will cause errors in phase assignment and consequent image artifacts. Additional errors result from current phase assignment algorithms being confused by the noise in the external respiratory signal. These errors may be remedied by using improved algorithms.\textsuperscript{159} Two 4DCT studies report errors in phase assignment using commercially available systems for 30 and 40% of patients.\textsuperscript{92, 160} As an
alternative to using an external respiratory signal for phase assignment, Sonke et al. developed a method to extract a respiratory signal directly from 2D projection images for 4D CBCT. The same approach may be used for deriving respiratory signals from projection images for 4D DTS. The accuracy of such methods would rely on a consistent correlation between the respiratory signal and the target motion.

It has been suggested in previous 4DCT studies that sorting images based on amplitude may be advantageous over phase-based sorting. Amplitude-based sorting is advantageous in that it renders more accurate size and shape information than phase-based methods, specifically for irregular respiration. This method may be appropriate when the clinical goal is to obtain accurate anatomic information. If temporal information is important, pure amplitude-based methods may not be appropriate, as each bin, and therefore reconstructed image, does not represent the same amount of time. Olsen et al. proposed a method which considers both amplitude and the relative amount of time a respiratory amplitude has been reached. This method results in images which are useful for spatial and temporal analyses, and the study reports less severe artifacts. The same principles apply to sorting projections for 4D DTS. Data acquisition would remain the same regardless of the sorting algorithm, with the key concept being that data must be acquired over the course of at least a full respiratory cycle for each gantry angle or small gantry angle interval if using the slow gantry rotation method. As discussed in Abdelnour et al., irregular respiration leads to missing
axial slices for amplitude sorted 4DCT images. In the same way, irregular breathing will lead to missing projections for amplitude sorted 4D DTS images. DTS images may be reconstructed with missing projections, but the final images will contain linear streak artifacts. The severity of the artifacts would depend on the number of missing projections. The sorting algorithm should be chosen according to the clinical goals of the study. If 4DCT and 4D DTS images will be compared, it is essential that the same sorting technique be used for both studies. We chose to implement a phase based sorting technique for this study because it is currently used clinically for 4DCT in most centers, including ours.

In addition to the experiments presented for this preliminary study, several 4D DTS image sets were reconstructed using far fewer projections. Images were reconstructed using as few as 5 projections over a 5° scan angle. The target in these images was as conspicuous as for images presented in this paper, but the reconstructed images contained aliasing artifacts similar to those shown in part of a previous study by Bachar et al. which was intended to investigate the effects using various scan angles and numbers of projections.\textsuperscript{138} It is appropriate to point out that scan angle, number of projections and distribution of projections are parameters that affect image quality and are entirely dependent on subject anatomy. As explained earlier in this article, the primary effect of decreasing scan angle is that the apparent slice thickness increases. Thus, the extent to which images are degraded by a reduction in scan angle depends
strongly on the anatomy. Future studies must include studies that investigate scan angle and image quality relationships for various anatomical sites. It will also be important to determine whether such relationships might be generalized to a specific site for all patients.

In this preliminary study, we made some comparisons between 4D DTS and 4D CBCT images for localization potential. These are only meant to illustrate a baseline comparison, given that adequate contrast can be achieved using DTS for a given anatomy. Utilization of DTS imaging is dependent on the appropriate choice of DTS scan angle for the anatomy to be imaged and requires clinical feasibility tests for specific sites.

Variations in respiratory motion parameters will also affect the quality of the resulting images. The highest achievable motion suppression for any 4D imaging technique is limited by the inherent extent of motion within the phase window. Thus, for a given respiratory period, increasing motion amplitude will increase the motion blur present in the phase images. For a given amplitude, a decrease in the period of respiration will increase the motion blur present in the phase images. Also if the profile is asymmetric and there are intervals of the cycle during which the target velocity is higher, the corresponding phase images will incorporate more motion blur as demonstrated in this study. These effects may be alleviated by decreasing the phase window with the expense of a greater number of required projections.
2.5 Conclusions

We have developed and implemented a technique for constructing 4D DTS images and have demonstrated how this imaging technique might be used to obtain kinetic information for tumors subject to respiratory motion in the treatment room. The study demonstrated how the extent of motion in three dimensions can be obtained by reconstructing coronal and sagittal images using limited arcs of projections acquired about AP and LR axes. Images at selected phases of respiration can be reconstructed using limited arcs of projections binned according to phase. This technique has been shown to provide 3D information at various phases of respiration and may facilitate accurate quantitative motion analysis. The positional accuracy was shown to be dependent on the extent of motion across the phase window. Motion artifacts in the SI dimension were substantially less severe when compared with 4DCT. 4D DTS allows verification of kinetic information in the treatment room, potentially facilitating more precise delivery of radiation to the targets affected by respiratory motion.

3 A New Framework for Slow Gantry Rotation Acquisition: Theory and Phantom Studies

3.1 Introduction

As discussed in great detail in Section 1.3.2, previously proposed techniques for acquiring projections for on-board 4D imaging using a 2D kV imaging device have not considered relationships between respiratory motion and acquisition and reconstruction
parameters. The resulting irregular and uncontrollable spacing between projections in sorted phase bins yielded inconsistent and uncontrollable image quality. Acquisition parameters cannot be properly determined without a comprehensive understanding of the relationships between patient respiratory motion, gantry motion, acquisition frame rate and reconstruction parameters.

We considered two possible methods for controllable acquisition of projections for on-board 4D imaging: slow gantry rotation and step-and-shoot methods. The slow gantry method refers to data acquisition at a constant frame rate as the source and detector rotate at a constant speed over a single sweeping motion. The step-and-shoot method would be conducted by rotating the source and detector to fixed locations and acquiring projections at each of those source locations. The step-and-shoot method has the advantage that the projections in the final phase bins would be spaced at regular intervals, while the interplay between gantry rotation and respiratory motion complicates projection spacing for the slow gantry method. The advantages of the slow gantry method are shorter acquisition time because projections are acquired while the gantry is moving and easier implementation because it is easier to simply adjust frame rate and gantry rotation speed than it is to add starts and stops to the acquisition sequence. For these reasons we have chosen to develop an acquisition framework for the slow gantry rotation technique.
The aims of the following study are to 1) propose a framework for slow gantry rotation acquisition that relates all acquisition and reconstruction parameters as well as patient respiratory parameters and 2) conduct experiments with a motion phantom to verify the relationships set forth in the framework. Portions of the following chapter have been previously published in Medical Physics.162 The journal has granted permission to reprint the work in this thesis.

3.2 Methods and Materials

3.2.1 Framework Theory

We begin the description of this theoretical framework by defining some parameters. \( \text{RC}_{\text{MIN}} \) is the shortest expected respiratory cycle duration for the patient, and \( \text{RC}_{\text{MAX}} \) is the longest expected respiratory cycle duration. The respiratory phase at a given point in the respiratory cycle is defined as the percentage of the respiratory cycle that has passed since the beginning of the cycle. The beginning of the respiratory cycle (0%) is end-inhalation. Phases for the points between 0% phases are determined by performing linear interpolation between consecutive 0% phases. The phase window (PW) is the range of phases that will be binned together to form a set of projections used to reconstruct a specific phase image. For example, if the PW is 10%, the 30% phase image will be reconstructed using projections tagged with phases between 25 and 35%. Throughout this thesis, we refer to ‘angular intervals’ between projections. The angular interval (\( \theta \) or AI) between two projections is the angle between the two lines that
connect the isocenter and the kV source locations for the two acquisitions. This is illustrated in Figure 3.1.

![Diagram of kV Source Trajectory and Isocenter](image)

**Figure 3.1 Angular interval (Θ) illustration.**

A \( AI_{\text{MAX}} \) is the maximum angular interval between consecutive projections in phase bins that will result from the portion of the scan when respiratory cycles are less than or equal to \( RC_{\text{MAX}} \). Therefore, \( AI_{\text{MAX}} \) is the maximum expected angular interval between any two projections in final phase bins. This is derived later in this section.

The frame rate refers to the number of projections acquired per second. The optimal frame rate \( FR_{\text{OPT}} \) is defined as the frame rate that acquires exactly one projection during each phase window (PW) of the shortest respiratory cycle \( RC_{\text{MIN}} \).

**Equation 3.1**

\[
FR_{\text{OPT}} = \frac{1}{\frac{PW[\%]}{100\%} \cdot RC_{\text{MIN}}}
\]

The following paragraphs thoroughly detail the theory behind this derivation. If the frame rate were lower than \( FR_{\text{OPT}} \), there would be phase windows for which no
projections were acquired. This would make it difficult to predict or control projection distributions within sorted phase bins and would unnecessarily extend the scan time. If one phase window passed without a projection acquisition, the angular interval between acquisitions for that phase window in the previous and subsequent respiratory cycles would be approximately twice as large as for cases where projections were acquired in the phase window in consecutive respiratory cycles. If the phase window was missed during multiple respiratory cycles, even larger gaps would occur in sorted bins. Setting the frame rate to acquire at least one projection per phase window in the shortest respiratory cycle sets an upper limit on the angular intervals that will occur between projections in sorted phase bins.

The hypothesized lowest frame rate would acquire at least one projection per phase window during the shortest respiratory cycle, but this means that multiple projections will be acquired during the longer respiratory cycles, since the phase window durations are longer. Projections acquired in single phase windows will be placed in the same phase bins. Since the gantry rotation is slow, these projections will be very closely spaced. Increasing the frame rate above FR\textsubscript{OPT} would increase the numbers of these tightly spaced projections and result in sub-optimal projection distributions containing ‘clusters’ of projections. Clustered projection distributions cause streaking in the reconstructions. Figure 3.2 illustrates this phenomenon.
Figure 3.2  Shepp-Logan phantom reconstructed with 90 projections spaced over 180°.  
a) projections are spaced 2° apart, b) projections are arranged in ‘clusters.’

Figure 3.2.a shows a Shepp-Logan phantom reconstructed using filtered backprojection 
and 90 projections spread over 180° with 2° angular intervals between consecutive 
projections.  Figure 3.2.b is an image of the same phantom also reconstructed with 90 
projections spread over 180° but with projections arranged in clusters.  Each cluster of 
projections has three projections with 0.5° angular intervals between, and each cluster is 
centered 6° apart.  Therefore, the pattern of angular intervals is 0.5, 5.2, 0.5, 0.5, 5.2, 
0.5°…

With the frame rate set according to Equation 3.1, the maximum angular interval 
(AI_{MAX}) between projections in sorted phase bins would occur if a projection was 
acquired at the beginning of one phase window, and the next acquisition for that phase 
window occurred at the end of the phase window following the longest respiratory 
cycle.  Figure 3.3 illustrates this and shows how the following relationship was derived.
Equation 3.2

\[
AI_{\text{MAX}} = \text{GRS} \left( RC_{\text{MAX}} + RC_{\text{MIN}} \frac{PW[\%]}{100} \right)
\]

Figure 3.3  Illustration of the derivation of the relationship between RC\text{MAX}, RC\text{MIN}, PW and AI\text{MAX}.

AI\text{MAX} is a theoretical limit for angular intervals between projections in sorted phase bins. Angular intervals as large as AI\text{MAX} may not occur if the longest respiratory cycle does not turn out to be as long as RC\text{MAX}. The above relationship can be rearranged to determine an appropriate GRS for given RC\text{MIN} and RC\text{MAX} and desired PW and AI\text{MAX}.

Scan time (ST) and number of projections acquired (NPA) can be calculated as follows:

Equation 3.3

\[
ST = \frac{SA}{\text{GRS}}
\]

or

\[
ST = \frac{SA \left( RC_{\text{MAX}} + RC_{\text{MIN}} \frac{PW[\%]}{100} \right)}{AI_{\text{MAX}}}
\]
Equation 3.4

\[ NPA = FR \times ST \]

or

\[
NPA = \frac{SA}{AI_{MAX}} \left( \frac{RC_{MAX} + RC_{MIN}}{100\%} \right) \left( \frac{PW[\%]}{100\%} \right) \left( \frac{RC_{MIN}}{100\%} \right)
\]

where SA is the scan angle and PW is the phase window (width of a phase bin) expressed as a percentage of the respiratory cycle. The second part of Equation 3.4 assumes that \( F_{ROPT} \) is used. Once validated, these relationships can be used to evaluate imaging protocols in terms of scan time and imaging dose.

3.2.2 Image Acquisition and Reconstruction

The slow gantry rotation acquisition was implemented using an On-Board Imager \( \text{OBI} \) \( kV \) imaging system (Varian Medical Systems, Palo Alto, CA). This imaging system was described at length in Section 2.2.1. Exposure parameters were 120 kVp, 50 mA and 30 ms per projection. The images were reconstructed using a modified Feldkamp-type reconstruction program developed by Godfrey et al.\(^{142, 163}\)

3.2.3 Frame Rate

According to the proposed framework for optimal acquisition using a slow gantry rotation technique, increasing the frame rate above \( F_{ROPT} \) would substantially increase projection density and thus imaging dose but would not substantially improve
image results, because the additional, closely spaced projections would contribute very little to the sampling.

Experiments in this section tested the hypothesis that $F_{ROPT}$ is the optimal frame rate for slow gantry rotation 4D imaging. A motion phantom was scanned using a slow gantry rotation protocol. The phantom was an International Electrotechnical Commission (IEC) body phantom mounted on a moving platform. It was programmed to exhibit short and long respiratory cycles (3 and 6 s). $RC_{MIN}$ and $RC_{MAX}$ were assumed to be 2.7 and 3.3 s for the short respiratory cycle and 5.7 and 6.3 s for the long respiratory cycle. Both respiratory cycles were scanned using a GRS of 1.1 °/sec and three different frame rates corresponding to $\frac{1}{2} \cdot F_{ROPT}$, $F_{ROPT}$ and $2 \cdot F_{ROPT}$. The frame rates as calculated by Equation 3.1 are shown in Table 3.1 for the 6 acquired data sets. We used 10 % phase windows for the FR calculation and for sorting the projections into phase bins.

**Table 3.1** Short and long respiratory cycles (3 and 6 s) were scanned using a gantry rotation speed of 1.1 °/s and frame rates shown in this table.

<table>
<thead>
<tr>
<th>Study #</th>
<th>RC (s)</th>
<th>FR w.r.t. $F_{ROPT}$</th>
<th>FR (fps)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>$\frac{1}{2} \cdot F_{ROPT}$</td>
<td>1.9</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>$F_{ROPT}$</td>
<td>3.7</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>$2 \cdot F_{ROPT}$</td>
<td>7.4</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>$\frac{1}{2} \cdot F_{ROPT}$</td>
<td>0.9</td>
</tr>
<tr>
<td>5</td>
<td>6</td>
<td>$F_{ROPT}$</td>
<td>1.8</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>$2 \cdot F_{ROPT}$</td>
<td>3.5</td>
</tr>
</tbody>
</table>
Projection images were sorted into 10 bins for each of the 6 data sets, and the projections in each bin were used to reconstruct phase images. The validity of Equation 3.1 was investigated by analyzing the projection distributions and reconstructed images. Projection distributions were analyzed using all of the data from the 200° scans. Subsets of the data corresponding to 40° DTS images were used for the image reconstructions. We expected to see substantial improvements in the images reconstructed using the FR\textsubscript{OPT} data sets over those images reconstructed using the lower frame rates. While the imaging dose and overall projection density were doubled with the doubling of FR\textsubscript{OPT}, we expected to see small improvements using the higher frame rates. Reconstructed images are presented in the results section. We expected that increasing the frame rates beyond FR\textsubscript{OPT} would increase the ‘clustering’ effect. Projection distribution data are also summarized in the results section.

3.2.4 Gantry Rotation Speed

A phantom study was conducted to verify that Equation 3.2 accurately explains the relationship between GRS, PW, AI\textsubscript{MAX} and RC\textsubscript{MAX}. The six data sets described in the previous section (Table 3.1) were used for these experiments. Recall that two respiratory cycles (3 and 6 s) were scanned. RCM\textsubscript{IN} and RCM\textsubscript{AX} were assumed to be 2.7 and 3.3 s for the short respiratory cycle and 5.7 and 6.3 s for the long respiratory cycle. Both respiratory cycles were scanned using a GRS of 1.1 °/sec and the three different frame
rates. We expected that the relationship in Equation 3.2 would hold for the $FR_{MAX}$ and $2 \cdot FR_{MAX}$ frame rates but not for the lower frame rates.

Projection images were acquired over $200^\circ$ arcs and sorted and binned into 10 phase bins for each of the acquisitions shown in Table 3.1. After sorting projections, the maximum angular interval between any two consecutive projections in phase bins should not exceed the $AI_{MAX}$ given by Equation 3.2, as long as the $FR$ is set to acquire at least one projection per phase window ($FROPT$). $AI_{MAX}$ values for the short and long respiratory cycles as calculated by Equation 3.2 were 4 and $7.6^\circ$, respectively. The actual maximum angular interval ($AI$) for each bin of each data set was obtained and compared with the $AI_{MAX}$ value. We expected that the actual $AIs$ for phase bins of data sets 1 and 4 would be greater than the $AI_{MAX}$ values, since the $FROPT$ criterion was violated. We expected that the actual maximum $AIs$ for the other data sets would be equal to or less than the $AI_{MAX}$ values.

### 3.3 Results

#### 3.3.1 Frame Rate

Figure 3.4 shows selected 4D DTS phase image reconstructions for the 3 s profile and all three frame rates. Images were reconstructed using $40^\circ$ scan angles and 10% phase windows. As expected, the images reconstructed from the data acquired at $FROPT$ are substantially improved over images reconstructed from the data acquired at $\frac{1}{2} \cdot FROPT$. Despite doubled imaging dose and doubled acquisition time, the images
reconstructed from the $2 \cdot FR_{opt}$ data do not show obvious improvements over the $FR_{opt}$ images.

![Figure 3.4 Selected 4D DTS phase images of the 3 s profile for acquisitions using various frame rates. The scan angle was 40°; the gantry rotation speed was 1.1 °/s, and the phase windows were 10%.](image)

The same phenomenon occurs with the images for the 6 s profile. These images are shown in Figure 3.5. These experiments support the theory that the optimal frame rate is the $FR_{opt}$ as defined by Equation 3.1.
Figure 3.5 Selected 4D DTS phase images of the 6 s profile for acquisitions using various frame rates. The scan angle was 40°; the gantry rotation speed was 1.1 °/s, and the phase windows were 10%.

Projection distributions in data sets acquired at $F_{R_{\text{OPT}}}$ were highly irregular and contained large angular intervals. Table 3.2 and Table 3.3 summarize how the projections were distributed in the $F_{R_{\text{OPT}}}$ and $2 \cdot F_{R_{\text{OPT}}}$ data sets. Table 3.2 gives data for the 3 s profile, and Table 3.3 gives data for the 6 s profile. The data in these tables show how increasing the frame rate above $F_{R_{\text{OPT}}}$ contributes to the ‘clustering’ effect as described in section II.A. Distribution data is discussed further in the next section as it relates to the relationship between GRS and $A_{\text{MAX}}$.

Table 3.2. Projection distributions for scans of the 3 s profile using frame rates of 3.7 fps ($F_{R_{\text{min}}}$) and 7.4 fps ($2 \cdot F_{R_{\text{min}}}$). Projections were acquired over a 200° arc at a gantry rotation speed of 1.1 °/s.

<table>
<thead>
<tr>
<th></th>
<th>Total Projection #</th>
<th># Large Intervals per Bin (range)</th>
<th>Ave. # Small Intervals per Bin (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$F_{R_{\text{min}}}$</td>
<td>758</td>
<td>59 or 60 (2.98 – 3.86°)</td>
<td>16.4 (0.27 – 0.30°)</td>
</tr>
<tr>
<td>$2 \cdot F_{R_{\text{min}}}$</td>
<td>1516</td>
<td>59 or 60 (2.88 – 3.58°)</td>
<td>92.2 (0.13 – 0.16°)</td>
</tr>
</tbody>
</table>
Table 3.3  Projection distributions for scans of the 6 s profile using frame rates of 1.8 fps ($FR_{MIN}$) and 3.5 fps (2×$FR_{MIN}$). Projections were acquired over a 200° arc at a gantry rotation speed of 1.1 °/s.

<table>
<thead>
<tr>
<th></th>
<th>Total Projection #</th>
<th># Large Intervals per Bin (range)</th>
<th>Ave. # Small Intervals per Bin (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$FR_{MIN}$</td>
<td>369</td>
<td>30 or 31 (5.49 – 7.77°)</td>
<td>5.4 (0.52 – 0.61°)</td>
</tr>
<tr>
<td>2×$FR_{MIN}$</td>
<td>716</td>
<td>30 or 31 (5.24 – 7.47°)</td>
<td>41.1 (0.27 – 0.31°)</td>
</tr>
</tbody>
</table>

### 3.3.2 Gantry Rotation Speed

The distributions of projections in sorted phase bins demonstrate that the developed framework for slow gantry rotation acquisition accurately defines relationships between acquisition parameters and projection distributions for 4D imaging using slow gantry rotation. The $A_{MAX}$ value for the 3 s profile was 4° according to Equation 3.2. The actual maximum angular interval in the data set acquired at $\frac{1}{2} FR_{OPT}$ was 27.9°. Large angular intervals occurred in every phase bin, demonstrating that the formalism does not hold if the $FR_{OPT}$ criterion as defined in Equation 3.1 is violated. Distribution data for the 3 s profile acquisitions at $FR_{OPT}$ and 2×$FR_{OPT}$ are shown in Table 3.2. The actual maximum angular interval in the data set acquired at the $FR_{OPT}$ was 3.86°, which is just below the 4° $A_{MAX}$. Each phase bin had 59 or 60 angular intervals between 2.98 and 3.86° over the 200° arc. Each phase bin also contained a number of small angular intervals ranging from 0.27 to 0.3°. These small angular intervals demonstrate the ‘clustering’ effect described in Section 3.2.3. The average
number of small intervals per phase bin was 16.4. Each phase bin in the data set acquired at 2 times the $FR_{opt}$ had 59 or 60 angular intervals which were between 2.88 and 3.58° and many angular intervals between 0.13 and 0.16°. The average number of small angular intervals per phase bin was 92.2. Twice as many projections were acquired using the higher frame rate, but all of the additional projections were acquired very close to other projections of the same phase and thus provided little additional information for image reconstruction. The findings for the 6 s profile demonstrated the same phenomenon. The phase bins from the data set acquired at half of the $FR_{min}$ contained very large angular intervals (up to 34.07°). Table 3.3 summarizes the projection distributions for the other two frame rates. The actual maximum $AIs$ were 7.77 and 7.47° for the $FR_{opt}$ and $2 \cdot FR_{opt}$ acquisitions, respectively. The $AImax$ value according to Equation 2 was 7.76°.

3.4 Discussion

This study has established a procedure for determining optimal acquisition parameters (gantry rotation speed and frame rate) for slow gantry rotation 4D imaging using a gantry mounted kV imaging system. This requires a determination of the patient’s shortest and longest respiratory cycles ($RC_{min}$ and $RC_{max}$). $RC_{min}$ and $RC_{max}$ should be determined by observing patient respiration. This process should be similar to that performed before a 4DCT scan. The patient’s respiration should be monitored (using a monitoring system such as RPM) for a few minutes before the scan. The longest
and shortest respiratory cycles should be noted. $R_{C_{\text{MIN}}}$ should be set below the shortest observed cycle, and $R_{C_{\text{MAX}}}$ should be set above the longest observed. If the duration of the patient’s breathing is very regular, $R_{C_{\text{MIN}}}$ and $R_{C_{\text{MAX}}}$ do not need to be set far from the observed shortest and longest cycles, but if the breathing duration is irregular, more latitude should be given to ensure appropriate scan results. The degree of irregularity which can be tolerated depends on the motion management approach and the goals of 4D imaging. Patients with highly variable durations in respiratory period would not be good candidates for phase window gating applications, but if the goal of the imaging is to verify the internal target volume, trajectory or mean position of a target, some irregularity in durations of breathing cycles may be acceptable. Phase bins inherently contain some motion artifacts. These artifacts are limited to the extent of motion that occurs within the phase window for regular breathing, but additional motion artifacts would result from irregularities. Some degree of irregularity would not prevent clinicians from extracting information about internal target volume, trajectory or mean position and may be tolerable as long as the $R_{C_{\text{MIN}}}$ and $R_{C_{\text{MAX}}}$ are set appropriately. Improper values would cause missing projections within phase bins or excessive projection acquisition and excessive imaging dose.

Determining appropriate gantry rotation speed and frame rate requires a set phase window. This too depends on the motion management technique and clinical goals. For example, if the objective is to match phase images with 4DCT phase images,
the phase window should match that of the 4DCT scan. If the objective is to treat during an interval of respiration, the imaging phase window should match the treatment window. Unlike for 4DCT, the imaging dose for 4D DTS does depend on the phase window. The phase window should be set as high as clinically tolerable to reduce imaging dose. These issues should be thoroughly investigated prior to the clinical implementation of on-board 4D imaging.

One final point of discussion is the phase assignment and sorting technique. In this study, consecutive inhalation peaks were assigned 0% phases, and linear interpolation was performed to generate phases for the remaining points. This is consistent with the technique commonly used for 4DCT.\textsuperscript{81} It may not, however, be the most appropriate technique for all clinical tasks. Patient waveforms are variable and may vary for the same patient from breath to breath. This has two noteworthy effects on the phase assignment. First, it is possible that peak inhalation will not occur at the 50% phase. For internal target volume delineation, it may be more appropriate to assign phases to both inhalation and exhalation peaks or to use an amplitude based sorting technique. The second consequence of waveform variation is that it will cause additional motion artifacts within phase bins. While we have not found this to be a major concern during 4DCT imaging in our clinic, it is something to consider on a case by case basis.
3.5 Conclusions

Three parameters must be appropriately determined for 4D DTS acquisition using the slow gantry rotation technique. These are scan angle (SA), gantry rotation speed (GRS) and frame rate (FR). We have shown in this article how these parameters are inter-related and how they depend on phase window (PW), shortest respiratory cycle (RCmin), and longest respiratory cycle (RCmax). We have also demonstrated how the three acquisition parameters (SA, GRS and FR) affect resulting projection distributions and hence the reconstructed images. We determined that the optimal way to increase projection density within sorted phase bins was to reduce gantry rotation speed and keep the frame rate low. In fact, increasing the frame rate such that multiple projections were acquired during single phase intervals greatly increased imaging dose but provided no substantial improvement in reconstructed images. This is true for 4D DTS and 4D CBCT imaging procedures with slow gantry rotation.

4 Lung Simulation Studies to Determine Required Acquisition Parameters

4.1 Introduction

Chapter 3 presented a theoretical framework for relating parameters for on-board 4D imaging using slow gantry rotation. This framework was tested using a motion phantom. The phantom studies validated the proposed relationships, but the anatomic simplicity and the inherently high contrast of the phantom did not allow a
characterization of the actual required scan angles and the $A_{\text{MAX}}$ values that would be needed for the implementation of this technique. Reasonable approximations of these parameters are required to estimate scan times and doses for actual patient studies. In this study we aim to determine approximate values needed for imaging lung tumors and estimate required doses and scan times.

4.2 Methods and Materials

4.2.1 Optimizing Scan Angle and Projection Spacing

In standard CBCT imaging, dose is optimized by reducing total mAs exposure, and the best images are reconstructed from many projections with low mAs per frame. This methodology is not quite practical for 4D imaging. As shown in Chapter 3, the optimal frame rate is set to capture one frame during each phase window of the shortest respiratory cycle. The gantry is rotating very slowly, so two projections acquired in the same phase window will be very closely spaced. Closely spaced projections contribute very little to sampling, so increasing the frame rate above optimal for 4D imaging has an effect that is not hugely different from simply increasing the mAs per projection. That being the case, for a given phase window, SA and $A_{\text{MAX}}$ are the most important parameters that can be manipulated for 4D imaging scan time optimization and dose reduction. The framework developed in Chapter 3 was used to conduct simulation studies to determine appropriate SA and $A_{\text{MAX}}$ values for lung imaging and to compare 4D DTS with 4D CBCT.
For the sake of image quality, it would be ideal to keep $A_{\text{I} \text{M} \text{A} \text{X}}$ on the order of what is currently used for CBCT scanning (approximately $0.5^\circ$ to avoid effects of under-sampling). However, $A_{\text{I} \text{M} \text{A} \text{X}}$ is proportional to the gantry rotation speed (Equation 3.2) and thus, scan time. A scan time of approximately 35 minutes would be required to maintain $0.5^\circ$ projection spacing in phase bins for a $200^\circ$ 4D CBCT scan on a patient with respiratory cycles ranging from 3 to 5 seconds. Much larger $A_{\text{I} \text{M} \text{A} \text{X}}$ values are needed to achieve reasonable scan times. This study is aimed at determining appropriate SA and $A_{\text{I} \text{M} \text{A} \text{X}}$ values for scan time optimization. The mAs per projection was constant for this study, so dose reduction with $A_{\text{I} \text{M} \text{A} \text{X}}$ increases was also reported.

Imaging dose and scan time are both proportional to the SA and inversely proportional to the $A_{\text{I} \text{M} \text{A} \text{X}}$ (proportional to $SA/A_{\text{I} \text{M} \text{A} \text{X}}$). (This is assuming constant mAs per projection.) The mechanisms by which $A_{\text{I} \text{M} \text{A} \text{X}}$ and SA affect reconstructed images are projection density and spatial sampling. Since both parameters affect the total number of projections and the spatial distribution of those projections, we found it appropriate to investigate these parameters simultaneously. We simulated DTS projection sets for various $SA/A_{\text{I} \text{M} \text{A} \text{X}}$ combinations by extracting sets of projections from lung CBCT scans. Projection data were acquired using an OBI system similar to the one described in Section 3.2.2. The exposure parameters were 125 kV, 80 mA, and 25 ms per projection. We studied three tumors in two patients (1 in 1 patient and 2 in the other). The approximate volumes of the tumors were 0.12, 0.24 and 1.53 cm$^3$. We sought to
minimize dose and scan time by finding optimal $SA/AI_{MAX}$ combinations. We investigated scan angles ranging from 20 to $120^\circ$ (20° intervals) with $AI_{MAX}$ values of 1.2, 2.3, 3.4 and 4.6°. All together, there were 24 combinations of $AI_{MAX}$ values and scan angles. The objectives of these investigations were to determine which combinations yielded visible images of the tumors and to determine the most efficient combinations in terms of dose and acquisition time. Once scan angle and $AI_{MAX}$ values were approximated, we calculated estimated doses and scan times for 4D DTS scans using the framework presented in the previous chapter.

4.2.2 4D DTS and 4D CBCT Comparisons

A second set of experiments was conducted using the same patient data to simulate comparisons between 4D DTS and 4D CBCT. Projection sets were extracted from the lung CBCT scans to simulate phase images at three different dose/acquisition time ‘levels.’ Images were reconstructed for scan angles ranging from 20 to $200^\circ$ at each level. The angular spacing between projections was adjusted for each scan angle to keep a constant $SA$ to $AI_{MAX}$ ratio for all images within a given level. This resulted in all images in a given level having the same acquisition time and dose.

Acquisition times and imaging doses for the simulated 4D scans depend on respiratory characteristics, so each level was associated with a dose range and an acquisition time range. The acquisition time ranges for the different levels were as follows: level 1 (0.45 to 1.06 min.), level 2 (0.92 to 2.12 min) and level 3 (1.84 to 4.24 min).
Doses relative to a standard CBCT (assuming constant mAs and kV settings) for the three levels were as follows: level 1 (0.12 – 0.36), level 2 (0.24 to 0.72) and level 3 (0.48 to 1.44). Note that doses and acquisition times for level 2 are twice those of level 1, and doses and acquisition times for level 3 are twice those of level 2.

4.2.3 Image Evaluation

Visual assessments of all images in this chapter were conducted to determine which SA/Al\text{MAX} combinations resulted in tumor visibility for each of the tumors. Normalized mutual information (NMI) was used for quantitative assessment. We calculated NMI between reconstructed DTS images and the corresponding fully sampled CBCT images. NMI was calculated using 2D region of interests (ROIs) of size 190 by 130 pixels.

Mutual information has been widely studied and used as measure of similarity between images for image registration.164-174 There are three ways to define mutual information, but all are identical and can be re-written into each of the other forms.175 One of the definitions is as follows:

\[ MI(X, Y) = H(X) + H(Y) - H(X, Y), \]

where \( MI(X, Y) \) is the mutual information shared by images \( X \) and \( Y \), \( H(X) \) and \( H(Y) \) are marginal entropies of images \( X \) and \( Y \), and \( H(X,Y) \) is the joint entropy. \( H(X), H(Y) \) and \( H(X,Y) \) are calculated as follows:
\[
H(X) = -\sum_{i=1}^{N} p_i \log p_i \\
H(Y) = -\sum_{j=1}^{N} p_j \log p_j \\
H(X,Y) = -\sum_{i=1}^{N} \sum_{j=1}^{N} p_{i,j} \log p_{i,j}
\]

where \( N \) is the number of grey scale values in each of the images, \( p_i \) denotes the probability of the \( i^{th} \) grey scale value in image \( X \), and \( p_{i,j} \) denotes the probability of the \( i^{th} \) grey scale value occurring in a pixel of image \( X \) with the \( j^{th} \) grey scale value occurring in the corresponding pixel of image \( Y \).

Mutual information gives a statistical measure of the information which is common to two random variables. Since the amount of information contained in a random variable depends on the number of values the variable could take (grey scale values in our case), the scales on which MI measurements are made are arbitrary. For this reason, we have chosen to use normalized MI. Several methods for normalizing MI have been proposed.\(^{176}\) There are multiple reasons for using normalized MI for image registration, but since our purpose is only to provide a common scale, the exact normalization method was not critical. We used the following normalization method described by Kvalseth.\(^{176}\)

\[
NMI(X,Y) = \frac{MI}{\min(H(X),H(Y))}
\]

It can be shown that this normalization method maps values on a 0 to 1 scale assuming the following limits on \( H(X,Y) \).
\[ H(X,Y) \geq H(X) \]
\[ H(X,Y) \geq H(Y) \]
\[ H(X,Y) \leq H(X) + H(Y) \]

4.3 Results

4.3.1 Scan Angle and Projection Spacing Optimization

Figure 4.1 shows coronal DTS images reconstructed for the tumor with approximate volume equal to 0.24 cm³. Figure 4.2 shows the sagittal DTS images for the same tumor. Each image is labeled with the SA, \( AI_{\text{MAX}} \) and number of projections used for the reconstruction. Figure 4.3 shows coronal DTS images for the smallest (0.12 cm³) and largest (1.53 cm³) of the three tumors.

Figure 4.1 Coronal image reconstructions of a lung tumor (approximate volume 0.24 cm³) using various scan angles and \( AI_{\text{MAX}} \) values.
Figure 4.2 Sagittal image reconstructions of a lung tumor (approximate volume 0.24 cm³) using various scan angles and AI\textsubscript{MAX} values.

Figure 4.3 Coronal image reconstructions of lung tumors (approximate volumes 0.12 and 1.53 cm³) using various scan angles and AI\textsubscript{MAX} values.
Even in the absence of a quantitative analysis, the images provide compelling evidence regarding appropriate starting points for \( SA/AI_{\text{MAX}} \) selection. First, we noted that for every scan angle, the dose and acquisition times for \( AI_{\text{MAX}} = 1.2^\circ \) are approximately double those of \( AI_{\text{MAX}} = 2.3^\circ \) images, but tumor visibility for all tumors (including the views not shown) was virtually unaffected (first vs. second rows). Moving to \( AI_{\text{MAX}} = 3.4^\circ \), we noted that dose and scan times were reduced by another 33%. There are some observable differences between the images in rows 2 and 3, but they do not prohibit tumor visibility in any of the cases we studied. The doses and scan times are about 24% lower for the \( AI_{\text{MAX}} = 4.6^\circ \) images than the \( AI_{\text{MAX}} = 3.4^\circ \) images, but some of the \( AI_{\text{MAX}} = 4.6^\circ \) images do show marked visibility impairment compared to the \( AI_{\text{MAX}} = 3.4^\circ \) images. We noticed that scan angle was far more important in achieving tumor visibility than projection spacing for all cases. Required scan angles were lower for coronal views than sagittal views. All three tumors were visible in the coronal view using 40 – 60\(^\circ\) scan angles. The largest tumor was visible in the sagittal view using a 40\(^\circ\) scan angle, but the two smaller tumors required 100 – 120\(^\circ\) scan angles for visibility in the sagittal view.
Figure 4.4 Relative doses and acquisition times for various scan angle/\text{AIMAX} combinations.

The maximum doses and acquisition times occur for the 120° scan angle and 1.2° \text{AIMAX} value. Figure 4.4 shows how doses and acquisition times compare for different scan angle/\text{AIMAX} combinations. Figure 4.5 and Figure 4.6 show NMI data for the coronal views corresponding to the images in Figure 4.1 and Figure 4.3. We show just these two plots as examples, but all of the NMI data support the visual observations that image improvements do not scale proportionally with dose or acquisition time. The NMI data and visual analyses show that optimal scan angles vary on a case-by-case basis, though for all cases we studied, substantial dose and acquisition time reductions could be achieved by using a 3.4° \text{AIMAX} value over a 1.2° value with little reduction in tumor visibility. There were, however, cases where an increase in \text{AIMAX} values at large scan angles did cause a substantial reduction in the NMI. This occurred for the case
shown in Figure 4.1 and Figure 4.5. Sagittal views required larger scan angles, especially for small tumors.

Figure 4.5 Normalized mutual information data for images shown in Figure 4.1.

Figure 4.6 Normalized mutual information data for images shown in Figure 4.3.
The following tables summarize reasonable acquisition parameters for typical respiratory profiles. The data are calculated assuming a $3.4^\circ AI_{\text{MAX}}$. Table 4.1 shows data for reconstructions with 10% phase windows, and Table 4.2 shows data for reconstructions using 15% phase windows. Acquisition times and ratios of 4D DTS doses to the dose from a standard CBCT are also shown in the tables.

Table 4.1  Acquisition parameters, acquisition time and dose estimation for various respiratory conditions, assuming a 10% phase window.

<table>
<thead>
<tr>
<th>$RC_{\text{MIN}} – RC_{\text{MAX}}$(s)</th>
<th>$FR$ (s$^{-1}$/s)</th>
<th>$GRS$ (°/s)</th>
<th>$ST$ (min) per $40^\circ$</th>
<th>Dose Relative to CBCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 – 3</td>
<td>5.0</td>
<td>1.03</td>
<td>0.68</td>
<td>0.31</td>
</tr>
<tr>
<td>2 – 4</td>
<td>5.0</td>
<td>0.77</td>
<td>0.91</td>
<td>0.41</td>
</tr>
<tr>
<td>2 – 5</td>
<td>5.0</td>
<td>0.62</td>
<td>1.13</td>
<td>0.51</td>
</tr>
<tr>
<td>3 – 4</td>
<td>3.4</td>
<td>0.77</td>
<td>0.91</td>
<td>0.28</td>
</tr>
<tr>
<td>3 – 5</td>
<td>3.4</td>
<td>0.62</td>
<td>1.13</td>
<td>0.35</td>
</tr>
<tr>
<td>3 – 6</td>
<td>3.4</td>
<td>0.52</td>
<td>1.34</td>
<td>0.41</td>
</tr>
<tr>
<td>4 – 5</td>
<td>2.5</td>
<td>0.62</td>
<td>1.13</td>
<td>0.26</td>
</tr>
<tr>
<td>4 – 6</td>
<td>2.5</td>
<td>0.52</td>
<td>1.34</td>
<td>0.30</td>
</tr>
<tr>
<td>4 – 7</td>
<td>2.5</td>
<td>0.44</td>
<td>1.59</td>
<td>0.36</td>
</tr>
<tr>
<td>5 – 6</td>
<td>2.0</td>
<td>0.52</td>
<td>1.34</td>
<td>0.24</td>
</tr>
<tr>
<td>5 – 7</td>
<td>2.0</td>
<td>0.44</td>
<td>1.59</td>
<td>0.29</td>
</tr>
</tbody>
</table>
Table 4.2 Acquisition parameters, acquisition time and dose estimation for various respiratory conditions, assuming a 15% phase window.

<table>
<thead>
<tr>
<th>$R_{\text{MIN}} - R_{\text{MAX}}$ (s)</th>
<th>$FR$ (s$^{-1}$)</th>
<th>$GRS$ (v/s)</th>
<th>$ST$ (min) per 40°</th>
<th>Dose Relative to CBCT</th>
</tr>
</thead>
<tbody>
<tr>
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<td>3.4</td>
<td>0.86</td>
<td>0.65</td>
<td>0.21</td>
</tr>
<tr>
<td>2 – 4</td>
<td>3.4</td>
<td>0.65</td>
<td>0.87</td>
<td>0.28</td>
</tr>
<tr>
<td>2 – 5</td>
<td>3.4</td>
<td>0.52</td>
<td>1.08</td>
<td>0.35</td>
</tr>
<tr>
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<td>0.19</td>
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<td>3 – 5</td>
<td>2.3</td>
<td>0.52</td>
<td>1.08</td>
<td>0.24</td>
</tr>
<tr>
<td>3 – 6</td>
<td>2.3</td>
<td>0.43</td>
<td>1.28</td>
<td>0.28</td>
</tr>
<tr>
<td>4 – 5</td>
<td>1.7</td>
<td>0.52</td>
<td>1.08</td>
<td>0.17</td>
</tr>
<tr>
<td>4 – 6</td>
<td>1.7</td>
<td>0.43</td>
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</tr>
<tr>
<td>4 – 7</td>
<td>1.7</td>
<td>0.37</td>
<td>1.52</td>
<td>0.25</td>
</tr>
<tr>
<td>5 – 6</td>
<td>1.4</td>
<td>0.43</td>
<td>1.28</td>
<td>0.17</td>
</tr>
<tr>
<td>5 – 7</td>
<td>1.4</td>
<td>0.37</td>
<td>1.52</td>
<td>0.20</td>
</tr>
</tbody>
</table>

4.3.2 4D DTS and 4D CBCT Comparisons

Figure 4.7 shows coronal images reconstructed for the three dose/acquisition time levels for the smallest and largest tumors. The smaller of the tumors is barely visible in the 40° image at level 1 but it not visible in any of the images with larger scan angles. Both tumors are visible in 40, 60, 100 and 140° images at level 2, and all of the images at level 3. The maximum NMI value at level 1 was for the 20° image. The maximum NMI values for the level 2 and level 3 images were for the 100 and 140° images, respectively. Tumor visibility was not achieved for CBCT images at levels 1 and 2, but it was achieved for some of the DTS images at those levels.
Figure 4.7 Coronal images reconstructed at three dose/acquisition time levels.

Coronal images for the third tumor are not shown here, but tumor visibility was achieved in 20 and 40° images at level 1 and 20, 40, 60 and 100° images at level 2. This tumor was visible for all level 3 images except the 200° CBCT image. NMI values were maximum at 40° for level 1 and 100° for both level 2 and level 3 images. Tumor visibility was not achieved for sagittal images of the two smaller tumors at these levels, because large scan angles and small $AImax$ values are needed for visualization. This was shown in the previous experiments. The largest tumor was visible in all of the sagittal images,
and NMI values at all levels were maximized at 200° scan angles. Adequate tumor visibility was easily achieved for coronal 4D DTS images of all three lung tumors at levels 1 and 2, while visibility was achieved only in level 3 images for 4D CBCT. These results suggest that 40° 4D DTS acquisition times will range from 0.45 - 2.12 min. vs. 1.84 - 4.24 min. for 4D CBCT. 4D DTS imaging will range from 0.12 - 0.72 times the dose of a standard CBCT scan vs. 0.48 - 1.44 times the dose of a standard CBCT scan for 4D CBCT. Patient studies are conducted in the next chapter to validate these findings.

4.4 Discussion

Acquisition parameters, acquisition time and dose relative to a standard CBCT were calculated for a wide range of respiratory parameters (shortest and longest respiratory cycles). Based on our clinical experience, most if not all patients will fall into one of the categories in Table 4.1 and Table 4.2. Doses for 40° scans are well below the doses for standard CBCT scans. In the extreme case that a 120° sagittal scan is needed in addition to a 40° coronal scan, the doses would range from 1 to 2 times the dose of a standard CBCT scan for reconstructions using 10% phase windows depending on respiratory characteristics. Acquisition times would range from 2 to 6 minutes. Both imaging doses and acquisition times can be reduced if the phase window can be increased above 10%.

Acquisition time and numbers of projections acquired are both proportional to scan angle and inversely proportional to AImax. The visual analysis indicated that the
required scan angle depended on patient specific anatomy and scan orientation (coronal or sagittal images). Our preliminary results indicate that 40° scan angles are adequate for coronal images of tumors in the lower lobes of the lungs. Scan angles ranging up to 120° were required for sagittal views. We believe that larger scan angles are required for sagittal views, because patients are typically wider in the later dimension than in the anterior-posterior dimension, meaning that lateral projections contain more ‘anatomic noise’ and statistical noise due to fewer photon detections. Our visual and NMI analyses show that scan angle is a more important factor in achieving good image results than projection spacing. Minimum required scan angles vary widely with tumor size and scan orientation, but we found that dose and acquisition time could be reduced to feasible levels while maintaining visibility by increasing the $AIMAX$. We found that 3.4° was adequate for all cases.

We find it prudent to suggest using case specific optimizations of scan angles and a common $AIMAX$ value for all 4D DTS lung scans. There are at least two ways case specific scan angles could be determined. One way would be to conduct an extensive study and create categories based on patient size, tumor size and tumor location. Another option would be to use a CBCT scan of a patient and simulate DTS reconstructions using different angles. The first acquisition (CBCT) would be more lengthy and require a higher dose, but an optimized scan angle could then be used for future scans of the same patient. Software to create the simulations would need to be
developed and implemented in order to use this method. Since the effects of $A_{\text{max}}$ were smaller and did not seem to depend on anatomy, we suggest using a value around $3.4^\circ$ for all cases to reduce dose and acquisition time. More studies should be conducted to ensure that our preliminary value of $3.4^\circ$ is generally appropriate.

Comparisons between 4D DTS and 4D CBCT showed that 4D DTS could provide coronal images with reduced acquisition time and imaging dose than 4D CBCT. Since the frame rate is set according to patient respiratory characteristics, it is not adjustable for dose or acquisition time manipulation. Gantry rotation and scan angle are the other variable parameters that affect both dose and scan time. The $SA/A_{\text{max}}$ investigations showed that projection spacing became increasingly more important as the scan angle was increased. However, for constant dose and acquisition time, the scan angle must be small or the $A_{\text{max}}$ large. The investigations with constant dose/acquisition time levels demonstrated that large scan angle/large $A_{\text{max}}$ value combinations did not result in tumor visibility for lower dose/acquisition time levels. Therefore, the only way 4D imaging can be conducted using doses and acquisition times as low as our levels 1 and 2 is to image with 4D DTS. It would be possible to reduce the gantry speed and therefore the $A_{\text{max}}$ value and also reduce the mAs per projection to keep the dose constant and potentially improve visibility for low dose 4D CBCT images. Since this was not studied, it is unclear whether 4D DTS would maintain the advantage over 4D CBCT if mAs was included in the optimization. However, the necessary reduction in gantry rotation
speed would require substantially extended scan times for 4D CBCT. For cases where both coronal and sagittal views are required, it may be prudent to image with 4D CBCT, since large scan angles are needed for small tumor visibility in the sagittal views and two 4D DTS scans at level two would require the same imaging dose and acquisition time as one 4D CBCT scan at level 3. For large tumors that do not require large scan angles for sagittal views and for situations where only coronal views are needed, 4D DTS can be performed using reduced imaging doses and acquisition times than 4D CBCT.

4.5 Conclusions

The investigations have led to the determination of appropriate acquisition parameters for various scenarios and provide insight about the feasibility of on-board 4D DTS imaging for lung patients. For 10% phase windows, we found that appropriate frame rates ranging from 2 – 5 frames per second, gantry rotation speeds ranging from 0.44 – 1.02 °/s, and aiming for a 3.4° maximum angular interval between projections were appropriate for dose and scan time optimization. Adequate tumor visibility was achieved for coronal 4D DTS images of all three lung tumors with acquisition times ranging from 0.45 - 2.12 min. vs. 1.84 – 4.24 min. for 4D CBCT. 4D DTS imaging doses ranged from 0.12 – 0.72 times the dose of a standard CBCT scan vs. 0.48 – 1.44 times the dose of a standard CBCT scan for 4D CBCT. This study has shown that 4D DTS images can be generated using reduced acquisition times and possibly reduced imaging doses.
compared to 4D CBCT when coronal views are sufficient for clinical goals or when tumors are large enough that small scan angles can be used for generating sagittal images.

5 Slow Gantry Rotation Acquisition Optimization: Lung Patient Studies

5.1 Methods and Materials

5.1.1 Slow Gantry Data Acquisition

In this study, projection data sets with slow GRS for three lung cancer patients were acquired at MD Anderson Cancer Center under institutional IRB protocol ID00-202 using a kV imaging system mounted on a linear accelerator (The Trilogy System, Varian Medical Systems, Palo Alto, CA). The imaging geometry and reconstruction technique were the same as for the system described in Section 3.2.2 except that the detector was operated in dual-gain readout mode to extend the dynamic range. The imaging parameters were 120 kV, 80 mA and 25 ms per projection. GRS, frame rates and total numbers of projections are listed for the three patients in Table 5.1.

Table 5.1 Patient respiratory and slow gantry scanning parameters.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>( R_{\text{MIN}} ) (s)</th>
<th>( R_{\text{MAX}} ) (s)</th>
<th>GRS (o/s)</th>
<th>FR (s(^{-1}))</th>
<th>Total no. projections</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.8</td>
<td>3.4</td>
<td>0.73</td>
<td>7.3</td>
<td>1983</td>
</tr>
<tr>
<td>2</td>
<td>1.6</td>
<td>4.7</td>
<td>0.73</td>
<td>7.3</td>
<td>2006</td>
</tr>
<tr>
<td>3</td>
<td>3.0</td>
<td>8.6</td>
<td>0.59</td>
<td>4.9</td>
<td>1679</td>
</tr>
</tbody>
</table>
Projections were acquired over single 200° gantry rotations. 4D images were then generated by 1) retrospectively analyzing projection images to acquire respiratory and phase signals, 2) assigning phases to projection images, 3) sorting of images into phase bins, 4) selecting subsets of projection data corresponding to desired scan angles, phase windows and frame rates, and 5) reconstructing phase images. Patient respiratory signals are typically generated by monitoring the motion of an externally applied surrogate marker or pressure sensing belt.\textsuperscript{79, 80, 110, 111} These methods have errors associated with signal acquisition, correlation between target and surrogate motions and correlation between signal acquisition and projection acquisition. We generated respiratory signals by manually tracking structures (diaphragm when possible) in the projection images. While this method is too time consuming to use clinically, we chose to use it in order to reduce confounding effects of signal acquisition and correlation errors in our study. We found that peak inspirations and expirations were easily determined by tracking structures in the projection images and assumed that the correlations between motions of the structures tracked in the projection images and the targets were better than correlations between target and externally applied surrogate motions. Furthermore, there is no error in correlating signal and projection acquisition times using this method. We used the same phase assignment technique used in our clinic for 4DCT imaging and in the 4DCT papers previously cited in this paper. The phase refers to the percentage of the respiratory cycle that has passed since end-
inhalation. End-inhalation peaks were labeled 0 % phase, and linear interpolation was performed to determine phases (0 – 100 %) for the projections in between consecutive 0 % peaks. Various subsets of the projection images were extracted and binned to generate 4D DTS and 4D CBCT data sets with differing scan angles, phase windows and frame rates. DTS and CBCT phase images were reconstructed using a Feldkamp type filtered back projection technique.142, 163, 177

5.1.2 Slow Gantry Protocol Validation

Equations 1 and 2 were validated using lung patient data sets (Table 5.1) by analyzing distributions of projections in sorted phase bins. Equation 1 asserts that for a given $\text{RC}_{\text{MIN}}$ and a desired PW, there is an optimal frame rate ($F_{\text{ROPT}}$) that should be used to eliminate large angular intervals in sorted phase bins and keep numbers of tightly spaced projections as low as possible. For each of the three patient data sets, we sorted projections into phase bins using various phase windows such that the actual frame rate was lower than the theoretical optimal ($0.5 \times F_{\text{ROPT}}$ & $0.75 \times F_{\text{ROPT}}$) and higher than the optimal ($1.25 \times F_{\text{ROPT}}$ & $1.5 \times F_{\text{ROPT}}$). Equation 2 asserts that angular intervals larger than $\text{AIMAX}$ will not exist in data sets for which the frame rate is set equal to or greater than $F_{\text{ROPT}}$. The distributions of projections in phase bins were analyzed and compared with these expectations.
5.1.3 Dose Reduction via Phase Window Expansion

4DCT images are the current standard for 4D imaging in radiation oncology. These images are created by sorting reconstructed axial images into like phase bins.\textsuperscript{80-82} The phase window refers to the range of respiratory phases that falls into a bin centered about a specific phase. For example, a 30 % phase bin with a 10 % phase window will contain images tagged with phases ranging from 25 to 35 %. 4DCT images are typically reconstructed with 10 % phase windows, but the data used to reconstruct the axial images are typically acquired using source rotation times of 0.5 to 1.0 s.\textsuperscript{79-82, 92, 105} Thus, for respiratory cycles ranging from 2 to 5 s, the axial images contain an additional 10 to 50 % of the respiratory cycle, making the effective phase windows 20 – 60 %. Phase images containing 60 % of the respiratory motion are often characterized by severe motion blurring or artifacts in 4DCT reconstructions,\textsuperscript{92, 178} but with 0.5 – 1.0 s gantry rotation times, effective phase windows of 20 – 30 % are the best that can be achieved with 4DCT.

Four-dimensional images generated using a gantry mounted 2D imaging device are inherently capable of far better temporal accuracy than 4DCT images because the 2D projections are acquired in milliseconds and directly tagged with phases. Thus, 4D DTS and 4D CBCT images could be reconstructed using 20 to 30 % phase windows and still maintain temporal accuracy comparable to the best 4DCT images.
According to the protocol for slow gantry acquisition, the optimal frame rate, and therefore dose are inversely proportional to the phase window. Thus, substantial decreases in imaging dose could be achieved by doubling or tripling the standard 10 % phase window, making 4DCT and 4D CBCT phase windows effectively similar. The tradeoff for increasing the phase window is a decrease in temporal accuracy (additional motion blur within phase images). The effects of increasing phase window and simultaneously decreasing frame rate on temporal accuracy to reduce dose were investigated in this study.

Decreasing the frame rate for conventional CBCT images would not be the most appropriate way to reduce dose. Rather mAs per projection would be lowered. Frame rate reduction in 4D imaging, however, does not result in decreased numbers of frames per reconstructed images. Rather, the frame rate is reduced because fewer segments of the respiratory cycle must be fully populated with projection data for image reconstruction.

Three subsets of data were reconstructed for each patient: full FR/10 % PW, \( \frac{1}{2} \) FR/20 % PW and \( \frac{1}{3} \) FR/30 % PW. Cutting the frame rate to half and one third reduced the dose by 50 and 67 %, respectively, while the appropriate simultaneous increase in phase window (Equation 1) maintained an almost constant number of projection images per sorted phase bin. Due to the constant GRS and varying PW, the \( A_{MAX} \) increased slightly with higher phase windows (Equation 2), resulting in slightly fewer projections.
per bin. This effect was marginal. 4D DTS (60° scan angles) and 4D CBCT (200°) images were reconstructed for 10 phases for each patient and for each PW/FR combination. We quantitatively analyzed the differences between images reconstructed using different FR/PW combinations by calculating the root mean squared deviation (RMSD) between phase images. RMSDs between full FR/10 % PW and 1/2 FR/20 % PW phase images were calculated. RMSDs between full FR/10 % PW and 1/3 FR/30 % phase images were also calculated. Each group of comparisons had 10 RMSDs (one for each phase bin). The RMSDs were calculated over a cubic volume of 190 × 190 × 190 pixels centered about the tumor for each of the 4 tumors. The average and standard deviations of these values were reported as percentages of the average pixel values of the full FR/10% PW images for each patient. Images and line profiles were used to visually characterize changes in temporal resolution with phase window/frame rate changes.

Estimated doses are reported for the three PW/FR combinations. The weighted CBCT dose index (CBCTDIw) for a standard CBCT scan (125 kVp, 80 mA, 25 ms, 630 projections) using Varian’s OBI system is 5.4 cGy.179 Doses for various reconstructions in this study were estimated by scaling based on the numbers of projections.

5.1.4 4D DTS for Dose and Scan Time Reduction

The intent of this part of the study was to determine the effect of scan angle on tumor visibility for four lung tumors (2 in 1 patient and 1 in each of the other 2 patients). Coronal 4D DTS images were reconstructed using 5, 10, 20, 30, 40, 60, 80, 100, 120 and
200° scan angles, and sagittal images were reconstructed using 5, 10, 20, 33 and 120° scan angles. We were not able to reconstruct sagittal DTS images with scan angles between 33 and 200°, due to the actual 200° scan being oriented about the anterior-posterior axis. Images were reconstructed for the 50 % phase using 30 % phase windows and 1/3 of the full frame rates. Selected images are shown in the results section. Scan times were calculated by dividing the total scan angles by the gantry rotation speeds and adding 12 seconds for gantry rotation between arcs for DTS cases. Doses were estimated using the method stated in the previous paragraph.

5.2 Results

5.2.1 Slow Gantry Protocol Validation

Projection distributions are shown using histograms in Figure 5.1. The largest angular intervals are not included in these charts, because including them would have extended the length of the charts far enough to impair the visibility of the majority of the data. Angular intervals up to 9.6° occurred in the 0.75×FR\text{OPT} groups, and angular intervals up to 16.9° occurred in the 0.5×FR\text{OPT} groups. Note that all of the tightly spaced projections fell into the 0.5° bins, but these intervals were much smaller than 0.5°. The intervals in these bins are displayed in histograms with smaller bins in the left of Figure 5.1.
Figure 5.1 Histograms showing projection distributions using various frame rates. The smaller histograms on the left show the distributions of the projections in the smallest bins on the right.

According to the protocol, actual angular intervals should not exceed $A_{\text{MAX}}$ values determined by Equation 3.2 as long as the frame rate is set at or above $F_{\text{OPT}}$. The consequence of setting the frame rate higher than $F_{\text{OPT}}$ is higher numbers of tightly spaced projections. $A_{\text{MAX}}$ values, actual maximum angular intervals, percentages of angular intervals exceeding $A_{\text{MAX}}$ values, and percentages tightly spaced projections (intervals that were less than $0.2^\circ$) are shown in Table 2 for each patient and each frame.
rate. The data show that the FRopt is the minimum frame rate that can be used to control the sizes of the large gaps between projection images in sorted phase bins, and it is also the maximum that should be used to minimize numbers of tightly spaced projections that contribute greatly to dose accumulation but not to image sampling.

Table 5.2 AI_{MAX} values, actual maximum angular intervals, percentages of angular intervals exceeding AI_{MAX} values and percentages of projections spaced less than 0.2° apart for cases using frame rates that are lower than, equal to and higher than optimal frame rate.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>X of FR_{OPT}</th>
<th>AI_{MAX} (°)</th>
<th>Max. AI (°)</th>
<th>% &gt; AI_{MAX}</th>
<th>% &lt; 0.2°</th>
</tr>
</thead>
<tbody>
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<td>2.5</td>
<td>11.3</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
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<td>1.2</td>
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</tr>
<tr>
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<td></td>
</tr>
<tr>
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</tr>
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<td>5.1</td>
<td>16.9</td>
<td>9.3</td>
<td>4</td>
</tr>
<tr>
<td>0.75</td>
<td>5.1</td>
<td>9</td>
<td>0.5</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>5.2</td>
<td>4.8</td>
<td>0</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>1.25</td>
<td>5.2</td>
<td>4.8</td>
<td>0</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>1.5</td>
<td>5.3</td>
<td>4.5</td>
<td>0</td>
<td>57</td>
<td></td>
</tr>
</tbody>
</table>
5.2.2 Dose Reduction via Phase Window Expansion

Figure 5.2 and Figure 5.3 show 60° 4D DTS coronal images reconstructed using 10, 20 and 30% phase windows and inversely proportional frame rates for the small and large tumors in patient 1, respectively. The figures also include profiles to show that motion blurring was not substantially increased with increased phase windows. The dashed lines show the locations from which the line profiles were drawn.

Figure 5.2 60° coronal DTS images for three phases (0, 20 and 50%) reconstructed using three phase windows. 20 and 30% phase window reconstructions correspond to 50 and 67% dose reductions compared to the 10% phase window reconstructions.
Figure 5.3  60° coronal DTS images for three phases (0, 20 and 50%) reconstructed using three phase windows. 20 and 30% phase window reconstructions correspond to 50 and 67% dose reductions compared to the 10% phase window reconstructions.

Figure 5.4 and Figure 5.5 show 60° 4D DTS coronal images reconstructed using 10, 20 and 30% phase windows and inversely proportional frame rates for the patients 2 and 3, respectively.
Figure 5.4 60° coronal DTS images for three phases (0, 20 and 50%) reconstructed using three phase windows. 20 and 30% phase window reconstructions correspond to 50 and 67% dose reductions compared to the 10% phase window reconstructions.
Figure 5.5 60° coronal DTS images for three phases (0, 20 and 50%) reconstructed using three phase windows. 20 and 30% phase window reconstructions correspond to 50 and 67% dose reductions compared to the 10% phase window reconstructions.

Figure 5.6 shows coronal 200° 4D CBCT images of patient 3. Note that in Figure 5.5 (DTS), the superior-inferior motion is more readily evident compared to in Figure 5.6. This is because the motion in the CBCT images is both superior-inferior and anterior posterior. Anterior-posterior motion is not evident in DTS images, because the apparent slice thickness is large enough that motion in that dimension is obscured. In both cases, we see that there is very little difference between the images using different phase windows.
Figure 5.6 60° coronal DTS images for three phases (0, 20 and 50%) reconstructed using three phase windows. 20 and 30% phase window reconstructions correspond to 50 and 67% dose reductions compared to the 10% phase window reconstructions.

Figure 5.7 contains axial slices of 200° 4D CBCT reconstructions showing both tumors in patient 1.
Figure 5.7 Axial slices of 50% phase images reconstructed using various phase windows. 20 and 30% phase windows correspond to 50 and 67% dose reductions compared to 10% phase window reconstructions.

Table 3 shows average and standard deviations of RMSDs (10 bins) as percentages of the average pixel values of the full FR/10 % PW for each of the 4 tumors studied.

Table 5.3 RMSD values.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Ave. RMSD (%) 20% PW (mean ± s.d.)</th>
<th>Ave. RMSD (%) 30% PW (mean ± s.d.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.a.</td>
<td>0.59 ± 0.04</td>
<td>0.77 ± 0.04</td>
</tr>
<tr>
<td>1.b.</td>
<td>0.59 ± 0.04</td>
<td>0.78 ± 0.07</td>
</tr>
<tr>
<td>2</td>
<td>0.58 ± 0.04</td>
<td>0.74 ± 0.04</td>
</tr>
<tr>
<td>3</td>
<td>0.68 ± 0.13</td>
<td>0.89 ± 0.16</td>
</tr>
</tbody>
</table>

This data demonstrates that for the cases we studied, 20 and 30 % phase windows can be used with very little additional motion blur in phase images, and the associated dose reductions are very substantial. Table 4 summarizes estimated 4D CBCT doses using the various phase windows. Further dose reduction using 4D DTS is detailed in the section below.
Table 5.4 Summary of dose reduction for CBCT phase window optimization.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>10% PW Dose (cGy)</th>
<th>20% PW Dose (cGy)</th>
<th>30% PW Dose (cGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 &amp; 2</td>
<td>17.0</td>
<td>8.5</td>
<td>5.7</td>
</tr>
<tr>
<td>3</td>
<td>14.4</td>
<td>7.2</td>
<td>4.8</td>
</tr>
</tbody>
</table>

5.2.3 4D DTS for Dose and Scan Time Reduction

Figure 5.8 and Figure 5.9 show coronal and sagittal images reconstructed using various scan angles for the larger of the tumors in patient 1.

Figure 5.8 Coronal images reconstructed at various scan angles.
Figure 5.9  Sagittal images reconstructed using various scan angles.

Figure 5.10 and Figure 5.11 show images of patient 2. Figure 5.12 and Figure 5.13 show the same images for patient 3. In all cases tumor visibility was clearly sufficient in coronal views using 30° scan angles.

Figure 5.10  Coronal images reconstructed using various scan angles for Patient 3.
Figure 5.11 Sagittal image reconstructions reconstructed using various scan angles for Patient 3.

Figure 5.12 Coronal image reconstructions using various scan angles for Patient 3
Figure 5.13  Sagittal images reconstructed using various scan angles for patient 3.

Tumor visibility in 33° sagittal images was greatly improved over projection images, but it is debatable whether or not tumor visibility is sufficient for localization. Figure 5.14 through Figure 5.17 show coronal and sagittal slices of 4D CBCT images and corresponding coronal and sagittal slices of 33° 4D DTS images for all of the patients in this study. 30 % phase windows were used to reconstruct these images. Scan times for the full 4D CBCT images were 4.6 minutes for patients 1 and 2 and 5.6 minutes for patient 3. Doses and scan times are linearly proportional to scan angle, so 30° coronal images would require between 41 and 50 s for these patients.
Figure 5.14 4D DTS and 4D CBCT images of the small tumor in patient 1. 30% phase windows were used for all reconstructions.
Figure 5.15 4D DTS and 4D CBCT images of the large tumor in patient 1. 30% phase windows were used for all reconstructions.
Figure 5.16 4D DTS and 4D CBCT images of patient 2. 30% phase windows were used for all reconstructions.
Figure 5.17 4D DTS and 4D CBCT images of patient 3. 30% phase windows were used for all reconstructions.

5.3 Discussion

This study has validated a comprehensive formalism for relating patient respiratory parameters and acquisition and reconstruction parameters. The formalism accurately accounted for relationships between patient respiration (including variations in patient respiratory cycle durations), gantry rotation speed, frame rate and phase window. It was shown that an optimal frame rate and gantry rotation speed can be
chosen such that the maximum size of the gaps between projections in phase bins can be explicitly controlled while minimizing the numbers of tightly spaced projections. The angular intervals for the tightly spaced projections were on the order of $0.1^\circ$ for all three patients studied. These are extremely small and contribute very little to image sampling. The data does show that these can be further reduced by using frame rates below $F_{ROPT}$ with the consequence of large gaps between projections in sorted phase bins. The actual maximum angular intervals were up to $9.6^\circ$ (4 times greater than the $\Delta_{IMAX}$) for frames rates that were 75 % of the $F_{ROPT}$. These kinds of gaps cause severe streaking artifacts for filtered back projection reconstructions. Frame rate reduction below $F_{ROPT}$ would require an additional technique such as the use of prior information\textsuperscript{152} or substitution of projections from other phase bins to help compensate for the gaps.

Phase windows were expanded from 10 to 20 and 30 % to maintain image quality while reducing frame rates (and thus doses) by 50 and 67 %. As described above, the temporal accuracy using a 30 % phase window is similar to that of 4DCT images reconstructed using 10 % phase windows. Thus, by current standards the temporal accuracy achieved here is quite good. It has been determined in previous studies that 4DCT image artifacts can be substantial, and they do tend to increase with tumor motion amplitude.\textsuperscript{92, 178} The largest peak-to-peak tumor motion amplitude in our studies was approximately 1 cm. Additional motion blurring may occur in larger phase
window images when the overall tumor motion is greater. Further studies should be conducted to fully characterize this effect with more patients and motion characteristics, but we believe that the temporal accuracies for 4D CBCT and 4D DTS using this technique will always match or exceed those currently achieved with 4DCT. Thus, using larger phase windows for on-board imaging to reduce dose would not require reconsideration on the margins set based on planning with 4DCT.

_Dose and Scan Time Reduction via Scan Angle Reduction_

While we were not able to reconstruct sagittal 4D DTS images using scan angles larger than 33°, data from the previous section indicate that larger scan angles may be needed to achieve adequate visibility. If 70° images were sufficient, 4D DTS images could be generated using total scan angles of 100°. Assuming 12 seconds for gantry rotation in between arcs, scan times could be reduced to 2.5 to 3 minutes for these patients. Imaging doses for the 4D DTS images would be 2.4 to 2.9 cGy, which is approximately half of the dose of a standard CBCT scan.179

_Altimate Dose and Scan Time Reduction Method_

Dose and scan time reductions have been previously investigated using this data by simulating increased gantry rotation speeds.180 This study by Ahmad et al. shows that doubling and tripling the gantry rotation speeds reduce scan times and doses by 50 and 67%. While the dose reductions are exactly the same as for our study, the scan time reduction is an additional benefit. The tradeoff for using the dose reduction technique
by Ahmad et al. is the addition of streaking artifacts that do not occur when dose reduction is achieved by reducing the frame rate as in our study. Readers may compare images reconstructed using both techniques by examining subfigures a, b and c of Figure 5 in the study by Ahmad et al. and the three subfigures of Figure 5 in our study. Both studies show dose reductions of 50 and 67 %, and the scan times in subfigures b and c from the study by Ahmad et al. are 50 and 67 % lower than in our study.

5.4 Conclusions

This study validated an optimal protocol for four-dimensional CBCT imaging with slow gantry rotation. This comprehensive protocol accounts for the relationships between respiratory motion, gantry motion and frame rate and incorporates irregularities in durations of patient respiratory cycles. The protocol allows a full-fledged patient specific optimization for slow gantry rotation imaging. The optimized protocol was used to demonstrate that expanded phase windows provide a means of dose reduction with only a small tradeoff in motion blur in the phase images. The optimized protocol facilitates consistent, controllable, high quality on-board 4D CBCT and DTS imaging.
6 Investigations on the Effects of mAs in 4D CBCT Imaging

6.1 Introduction

Kilovoltage cone-beam CT integrated on a linear accelerator for image guided radiation therapy (IGRT) is a relatively new development. The earliest proposals were between 1999 and 2002, and it was a few years later before clinics began reporting on the integration and clinical use of commercially developed equipment. In 1976, Barrett et. al. theoretically demonstrated that the statistical laws regarding signal and noise for radiography also applied to tomographically reconstructed images. In 2006 Daly et. al. verified this for the case of cone-beam CT with a flat panel detector. Daly et. al. quantitatively assessed image quality by computing contrast-to-noise (CNR) at various dose levels and also for scans with various numbers of projection images. In these studies they determined that the aliasing artifacts caused by using limited projection views did not affect the noise or the CNR dependence on variations in dose. In other words, they found that the high frequency noise variations in the reconstructions were directly dependent on dose. They found that CNR increased with the square root of the dose, as predicted by Barrett et. al. In the case of 4D CBCT imaging, the numbers of projections (and hence the dose) vary from phase bin to phase bin. The objective of the following study is to characterize the variations in image
quality between phase bins (due to fluxuations in dose) and compare the magnitude of this effect with the effect of changing the mAs per projection.

6.2 Methods and Materials

6.2.1 Imaging Device and Motion Phantom

We have recently developed and built an imaging system in our laboratory which is nearly equivalent to the OBIs mounted on Varian’s linear accelerators as described in Section 2.2.1. The kV source, flat-panel detector and specifics of the acquired projection data are similar. Our system has two opposing systems, but we only used one of the systems for this experiment. There are a few differences between the OBIs and our system. The Varian OBI is mounted on a rotating gantry, so the source and the detector rotate about an isocenter. Our source and detector are stationary, and the object to be imaged is placed on a stage that rotates about the isocenter. The source-to-isocenter distance (SID) and source-to-detector distance (SDD) are 100 and 150 cm, respectively. These are the same for the OBI. The main consequence of the different setups is that geometric offset corrections must be processed differently in the reconstruction algorithms. The second difference between our system and the OBI is that our system has been set up such that the rotation speed, frame rate and mAs per projection may be easily adjusted. This system is therefore ideal for implementation of 4D CBCT according to the framework developed in Section 3. The imaging system is shown in Figure 6.1.
Figure 6.1 Dual detector imaging system.

We were not able to use the dynamic thorax phantom used in earlier studies on with this system, as the motion would be in the same plane as the source and detector. Instead we used a motion platform developed by Brainlab for quality assurance purposes. This apparatus, as shown in Figure 6.2.a has two moving platforms that move in orthogonal dimensions. A soft tissue equivalent sphere (physical density: 1.04 g/cc, electron density w.r.t. water: 1.003) with a 2 cm diameter surrounded by 1 cm of lung equivalent material (physical density: 0.21 g/cc, electron density w.r.t. water: 0.207) was placed on the smaller platform which moved up and down. The respiratory cycle was set at 4.5 s, and the peak-to-peak motion amplitude was set at 3 cm. The soft
tissue equivalent sphere and surrounding lung tissue equivalent material are shown in Figure 6.2.b.

![Moving platform developed by Brainlab. Soft tissue equivalent sphere surrounded by lung equivalent material.](image)

The shortest and longest respiratory cycles (RC_{MIN} and RC_{MAX}) were assumed to be 4.3 and 4.7 s, respectively. The 4D imaging parameters (frame rate and stage rotation speed) were set according to the framework developed in Section 3, where stage rotation speed (SRS) is the equivalent of gantry rotation speed (GRS). Images were acquired assuming a 15% phase window. According to Equation 3.1, the frame rate was set at 1.6 frames per second, and according to Equation 3.2, the SRS was set at 0.32°/s in order to achieve a maximum angle between projections in phase bins (AIMAX) of 2.0°. A total of 873 projection images were acquired for each scan over 200° scan angles. All scans were conducted using a beam energy of 50 kV. We conducted four scans using 0.25, 0.5, 1.0
and 2.0 mAs per projection. All other parameters were fixed. Images were sorted and binned using the method described in Section 5.1.1. Phase images were reconstructed using a Feldkamp type filtered backprojection method implemented in Matlab. Reconstructed images had a 0.5 mm$^3$ voxel size.

Signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) were computed for all phase images. Six 121 pixel regions of interest (ROIs) were defined in each reconstructed phase image: one in the soft tissue target and the other five in the background as shown in Figure 6.3.

![ROIs = 121 Pixels](image)

**Figure 6.3** ROI definitions for SNR and CNR computations.

The target is in its lowest position in the phase image in the above figure. As the high density stage moved up and down, it caused artifactual variations in the background above the locations where the background ROIs are defined. This is the reason for the positioning of the these ROIs. SNRs were computed by dividing the mean pixel value in
the target ROI by the average of the standard deviations of pixel values in the 5 background ROIs.

\[
SNR_{\text{Measured}} = \frac{\mu_{ROI_T}}{\frac{1}{5} \sum_{ROI_B=1}^{5} \sigma}
\]

CNRs were computed by dividing the differences in the mean pixel values in the target ROIs and the average of the mean pixel values in the background ROIs by the average of the standard deviations in pixel values in the background ROIs.

\[
CNR_{\text{Measured}} = \frac{\left| \mu_{ROI_T} - \frac{1}{5} \sum_{ROI_B=1}^{5} \mu \right|}{\frac{1}{5} \sum_{ROI_B=1}^{5} \sigma}
\]

### 6.3 Results

Each scan had 10 phase bins, distributed from 0 to 90%. As expected, the numbers of projections per phase bin varied, and the numbers in each phase were almost constant for the four scans using different mAs. 0, 10, 40, 60 and 90% bins had either 121 or 122 projections. 20, 30, 70 and 80% bins had 145 or 146 projections, and the 50% bins had 217 or 218 projections.

The programmed motion profile used a relatively high peak-to-peak motion amplitude (3 cm). The waveform was set to be sinusoidal, but we noticed that there was
a distinct pause when the target was at its lowest position. The motion appeared to be quite fast, so the inherent contrast due to motion blurring varied substantially between phases due to motion blurring. Sample phase images of different phases and at different mAs are shown in Figure 6.4.

![Sample phase images of different phases and at different mAs](image)

**Figure 6.4** Reconstructed 4D CBCT phase images at various dose levels (mAs per projection)

The numbers of projections for given phase bins was constant for the four different mAs scans. Also, the motion blurring in a phase image is constant with varying mAs. Thus, the changes for given phase bins (different mAs per projection) are due entirely to dose changes. According to the works presented by Barrett et al and Daly et al, the SNR and CNR should increase with the square root of the dose. We measured entrance doses on the detector for a range of mAs values to determine exactly how the
SNR and CNR should fall with our decreased mAs. Entrance doses were measured using an Unfors Xi R/F Detector (model 5101049-D) (Unfors, Bilddal, Sweden). The 2 oz. detector consisted of a carbon fiber ion chamber with a built in temperature and pressure correction system. Measurements are reportedly accurate within 5%. The detector was taped to the face of our flat panel detector perpendicular to the x-ray tube axis (as recommended in the detector manual). Entrance doses were measured for 2.0, 1.0, 0.5, 0.4, 0.315, 0.25, 0.2, 0.16, 0.125, and 0.1 mAs per projection. These mAs levels were the complete set of allowable levels for our system. Nine projection measurements were acquired at each dose level.

The figure below shows the measured entrance doses plotted as a function of the set mAs. The error bars are set based on the fact that the detector supposedly measures dose with a 5% accuracy. Entrance dose was linear for the lower doses, but it was not precisely linear at 1.0 and 2.0 mAs per projection.

Figure 6.5 Measured entrance doses plotted as a function of the set mAs
Theoretical SNRs and CNRs for the 0.25, 0.5, and 1.0 mAs phase images (relative to the SNR and CNR measured in the 2.0 mAs images) were calculated by dividing the 2.0 measured mAs by the square root of the dose changes. We compared the predicted theoretical values with the measured values. Figure 6.6 shows measured SNR values compared with theoretical SNR values for 0, 40, 60 and 80% phase bins.

Figure 6.6 Measured SNR values compared with theoretical calculated SNR values for selected phase bins.

The measured SNR data roughly follow the expected trends, though all of the SNR values for the lowest dose level are lower than predicted. The SNR varied between
phase bins as expected (numbers of projections per bin and motion blur varied between phase bins). The average SNR values across all phase windows were 71.8, 50.5, 35.0 and 20.7 for the 2.0, 1.0, 0.5 and 0.25 mAs per projection dose levels, respectively. The decreases in SNR were somewhat greater than the theory suggested they would be, with the greatest discrepancy being with the lowest dose level. The ratios of SNR values for the lower three dose levels to the SNR for the 2.0 mAs dose level for each phase window and each phase image are shown below in Figure 6.7. The solid lines represent the theoretical ratios. The theoretical ratios were calculated by dividing the square root of the measured entrance dose by the square root of the entrance dose measured for the 2.0 mAs scan.

![Ratio of SNR to SNR\textsubscript{2.0 mAs}](image.png)

**Figure 6.7** Ratios of SNR values for the lower three dose levels to the SNR for the highest dose level for each phase window. The solid lines show the predicted ratios.
Figure 6.8 Contrast to noise ratios for all phase bins and all four dose levels.

Figure 6.8 shows measured CNR values for all phase bins and all four dose levels. CNR varies from phase bin to phase bin. These variations appear to be related to contrast changes due to motion blurring in some cases. 30 and 70% phase windows have substantially more motion blurring than the other phases, and this appears to degrade CNR for the higher dose levels. The 50% phase windows have between 50 and 80% more projections than the other windows, and this has an effect on CNR. CNR values for the 50% phase windows were 16, 34, 11 and 26% higher than the averages of the other phase windows for the 0.25, 0.5, 1.0 and 2.0 mAs per projection dose levels, respectively.
The average measured CNR values across all phase windows were 59.4, 40.0, 26.6 and 14.8 for 2.0, 1.0, 0.5 and 0.25 mAs per projection dose levels, respectively. The CNR values were lower than the predicted values and more so for the lower dose levels. The trends were the same at the trends seen in the SNR study, as expected.

6.4 Discussion and Conclusions

Acquisition parameters (frame rate, gantry/stage rotation speed and phase window) for on-board 4D imaging are adjusted simultaneously to give an approximate number and distribution of projections per phase bin. Any one of these parameters alone is not directly related to dose in and of itself, since they are adjusted together according to the framework developed in Section 3. Thus, the photon fluence (or dose) is an independent parameter that is expected to affect image quality according to the principles derived and experimentally verified for CBCT. There is, however, an expected variation in image quality between phase images for 4D CBCT due to the variations in motion blurring and numbers of projections per phase bin. It was beyond the scope of this study to fully characterize these effects for all motion profiles, but this study provides a general characterization for one scenario.

Variations in Image Quality Due to Variations in Motion Blurring

The variations in motion blurring (and thus target contrast) between phase windows depends on the patient’s motion profile. These variations will be minor for small motion amplitudes and for profiles that exhibit fast inhale/exhale. The motion
blurring in certain phase windows increases for segments of the respiratory cycle during which internal anatomy moves quickly. The profile we chose to investigate was an extreme case scenario. The peak-to-peak motion amplitude was 3cm, which is at the upper limit of what has been observed. In addition, there was a short pause (which we were unable to measure the duration of) during inspiration. This means that the target moved very fast during two phase windows (30 and 70%). This is evident in Figure 6.4. The extent to which motion blurring affects target CNR in the high motion phase windows will vary from patient to patient, but even in this extreme case, the effect was not substantial enough to isolate it from the other factors affecting image quality and only affected 2 of the 10 phase windows.

*Variations in Image Quality Due to Variations in Numbers of Projections per Phase Bin*

All of the phase bins with the exception of the 50% phase bins had either 121 – 122 or 145 – 146 projections. There were no observable differences in image quality between these two groups. While there is most likely an existing difference, the other factors affecting CNR and SNR were prominent enough to obscure any trends. The 50% phase windows had either 217 or 218 projections per bin, which is 50% greater than the bins with 145 or 146 and 80% greater than the bins with 121 or 122. CNR values for the 50% phase windows were 16, 34, 11 and 26% higher than the averages of the other phase windows for the 0.25, 0.5, 1.0 and 2.0 mAs per projection dose levels, respectively. This data suggests that the effect is not exclusively a result of dose. The 50 to 80%
discrepancy in projection numbers between phase windows is an extreme case. In patient cases, the breathing typically exhibits some irregularity in respiratory cycle durations, which causes a more even distribution of projections between phases. We believe that an expectation of a possible 30% variation in image quality due to variations in projection numbers between phase bins is a very conservative estimate.

SNR and CNR Dose Dependence

This study has shown that average SNR and CNR increased with the applied mAs per projection. The average SNR values across all phase windows were 71.8, 50.5, 35.0 and 20.7 for the 2.0, 1.0, 0.5 and 0.25 mAs per projection dose levels, respectively. The average measured CNR values across all phase windows was 59.4, 40.0, 26.6 and 14.8 for 2.0, 1.0, 0.5 and 0.25 mAs per projection dose levels, respectively. The CNR and SNR falloffs were greater than predicted by Barrett. At this time it is unclear why our results did not exactly follow these predictions.

7 Concluding Remarks and Future Directions

7.1 Concluding Remarks

Prior to the beginning of this work, proposed techniques for on-board motion imaging were limited in that imaging parameters were not optimized based on patient respiration. The earliest 4D CBCT imaging proposals simply sorted projection images that were acquired according to standard CBCT imaging protocols. This resulted in severe under-sampling artifacts. A later study imaged lung patients using very high
frame rates and slow gantry speeds to better populate phase bins with projection images, but the doses were two to three times greater than doses for standard CBCT scans (10.4 to 14.2 cGy), and scan times were impractically long (4.5 to 7 minutes).

The work in this study successfully demonstrated various methods for reducing dose while avoiding under-sampling artifacts. Phantom studies demonstrated that motion could be assessed with sub-millimeter accuracy using 4D DTS. The accuracy for determining the limits of motion (in 3 dimensions) was limited only by the image resolution, was 0.5 mm in our phantom study. Patient 4D DTS studies demonstrated that tumor contrast for the lung patients we studied could be achieved using 30° scan angles for coronal views. Scan times for those cases were between 41 and 50 seconds. Image doses for those patients were between 1.56 and 2.13 cGy. These doses are well below doses for standard CBCT scans. Coronal 4D DTS images are a fast, low dose alternative to 4D CBCT for cases when clinicians are primarily concerned with superior-inferior and/or lateral motions. Anterior-posterior motion could be analyzed using an additional sagittal 4D DTS scan. We found that sagittal DTS images required larger scan angles, though we did not have enough clinical patient data to make solid conclusions regarding necessary scan angles (or therefore, scan times or doses).

Another major contribution of this work was that we developed a comprehensive framework for relating acquisition parameters (frame rate, gantry rotation speed, phase window and scan angle) with patient respiratory parameters
(shortest and longest expected respiratory cycles). These relationships were validated experimentally, and patient studies were conducted to determine protocols for optimizing acquisition parameters (much like the process conducted for 4DCT). We determined that the optimal frame rate is that which acquired one projection per phase window during a patient’s shortest expected respiratory cycle. If the frame rate is set lower than this, large gaps exist between consecutive projections in phase bins, causing severe under-sampling artifacts in the reconstructed images. The benefits of increasing the frame rate are minimal, as the gantry is moving very slowly, and thus, the additional projections are not spaced far enough apart to provide much additional information. In the patients we studied, the ‘extra’ projections were on the order of 0.1° apart. That being the case, the only way to improve sampling is to slow the gantry rotation speed. In order to achieve phase bins with projections spaced approximately 0.5° apart, for a patient with a respiratory cycle ranging from 3 to 5 seconds, the gantry rotation speed would have to be on the order of 0.094°/s. This would correspond to a 35 minute scan time, which is impractical. If we accept approximately 3.5° separations between projections in final phase bins, the scan time is still 5 minutes, and we also start to see some under-sampling artifacts. We found that the only way to avoid under-sampling artifacts while reducing scan time is to use 4D DTS.

We recognized that the temporal accuracy of 4D imaging using a 2D on-board imager far exceeds that of 4DCT. We theoretically considered the imaging dynamics of
our system compared with those of 4DCT and concluded that phase windows for 4D imaging using an on-board 2D imaging device can be expanded from the conventional 10% and maintain the same temporal accuracy achieved by 4DCT. We conducted patient investigations and found that differences between images reconstructed using 10 and 20% phase windows were on average 0.59 to 0.68% different, and differences between images reconstructed using 10 and 30% phase windows were on average 0.74 to 0.89% different. These were for 4 lung tumors exhibiting peak-to-peak motions of 2 mm to 1 cm. Use of 20 and 30% phase windows results in approximately 50 and 67% dose decreases for on-board imaging with a 2D system.

To conclude, we have shown that coronal 4D DTS images can be conducted using doses and scan times well below those used for standard CBCT scans. This is a practical procedure for superior-inferior and anterior-posterior motion analysis in the treatment room and can be easily implemented using hardware already installed in many treatment rooms. 4D CBCT scans can be conducted using doses that are similar to the doses for standard CBCT scans, though scan times are currently around 5 minutes to achieve projection spacing in phase bins of approximately 3.5°.

7.2 Future Directions

Iterative Reconstruction

The most commonly used algorithm for CBCT and DTS reconstructions is a modified Feldkamp type filtered back projection (FBP) algorithm. A ramp filter,
which preferentially filters out low frequency information, is typically used for FBP reconstruction. This amplifies high frequency noise. Under-sampling artifacts are also particularly problematic for FBP algorithms when there are gaps between projection views or irregularly spaced projection views are available. As shown in this work, 4D imaging using a 2D imaging device necessarily results in limited, irregularly spaced projection data sets with larger than optimal gaps between projection images. Furthermore, imaging dose is a concern since the goal is to fully sample an imaging volume at multiple respiratory phases. With its tendency towards under-sampling artifacts for limited projection views and high frequency noise amplification for low dose images, FBP is not an ideal reconstruction technique for achieving high quality 4D images.

Iterative image reconstruction methods inherently process noise better than FBP methods and have the ability to impose regularizing constraints. For these reasons, iterative methods may be better suited for reconstructing typical 4D imaging data sets. Many investigators have found benefits in using iterative reconstruction methods for reconstructing images in cases where limited and/or irregularly spaced projection data sets are available.\textsuperscript{191-194} We conducted a very preliminary trial using an ordered subset transmission reconstruction (OSTR) method proposed by Erdogan and Fessler\textsuperscript{195}. The reconstruction application was developed by Dr. James Bowsher. We found that there were some technical limitations with the reconstruction program that made a
comprehensive study impractical at this time. We reconstructed some test images that demonstrate how noise and aliasing artifacts present differently using FBP and OSTR reconstruction methods.

FBP and OSTR images were reconstructed for the 50% phase (30% phase window) using data from patient 1 in Chapter 5. The projection images were sorted and binned as described in Section 5.1. Subsets of projections were extracted to represent extremely limited projection views (corresponding to very fast 4D scan times). Table 7.1 shows the scan angles, gantry rotation speeds and numbers of projections for each of the test cases.

Table 7.1 Summary of the data sets used in FBP and iterative reconstruction comparisons and numbers of projections for each.

<table>
<thead>
<tr>
<th>Reconstruction No.</th>
<th>Scan Angle (°)</th>
<th>No. Projections</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1 (2.19°/s GRS)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>200°</td>
<td>70</td>
</tr>
<tr>
<td>2</td>
<td>80°</td>
<td>29</td>
</tr>
<tr>
<td>3</td>
<td>40°</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>20°</td>
<td>9</td>
</tr>
<tr>
<td><strong>Group 2 (4.40°/s GRS)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>200°</td>
<td>35</td>
</tr>
<tr>
<td>6</td>
<td>80°</td>
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</tr>
<tr>
<td>7</td>
<td>40°</td>
<td>8</td>
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</table>
Figure 7.1 FBP (left) and OSTR (right) reconstructions for a 200° scan using a total of 70 projections.

Figure 7.1 shows the 200° images (70 total projections) reconstructed using both FBP (left) and OSTR (right) methods. This was the largest number of projections we were able to reconstruct using the OSTR method. Figure 7.2 – 7.9 show FBP and OSTR images for the other test cases. The top and bottom images are different slices of the same patient. Five structures are denoted in the following images. These structures are labeled 1 – 5, in an order corresponding to what we believe to be easiest to most difficult to delineate.
Figure 7.2 FBP (left) and OSTR (right) reconstructions using 29 projections over an 80° scan angle.

Figure 7.3 FBP (left) and OSTR (right) reconstructions using 15 projections acquired over 40°.
Figure 7.4 FBP (left) and OSTR (right) reconstructions using 9 projections over a $20^\circ$ scan angle.

Figure 7.5 FBP (left) and OSTR (right) images reconstructed using 35 projections over $200^\circ$ scan angles.
These reconstructions clearly demonstrate that the two reconstructions process noise differently. In addition, the OSTR images appear to present without under-sampling artifacts. This appears to be particularly promising for 4D CBCT images, as the FBP reconstructions have severe artifacts. The reconstruction program we currently have available requires far too much time for optimization of the OSTR method to be practical. Many investigators are currently developing accelerated iterative reconstruction applications using graphics hardware and other programming techniques. When these become available, a comprehensive exploration of iterative reconstruction may show great improvements in image quality for the limited and irregular data sets typical of 4D imaging using a 2D kV imaging system.
4D DTS Clinical Trials

The studies conducted in this work were preliminary feasibility and technique characterization studies. The techniques and concepts developed and investigated in this work should be tested further using more patients. Target visibility (particularly for DTS) depends on many patient specific factors including patient size, tumor size, tumor location and peak-to-peak motion amplitude. We found in our studies that sagittal DTS images required larger scan angles than coronal, though we were unable to make conclusions about appropriate scan angles with our patient data. Comprehensive studies using more lung patients with projection data acquired over various scan angles centered about a lateral axis should be conducted to determine appropriate scan angles. More extensive clinical studies should be conducted to determine appropriate imaging protocols that could be used clinically. It should be determined whether a set scan angle can be used for all patients or whether scan angles should be set on a patient specific basis depending on patient size, tumor size, tumor location and/or tumor motion parameters.
Appendix A: DTS Evaluation Metric

We have found that metrics which are typically used for image quality characterizations are not very meaningful for characterizing the effects of varying scan angle for DTS images. The reason for this is that as the scan angle varies, so does the anatomy which is included in the imaging field. As an example, it may be seen for a particular object that if the scan angle is increased from 40 – 50°, a high density object that did not shadow the target in other projections does in the additional projections, causing a decrease in contrast with increasing scan angle. If signal is measured as an increase in attenuation, the same phenomenon may cause an artificial increase in signal for a particular target. Metrics like signal-to-noise (SNR) and contrast-to-noise (CNR) were initially derived for 2D radiographic images. They have been used for some 3D evaluations, but they do not have much meaning in the case of reconstructions using projections over a limited scan angle. We have attempted to use these metrics to characterize image quality as a function of scan angle. We were unable to differentiate between actual changes in CNR or SNR and effects of the anatomy included in the projections. For these reasons, we believe that image quality in the traditional sense is of little use in determining appropriate scan angles for DTS imaging.

It is important to recognize that the degree to which a DTS image matches with a CBCT image is strongly dependent on the orientation and number of projections with respect to the particular subject anatomy. This is the nature of DTS imaging. No metric
will be able to characterize DTS image quality as a function of scan angle with results that will apply universally for various anatomies.

The purpose of the following study was to compare three potential metrics for quantifying similarity between DTS and CBCT images. These metrics do not rely on assumptions about image content or the nature of image acquisition. They are simply intended to provide a measure of how well a DTS image compares with a CBCT image. The primary intent of the metric we will adopt for these studies is to characterize image fidelity on a wide scale. Does the image contain severe artifacts that reduce visibility? Is the reconstructed image geometrically similar to the CBCT? Thus, we have reconstructed DTS images for scan angles ranging from 10 – 180° for a simple phantom which is easy to analyze visually. Each of the metrics was used to evaluate the DTS images as compared to the CBCT images, and we chose to use the metric for which the analysis matched our visual analysis. Three metrics were investigated: normalized image subtraction (NIS), normalized threshold comparison (NTC) and normalized mutual information (NMI). These metrics are described below.

*Normalized Image Subtraction*

NIS is a simple metric by which two images are normalized such that their minimum and maximum values are the same, and a pixel by pixel subtraction is computed to determine a difference quantity. To ensure that noise does not contaminate
the images, high and low values are computed for each image after 4 x 4 pixel binning.

NIS is computed as follows:

\[ NIS_{X,Y} = \sum_i \sum_j |X(i,j) - Y(i,j)| \]

X and Y are the DTS and CBCT images, and \( i \) and \( j \) are pixel row and column indices.

**Normalized Threshold Comparison**

NTC is a slightly more sophisticated version of image subtraction. For this method, the two images are normalized as described above for NIS. Each set of corresponding pixels is then compared based on a preset threshold. If the difference between the pixels are less than the threshold, they are deemed similar; if the difference is greater than the threshold, they are deemed different. The percentage of pixels deemed different is then computed. The primary advantage of this method over NIS is thought to be that there is an ideal value (1), and the results may be more easily interpreted. For NIS, the results are arbitrary and can only be used for general comparisons with other tests. NTC is computed as follows:

\[ NTC_{X,Y} = 1 - \left[ \sum_i \sum_j |X(i,j) - Y(i,j)| \right] \div TNP \]

X and Y are the DTS and CBCT images; \( i \) and \( j \) are row and column indices; \( T \) is the comparison threshold expressed as a percentage of the total image variation after
normalization, and $TNP$ is the total number of pixels in each image. We performed experiments using thresholds of 2, 4 and 8%.

*Normalized Mutual Information*

NMI is a comparative metric that does not rely on assumptions about image content or relationships between intensities in different images. Mutual information quantifies similarities by measuring a statistical dependence between two images. It quantifies the extent to which the information in one image can predict the information in the other. For these reasons, MI has been used in multi-modality image registration\textsuperscript{196, 197} and is ideal for comparing DTS and CBCT reconstructions which are reconstructed using different numbers of projections. NMI was defined in Section 4.2.3.

These three methods were implemented and tested. Images of a simple phantom were reconstructed at various scan angles (10-90° at 10° intervals), and the trends from each of the potential metrics were compared with visual analyses. The reconstructions are shown below in Figure A 1.
We visually determined that the artifacts diminished with increasing scan angle, with the exception that the 40° image looked somewhat worse than the 30°. Generally, the artifact reduction from 10 to 20° and from 20 to 30° appeared substantial, while the improvements were far more subtle from 50° upwards. Figure A 2 shows the results for image analysis using normalized image subtraction. Figure A 3 shows the results for the normalized threshold comparisons with 3 and 6% thresholds. Neither of these methods appear consistent with visual analysis.

Figure A 1: Phantom reconstructions for comparison with potential analysis metric results.
Figure A 2: Normalized image subtraction data.

Figure A 3: Normalized threshold comparison data.
The results using the NMI method are shown in Figure A 4. The trend using this method corresponds to the visual analysis. While this metric cannot be used to quantify image quality in absolute terms, we believe that it can be used to quantify the overall similarities of image pairs with the overall similarities of other analogous image pairs. We believe it to be well suited for task such as investigating the effects of DTS scan angles on artifacts in reconstructed images.
References


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