Fluence Field Modulated Computed Tomography

by

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Abstract

Dose management in CT is an increasingly important issue as the number of CT scans per capita continues to rise. One proposed approach for enhanced dose management is to allow the spatial pattern of x-ray fluence delivered to the patient to change dynamically as the x-ray tube rotates about the patient. The changes in incident fluence could be guided using a patient model and optimization method in order to deliver user-defined image quality criteria while minimizing dose. This approach is referred to as fluence field modulated CT (FFMCT). In this work, a framework and optimization method was developed for evaluating the dose and image quality benefits of FFMCT, both in simulated and experimental data. Modulated fluence profiles were optimized for different objects and image quality criteria using a simulated annealing algorithm. Analysis involved comparing predicted image quality maps and dose outcomes to those using conventional methods. Results indicated that image quality distributions using FFMCT agreed better with prescribed image qualities than conventional techniques allow. Dose reductions ranged depending on the task and object of interest. Simulation studies using a simulated anthropomorphic phantom of the chest suggest an average dose reduction of at least 20% compared to conventional techniques is possible, where local dose reductions may be greater than 60%. Across different imaging tasks and objects, integral dose reductions ranged from 20-50% when compared to a conventional bowtie filter. The results of this study suggest that given a suitable collimator approach, FFMCT could reap significant benefits in terms of reducing dose and optimizing image quality. Though the tradeoff between image quality and imaging dose may not be eliminated, it may be better managed using an FFMCT approach.
For my family.
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<td>Automatic Exposure Control</td>
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<tr>
<td>ALARA</td>
<td>As Low as Reasonably Achievable</td>
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<tr>
<td>CNR</td>
<td>Contrast-to-Noise Ratio</td>
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<tr>
<td>FBP</td>
<td>Filtered Backprojection</td>
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<td>FFMCT</td>
<td>Fluence Field Modulated Computed Tomography</td>
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<td>FFT</td>
<td>Fast Fourier Transform</td>
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<td>IMCT</td>
<td>Intensity Modulated Computed Tomography</td>
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<td>IMRT</td>
<td>Intensity Modulated Radiation Therapy</td>
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<tr>
<td>IQMₘₚ</td>
<td>Image Quality Map (for standard deviation)</td>
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<tr>
<td>LAR</td>
<td>Lifetime Attributable Risk</td>
</tr>
<tr>
<td>LNT</td>
<td>Linear No Threshold</td>
</tr>
<tr>
<td>NIST</td>
<td>National Institute of Standards and Technology</td>
</tr>
<tr>
<td>NPS</td>
<td>Noise Power Spectrum</td>
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<tr>
<td>ROI</td>
<td>Region of Interest</td>
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<tr>
<td>SER</td>
<td>Scanning Equalization Radiography</td>
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<td>SNR</td>
<td>Signal-to-Noise Ratio</td>
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<td>SDVH</td>
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<td>Tube Current Modulation</td>
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Chapter 1
Introduction to Fluence Field Modulation in CT

1.1. Motivation

1.1.1. A Rapidly Advancing Field

Computed tomography (CT) is an advanced medical imaging modality, which produces three-dimensional (3D) images for clinical applications, including diagnosis of disease (e.g., of cancer), and guidance of treatment (e.g., in image guided radiation therapy (IGRT)). During a CT scan, an x-ray source rotates around a patient while a detector records a series of digital radiographs (or projections) at regular angular intervals (see Figure 1-1). The collection of 2D projections is then used to infer a 3D image of the patient anatomy using established mathematical relationships between the two data sets.

Technology in CT has shown considerable advancement since the first medical CT scanner was introduced by EMI in the early 1970’s. The earliest acquisitions required about 4 minutes to acquire a low resolution image of a single head section. In comparison, the increased detector size and speed of dynamic volume CT scanners has improved to the point where a complete organ can be scanned in a single rotation, within a fraction of a second, and at sub mm resolution. Another example of the advancement of CT technology is the advent of dual energy CT (projections taken at two different beam energies), which has introduced the capacity for additional tissue discrimination. Despite these advancements, a main disadvantage of CT is that it employs ionizing radiation in order to image the patient.
1.1.2. Biological Effects of Ionizing Radiation

When X-rays interact with tissue, there is the potential for cell damage. An X-ray can damage a cell either by direct interaction with a cell molecule, or indirectly by creating free radicals in water which then subsequently induce DNA damage. DNA damage can result in one of three outcomes. The cell can either repair itself, die or be incorrectly repaired such that the function of the cell becomes altered. The effect of damaged surviving cells can manifest either as deterministic or stochastic effects. Deterministic effects occur after some threshold of dose is reached, and are typically not observed in CT scanning procedures except rare cases generally involving operator error. Stochastic (probabilistic) effects refer to cancer resulting from radiation exposure. Usually, risks of cancer are based on the linear, no threshold (LNT) model, which describes a linear relationship between radiation dose and incidence of cancer in a population. Given that this model predicts that no amount of radiation is free of increased cancer risk, the principle of maintaining radiation exposure “As Low As Reasonably Achievable (ALARA)” is employed in order to limit unnecessary dose and cancer risk to patients.

1.1.3. CT Radiation a Rising Concern

Recently, concerns regarding the potential risks of radiation dose due to computed tomography (CT) scans have been heightened immensely. This increased concern has been largely stimulated by a number of reports and papers within the last five years\textsuperscript{1-6} that have indicated both
that the number of CT procedures being performed per capita is on a steady incline (estimates
show roughly 10% per year in both the US and the United Kingdom\textsuperscript{7}), and that the lifetime
attributable risk (LAR) of cancer may be non-negligible for certain procedures, especially when
patients receive multiple CT scans\textsuperscript{1,4,5,8}. One study\textsuperscript{1} estimates that on the order of 2% of future
cancers in the USA may be attributable to radiation from current CT scanning procedures. The
drive to increase awareness among health professionals is perhaps most notable through the
widespread campaigns Image Gently\textsuperscript{9} and Image Wisely\textsuperscript{10}, which have the general mandate of
providing education on available approaches for limiting dose to pediatric and adult patients,
respectively. Image noise\textsuperscript{†} and radiation dose generally share an inverse relationship in CT. The
goal is to achieve an image of sufficient quality for diagnosis, treatment planning or treatment
guidance while limiting dose as much as possible.

1.2. Conventional Modulation in Computed Tomography

Essential to the appropriate use of CT is the appropriate selection of the imaging technique,
based on the patient’s age, anatomy (e.g., size), and the imaging task (e.g., tracking an
interventional instrument, surveillance imaging of lung nodules, or diagnosing a suspicious soft-
tissue lesion in the abdomen). This selection inherently involves balancing the tradeoff between
image quality and ionizing radiation delivered to the patient. While this tradeoff is always a
compromise, more efficient management of x-ray exposure can aid in alleviating the radiation
risks to the patient.

Some forms of modulation of the incident x-ray beam are used in conventional practice with the
aim of reducing dose to the patient without sacrificing image quality. Fundamentally, noise in
the 2D projections, which ultimately propagates through the final reconstructed image, is related
to how many photons reach the detector; fewer photons result in noisier projections. As the x-
ray beam rotates about the patient, lateral views of the patient inherently attenuate more of the x-
ray beam than posterior-anterior views where the path length through the body is shorter.
Increasing the exposure to compensate for the noise in these projections means potentially

---

\textsuperscript{†} Image noise is defined as random statistical fluctuations from the mean expected value in the image. The larger
the magnitude of the noise, the more obscure the details in the image become.
overexposing the patient in remaining views. This observation led to the development of automatic exposure control (AEC)\textsuperscript{11-19}, which can employ a combination of angular\textsuperscript{11,20-25} and z-axis\textsuperscript{26-29} tube current modulation (TCM). The goal of TCM is to lower the intensity of the x-ray beam during portions of the scan where the patient thickness is smaller and therefore less attenuating, as depicted in Figure 1-2 (a). In combination with TCM, bowtie filters\textsuperscript{30-32}, placed in front of the beam, attempt more uniform exposure levels at the detector, by decreasing exposure to thinner regions of the patient, as illustrated in Figure 1-2 (b). Additional collimation of the beam\textsuperscript{33-37} has also been proposed for further reduction of dose to the patient by maintaining higher exposure within a limited, central region of interest (ROI). These approaches indicate a steady trend towards more patient and task-specific fluence plans, and collectively, make great strides towards the reduction of patient radiation dose. However, filters and/or collimators that are fixed in the field of view throughout the CT scan are greatly limited in their ability to compensate for the complex heterogeneity of attenuation presented by real patient anatomy across the incident x-ray field.

![Figure 1-2](image-url)

**Figure 1-2:** (a) Conceptual illustration of tube current modulation in CT. A lower X-ray intensity is utilized in anterior-posterior views of the patient, where the path-length through the patient is less than in lateral views. (b) Illustration of a bowtie filter in conventional CT. The bowtie filter decreases exposure to the patient more greatly at the lateral ends, where the patient thickness is smaller and less attenuating.

1.3. Fluence Field Modulation in Computed Tomography

1.3.1. Proposed Approach

Contrary to the fixed filtration patterns in conventional use, a distinct approach has been proposed by Graham et. al\textsuperscript{38,39} that would allow the fluence (number of photons per unit area) to change both as a function of position across the detector, $\xi$, and angular position, $\theta$, around the
patient, as depicted in Figure 1-3. This flexible fluence delivery would be better equipped to manage complex changes in attenuation across the field of view which can change significantly for different projection angles. Provided a patient model and a method for predicting the distribution of image quality exists, the modulation pattern could be optimized to potentially achieve spatially varying, user-prescribed, image quality characteristics (e.g., noise), while limiting dose.

Figure 1-3: Schematic illustration of method proposed in fluence field modulated computed tomography (FFMCT). The pattern of fluence is able to change between projections, as a function of $\xi$ and $\theta$, in contrast to conventional methods where the pattern of fluence is fixed (e.g., using a bowtie filter). The geometry is shown using parallel-ray geometry, but the concept is equally valid for alternative geometries.

In many cases, the image quality required may vary regionally within an image, depending on the task. For example, bony anatomy can generally be seen clearly in relatively noisy data, while visualization of the prostate requires very low noise because of its low contrast with respect to surrounding tissue. In another instance, one may only be concerned with locating the tip of a surgical instrument with respect to an anatomical landmark. Yet another example might be a repeat diagnostic CT scan to explore a suspicious anomaly, in which case one may only desire high image quality near the suspicious lesion. Therefore, the prescription of image quality may take on different shapes and/or have regionally varying properties depending on the application. Since FFMCT inherently has the ability to reduce high exposure where unnecessary for a given task, a main advantage of FFMCT is thought to be its potential for reduced dose to the patient;
further, increased control over dose allocation could allow for dose minimization to specific radiation sensitive tissue (e.g., lens of the eye). In addition, more uniform noise properties for defined ROIs may be achievable since anatomical variations can be compensated for on a projection-to-projection basis.

One application employing x-ray fluence modulation is intensity modulated radiation therapy (IMRT) where the modulation attempts to deliver high dose to a cancerous lesion while sparing healthy tissue. The proposed approach shares parallels with the approach used in intensity modulated radiation therapy (IMRT), except “image quality plans” replace the target “dose plans” of IMRT. These strong parallels initially prompted reference to this approach as intensity-modulated CT (IMCT), which has also been recently used in the literature; however, the revised terminology fluence field modulated CT (FFMCT) more accurately describes the relevant physical quantities, and is less likely to be confused with the standard but distinct practice of TCM used today.

Currently, no modulator has been developed for CT scanners that would allow the flexibility proposed. Application of fluence modulation specific to patient anatomy in imaging was first explored in 2D x-ray imaging, where it has been referred to as scanning equalization radiography (SER); techniques developed in that field have included moving slits and dynamically varying apertures for varying the incident fluence field and patient specific filters. The feasibility of similar techniques has begun to be explored for dynamic beam modulation in CT systems. Other approaches for fluence field modulation under investigation include sliding wedges and multiple sources in inverse geometry CT. This work attempts to explore the merits of FFMCT and also to compare to some extent plausible methods of delivering modulated fluence field patterns, such as those currently proposed in the literature.

1.3.2. Hypothesis

The underlying hypothesis behind this work is that:

*Fluence field modulation can be employed to satisfy user-prescribed, regionally varying, image quality objectives in CT while reducing the total dose to the patient and/or the local dose to site-specific radiation sensitive tissue.*
1.3.3. Specific Aims

This project proposes a general framework for FFMCT and aims to study its capacity to meet dose and image quality objectives for anatomically relevant objects, using simulated and real data. The specific aims are listed and detailed briefly below:

1. *Develop a framework and optimization scheme for FFMCT*

The basic concepts for FFMCT and a basic optimization scheme were first discussed by Sean Graham in his M.Sc. thesis. However, a developed framework and robust optimization method for advanced investigation into the potential for image quality and dose benefits of FFMCT were not established. Initial FFMCT optimizations required very long computation times for small cylindrical data sets (greater than 7 hours on a Pentium 2.6 GHz machine for a 64x64 pixel dataset limited to 90 projections), and severely limiting assumptions (e.g., symmetrical, uniform object). The first aim was therefore to detail a general framework for FFMCT and develop a more computationally efficient and flexible optimization scheme for the study of and potential implementation of FFMCT. This aim is developed in Chapters 2-5 of this dissertation in conjunction with the aims described below.

2. *Evaluate (local and total) dose and image quality benefits of FFMCT in simulation*

Flexibility in managing the incident x-ray fluence field suggests the ability to meet user-prescribed image quality criteria, while decreasing exposure to sensitive tissue and/or the total dose to the patient. The second aim of this work was therefore to explore the capacity to meet image quality objectives via simulations based on the framework and optimization method posed in Aim (1), as well as the capacity for dose reduction (local and total). Meeting prescribed image quality objectives while minimizing dose is explored using simulated and real data in Chapters 4 to 6 of this treatise. The potential for specific local dose reductions is treated in Chapter 3.

3. *Evaluate and compare constrained modulation schemes/compensator options for FFMCT*

An ideal modulator would allow the fluence profile to change freely between projections. However, most real modulators will likely introduce some forms of constraints on the modulation. A suitable collimator design for FFMCT is not obvious. The third aim of this work is therefore to evaluate potential constrained compensator approaches with less flexible
modulation capabilities and compare these against that of an ideal modulator as well as to conventional compensator approaches. This aim is explored with detailed image quality and dose comparisons in Chapter 4.

4. Application of FFMCT to experimentally acquired phantom data
Simulation studies employed make use of some simplifying assumptions such as that of an ideal detector. In real systems, factors such as electronic noise, and noise correlations between pixels must be considered in the noise prediction model. In addition, accurate modeling of noise propagation requires accounting for the particular acquisition geometry employed (e.g., source to rotation axis distance, field of view, etc.). These factors are system specific. The last aim of this work is therefore to account for system dependent factors in the application of fluence field modulation to a real experimental CT system, and further to evaluate whether FFMCT applied to a real system produces results consistent with simulation studies. In Chapter 5, this aim is developed using phantom data acquired with an experimental cone-beam CT unit.
Chapter 2
Theory and Framework for FFMCT

2.1. Theory

This chapter summarizes the relevant theoretical developments that provide the underlying principles for fluence field modulation\textsuperscript{38,39,47}. The key outcome is that modulation of a monoenergetic x-ray beam affects the noise distribution in reconstructed data but not the expectation value (mean signal). This result suggests that region-specific noise characteristics in CT can be planned and achieved by appropriate modulation of the incident x-ray fluence, assuming that some \textit{a priori} information about the object is available. This \textit{a priori} knowledge may come from a previous CT scan, or a population based model.

The imaging geometry assumed in this work is shown schematically in Figure 2-1. The object is described by an attenuation function, $\mu(\mathbf{r})$, where $\mathbf{r} = (x, y, z)$ is a position vector whose components are the spatial coordinates in the object space. In parallel-ray geometry, and considering a monoenergetic beam, the incident and transmitted fluence are defined as $N^o(\theta, \xi)$ and $N(\theta, \xi)$ respectively, where $\xi$ parameterises the ray location at projection angle $\theta$ (see Figure 2-1), and where the fluence is defined in terms of photon counts per unit area of the detector pixel. Rotation of the imaging system takes place in the z=0, x-y plane. The methodology may be extended to variation along z as well, but we limit our investigation to a single axial plane. Reconstruction of the object is achieved via filtered backprojection.
Figure 2-1: Schematic diagram and nomenclature of parallel x-ray beam geometry used in this study.

Assuming an ideal detector, the projection $P(\theta, \xi)$ can be derived from Beer’s law$^{38,39,47}$, and is calculated from the natural logarithm of the ratio between incident and exit fluence:

$$P(\theta, \xi) = \ln(N^o(\theta, \xi)/N(\theta, \xi)),$$

(2.1)

Modulation of the fluence can be modeled by multiplying the incident fluence with a spatial modulation factor, $m(\theta, \xi)$, such that the incident and transmitted fluence become $m(\theta, \xi)N^o(\theta, \xi)$ and $m(\theta, \xi)N(\theta, \xi)$, respectively$^{33,34}$. Substituting these terms into Eq. (2.1) gives the modulated projection,

$$P_m = \ln(mN^o/mN) = \ln(N^o/N) = P,$$

(2.2)

where the spatial dependencies have been dropped for simplicity, and it is seen that the expectation value of the projection is independent of the applied modulation factor. However, the variance of the measured projection value is known to be related to the expectation value of the number of photons that arrive at the detector. From Poisson statistics, the predicted variance (assuming an ideal detector) of $P_m(\theta, \xi)$ is$^{47}$
\[ \text{var}(P_m(\theta, \xi)) = \frac{1}{m(\theta, \xi)N(\theta, \xi)}. \]  

(2.3)

The variance at \( r \) of the reconstructed object, \( f(r) \), can then be found from an application of filtered backprojection\(^\text{47} \):

\[ \text{var}(f(\bar{r})) = \left(\frac{\pi \tau}{M_{\text{proj}}}\right)^2 \sum_{\theta \in \Omega} \sum_{\xi \in K} \frac{1}{m(\theta, \xi)N(\theta, \xi)} h^2(x \cos \theta + y \sin \theta - \xi), \]  

(2.4)

where \( M_{\text{proj}} \) is the number of projections, \( \tau \) is the width of the detector pixels, \( h \) is the convolution kernel in the filtered backprojection operation, and \( \Omega \) and \( K \) are the sets of projection angles and detector positions respectively. Assuming that the transmitted x-ray fluence is a predictable quantity (via \textit{a priori} knowledge of the object), this result suggests that prescribed noise qualities at arbitrary points of interest can be achieved by appropriate selection of the modulation factor. The selection of spatially-varying modulation factor will herein be referred to as the \textit{modulation profile} (which can be represented in 2D as a function of \( \theta \) and \( \xi \)). Although the modulation profile is found using \textit{a priori} knowledge, it is further assumed that small deviations in soft tissue anatomy, which may be the subject of subsequent scans, will not change the result appreciably.

Backprojection introduces noise correlations between voxels due to the convolution filter applied and the inherent “smearing” of filtered projection values over ray paths. Therefore it is not possible to achieve an arbitrary noise prescription over the entire object. However, one can define a desired quality metric, \( \hat{Q}(\bar{r}) \), for all points and attempt to find a modulation profile that generates results as close to this criterion as possible. The problem may be defined in terms of finding the optimal modulation profile, \( \hat{m} \), such that

\[ \hat{m} = \arg \min_{m \in M} \left( \sum_{\bar{r} \in S} (\hat{Q}(\bar{r}) - Q_m(\bar{r}))^2 \right). \]  

(2.5)

where \( M \) is the set of all feasible modulation profiles \( m \), \( Q_m(\bar{r}) \) is the modulation-dependent, spatially variant quantification of the image quality within the object, and \( S \) is the set of spatial coordinates occupied by the object of interest. An attempt to solve this problem can be made
using an iterative optimization method, where the bracketed expression represents the cost function. If \( Q_m(\tilde{r}) \) represents the variance of the noise, then its value can be updated at every iteration using Eq. (2.4) for each new potential selection of modulation profile. It is also possible to impose constraints on the solution, such as limiting the dose \( D(\tilde{r}) \), and to introduce weighting factors, such that the minimization problem becomes

\[
\hat{m} = \arg \min_{m \in M} \left( w_Q \sum_{\tilde{r} \in S} W_Q(\tilde{r})(\hat{Q}(\tilde{r}) - Q_m(\tilde{r}))^2 + w_D \sum_{\tilde{r} \in S} W_D(\tilde{r})(D_m(\tilde{r}))^2 \right), \tag{2.6}
\]

where \( D_m(\tilde{r}) \) is the local, modulation dependent, dose in mGy (or alternatively, the integral dose in Joules), \( W_Q(\tilde{r}) \) and \( W_D(\tilde{r}) \) are predefined, spatially-varying weighting factors that can be used to prioritize image quality and dose at specific locations, respectively, and \( w_Q \) and \( w_D \) weigh the relative importance of the relative image quality and dosimetric terms. Weights \( w_Q \) and \( w_D \) are normalized such that each term in Eq. (2.6) is unitless.

### 2.2. Proposed Framework

The proposed framework for implementation of FFMCT is depicted in flowchart form in Figure 2-2; Figure 2-3 illustrates the main concepts in graphical form. This process requires an initial digitized representation of the object (e.g., an image from a previous CT scan or a population-based model). An image quality plan, based on the imaging task, can then be made by prescribing desired image quality criteria (e.g., SNR, CNR, etc.) to ROIs within the image. Note that the image quality prescription can be uniform within a given ROI or regionally varying depending on the task. This plan can also incorporate regions of desired dose minimization (e.g., to delineated radiation sensitive tissue such as the lens of the eye). Given that arbitrary image quality criteria are likely unachievable and that compromises with dose are likely necessary, weighting factors that prioritize the ROIs are introduced. Priority weighting could align with an entire ROI or within subregions. Additionally, tolerances on specific regions of interest could be specified within this framework, but are not implemented in this work. Once the desired plan is formed, an optimization algorithm seeks a modulation profile that achieves the desired criteria via minimization of a cost function. In practice, if the predicted noise and dose distributions for
the output modulation profile are not satisfactory, the user could repeat the optimization using a different weighting scheme or by making modifications to the initial criteria. Finally, the output modulation profile is implemented in a physical setting by a method of spatial compensation that is yet to be specified. Current CT scanning techniques do not allow for arbitrary, patient-specific modulation patterns. Developing suitable techniques for modulation in an FFMCT system is the subject of ongoing work and is treated in the context of modulation constraints in Chapter 4, and is also discussed in Chapter 6.

![Diagram of the proposed general framework for fluence field modulated CT](image)

**Figure 2-2**: The proposed general framework for fluence field modulated CT. Optimizing the modulation profile can be viewed as an inverse planning stage, similar to the inverse planning in IMRT.

### 2.3. Alternative Reconstruction Methods

It is important to note that while dose is independent of the reconstruction algorithm, noise and related image quality metrics will in general be highly dependent on the reconstruction method and associated parameter selections (such as the choice of the convolution filter in filtered backprojection). While this work considered filtered backprojection, alternative reconstruction methods, such as locally filtered backprojection, could be employed provided that predictive models exist that relate fluence to a given quality metric. Recent developments on noise
predictors\textsuperscript{48,49} for statistically based iterative methods also suggest that the optimization need not be restricted to linear reconstruction methods.

Figure 2-3: Graphical flow chart illustrating the different stages of FFMCT. The main concepts include using a patient based model to define an image quality plan, then seeking modulated fluence fields that aims to achieve the prescribed plan, and finally acquiring the modulated set of projections and reconstructing the FFMCT image. The dashed ellipses identify hypothetical regions of prescribed high image quality (low noise in this case) data. However, the image quality plan could define one or multiple irregularly shaped regions of interest with prescribed image quality that varies regionally, depending on the task; the plan could also include one or more metrics (e.g., contrast-to-noise ratio, dose, etc.).
Chapter 3
Simulation Study for Noise and Dose Optimization

In this chapter the potential benefits of FFMCT are evaluated under an idealized setting (e.g., considering a monoenergetic beam without scatter contribution) by optimizing incident x-ray fluence fields for noise and dose objectives. Recall that in the proposed framework, desired (regionally varying) image quality metrics (e.g., signal-to-noise ratio (SNR(x,y)), contrast-to-noise ratio (CNR(x,y))) along with dosimetric constraints (e.g., Dose(x,y)) are defined for a given patient model (e.g., from a prior CT scan). A solution to the inverse problem of generating modulated fluence fields to meet the specified criteria is then sought via an optimization method that attempts to minimize a cost function. This methodology is tested using a suite of simulated test objects of increasing complexity, and by generating modulated fluence fields that seek to meet specified SNR distributions under dose minimization constraints. Finally, the results are evaluated in terms of resulting regional SNR and dose distributions. These results were published in Medical Physics and are reproduced here with permission.

3.1. Inverse Modulation Algorithm

3.1.1. Simulated Annealing Method

An approximate solution to Eq. (2.6) was sought using an optimization scheme that belongs to the class of simulated annealing methods. Simulated annealing is generally more computationally intensive than alternative methods, but has the advantage of very good global convergence properties provided enough iterations are performed. The reliability of this
technique served the objectives of this work. Some efforts were also made to speed up the optimization process and are described later for completeness.

A detailed description of general simulated annealing methods can be found elsewhere. In brief, the simulated annealing algorithm proceeds towards an optimized modulation profile by randomly selecting a new profile near the current one, and then comparing the two. New profiles that yield decreases in cost function value are automatically accepted, while estimates that yield a higher cost function value are accepted with a probability defined by

$$P_n = \exp \left( - \frac{\Delta C_n}{T_n} \right),$$

(3.1)

where $n$ is the iteration count, $\Delta C_n$ is the change in the unitless cost function $C_n$, and $T_n$ is the unitless “temperature” of the system. The temperature decreases as the iteration number increases, thereby reducing the probability of accepting a cost function increase as the iterations progress. The rate of change of $T_n$ is referred to as the cooling schedule. In this work, an inhomogeneous, exponential cooling schedule was used

$$T_n = T_0 e^{-\alpha n},$$

(3.2)

where $T_0$ is the initial temperature, and $\alpha$ is a constant that regulates the cooling rate. The simplest choice for a stop criterion is when a minimum temperature or a maximum number of iterations is reached. In the present work, the cooling rate constant was defined as

$$\alpha = a / N_{\text{iters}},$$

(3.3)

where $a$ is an empirically determined constant and $N_{\text{iters}}$ is the number of iterations to be carried out, so that the final temperature is independent of the number of iterations selected by the user.

### 3.1.2. Fluence Field Estimate Generator

The modulation profile was represented in simulation by a discrete set of modulation bins (bixels). At each iteration, $n$, a new profile was generated by randomly selecting a subset of bixels, and changing their value by a random deviation. This deviation was bounded by a
maximum and minimum value, where the maximum bound decreased linearly as a function of iteration number and the minimum was set by the desired resolution. Reducing the maximum bound effectively reduces the search space and supposes that as the temperature cools a more optimal solution will likely not differ greatly from the current one. Though this change to the algorithm resulted in approaching similar results in fewer iterations, it should be noted that the change was based on empirical observations and differs from formulations of simulated annealing on which proofs of global convergence properties strictly hold true. Random number generations were implemented using the rand function in Matlab® (based on the Marsaglia “borrow and subtract method”, Matlab R14, The Mathworks, Natick MA).

3.1.3. Speed Improvements

A. Neighbour Selection

Several refinements were made to the simulated annealing algorithm proposed for modulation profile optimization by Graham. One major change was the neighbour generator (i.e., the method used to choose a new profile at each iteration). In the previous algorithm, a large random number of modulation factors were changed that spanned over all projection views. In the updated version, changes in modulation factors are made to only a few random projections. While this change was found to have little effect on the number of iterations required for convergence, the time for each iteration to be performed is greatly reduced. This reduction occurs because the previous method required backprojection over all projection views for evaluation of Eq. (2.4), while the updated method only requires updating the few projection views where changes occurred; the relative speed improvement is on the order of approximately 20 times.

B. Modulation Profile Refinement by Multiple Passes to the Optimization Algorithm

To further avoid long computation times, a scheme was developed that employs multiple passes to the optimization script. In the first pass, the modulation profile is constrained to have reduced resolution in modulation factor and bixel size. The output solution under this constraint is then used as a first estimate in a subsequent pass at a finer resolution. Constraining the resolution of the modulation profile in the initial stages reduces the number of variables to optimize, allowing an approximate solution to be achieved more quickly. The process is continued until a
predefined resolution in bixel size and modulation factor is reached. Pseudocode for the modified simulated annealing optimization algorithm is provided in Figure 3-1, where the variables employed are defined in Table 3-1. A comparison was made between results achieved using the multi-pass method and a single pass at finest resolution, with the outcomes reported in the Results section.

Figure 3-1: Multi-pass optimization pseudocode for determining modulation profiles that achieve prescribed SNR patterns in FFMCT.
3.1.4. Enhanced Capabilities

A. Dose Estimation

The previous optimization algorithm was limited to symmetrical objects and symmetrical image quality objectives in order to reduce optimization time. In the current algorithm these assumptions were removed and no restrictions on object shape or image quality objectives are required. Dose estimates were also previously based on the difference between incident and transmitted fluence, and only considered total dose based on a uniform phantom. In the updated algorithm, local voxel to voxel dose, $D(\vec{r})$, was estimated using the collision kerma, $K_c(\vec{r})$, where

$$D(\vec{r}) = K_c(\vec{r}) = \Psi(\vec{r}) \frac{\mu_{en}(\vec{r})}{\rho(\vec{r})},$$

and where $\Psi(\vec{r})$ is the primary energy fluence assuming each photon has an energy of 60 keV, $\mu_{en}(\vec{r})$ is the mass-energy absorption coefficient, and $\rho(\vec{r})$ is the material density. Material density and mass-energy absorption coefficients were defined using values from the National Institute of Standards and Technology (NIST) database. This method of dose calculation provides the option for local dose deposition in areas such as the eyes to be limited during a scan, which has been added as functionality in the optimization routine via the local weighting terms in Eq. (2.6).

<table>
<thead>
<tr>
<th>Variable name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$d_{pix}$</td>
<td>Pixel dimension</td>
</tr>
<tr>
<td>$s_x, s_y$</td>
<td>Image dimension in x and y (voxels)</td>
</tr>
<tr>
<td><strong>theta</strong></td>
<td>angular displacements of projections</td>
</tr>
<tr>
<td>$m_j$</td>
<td>Modulation profile at iteration $j$</td>
</tr>
<tr>
<td>$l_o$</td>
<td>initial number of photons per bin</td>
</tr>
<tr>
<td>$j$</td>
<td>iteration number</td>
</tr>
<tr>
<td>$T_j$</td>
<td>Temperature at iteration $j$</td>
</tr>
<tr>
<td>$C_j$</td>
<td>Cost function value at iteration $j$</td>
</tr>
<tr>
<td>$N_{divs}$</td>
<td>Number of resolution changes</td>
</tr>
<tr>
<td>$f$</td>
<td>Object function</td>
</tr>
<tr>
<td>$Q$</td>
<td>Target image quality</td>
</tr>
<tr>
<td>$\alpha$</td>
<td>Cooling rate factor</td>
</tr>
<tr>
<td>$N_{iters}$</td>
<td>Maximum iteration number</td>
</tr>
<tr>
<td>$\Delta_{max}, \Delta_{min}$</td>
<td>Maximum and minimum allowed change in modulation factor</td>
</tr>
<tr>
<td>$k_{devs}$</td>
<td>Number of modulation factors that can change value per iteration</td>
</tr>
</tbody>
</table>
B. Application to Higher Resolution Images

Another change to the algorithm involves application of the modulation profiles to higher resolution objects. Extension to high resolution images is made by downsampling the object of interest initially and acquiring a modulation profile for the low resolution image. The modulation can then be upsampled to the scale of the original image. Noise relationships between low and high resolution images are available in the literature for standard filtered backprojection methods and are used to translate predicted noise between the low and high resolution images (see further discussion below in Section 3.2.1). A comprehensive table of additional changes/improvements made to Graham’s original algorithm is found in Appendix A.

3.1.5. Simulated Annealing Parameter Selections

The number of bixels that can change in a given iteration is a free parameter set by the user. Setting this parameter too high was found to result in substantially increased computation time due to the computationally intensive stage of updating the SNR using Eq. (2.4) without yielding significant improvement in the results. Therefore, a minimum number of bixels was changed at each iteration.

Heuristics suggest that the initial temperature in the simulated annealing algorithm should be chosen such that both decreases and increases in the cost function have similar probability. In the first pass, where the initial guess is assumed to be blind, this choice suggests a temperature on the order of $\Delta C$. A limited number of iterations can be run initially (approximately 200 was found to be sufficient) to determine the order of $\Delta C$ in this case. In subsequent passes, the initial guess is assumed to be a better approximation, which suggests the initial temperature must be significantly less than $\Delta C$. Choosing the appropriate initial temperature values in these cases was therefore performed empirically by observing the cost function behaviour after approximately a thousand iterations, ensuring that neither decreases nor increases in cost function value dominate initially. The cooling rate was selected so that near the maximum number of iterations the algorithm approaches the so-called “greedy” algorithm, where only decreases to the cost function are allowed. Maximum iterations for each pass scaled approximately with the number of bixels. However, relatively long iteration counts (with respect to the number of bixels) were used in the first pass to allow for a very good initial guess, and for the last pass to allow for the system to
stabilize at a very low cost function value. Convergence to the optimal solution is not guaranteed, unless a very large number of iterations are used\textsuperscript{57}; further, changes from conventional implementation of simulated annealing that have been made to increase speed as defined in the previous chapter break from conventional formulations of simulated annealing on which proofs of convergence have been built. However, confidence in the results was increased by observing the repeatability of outcomes under varied initial estimates in independent trials, and comparing the output to known solutions for the trivial case of a uniform cylinder.

3.2. Experiments

3.2.1. Test Parameters and Image Quality Criteria

All experiments were carried out in simulation using Matlab\textsuperscript{®}. A suite of three different objects, illustrated in Figure 3-2, was designed to test the algorithm under increasing levels of complexity. Figure 3-2 (a) and (b) represent cylindrical and oblong shaped water phantoms, respectively, while (c) represents a simplified anthropomorphic lung phantom with three distinct attenuation coefficients: air, water and bone. Algorithm parameters were determined as described above with a summary provided in Table 3-2; optimization code was written in Matlab\textsuperscript{®} and run on a laptop running an Intel\textregistered Core\textsuperscript{TM} Duo Processor T2300 (Intel Corp., Santa Clara CA). Parallel-beam projections were considered over 180\degree at 192 equiangular intervals. A larger number of projections could have been used but was avoided to reduce optimization time. To further reduce optimization time, modulation profiles were generated for low resolution images (64×64 voxels, 0.54×0.54×0.5 cm voxel dimension) and later applied to high resolution cases. The number of bixels in the modulation profile was therefore 64 (detector bins) × 192 (projection angles). Modulation factors were determined with respect to a uniform incident fluence field.

Image quality was defined in terms of the ratio of the attenuation coefficient of water relative to the standard deviation of the voxel signal. This ratio has the same units as SNR, with a similar interpretation, and to simplify nomenclature will be referred to as the SNR. It should be clear, however, that since the signal is an arbitrary constant value, the image quality metric is strictly a measure of the standard deviation of the voxel signal and not its mean. Image quality plans were prescribed on the low-resolution images in terms of arbitrarily chosen, target SNR values defined
for ROIs, as illustrated in Figure 3-2. Relationships between noise and spatial resolution are available in the literature\textsuperscript{56,58}. Under the present assumptions and using the Ram-Lak filter for filtered backprojection, a resolution increase of \( f \) in \( x \) and \( y \) results in a variance increase of \( f^3 \).

The target high SNR specification of 1100 in the low resolution images therefore corresponds to a standard deviation of 1\% with respect to water for a 1.08 mm voxel size, or 1.4\% for a 900 \( \mu \)m voxel size, in the \( x \) and \( y \) directions, where the dimension in \( z \) is fixed; similarly, target SNR values of 550 and 220 correspond to standard deviations of 2 and 5\%, respectively, with respect to water and for a 1.08 mm voxel size.

![Figure 3-2: Suite of CT test objects of varying complexity: (a) circular, (b) oblong and (c) anthropomorphic axial chest slice. For each object, desired noise characteristics are defined in terms of regional water signal-to-noise ratio (SNR). In addition, two different weighting schemes (uniform and non-uniform) were examined, which adjust the relative importance of each region of interest. Uniform weighting allows the algorithm to treat each region with equal importance while the non-uniform weighting emphasizes specific image quality objectives (see right column). Similar weighting schemes were also used to prioritize dose minimization objectives; dashed circles identify target low dose regions of interest for a non-uniform dose weighting scheme (i.e., optimization using a “local dose constraint”). Analysis of noise outcomes using fluence field modulation were made at locations A, B and C.](image-url)
3.2.2. Cost Function and Weights

It is possible for different modulation profiles to satisfy specific image criteria but have different dose outcomes. The algorithm, therefore, attempts to generate a solution that achieves the specified SNR criteria while limiting dose by minimizing the cost function, defined as

\[
C_n = \frac{\sum_{x,y} W_{S_{x,y}} (\text{SNR}_{x,y} - \text{SNR}_{m_{x,y}})^2}{\sum_{x,y} W_{S_{x,y}}^2} + \frac{\sum_{x,y} W_{D_{x,y}} D_{m_{x,y}}}{\sum_{x,y} W_{D_{x,y}}^2},
\]

where \( W_{S} \) and \( W_{D} \) are regionally varying weights on the desired signal to noise ratio, \( \text{SNR} \), and dose, \( D \), respectively, subscript \( m \) denotes dependence on the selected modulation profile as before, subscripts \( 0 \) and \( n \) denote the initial and current iteration number respectively, and subscripts \( x,y \) denote the dependence of the variables on the spatial coordinates in the \( z=0 \), \( x,y \) plane. The weights \( W_{S} \) and \( W_{D} \) can be selected depending on task-specific priorities on image quality or dose. Note that the denominators are constant normalization factors, which make each term unitless, and which could be included in a single weighting for each term in the form of Eq. (2.6). Two different types of weighting schemes for the SNR distributions were investigated in this study – uniform weighting and region specific (or non-uniform) weighting. The non-uniform weights were assigned (for simplicity) to the same regions used to specify the SNR, boosting priority to the high and intermediate SNR regions as illustrated in Figure 3-2.
However, correspondence between the regions of SNR and the weighting functions is not a general requirement.

Similarly, two different dose weighting schemes were also implemented, which will be referred to in terms of a total dose constraint, where each voxel was assigned a unity weighting, and a local dose constraint, where select subregions were assigned a weighting of 1.5 and surrounding regions were assigned a low weighting of 0.1 (i.e., priority was given to minimizing the dose in the specified subregions). The selected subregions correspond to the regions bounded by the dashed circles shown in Figure 3-2 and were applied only to the case of the non-uniform SNR weighting for the cylindrical and anthropomorphic objects.

3.2.3. Analysis

Regional dose (in mGy) and SNR results were quantitatively compared to results using a bowtie filtered fluence pattern. Comparisons of integral dose (in Joules) were also made by integrating the predicted dose over the volumes. The bowtie filter was modeled under the assumption that each object is a uniform water cylinder with diameter equal to the maximum cross-sectional width of the object, and where the transmitted fluence is uniform across the detector. The bowtie filter can be described by a modulation factor, $m_b$, that varies in $\xi$ such that:

$$m_b(\xi) = e^{2\mu_0 \sqrt{R^2 - \xi^2}} \quad |\xi| \leq R$$

(3.6)

where $R$ is the radius of the modeled cylinder. The bias of the incident fluence was adjusted such that the average SNR within the high SNR ROI was the same as that achieved using the optimized modulation profile (for the non-uniformly weighted FFMCT case only). Simulations of reconstructions (64x64 voxels, 0.54x0.54x0.5 cm voxel dimension), generated from projections with added Poisson distributed noise, were also used to validate the accuracy of the analytic noise model implemented. Mean signal and standard deviation values over 100 trials were evaluated for small regions (3x3 voxels) at select locations in the reconstruction (see Figure 3-2) and compared with predicted values.

3.3. Results
3.3.1. Total Dose Constraint

Computation time when implementing the multi-pass method using the parameters specified in Table 3-2 was approximately 95 minutes. When compared to a single pass at finest resolution, the multi-pass method achieved a better overall result in reduced computation time, as shown by the respective cost functions plotted in Figure 3-3. Successive refinement of the modulation profile and the corresponding SNR distribution after each subsequent pass to the optimization script is also illustrated in Figure 3-4, for the case of the cylinder (uniform weighting, total dose constraint). It was noted that only relatively minor improvements to the cost function and the SNR distribution were observed after three passes. Sample output modulation profiles generated for the oblong and anthropomorphic test objects are also shown in Figure 3-5. Light and dark regions correspond to high and low modulation factors, or equivalently, high and low fluence passed to the object, respectively; transmission ranged from 1% to approximately 110% of the reference uniform fluence. The complexity of the profile was observed to increase with greater complexity of the object of interest, as is particularly seen in Figure 3-5 (b).

![Figure 3-3: Cost function versus time for the multi-pass and single pass methods. Convergence is approached more quickly in the multi-pass method, where the initial pass optimizes a low resolution modulation profile, and where the constraint on resolution is increasingly relaxed in subsequent passes. Inset shows the first and second passes of the multi-pass method (separated by the dashed line) shown at a finer time scale. Both increases and decreases in the cost function are permitted at the beginning of each pass, as is characteristic of simulated annealing optimization.](image-url)
Figure 3-4: Refined modulation profiles shown after each successive pass (n=1..5) to the optimization routine, where resolution (spatial and degree of modulation) is refined at each pass. SNR patterns generated for each modulation profile show increasingly smoother distributions as n increases (right column).
SNR distributions predicted using fluence field modulation under a total dose constraint are compared to that using bowtie filtration in Figure 3-6. In all cases, application of fluence field modulation resulted in SNR distributions similar to the prescribed values, and largely distinct from those produced using a bowtie filter. With increased complexity of the object structure and composition (i.e., for the case of the anthropomorphic phantom), the FFMCT results exhibited significantly better uniformity of image quality over the ROIs when compared to the bowtie filter (see Figure 3-6), which exhibited a larger range of SNR values within the target ROIs. Compared to the prescribed values, results using FFMCT show more gradual transition of image quality at ROI boundaries, particularly between the intermediate and low image quality regions in the cylindrical and oblong phantoms. Predicted (analytical) outcomes versus prescribed values at specified locations (see Figure 3-2) are also listed in Table 3-3. In general, the non-uniform weighting scheme resulted in better agreement of the high SNR ROI with the prescribed values (to within 6% at location A), but increased the disparity between the target and resulting values of surrounding regions (see Table 3-3 and Figure 3-6).

![Normalized modulation profiles generated for (a) oblong, and (b) anthropomorphic test objects using the uniform weighting scheme. Complexity of the modulation profile is observed to increase with complexity in object shape and composition.](image-url)
Mean signal values over 100 trials were evaluated for small regions at select locations in the reconstruction (Figure 3-2) with the results presented in Table 3-3. Note that the reference column in Table 3-3 refers to the reconstruction values without added noise to the projections; these values may differ slightly from the values defined for the test objects because of inherent inaccuracies in the reconstruction (e.g., aliasing artifacts due to limited projection numbers). The mean signal value over 100 trials had excellent agreement with the reference value in all cases (to 5 significant digits), independent of the modulation applied, as expected. The measured SNR values also agreed well with the analytical outcomes.

Figure 3-6: Image quality maps showing spatially dependent SNR values for constant (bowtie) modulation and for fluence field modulation patterns generated using two different weighting schemes for (a) cylindrical, (b) oblong and (c) anthropomorphic phantoms. Greater priority to the high SNR region (i.e., non-uniform weighting) results in better agreement with prescribed values but also some tradeoff in the SNR values of surrounding regions. Test objects are reproduced to the right for reference.

For better visualization of the effect of modulation on reconstructions, high resolution images were generated for each phantom. Figure 3-7 (a) shows the reconstructed image (1.08×1.08 mm) of the cylindrical phantom with modulation (non-uniform weighting) juxtaposed against the image without modulation. This comparison illustrates that the SNR performance is comparable to the unmodulated case in the high SNR ROI, and significantly decreased in surrounding
regions. For enhanced visual comparison between the high and low SNR regions, circular “inserts” were also simulated in the images, where the inserts have a 2% larger signal value than surrounding material. Similar results for the reconstruction of the oblong water phantom (0.9×0.9 mm) are also seen in Figure 3-7 (b). Finally, an image of the anthropomorphic phantom was also generated (0.9×0.9 mm), with an added anomaly of 4% signal deviation from water juxtaposed against the cavity (“lung”) wall, as seen in Figure 3-7 (c). In this image, the bony anatomy is clearly visualized in the low SNR regions, while visualization of the low contrast lesion is enhanced by the higher local image quality.

Predicted dose distributions for the modulation patterns optimized using the total dose constraint are illustrated in Figure 3-8 for the FFMCT and bowtie filtration cases. Increasing the priority of the high-SNR region resulted in higher overall doses delivered for all objects (see Table 3-3 for doses calculated at select locations). Compared to the bowtie filtered case, significant dose reduction was observed for all three phantoms using FFMCT. Integral doses for the cylindrical, oblong and anthropomorphic phantoms (non-uniform weighting) were found to be 52%, 48% and 61% of those resulting from the bowtie filter, respectively. Difference images show local dose increases also occurred, to a maximum of 0.4, 0.2 and 0.1 mGy for the anthropomorphic, oblong and cylindrical phantoms, respectively. Also notable is that modulation of the fluence field introduced greater irregularity in the dose distribution patterns.

3.3.2. Local Dose Constraint

Figure 3-9 shows the resulting SNR patterns and dose distributions for the cylindrical and anthropomorphic phantoms when a local dose constraint (with a non-uniform SNR weighting) was implemented in the optimization cost function; results for the total dose constraint are also reproduced in Figure 3-9 for easier comparison. Integral dose within the target low dose regions (bounded by the dashed circles in Figure 3-2 and Figure 3-9) were reduced by 31% and 44%, compared to that of the total dose constraint, and 47% and 55%, compared to that of the bowtie filter, for the cylindrical and anthropomorphic phantoms, respectively. The local dose reduction was greatest where higher relative doses were observed in the total dose constraint case; the overall effect was a more uniform, lower dose resulting within the target low dose regions. In the remaining volume both increases and decreases were observed (see difference images in Figure 3-9), with a maximum local increase of 0.4 mGy for both phantoms. Integral dose over
the entire volume was found to have decreased in both cases: marginally for the cylinder (by less than 0.5%), and by 5% for the anthropomorphic phantom (relative to the case of the total dose constraint).

Figure 3-7: (a) Water phantom in high resolution (1.08 x1.08 mm) with modulation (left) and without modulation (right). (The modulated case represents the case of the non-uniform SNR weighting.) Three equivalent circular “inserts” with a signal deviation of 2% above water have been added in both the high and low SNR regions for better visualization of the effect of the variable SNR performance. (b) Oblong water phantom in high resolution (1.08 x1.08 mm) showing similar effect of modulation on regional noise characteristics. (c) Anthropomorphic phantom observed at high resolution (0.9 x 0.9 mm) with a simulated lesion with 4% signal deviation from water. Close-up of lesion is also shown to the right. Window level has been reduced from full dynamic range in these images to enhance the contrast of the lesion/inserts. Bony vertebra is visualized easily in both low and high quality data. Images of the relative SNR distributions are also displayed in the bottom left corners.
Figure 3-8: Estimated doses with and without modulation applied to the incident fluence (values shown in mGy). The difference image represents the dose of the non-uniformly weighted (high SNR priority) modulation pattern minus the dose from a bowtie filtered fluence field. Dose reductions are generally highest at peripheral regions. Dose increases are also seen near the target high SNR ROI.

**TABLE 3-3.** Results for mean signal, SNR, and dose at sampled regions of simulated phantoms under modulation for two different weighting schemes. SNR values are reported with respect to water. The ± column reports the estimated standard error.

<table>
<thead>
<tr>
<th>Weight Object</th>
<th>Location</th>
<th>Mean Signal (× 10⁻¹ cm⁻¹)</th>
<th>SNR (H₂O)</th>
<th>Dose (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uniform Cylinder</td>
<td>Reference</td>
<td>2.0228</td>
<td>2.0229</td>
<td>0.0001</td>
</tr>
<tr>
<td></td>
<td>Noise Sim</td>
<td>2.0202</td>
<td>2.0201</td>
<td>0.0003</td>
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<tr>
<td></td>
<td>Prescribed</td>
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<td>340</td>
<td>340</td>
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<tr>
<td></td>
<td>Analytic</td>
<td>1100</td>
<td>920</td>
<td>940</td>
</tr>
<tr>
<td></td>
<td>Noise Sim</td>
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<td>430</td>
</tr>
<tr>
<td></td>
<td>Prescribed</td>
<td>1100</td>
<td>730</td>
<td>750</td>
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<td>380</td>
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Figure 3-9: SNR patterns and corresponding dose distributions resulting from modulated fluence fields optimized using a local dose (LD) constraint compared to those using a total dose (TD) constraint for (a) cylindrical and (b) anthropomorphic phantoms. The local dose constraint prioritized the regions bounded by the dashed circles to receive a low dose while seeking a modulation profile that would achieve the prescribed SNR values. Difference images show reductions in dose within the low dose target regions for the LD case with some tradeoff in achieving prescribed SNR values.

Local dose reductions were accompanied with some tradeoff in SNR values. Greatest decreases in SNR were observed at or near where the low dose ROIs overlapped with the target high SNR ROIs, as seen in the SNR difference images in Figure 3-9. Near these overlapping regions, a maximum decrease of 17% in SNR was observed for the case of the cylinder and 25% for the anthropomorphic phantom. In the case of the anthropomorphic phantom, some improvements in SNR were also observed within the target high SNR ROI, such that the values more closely approached the prescribed values. The mean SNR within the high SNR ROI decreased only moderately, with differences of 4% and 3% for the cylindrical and anthropomorphic phantoms, respectively. While variations were observed as described above, the overall SNR patterns observed were similar to those generated using a total dose constraint.
3.4. Discussion

In this study, regionally varying SNR patterns were prescribed for a suite of simulated test objects of varying degrees of complexity. Modulation profiles that achieve these patterns were sought using an optimization routine, based on minimizing a cost function that included image quality (defined with respect to image noise) and dose terms. When compared to results using a bowtie filtered x-ray fluence, the modulation profiles allowed for distinct SNR patterns, with localized regions of high and low image quality, similar to the patterns prescribed. Although the results showed that highly contoured and regionally varying SNR patterns are possible, they also indicated that some tradeoffs will inevitably be met when attempting to satisfy widely varying image quality criteria in adjacent ROIs (i.e., adjacent regions of very high and very low image noise). More specifically, increasing agreement of a particular ROI to the image plan can be made by prioritizing that region in the cost function, but at some expense in achieving surrounding values to arbitrary specification. The gradients between image qualities at ROI boundaries also appeared to have variable levels of sharpness. The rapidness with which image quality can change between distinct regions and its level of conformity to a prescribed shape are probably dependent on the complexity of the pattern, the amount of disparity between image qualities between ROIs, as well as on the reconstruction method itself, which introduces correlations between the noise.

Furthermore, the results were fairly robust under increased complexity of the test object. In the case of the anthropomorphic object, uniform high SNR values were achieved in a zone that had highly disparate image quality in the case of the bowtie filter. This result suggests that fluence field modulation can offer an improvement over fixed or restricted fluence patterns by better accommodating anatomical variations in order to achieve prescribed image quality. Evaluations of high resolution images also indicated that small perturbations will not change the output modulation profile greatly, as was expected. This outcome is important where multiple scans are made to observe changes in anatomy. Future work should explore the limits of this assumption, for example, when tracking a surgical tool which would introduce very high contrast changes to the image. Although the image quality plans analyzed in this study were defined using SNR values, alternative image quality metrics could be used such as CNR, or combinations thereof.
Evaluations of dose also demonstrated significant reductions when compared to the bowtie filtered fields. Although some regions did observe an increase in dose, the majority of the volumes experienced decreases, with integral dose reductions ranging from 39-52%. Dose increases were also relatively small (<0.5 mGy) and were associated with regions where image quality was improved. Dose reduction was particularly pronounced in the periphery of the objects. When modulation profiles were optimized using local dose constraints, further dose reductions (approximately 30-40% integral dose) were observed within the target low dose ROIs, while increases (relative to the total dose constraint) occurred in surrounding regions. This result is reasonable since local decreases in dose are related to decreases in fluence through those regions which may compromise the SNR objectives unless compensated by an increase in fluence (and therefore dose) elsewhere. The decreased dose to dense bony anatomy in the case of the anthropomorphic phantom may explain why the total integral dose actually decreased notably (by 5%) in that case. Local dose constraints also resulted in some tradeoffs in SNR in the target high SNR regions. However, these tradeoffs occurred primarily in regions that were near or overlapping the target low dose regions. While larger dose reductions could potentially be yielded by increasing the corresponding weights, this result suggests a limit with respect to how low a dose can be achieved in a region of interest while still achieving SNRs near the prescribed values, particularly when the target low dose and high image quality regions coincide. Furthermore, an arbitrary lower limit on the modulation factor of 1% with respect to the reference uniform fluence was imposed in this study, which implicitly places a lower limit on dose. In practice this limit may be determined by the dynamic range and sensitivity of the detector (and as such defined in terms of a minimum output fluence as a function of $\xi$). In addition, the start and end angles of the CT scan were fixed during the optimization; this constraint could be relaxed to further optimize dose reduction to ROIs.

Dose reductions reported are relative to a fixed bowtie fluence field, and therefore exclude the benefits that might be afforded by angular TCM. The extent to which TCM optimized with a bowtie filter can achieve similar results to that of the ideal modulation considered in this study is an interesting area of research and is investigated in more detail in the next chapter. Although a direct comparison with other research cannot be made due to the many simplifying assumptions made in this work, reported dose reductions using angular TCM at comparable anatomical sites (11-27% for thorax, 10-23% for abdomen, 14-37% for pelvis) are substantially lower on average.
than the potential reductions suggested here. In addition, angular modulation has primary benefit for anatomical sections where attenuation changes appreciably in orthogonal views, suggesting that combining TCM with the bowtie filter would not further reduce the dose in the cylindrical case, and may have limited impact on the anthropomorphic phantom described. Further note that the reported dose reduction for the anthropomorphic phantom is considered to be a conservative estimate. The reason behind this last belief is that the comparison was made with a bowtie filtered fluence that achieved the same average SNR over the target high SNR region. This meant that a large range of SNR values were permitted in the case of the bowtie filter, where a substantial fraction of those values were significantly lower than the target prescribed values, as well as those achieved using FFMCT. Had the comparison been made to a bowtie filter achieving the same minimum SNR (within the high SNR ROI), the reported dose reduction would likely be substantially higher. It is further noted that the dose model ignores any backscatter contribution. Though typically backscatter contribution would be high at energies used in CT, this study is confined to a single axial slice, where the majority of the backscatter would not contribute significantly to dose within the slice. Practically, more advanced dose models that consider backscatter contribution will need to be employed for larger field of views.

Another important aspect to note is that the noise model chosen incorporated only Poisson distributed noise and does not take into account detector imperfections such as electronic noise\textsuperscript{58,60}. Modeling detector specific noise characteristics for application to real CT systems is the subject of Chapter 5. Note that though the geometry presented is simplistic, the general framework presented is also more broadly applicable to alternative geometries, including cone-beam CT and inverse geometry CT\textsuperscript{61,62}. Chapter 5 also investigates the application of system specific fan-beam noise prediction models to FFMCT. Other simplifying assumptions were also made (e.g., monoenergetic beam, scatter free), the implications of which ultimately require further investigation, and may depend in large part on the design of the modulator.

In addition, the optimization routine was chosen because it is known to provide good results and is easily implemented. In particular, it offers the advantage over the method of steepest descent of being able to escape local minima well. Although typically very slow, a “multi-pass” method was developed and found to greatly increase the speed of the algorithm. Other steps could also have been implemented to further speed up the optimization time. For example, some results could be anticipated (e.g., uniform noise is anticipated from a uniform transmitted fluence in this
case) and incorporated as starting points for the algorithm. In practice, more advanced optimization schemes would likely be employed and can easily be substituted for the presented method in the general framework outlined.

The results of this study indicate that FFMCT may have a positive impact on the dose and utility of CT examinations if feasible methods are found for its implementation. The overall dose reduction could allow for more frequent scanning protocols than are currently used, and with greater utility of each scan. In image-guided head and neck surgery, for example, higher image quality could be prescribed within the region of a tracked surgical instrument, allowing for poorer image quality in other regions, under the additional constraint that dose delivered to the lens of the eye is limited. Advantages of this approach are not limited to image-guidance but could also be used in diagnostic CT where the region of interest is well localized, or when follow-up multiphase scans may be necessary.

3.5. Conclusions

The results of this initial study support the hypothesis that FFMCT can be used to achieve: (a) regionally-defined, user-prescribed, task-based image quality plans, and (b) reduced radiation exposure to the patient through more efficient management of x-ray fluence. However, it also highlights the dependence of this reduction on the scanning parameters, object shape, specified SNR pattern and corresponding weights. The tradeoff between image utility and dose to the patient cannot be eliminated; however, we have introduced a methodology that allows these tradeoffs to have a more regional dependence based on the specific imaging task.
Chapter 4
Comparison of Compensator Approaches

As mentioned in the introduction, application of fluence field modulation specific to patient anatomy was first explored in SER\(^42\); techniques for varying the incident fluence profile\(^44\) that have been developed for SER units have included moving slits and dynamically varying apertures. Similar techniques have also begun to be explored for dynamic beam modulation in CT systems\(^45\). Other distinctly different approaches under investigation include sliding wedges\(^41\) and multiple sources\(^46\) in inverse geometry CT\(^61\).

In the previous chapter, potential dose and image quality benefits of FFMCT were considered in simulation assuming an ideal modulator. However, real physical modulators (see examples above) will likely have more limited flexibility over the modulation that can be implemented, depending on the modulator design and/or time constraints. Some research\(^41,46,63\) has suggested that more limited modulation may be sufficient for meeting user-prescribed image quality and reduction of dose. The study in this chapter attempts to compare the relative effectiveness of FFMCT for noise and dose optimization under the imposition of several different modulation constraints, which are meant to represent realistic physical system constraints.

Though FFMCT may reap benefits in a broad range of applications, imaging of the thorax presents an interesting application for several reasons. In particular, the large attenuation differences presented by soft tissue, bone and lung can introduce highly non-uniform noise characteristics\(^64,65\). Further, dose reduction in thoracic imaging applications such as cardiac CT\(^66,67\) and lung-screening\(^68,69\) could potentially increase the benefit-to-risk ratio in these applications, and extend their utility to a larger percentage of the population. This study
therefore examines three distinct imaging applications of the thorax: lung-screening, cardiac CT, and routine diagnostic chest imaging, as test applications for constrained FFMCT. This study builds on the preliminary findings presented at the 1st CT Meeting\(^{63}\) and the CRPA Annual Conference\(^{65}\). Content from this chapter has also been submitted to Medical Physics and is reprinted here with permission\(^{70}\).

### 4.1. Methods and Materials

The methodology used in Chapter 3 was similarly followed in the experiments performed in this chapter, with the exception of some changes in parameters and imposition of constraints as described below.

#### 4.1.1. Simulated Thoracic Phantom

The phantom chosen for this study was a simulated anthropomorphic chest slice, containing bony, adipose, soft, and lung tissue equivalent regions, as depicted in Figure 4-1 (a). This phantom was simulated by a combination of thresholding and manual segmentation of these features from a high resolution CT scan of an anthropomorphic phantom\(^{71}\), and assigning tissue attenuation values according to the National Institute of Standards and Technology (NIST). A single axial slice, corresponding to a slice through the T6 vertebra was used. The phantom was selected in part because it represents highly heterogeneous tissue in terms of attenuation coefficient, which is known to introduce highly non-uniform noise characteristics as seen in Chapter 3.

#### 4.1.2. Optimization and Image Quality Metrics

As discussed in previous chapters, different modulation profiles may satisfy the same image quality criteria but have different dose outcomes. Optimization therefore attempts to find a solution to the minimization problem defined in Eq. (2.6), with the aim of achieving the specified image quality criteria while minimizing dose\(^{40}\).

Prescriptions for image quality were defined in terms of target standard deviations in Hounsfield units (HU); within the cost function, \(Q(r)\) was defined as the related quantity of variance of the reconstructed signal:
\[ Q(\bar{r}) = (n(\bar{r}))^2 \]  

(4.1)

where \( n(\bar{r}) \) is the signal standard deviation at location \( \bar{r} \). A lower \( Q \) value therefore indicates better image quality (lower noise). It is noted here again that other quality metrics, such as SNR or CNR, could have alternatively been used, or added as additional terms in the optimization.

Dose deposition can be modeled from the collision kerma, \( K_c(\bar{r}) \), as defined in Eq. (3.4), which accurately represents the dose at energy levels used in computed tomography. Fluence at each voxel was decreased according to the Beer-Lambert law as before, with an added inverse square dependence on distance from the source in order to more closely approximate a realistic dose distribution in the phantoms. Here, \( D_m(\bar{r}) \) of Eq. (2.6) represents the local integral dose obtained by multiplication of \( D(\bar{r}) \) by the estimated mass of the voxel at location \( \bar{r} \).

Solutions to the optimization problem were sought using a simulated annealing optimization method, described in detail in the previous chapter and in publication\(^ {40} \). Computation of Eq. (3.4) at each iteration required a prediction of the variance as a function of voxel position, which was calculated using Eq. (2.4). As in Chapter 3, the computation time required for the optimization was reduced by using a lower resolution image for the input model and for the target image quality plans (64×64 bins, 0.78×0.78×0.5 cm voxel dimension), which restricted the maximum number of modulation bins to 64.

4.1.3. Weight Selection

The first term in Eq. (2.6) causes the solution to trend toward the prescribed variance criteria while the second term attempts to lower the dose as much as possible. Noise correlations between voxels are inherent due to the process of filtering and the backprojection of values over ray paths using FBP. Due to these correlations, arbitrary image quality plans may not be possible. A higher value of \( W_Q(\bar{r}) \) (by a factor of 100) was therefore assigned to the prescribed high quality ROIs for all cases in order to prioritize those regions. The local dosimetric weighting, \( W_p(\bar{r}) \), could similarly be tuned to prioritize a region for low dose. However, in this study, the weighting was set to unity for all voxels such that each voxel has equivalent priority in
the optimization scheme with respect to dose minimization. In addition, setting the weight, $w_D$, too high relative to $w_Q$ can result in image quality outcomes that are lower than prescribed in favour of a lower total integral dose; on the other hand, allowing $w_D$ to approach zero results in slower convergence to a low dose solution since the relative importance of dose versus image quality is reduced. In this work, a relative weighting of 10:1 for $w_Q$ and $w_D$ was employed, as ratios higher than this resulted in only weak changes to average image quality (<1%) at the expense of longer optimization times. Specific outcomes utilizing these parameters for the various imaging scenarios are discussed in the results section.

### 4.1.4. Imaging Tasks and Image Quality Prescriptions

In this study we considered the case of a single slice acquisition of the phantom described in section 4.1.1, optimized for three different imaging applications:

1. Routine Chest Exam
2. Lung-Screening
3. Cardiac CT

Figure 4-1 (b-d) illustrates the image quality map ($IQM_{sd}$) representing the prescribed (regionally varying) standard deviation for each of the applications above; white regions correspond to the areas where high image quality was prescribed while the gray areas define the target low image quality regions. Here, we define high image quality as a target standard deviation of 10 HU at a voxel resolution of 1×1 mm in the x and y plane (0.5 cm slice thickness) and low image quality as a standard deviation of 50 HU. The high image quality ROIs were chosen such that they fully encompass the clinically relevant regions associated with each of the thoracic imaging cases; the deemed clinically relevant regions are illustrated on the reference phantom image in the upper left corners of Figure 4-1 (b-d). Previous research\(^{40}\) suggests that the transition between the low and high image quality prescriptions cannot be made arbitrarily steep. Therefore, a less steep transition was implemented before optimization by convolving the low image quality prescription with a 3×3 Gaussian kernel (the high priority target values were left unchanged). Note that the resolution of the illustrated quality maps is lower than that of the input model for the reasons described above (Section 4.1.2).
Figure 4-1: (a) Illustration of the simulated anthropomorphic chest phantom used in this study. Prescribed image quality distributions, where white is equivalent to high image quality, are shown for the cases where the scanning priority is (b) the entire patient cross-section, (c) the lung and (d) the heart. The associated clinically relevant region of interest delineated on image (a) is shown in the upper left hand corner of images (b) –(d).

4.1.5. Modulation Constraints

Several cases of constraints for modulation were considered and are described below. The constraints are meant to model restrictions that might be imposed by real physical modulators. Examples of possible associated modulator designs are also indicated, although the reader should note that there may be a range of modulation techniques that could result in the same or similar modulation profiles.

i. 64 Modulation Bins per Projection

This case allows each modulation factor (64 bins per projection) to change independently of one another. The number of factors per projection corresponds to the reduced number of detector bins considered in the optimization as described above, and in this respect can be considered to be “unconstrained”. It should be noted that when applied to higher resolution images, this case
still represents a constrained modulation since the number of factors per projection is fewer than the number of detector bins.

ii. 16 Modulation Bins per Projection

This constraint reduces the number of modulation factors allowed per projection, and can be described mathematically as

\[ m(\xi, \theta) = c_n(\theta), \]
\[ 8n - 7 \leq \xi \leq 8n, \]
\[ n = 1, 2, ..., 16 \]  

(4.2)

A system of this nature could potentially be implemented by a set of wedges as suggested by Szczykutowicz et al.\(^{41,72}\) and Hsieh et al.\(^{73}\), or a multi-source array in inverse geometry as proposed by Sperl et al.\(^{46}\).

iii. Modulation Constrained to a Bowtie Filter

Under this constraint, only the relative bias of tube current can change from projection to projection while the modulation profile in any projection is constrained to the shape of a bowtie filter. The bowtie filter was designed to match a cylinder with a diameter that would fully encompass the simulated phantom. In this case, the modulation can be defined as

\[ m(\xi, \theta) = c(\theta)m_b(\xi), \]
\[ m_b(\xi) = e^{2\mu/(\sqrt{R^2 - \xi^2} - R)} \]  

\[ \left| \xi \right| \leq R \]  

(4.3)

where \( R \) is the radius of the matched water cylinder. This constraint models the functionality of TCM, but optimizes the tube current based on the task and the patient model, rather than employing a sinusoidal pattern or using a detector based measure for guiding the current modulation.

iv. Two Exposures: One Full Field Exposure Plus One Collimated Exposure

This constraint is characterized by the superposition of two exposures where the first is a uniform fluence field and the second is a reduced field of view. Mathematically, the modulation is constrained such that
\[ m(\xi, \theta) = m_1(\theta) + m_2(\xi, \theta) \]
\[
\begin{cases} 
= c(\theta), & \xi_1 \leq \xi \leq \xi_2 \\
= 0, & \xi < \xi_1, \\
= 0, & \xi > \xi_2 
\end{cases}
\]

One embodiment that could deliver a modulated fluence field of this type could be a dual source CT scanner, where one source delivers fluence to the entire object and the second is collimated to a smaller region as described by Heuscher et. al\textsuperscript{45}. This concept is similar to the window filters proposed in region of interest imaging, except the collimated field of view is allowed to dynamically change size and location from projection to projection.

To prevent erratic displacements and aperture sizes of the second exposure from projection to projection, an additional velocity constraint was placed on the system, such that the displacement of either boundary of the second exposure was limited to 5 modulation bins between projections.

v. **Modulation Constrained to a Custom Patient and Task Specific Filter**

The last constraint is similar to that of case (iii), except the filter is not predefined, but is instead determined as part of the optimization routine. In this case, the constraint can be defined as

\[ m(\xi, \theta) = c(\theta)m_1(\xi). \]

The modulation can be thought of as using a filter that is fixed in place, but has a shape optimized for the task and the specific anatomy of the patient.

In the above cases, the lower limit for modulation was taken to be 1% of the reference fluence; resolution of the modulation factors was similarly restricted to 0.01 [unitless], except for the bowtie filter case (case (iii)) where this resolution constraint was imposed on \( c(\theta) \) but not on the modulation factor \( m(\xi, \theta) \). For easier reference in the following text, cases (i) to (v) above will be referred to as: unconstrained, 16 bins, bowtie filter, two exposure and custom filter cases, respectively.
4.1.6. Analysis

Results for each of the cases defined above were compared with respect to the resulting average image quality, and the uniformity of image quality within the prescribed high priority ROI. The results were also compared against results using uniform fluence fields. Mean image quality and uniformity was evaluated in several ways, including bar plots showing the mean image quality within the region of interest, standard deviation-volume histograms, and the root mean square error (RMSE), defined as

\[
RMSE = \sqrt{\frac{\sum_{r \in A} (\hat{n}(\tilde{r}) - n_m(\tilde{r}))^2}{N_A}},
\]

(4.6)
calculated between the prescribed standard deviation \( \hat{n}(\tilde{r}) \) and the predicted standard deviation \( n_m(\tilde{r}) \) for each case, where \( N_A \) is the total number of voxels considered within a region \( A \). The RMSE was calculated first for \( A \) containing voxels within the high priority region alone, and then again where \( A \) included all voxels across the object. Error bars in the mean image quality bar plots indicated variability in the magnitude of noise across the high priority ROI, and so provide a measure of the uniformity of the noise in the different scenarios.

Since optimization was performed on low resolution images, several examples of high resolution (1×1 mm in the x-y direction) reconstructions were also created by adding Poisson noise to the projection data based on the fluence arriving at the detector for the different modulation profiles; a simulated lesion was added in one of the high resolution reconstructions to enhance visualization of the change in image quality. Difference images between the noisy reconstructions and a reference reconstruction without noise are also provided in order to better visualize the underlying noise component. In order to validate the accuracy of the predictive noise model, a high resolution reconstruction of a single modulation case was repeated 100 times with distinct random instances of noise added to the projection data in the manner described above. The standard deviation of the reconstructed value of each voxel was then calculated over the 100 reconstructions. The mean standard deviation over a small subregion of voxels is reported and compared with prediction at the centre of the small ROI.
Finally, dose comparisons were made on the basis of the integral dose (in kg·Gy) resulting from each modulation profile across the entire object, defined as

\[ D_i = \sum_{r \in S} D(\bar{r}) m_r(\bar{r}) = \sum_{r \in S} D_m(\bar{r}) \] (4.7)

where \( m_r(\bar{r}) \) represents the estimated mass of the voxel at \( \bar{r} \), and \( S \) is the set of spatial coordinates occupied by the object of interest. Integral doses were normalized to the case of a uniform fluence field that would provide the same minimum image quality (i.e., maximum noise) within the target ROI as in the worst observed modulated case. As an additional comparison, effective dose was also estimated based on approximate organ masses for a 62 kg male, and by applying the effective dose weights defined by the International Commission on Radiological Protection (ICRP).

4.2. Results

Figure 4-2 shows the resulting modulation profiles for each of the three thorax CT imaging tasks under different modulation constraints. Since the modulation factors are calculated with respect to a uniform fluence field, the modulation profiles shown are proportional to the incident fluence. Each predicted IQMsd (i.e., standard deviation map) is shown below the corresponding modulation profile. For reference, the last column in Figure 4-2 shows the target IQMsd as well as the result using a uniform fluence field (i.e., the case with no modulation). Note that the window level for image quality in Figure 4-2 is centred about the high image quality target values. Several observations are noted below with respect to the results shown in Figure 4-2. Observations with respect to the modulation profiles arising under the different constraints are described first followed by descriptions of each corresponding predicted IQMsd.

4.2.1. Modulation Profiles

Focus is initially on the results for the routine diagnostic CT scan (Figure 4-2(a)). Notably, the larger number of degrees of freedom in the unconstrained case presents a more complex fluence pattern compared to the remaining constrained modulation cases. The constrained cases appear largely distinct from that of the unconstrained case due to the imposition of the relative constraints. For example, in the two exposure case, each projection (i.e., each column) consists of two distinct fluence values, corresponding to a lower initial exposure, and a secondary
collimated exposure, as defined in the Methods section. However, some similarities between the modulation profiles can be seen. For example, the peak fluence values in the unconstrained case occur at approximately 90 degree intervals, corresponding to regions where the attenuation of incident fluence is great due to the superposition of bony features. This pattern remains consistent for the remaining constrained modulation cases (ii-v). Likewise, angular intervals where relatively low fluence occurs are generally consistent for each modulation type.

Comparing the unconstrained FFMCT scenario across different thoracic imaging tasks (Figure 4-2 (a-c), case (i)), we observe that the pattern in modulation profile changes for each task. Notably, in the lung-screening task (Figure 4-2(b), case(i)), the fluence at 0 and 180 degrees is diminished as compared to the routine diagnostic application (Figure 4-2 (a), case(i)); in contrast, the fluence in the cardiac optimized case (Figure 4-2(c), case (i)) is decreased at the 90 and 270 degree intervals as opposed to the 0 and 180 degree locations. In the case of the lung-screening task, the decreases are associated with less fluence through the vertebra and cardiac region but not the lungs, while in the cardiac optimized scenario, the reduction decreases fluence through regions surrounding the heart, but not the ROI bounding the heart itself. Note that the locations of the changes in peak fluence are also consistent across the different modulation constraints. Another general observation is that the region of higher intensity fluence is constrained to a smaller region in the cardiac optimized case, as would be expected since the ROI itself is smaller here than in the other cases.

Several other specific observations can also be made with respect to the different modulation constraints. Modulation profiles for the 16 bin case appear to have similar patterns to the unconstrained case except that they are in lower resolution, which would be expected since the number of modulation bins was reduced by a factor of 4. When fluence is constrained to the shape of a bowtie filter (case (iii)), the pattern of changes in mAs per projection (e.g., peaks and valleys in tube current) is distinct for each imaging application. In the two exposure case (case (iv)), the collimation of the second exposure introduces locally high mAs values that correlate spatially in various instances with the locally high mAs regions of the unconstrained case. Further, the collimated exposure does not in general maintain an aperture size that would encompass the entire high priority ROI, as can be seen from Figure 4-3, which shows where the collimated exposure overlaps the prioritized ROI in sinogram space for the lung optimized scenario as an example. Lastly, the custom filter case (case (v)) has similar mAs fluctuations to
that of the bowtie filter. However, flexibility in filter shape results in further variations across the general profile; in the cardiac optimized case, the region of high exposure is reduced substantially along the detector direction compared to the bowtie filter.

Figure 4-2: Modulation profiles (upper rows) as functions of detector position ($\xi$) and projection angle ($\theta$) under different modulation constraints with each resulting IQM$_{sd}$ (lower rows) shown in Hounsfield units for the case of (a) diagnostic (b) lung-screening and (c) cardiac CT scans. The rightmost column indicates the prescribed standard deviation for the corresponding imaging application and the IQM$_{sd}$ for a reference uniform fluence field. Upper left hand corner of each prescribed IQM$_{sd}$ shows the clinically relevant region of interest for each scenario overlain on the illustration of the anthropomorphic chest slice.
Figure 4-3: Illustration of the overlap between the collimated exposure and the prioritized ROI for the lung optimized, two exposure case. The gray region depicts where the lungs are projected onto the detector, while the white region indicates overlap of the lungs with the collimated exposure. In many instances, the collimated field of view is substantially less than the ROI.

4.2.2. Image Quality

As may be observed from Figure 4-2, all instances of modulated fluence resulted in an IQMsd with better conformity to the prescribed IQMsd than the uniform fluence field case (see reference column). Moreover, greatest conformity with the target image quality plan was achieved using the ideal unconstrained modulator (case (i)) for all imaging tasks, as expected.

Figure 4-4 illustrates the mean image quality for each imaging task and modulation constraint within the high priority ROI. Error bars on the bar plots represent two standard deviations from the mean. With respect to the mean image quality, all modulation profiles achieved good agreement with the planned objective, where each case deviated less than 2.5% from the target. Uniformity of image quality within the high priority region of interest varied, as indicated by the extent of the error bars. For comparison, the case of a uniform fluence field is also included; as seen, both unconstrained and constrained cases of FFMCT provide better uniformity of image quality than that of the reference uniform fluence. Cases employing fixed filters (cases (iii) and (v)) show improved uniformity over the reference field by approximately the same degree, with the custom filter case (case (v)) showing modest improvement over that of the bowtie filter (case (iii)). Uniformity is further increased in the remaining cases, where the profile with 16 modulation bins (case (ii)) resulted in an outcome closest to that of the unconstrained case.
Figure 4-5 displays the distribution of image quality in terms of standard deviation-volume histograms (SDVHs) for the diagnostic, lung-screening and cardiac CT screening cases respectively. Each point on the SDVH represents the percentage of the volume within the high priority ROI that has a predicted standard deviation equal to or greater than the corresponding value on the x-axis. The ideal distribution would appear as a step function at 10 HU, indicating that 100% of the volume meets the prescribed value with no percentage above or below. A broader distribution indicates less uniformity. Similar to the observation of Figure 4-2, cases (ii) and (iv) yield better overall uniformity of image quality than the cases where the profile is fixed throughout the scan. These cases also yield similar performance except for the routine diagnostic application, where greater deviation occurs between the curves. Note that all of the modulated cases achieve significantly better uniformity than the reference uniform fluence field case.
Figure 4.5: Standard deviation-volume histograms (SDVHs) for the (a) routine diagnostic CT (b) lung-screening and (c) cardiac CT cases over the corresponding regions of interest. The vertical axis represents the percent of volume that has a standard deviation equal to or greater than a given standard deviation in HU along the horizontal axis. Broader curves represent less uniformity in image quality (i.e., noise). The ideal curve would be a step function at the target of 10 HU, indicating that 100% of voxels in the volume have a standard deviation of 10 HU.
A measure of overall agreement with the prescribed values for both the high and low priority regions is provided in Figure 4-6, which illustrates the average root mean squared error (RMSE) across thoracic imaging applications for each type of modulation constraint. Errors for the high priority region alone and for the low and high priority regions combined are shown. Note that a break exists in the vertical axis where a change in scale also occurs. In general, the combined error is approximately an order of magnitude greater than the error within the high priority region of interest alone, indicating a larger discrepancy with achieving the low image quality priority ROI for each case. The combined error follows the same trend as that of the error within the high priority region of interest. As an average measure of achieving the prescribed image quality, best performance was achieved using the ideal unconstrained modulator, followed by the case with reduced resolution (case (ii)), two exposures (case (iii)), a custom fixed modulator (case (v)) and the bowtie filter (case (iv)), respectively.

Figure 4-6: Average root mean square error between the predicted outcomes and the prescribed values across thoracic imaging applications for different constraints in FFMCT. The break in the vertical axis marks a change in value and scale. The errors corresponding to the prioritized regions of interest are approximately an order of magnitude less than the total error.

Several examples of high resolution reconstructions applying the optimized modulation profiles are shown in Figure 4-7 (a), and difference images between the noisy reconstructions and a reference case without modulation are shown in Figure 4-7 (b). Validation of the noise prediction model has been shown elsewhere 40,47, but is included here with respect to this data for
completeness. The noise model employed (Eq.(2.4)) implicitly assumes a nearest-neighbour interpolation method during backprojection; however, in practice, the nearest-neighbour method yields aliasing artifacts, which in this case are on the order of the noise in the high quality ROI. Noise analysis was therefore performed on reconstructions using the nearest-neighbour method, but for illustration purposes the reconstructions shown in Figure 7 were generated using a linear interpolation method to better visualize the pattern of noise irrespective of aliasing artifacts. The mean standard deviation within the enclosed region in Figure 4-7 (b) was found to be 10.2 HU with a percent error of less than 1% with the mean predicted value within the same region. Use of linear interpolation instead of the nearest-neighbour method has the effect of further reduction of the standard deviation, in this case by approximately 32% (to 6.9 HU).

Several qualitative observations can also be made with respect to the image reconstructions. The reconstructions in Figure 4-7 (a) are windowed about the mean soft tissue value in order to highlight noise manifestation about the soft tissue. Outside of the region of interest for the lung and cardiac CT cases, the presence of noise increases. Streak artifacts are also present suggesting the noise in this region is not spatially uniform (i.e., is correlated in certain directions). Note from the images however, that the added presence of noise outside of the ROI does not adversely impact the visualization of bony anatomy. An added soft tissue lesion with a deviation of approximately 3% in signal value is shown in Figure 4-8, corresponding to the boxed-in region in Figure 4-7 (a). The lesion is identifiable within the high image quality ROI but would be obscured by the noise in the low image quality ROI.

4.2.3. Dose

Figure 4-9 (a) shows the integral dose comparison for the three thoracic imaging applications under the different constraints. In this figure, integral doses are normalized to the case of a reference uniform field that would provide the same minimum image quality (i.e., maximum noise) within the high quality target ROI as the case of the bowtie filter diagnostic scan. As an additional reference point, the dashed line in Figure 4-9 indicates the dose that would be required to meet the same criterion using a bowtie filter with static tube current. Significant dose reduction compared to the uniform reference field is observed for all cases. The modulated fixed filter cases (bowtie and custom filter) observe greater total integral dose than the
Figure 4-7: (a) High resolution reconstructions produced using projection data with added simulated Poisson noise for different modulation profiles (see corresponding modulation profiles in Figure 3). Top left corner of each image shows the region of interest of clinical relevance. A simulated lesion with 3% signal deviation from the mean soft tissue value is added to the lung scenario (see boxed region). The display scale was narrowed to highlight the different noise manifestations between image reconstructions. (b) Difference images between the reconstructions in (a) above and a reference noiseless reconstruction image. Top left corner of each image shows a representation of the predicted IQM_{sd}. The noise distributions of the images in (b) can be seen to follow the same trend as the distribution within the predicted IQM_{sd}. A comparison between simulated results and the predicted values was performed on the region contained within the dashed ellipse for validation of the noise prediction model.

Figure 4-8: Enlarged image of boxed region in Figure 4-7. The arrow points to a simulated lesion with a 3% signal deviation from the mean soft tissue value of the anthropomorphic phantom. Streak artifacts to the right of the image correspond to the defined lower image quality region. Streaks are a result of spatial non-uniformity in the image noise (i.e., directional noise correlations). The lesion is visible within the high image quality region but would not be visible within the low image quality region of interest due to the increased noise content.
reference bowtie filter with uniform tube current for the routine diagnostic application. The increase in dose in these cases is associated with greater uniformity of image quality (see Discussion section for interpretation of this result). In general the trend in dose follows the same trend as the error between predicted and prescribed image quality. Mean integral doses across thoracic imaging applications for cases (i) to (v) relative to the uniform case were 53, 57, 76, 62, and 74 %, respectively. Note that the integral doses for the bowtie and custom filter were similar except for the case of the cardiac CT scan. Figure 4-9 (b) compares the results based on effective dose estimates for each of the cases. In general, the same trends were observed though the gap between cardiac and lung-screening cases widened notably for the unconstrained (64 bin) and 16 bin cases.

![Graph showing normalized effective and integral doses](image)

**Figure 4-9:** (a) Relative integral dose normalized to the case of a uniform fluence field that would provide the same minimum image quality as that of the worst case FFMCT scenario. For additional reference, the dashed line shows the integral dose of a bowtie filter with uniform tube current that would meet the same minimum image quality. (b) Relative effective doses normalized to the same reference uniform fluence field. Similar trends are observed as in (a), though a larger gap is observed between the relative doses of the cardiac and lung-screening cases for the 64 bin and 16 bin scenarios.

**4.3. Discussion**

This study was carried out to evaluate: a) whether there exist potential noise and dose benefits when applying FFMCT to specific imaging tasks of the thoracic region, and b) to compare the relative effectiveness of FFMCT applied under different physical constraints. The results indicated that FFMCT can reduce dose in varied thoracic imaging tasks while meeting user-prescribed image quality criteria to a higher degree than can be achieved by conventional...
methods in practice today, even when the modulation pattern is subject to significantly limiting constraints.

When the modulation profile was constrained to the shape of a bowtie filtered fluence, the scenario was essentially reduced to the conventional practice of employing a bowtie filter with TCM. This case can therefore be considered the best case scenario employing conventional techniques. However, an important difference with conventional practice is that the modulation of the tube current was optimized using an *a priori* reconstruction of the object and employing voxel independent noise and dose prediction models. One interesting outcome of this study was that the optimized TCM for the bowtie filter varied significantly depending on the imaging task; in particular, the angular ranges where peak and minimum fluence occurred changed depending on whether the application was optimized for a routine diagnostic scan, lung-screening CT, or cardiac CT. In other words, as the high priority ROI varied in size and location, the optimized TCM profile changed markedly. Further, tube current peaks appeared to be associated with projections where largely attenuating features (e.g., the vertebra and sternum) would impact the image quality within the target ROI, suggesting that the presence of heterogeneous attenuation coefficients influences the optimal choice of TCM depending on the task (or image quality prescription). Dose reductions were also observed for the cardiac and lung-screening cases compared to the routine diagnostic CT case (approximately 15 and 10% respectively). These results suggest that the application of filters or compensators currently in standard practice today could be better optimized using the proposed optimization methodology of FFMCT. Another finding using the bowtie filter was that when optimizing for uniformity in image quality (defined here as noise, or standard deviation of the signal), the resulting dose is higher than when compared to a bowtie filter with uniform fluence that would deliver the same *minimum* image quality (but lesser uniformity). This result is in agreement with studies in TCM that indicate that the tradeoff between dose and noise may be best managed at a point between the case of a static tube current and that of a modulated tube current that would result in maximum uniformity\(^{11}\). Further study is likely necessary to determine where the optimum balance lies in other instances of constrained and unconstrained FFMCT.

Though general trends of high and low image quality were found to agree with that of the prescribed plans with varied success, agreement with the low image quality prescription was poorer than the prioritized high image quality ROI. This result suggests that arbitrarily high
differences in image quality may not be achievable, and is consistent with findings\textsuperscript{40,63} described in Chapter 3. Limits on the extent that the magnitude of the noise can be controlled from voxel to voxel are inherent due to the correlations of noise introduced along backprojection paths\textsuperscript{47}, and the pre-defined lower limit in incident fluence per detector bin (in this case, 1% of the incident uniform beam), which places an upper limit on the maximum noise. This result also lends support to the value of applying weights for prioritization of different ROIs within the image quality prescription. In addition, streak artifacts in the lower image quality region point to spatial non-uniformity of the noise present which may be an inherent consequence of regionally varying image quality targets; however, mitigation of spatial non-uniformities in noise might be possible with additional penalties added to the cost function. Note that the lower limit on incident fluence per detector bin was sufficient here to avoid photon starvation artifacts; in practice, however, a tolerance based on minimum expected detector counts would likely be necessary.

The benefit of creating a customized filter for each task instead of applying a conventional bowtie filter was seen to be relatively marginal in terms of delivering more uniform image quality within the target ROI, but was significant in terms of dose reduction when the region of interest was limited as in the cardiac CT scan. This result suggests that when using a fixed filter, appropriate selection of TCM bears more importance than the choice of filter shape itself on image quality, while the width of the filter with respect to the ROI is the most important factor with respect to dose. Where off-centre ROIs are defined, such as with the lung optimized scan, the shape of a fixed-filter generally ought to be such that greater fluence can pass to the defined ROI in any given view. Note that for small, off-centre ROIs, the high exposure region allowed by the filter could be reduced in size by shifting the patient relative to the imaging system, as recently proposed in region of interest imaging applications\textsuperscript{75,76}.

The relative effectiveness for achieving prescribed high quality image data was seen to increase considerably when moving from a fixed filter modulation constraint (i.e., bowtie or custom task/patient specific filter), to a method that allows for variation in the fluence pattern at each projection. The simplest case for dynamically modulating the beam, a single exposure followed by a collimated exposure of variable width and location, approached the target image quality and uniformity of the unconstrained case for both the lung-screening and cardiac CT imaging applications. Though the image quality results were less comparable for the diagnostic CT scan,
the results were still markedly improved over that of the fixed filter cases. Similarly, dose was also generally reduced in constrained FFMCT scenarios that allow for dynamic modulation of the fluence pattern as opposed to a fixed filter. These results support the advent of dynamic modulation of the fluence field across the field of view of the detector for enhanced management of dose and noise in CT.

We note that comparison of relative dose outcomes should not be weighed without consideration of the respective image quality outcomes. For example, though the dose outcomes of the custom filter and the two exposure cases were similar for the cardiac CT application, the custom filter case had poorer uniformity with a greater percentage of voxels having lower image quality than that of the two exposure case. It should also be emphasized that doses were normalized with respect to that of a uniform fluence field that would not exceed the maximum noise of any of the observed cases. If the uniform fluence field had been chosen to have the same average image quality instead, the normalization factor would have been smaller, but this case would also have considerably noisier regions than any of the observed cases, as seen in the relative bar plots (Figure 4-4), and so the former was considered a more intuitive reference point. It is also noted that approximations of effective dose tended to follow the same trends as the integral dose comparisons. One important distinction observed was a broader gap between the relative dose reduction between cardiac and lung-screening tasks for the unconstrained and 16 bin scenarios; this result was seen to be largely influenced by the contribution of dose the lung to its higher relative radiosensitivity weighting in the calculation of effective dose. Another important point is that the image quality prescription implicitly makes uniformity of noise an important attribute, where noise either above or below the target is penalized in the cost function. An alternative image quality definition where only image quality falling below a target value is penalized may result in a different set of SDVH plots and also broaden the respective differences in dose.

The two exposure routine diagnostic and lung-screening cases also suggest a break in the conventional school of thought that has arisen in proposed models for static and dynamic window filters, essentially that the collimated field of view or secondary exposure should encompass the ROI in each view. Here again, the presence of heterogeneous attenuation coefficients appears to demand more complex modulation profiles than would be expected for a homogeneous phantom.
One limitation of the study was that the scatter contribution from within the phantom was ignored; however, since only a single slice was considered, scatter contribution to dose and signal is expected to be small (assuming collimation in the z direction coincides with the slice width). Work remains to study the implications of scatter on image quality and dose contribution, which may be quite large in larger volumes and has been shown to potentially introduce large artifacts when employing dynamically modulated beams. However, provided adequate corrections are made, previous work in region of interest imaging suggests that image quality may be improved by scatter reduction within the high image quality regions of interest; similarly, reductions in primary fluence suggest reductions in dose due to scatter as well. In addition, sources of scatter as well as changes to the quality of the x-ray beam (beam-hardening) may arise from the modulators. Evaluation of the extent of these effects and possible corrections depends on the modulator design and is outside the scope of this work, but is important in ultimately deciding on a modulation strategy and determining the feasibility of any particular approach. We emphasize that there may be multiple means of delivering the same modulated primary fluence field. Another limitation of this study was the simplifying assumption of parallel beam geometry; future work will benefit from noise and dose prediction models applied to direct fan-beam reconstruction. However, the present study is thought to provide a useful first order comparison of the relative limitations and capabilities of different constrained modulators which are likely reflected in other geometries. One aspect of FFMCT that was not explored in this study, but that has been shown previously to have potential in the ideal modulator case, is the capacity for local dose sparing; evaluation of the relative capacity for achieving similar image quality plans with different dose distributions such that the total effective dose is minimized also merits further study. It should also be noted that the noise propagation model depends on the reconstruction method. An FFMCT approach could potentially be applied to other reconstruction techniques, including non-linear approaches, provided noise models are available; however, it would likely not be prudent to make inferences with respect to non-filtered-backprojection approaches based on the results of this paper without further investigation. Finally, the relative mechanical feasibility of implementing any given method is not evaluated here. Notwithstanding, the constrained modulator approaches modeled here are thought to represent cases that may be simpler in design than one that would approach the ideal case, yet may still reap significant benefits in terms of dose reduction and image quality optimization over conventional static shaped filters.
4.4. Conclusions

The results of this study support the hypothesis that FFMCT can be employed to lower dose to the patient while achieving image qualities prescribed by the user. Specifically, potential benefits were found for three distinct thoracic imaging tasks with distinct ROIs. Introducing constraints on modulation was found to limit agreement with prescribed image quality and dose reduction, but still offer the benefits of FFMCT over conventional techniques. Allowing the pattern of incident fluence to change across the detector for different projection angles was found to provide a distinct advantage in noise and dose management over the use of fixed filters.
Chapter 5
Experimental Validation

In this Chapter, evaluation of FFMCT is repeated using real data. Real CT systems employ x-ray beams with a polychromatic spectrum and use non-ideal detectors. In lieu of a physical modulator to implement prescribed fluence modulation, we instead synthesize modulated projections from projections acquired at different settings, as described in the methods below. The benefit of this approach is that it allows for testing the FFMCT models using real data, which are subject to detector imperfections and require system specific modeling and processing, independent of confounding factors introduced by the collimator itself (e.g., additional scatter, beam hardening, etc.). Therefore, any artifacts that are introduced in the images can likely be identified as due to poor noise characterization of the detector, projection processing, or other modeling error irrespective of the physical modulator. Artifacts resulting from an actual modulator are then likely easier to parse in future investigations from that of the ideal situation from synthesized projections. Some of the findings within this chapter have been reported in conference proceedings\textsuperscript{77,78} and are reproduced here with permission.

5.1. Methods

5.1.1. Apparatus

Experiments to evaluate the dose and image quality benefits of FFMCT were performed using a cone-beam CT benchtop in circular geometry, collimated to 64 detector rows about the central plane for simulation of a single slice CT acquisition. In this setup, an amorphous silicon flat panel detector (Paxscan 4030A, Varian, Palo Alto) with 194 $\mu$m pixel pitch, and a 600 kHU x-
ray tube (Rad-94, Varian, Palo Alto) were fixed in position, with the phantom mounted on a precision rotation stage, as shown in Figure 5-1. A cylindrical water phantom (5 cm diameter) was constructed containing acrylic spheres and Teflon rods, and is illustrated in Figure 5-1 (b). Acrylic spheres were chosen because of their low contrast with respect to water simulating soft tissue lesions, while Teflon simulates high contrast material such as bony anatomy. The phantom size was kept small relative to the full field of view in order to limit scatter artifacts from the object; the small size of the object also allowed the use of the simplified parallel ray assumption in the optimization script for noise propagation described in previous chapters.

![Figure 5-1: (a) Photo of experimental cone-beam CT unit. In this arrangement the x-ray tube and the detector are stationary, and the phantom rotates about a central axis on a rotation stage. When collimated to a central row, the imaging data is equivalent to conventional fan-beam computed tomography. The phantom mounted on the rotation stage is for illustrative purposes only, and was not imaged in the present experiment. (b) The phantom design used in this experiment consists of a 5 cm acrylic tube filled with acrylic spheres of varying sizes, teflon rods, and water. The water and acrylic provide low contrast details while the teflon rods introduce very high contrast material.]

In order to generate a projection with a modulated fluence pattern, multiple scans of the object were taken of the phantom at different mAs settings (from 0.4 – 4 mAs per projection). A set of synthesized modulated projections were then constructed from the available projection sets, according to the modulation profile defined by the optimization method. Lead collimators reduced the field of view in the z direction to about 64 detector rows. Collimation serves to reduce scatter in the projection data from the object. The cylinder was centred on the rotation axis and each projection was 512 pixels in length (corresponding to a 6.4 cm field of view). Details about the acquisition geometry and relevant settings are provided in Table 5-4.
Table 5-4: Acquisition Details

<table>
<thead>
<tr>
<th>System Parameter</th>
<th>Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source to Detector Distance (SDD)</td>
<td>156 cm</td>
</tr>
<tr>
<td>Source to Rotation Axis Distance (SAD)</td>
<td>100 cm</td>
</tr>
<tr>
<td>Reconstructed Field of View</td>
<td>6.4 cm (diameter)</td>
</tr>
<tr>
<td>Filtration</td>
<td>0.1 mm Cu + 5.1 mm Al</td>
</tr>
<tr>
<td>Tube current</td>
<td>0.4 – 4 mAs</td>
</tr>
<tr>
<td>Tube potential</td>
<td>80 kVp</td>
</tr>
</tbody>
</table>

5.1.2. Optimization Method

Optimization was carried out using the simulated annealing method described in detail in Chapter 3. The input model of the object was taken from a reconstruction of the object using a 1.25 mAs/projection setting. The noise in the projection data is modeled in the optimization routine as having two primary components: Poisson noise (based on photon counting statistics) and electronic noise, as discussed in subsequent sections below (see Section 5.1.4). Recall that the noise model employed in the optimization algorithm (see Eq. (2.4)) relies on the assumption of parallel ray geometry. In the present case, the object of interest is relatively small and the divergence of the beam was ignored during optimization, allowing for the continued use of the noise model by Kak and Slaney. After optimization, the noise model proposed by Zhu et al. was then used, which was derived for fan-beam geometry with a flat detector, with the aim of generating a more accurate final prediction of variance for the given modulation profile. The derivation by Zhu et al. also explicitly accounts for the effect of correlations between pixels, as described in Section 5.1.4. Such an approach could be employed in practice, where a simplified model is used to generate a modulation profile, and a more complex approach used post-optimization to verify that the profile and resulting image quality outcomes are acceptable. However, more complex noise models could also be used explicitly in the optimization method if implemented efficiently.
The optimization was constrained such that modulation of the incident fluence was restricted to 64 detector bins (where each bin represents 8 pixels in a row), and was further constrained to allow only one of 11 modulation factors. The first constraint aids in reducing optimization time while maintaining sufficient resolution for achieving desired image quality metrics, as in previous chapters. Although not meant to represent a particular collimator design, the number of bins also coincidentally corresponds to the number of intervals currently applied in tomotherapy where fluence profiles are similarly modulated for radiation therapy delivery. The second constraint was due to the limited number of mAs settings permitted using the pulsed radiographic mode on the control console.

Figure 5-2: (a) Prescribed SNR distribution for the small cylinder phantom slice. Here, SNR refers to the standard deviation of the noise distribution with respect to a reference water signal. The target SNR values in the optimization script are high because a decreased resolution image is utilized. (b) Local weights applied to the image quality term in the optimization cost function. Priority weighting in the optimization script is given arbitrarily to region A.

5.1.3. Image quality prescription and weights

Image quality was defined in the same manner as in Chapter 3, and is defined as the ratio of a reference water signal relative to the magnitude of noise (i.e., the standard deviation of signal measurements). A value of 100 is therefore interpreted as noise having a magnitude of 1% of the signal of water (or 10 HU). As in Chapter 3, the metric will simply be referred to as SNR for simplicity, though the reader should continue to keep in mind that the measure presented here is
strictly a measure of the inverse of noise, since the reference signal is a constant value. Though defining image quality in terms of target standard deviation values, as in Chapter 4, is intuitive, using the inverse of noise has the advantage of being proportional to the fluence, which may tend to be more stable in the cost function since dose is also proportional to fluence.

Here, the prescriptions of SNR were based on predicted values at the lower and upper range of mAs settings available. At highest reconstruction resolution (125 × 125 × 125 µm), noise near the centre of the phantom ranges from approximately 80 HU at 4 mAs to 200 HU at 0.4 mAs, corresponding to SNR values of 12.5 and 5, respectively. Therefore, these values were taken as the approximate target high and low image quality values. Using the approximate relationship derived by Li et al., the high image quality value would translate to noise on the order of 10 HU, or an SNR of 100, for a reconstruction resolution of 0.5 × 0.5 mm (125 µm slice thickness) for comparison. Figure 5-2 shows the relative distribution of target SNR values defined for the phantom; note that the scale in Figure 5-2 shows higher relative SNR values than stated above due to the reduced resolution of the input data.

In this experiment, a higher global weight was attributed to the image quality term in Eq. (2.6), with a ratio of 200:1. The local dose weight was set to unity, giving equal dose reduction priority to each voxel. A higher weighting on image quality was attributed arbitrarily to region A as depicted in Figure 5-2 (b), with a ratio of 2:1 with respect to the surrounding voxels. The purpose of prioritizing region A was to observe the effect of changing the locally varying image quality weight on the output modulation profile and final SNR distribution.

Dose was calculated as in previous chapters (see Eq. (3.4)) with an added inverse square dependence on distance from the source in order to more closely approximate a realistic dose distribution in the phantom, as used in Chapter 4.

5.1.4. Noise modeling of the Detector

A. Electronic Noise

The electronic noise in the detector is assumed to be fluence independent (i.e., the magnitude of electronic noise is the same irrespective of the mean photon counts at the detector). Electronic noise is measured by acquiring 100 dark field images (i.e., images with zero incident fluence)
and measuring the variance in the pixels after subtracting the mean. The magnitude of electronic noise may fluctuate from pixel to pixel in the detector, but here was assumed to be shift-invariant; therefore, the average variance value across pixels was used to describe the magnitude of the noise.

B. Poisson Noise

The variance in flat panel detectors is inherently less than what would be predicted purely from Poisson statistics. Siewerdsen et al.\textsuperscript{79} describe in detail the various stages of detector readout and the associated gain and blurring that cause this effect. Though accurate modeling of the different factors involved is quite complex, a simplified empirical model describing the variance in a detector reading, based on the results of Siewerdsen et al.\textsuperscript{79}, was used instead:

\[
\text{var}(N) = aN + d^2
\]  

(5.1)

where the factor \(a\) is an empirically determined parameter meant to account for the reduced variance of the pixels due to blurring effects in the detector, and \(d\) is the measured standard deviation of the noise in the dark fields (i.e., “electronic noise”). The fit to experimental data using this model is shown in the results section. This model is meant to provide a better estimate of the pixel variance as a function of mean pixel value; however, it does not provide any information about the nature of the correlation of the noise between pixels. As shown by Zhu et al.\textsuperscript{64}, the noise correlations that exist in real detectors need to be accounted for explicitly in the noise model or the predicted variance in the reconstruction will be in error. For optimization purposes, we attempt to compensate for this effect by comparing the model output assuming the noise is white with the actual outcome in a reconstruction using real data and deduce a correction factor (specific to the detector and pixel resolution).

5.1.5. Fan-beam Prediction Maps

As discussed above, the optimization algorithm is employed under the assumption of parallel ray geometry as in previous chapters, with the inclusion of an additional variance term describing the electronic noise, and two correction factors: the first to account for the reduced predicted variance in projection data due to correlations, and the second to account for additional reduction in the variance within the reconstruction due to the same correlations.
After the modulation profile is output by the simulated annealing algorithm, a variance map based on the approach by Zhu et al. is then calculated. This approach was derived for the fan-beam case with a flat panel detector, which corresponds with the present experiment. Further, it explicitly includes the transfer function for the noise which describes the nature of the noise correlation between pixels. From Zhu et al.’s algorithm, the variance in the image reconstruction data is given by

\[
\text{var}(f(r)) = \sum \frac{1}{l^2(r)} B \left( \frac{w^2}{N^2} v^2 (g * h)^2 \Delta u, \theta \right) \Delta \theta^2
\]  

(5.2)

where \( B \) represents the filtered backprojection operator, \( l \) and \( w \) are weighting terms applied in fan-beam filtered backprojection, \( \Delta u \) is the pixel width at the detector, \( \Delta \theta \) is the angular increment between projections, \( v \) is the variance in the projection data, and \( g \) is the transfer function governing the noise correlations between detector pixels. Dependencies on angular and detector position have been dropped to simplify the equation. Eq. (5.2) was derived assuming a white noise field, with variance \( v \), that is subsequently convolved with the transfer function \( g \). Therefore, \( v \) for the Poisson component would not be described by \( aN \) as defined in Eq. (5.1), since this value would represent the variance after convolution with \( g \). Eq. (5.1) is therefore not convenient since we cannot directly measure \( v \). However, once the function \( g \) is determined, the relationship between the variance of a hypothetical white noise field, and the variance of the same field after convolution with \( g \) can be found empirically in order to derive a proportionality constant. Therefore, for the Poisson component of noise

\[ v = abN \]  

(5.3)

where \( b \) represents the empirically determined proportionality constant between noise fields before and after convolution with \( g \). Since the electronic noise is independent of the Poisson noise, it can be considered separately. The proportionality constant and a separate transfer function can also be determined for the electronic noise component.

\[ \text{‡} \]

Here we change the variable names used in Zhu et al.’s algorithm to agree with the notation used here.
Some important distinctions from Zhu et al.’s paper should be noted here. First, in their paper, Zhu et al. derive separate equations for Poisson and electronic noise. The second derivation is more general and is the form used in Eq. (5.2). Further, in Zhu’s paper, the transfer function \( g \) is used synonymously with the modulation transfer function (MTF). However, the transfer function described is proportional to the root of the magnitude of the noise power spectrum (NPS). The MTF and NPS are related functions but need not share the same profile or shape; therefore in the present study \( g \) is not assumed to be the MTF as executed in their paper. Further, as noted above, the electronic noise and the Poisson noise may not exhibit the same correlations between pixels, and so \( g \) should be evaluated separately for each.

5.1.6. Noise transfer function

Since only a single slice acquisition is modeled here, the transfer function is modeled as if correlations are only between pixels within the single detector row. Characterization of correlations in two dimensions is possible, but would require a different noise propagation model. The electronic noise and Poisson noise were analyzed separately. Analysis of the electronic noise was performed by acquiring 100 dark acquisitions without any fluence incident on the panel. Each pixel has an inherent bias associated with it that first needs to be subtracted: the mean pixel values are calculated by averaging the 100 acquired projections, and is then subtracted from the corresponding pixel in each dark field. Each individual dark field is then zero meaned to eliminate any additional variation in bias between dark fields, and each field is zero padded to 1024 pixels. Zero padding is a necessary step prior to application of convolution by multiplication in the Fourier domain.

The transfer function is described in the Fourier domain as the variation in magnitude between different frequency bins. A white noise field would be characterized by a flat profile in the Fourier transform, while correlated noise (sometimes called \textit{coloured} noise) would exhibit different magnitudes between frequency bins. Analysis of correlations is therefore performed by calculating the discrete linear Fourier transform of each dark field using the Matlab fast Fourier transform (FFT) function. The magnitude of the Fourier components is visualized by plotting the absolute value of the FFT. For better statistics we average the result over the 100 dark field images (processed as described above) and observe the FFT. As shown in the results section, the
electronic noise was found to behave as a white noise field, so no further steps in analysis were required in terms of calculating the transfer function for electronic noise.

The steps above were repeated for flood fields (radiographs taken with incident fluence greater than zero and no object in the field of view), with tube current settings ranging from $0.4 - 1$ mAs. The magnitude of the FFT squared is proportional to the variance of the signal per frequency bin. The flood fields contain both Poisson and electronic noise. Variances of independent noise sources are added in quadrature, so the electronic noise component can be separated from the Poisson noise component by first squaring the mean absolute FFT of the flood fields and then subtracting the square of the FFT of the electronic noise. Taking the square root of the result provides a measure of the FFT of the noise due to Poisson statistics alone. Finally, the transfer function was modeled in the Fourier domain by fitting a Gaussian curve to the FFT. In order to calculate the proportionality constant in Eq. (5.3) white noise fields were generated and then convolved with $g$. Variance was calculated before and after the convolution and the results compared to derive $b$. Calculation of $g$ in the real domain would require an inverse FFT of the fitted function in the Fourier domain. However, practically, the convolution in Eq. (5.2) of $g$ and $h$ is done directly in the Fourier domain and therefore this last step is not required.

5.1.7. Projection Processing

Radiographs are processed such that the natural logarithm is taken of the measured fluence field at the detector relative to the incident fluence field on the object of interest (see Eq.(2.2)). The average incident fluence is typically calculated by acquiring flood field images without any object in the field of view. Typically, a large number of flood fields are averaged to reduce the error in the measure of the incident fluence field. In the present case, each modulated projection therefore requires a corresponding modulated incident flood field. This modulated flood field can be created as a composite of individual flood fields taken at different mAs settings, in the same way that the modulated radiograph is created, but without the object in place. However, the dynamic range of the detector is saturated for flood fields greater than 1.25 mAs. Therefore the flood field images for current settings above 1.25 mAs were extrapolated from the available flood field images at lower values.
5.1.8. Analysis

Image quality and dose outcomes predicted from the optimization algorithm were compared to predictions for that of a bowtie filter that would produce on average the same image quality within the priority weighted region of interest. The shape of the bowtie filter was designed to match that of the small cylinder rather than a standard larger bowtie filter that might be used for patients, for a more fair comparison (see Eq. (3.6) for the mathematical description of the bowtie filter). The optimized fluence modulation profile was then used to dictate the generation of the high resolution, FFMCT projection sets, synthesized from the set of projections taken at different mAs settings. An FFMCT reconstruction of the phantom was then created using the projection data, using a 125 μm voxel size. The reconstruction with modulation was then compared to a reconstruction of the same slice reconstructed using an unmodulated, 1.25 mAs/projection tube current setting for a visual comparison. A variance map for the high resolution case was generated using Eq. (5.2). Variance measurements in the FFMCT reconstructed data were then compared to the predicted variance map for evaluation of the accuracy of the fan-beam prediction model in conjunction with the noise modeling of the detector specific to the imaging system used.

5.2. Results and Discussion

5.2.1. Detector variance modeling

Variance as a function of mean detector signal is shown in Figure 5-3. Results show good agreement with the fit to the linear model proposed in Eq. (5.1). The clusters of data points in Figure 5-3 correspond to flood field data sets acquired at different six different mAs settings (from 0.4 to 1.25 mAs). Each data point on the graph corresponds to the measured variance of a pixel over 100 projections as a function of the pixel’s mean value. Where multiple pixels had the same mean (rounded to one count), the variance between the pixels was averaged and the data point was weighted more heavily in the least mean squares fit (proportional to the number of pixels averaged). Note that within each flood field a relatively large distribution of mean signal values is present. This distribution may be due partially to inherent differences between pixel sensitivity, but is likely mostly due to the heel effect where the intensity of X-rays varies inherently across the field of view due to the nature of the X-ray production. This effect was
ignored in the optimization algorithm, which assumes a uniform incident reference field and estimates the output by simulating projection sets, but is accounted for in the subsequent final prediction of noise using Zhu et al.’s algorithm where the projection sets utilized are the actual experimentally acquired projections.

![Graph showing variance as a function of mean pixel counts](image)

**Figure 5-3:** Variance as a function of mean pixel counts shows linear behaviour with increased mean detector count. The factor $a$ is empirically determined by a weighted least mean squares (lms) fit. The variance was calculated over 100 projections, and for 6 different tube current settings. Where multiple pixels evidenced the same mean value, the variances across those pixels were averaged and a higher weighting applied to the data point in the lms fit.

### 5.2.2. Image quality and dose

The optimized fluence modulation profile is shown in Figure 5-4 as a function of projection angle and detector bin. In this case, the high fluence region in the modulation profile clearly correlates with the spatial position of the prioritized high image quality ROI. A secondary region of fluence moderately higher than the background is also seen which corresponds spatially to region B in Figure 5-2 (a). An important observation here is that the simplicity of the pattern suggests that a simplistic collimator approach, such as the two-exposure collimator approach detailed in Chapter 4 could potentially result in similar results.
The resulting predicted SNR map for the FFMCT case is also compared to the case of a bowtie filter in Figure 5-5. Of the two regions specified for high SNR in the FFMCT case, the prioritized region achieved much better agreement with the objective than the low priority region. However, increased SNR with respect to the surroundings is also evident to a more limited extent within the low priority region. Another observation is made that the contour changes in the high SNR target region were smoother than those specified in the target SNR prescription. This result agrees with results from previous chapters and further suggests limitations in the target delineation capabilities of the system exist, particularly when there are “kinks” or sharp changes in the plan, although reducing the constraints on the system (e.g., greater number of modulation factors) could possibly achieve better results. Compared to the case of the bowtie filter, both techniques in this case were able to achieve relatively uniform image quality within the target prioritized region, as might be expected since the bowtie filter is designed for a cylindrical body. However, the FFMCT case constrained the region of high SNR such that it was well localized to the priority region of interest prescribed in the target plan, reducing the SNR elsewhere.

Figure 5-4: Modulation profile as a function of row position along the detector and projection number (320 projections over 360 degrees). Highest fluence correlates with the prioritized high image quality ROI. A secondary region of higher fluence correlates with the second (non-prioritized) high image quality ROI.
Figure 5-5: (a) SNR distribution predicted using FFMCT. Bottom right corner shows the prescribed SNR values. (b) SNR distribution using a bowtie filter matched to the size of the cylinder and providing the same mean SNR value within the target high priority ROI in (a).

Figure 5-6: Ratio of dose distribution using FFMCT relative to the dose distribution using a bowtie filter. Total integral dose reduction is 52%, while local dose reductions range up to 65%. Few voxels experience greater dose in this case than would occur using the bowtie filter.

Figure 5-6 shows a ratio of the dose map using FFMCT to that of the bowtie filter. Local dose decreases reached as high as 65%, and overall, the decrease in the integral dose was estimated at 52% for this object. Comparison with the bowtie filter is made here only to first order using the parallel ray assumption. However, since the phantom is relatively small (i.e., the fan angle is not large), the divergent effects introduced due to the fan-beam geometry are not considerably great.
Further, scatter and beam hardening are considered in this case to be minimal because the phantom size is small and also because the beam was highly collimated (to about 8 mm at the isocentre). However, larger phantoms and fields of view will likely demand more accurate dose modeling that accounts for effects such as beam hardening and scatter.

Figure 5-7: Average magnitudes of FFTs for simulated and real data. The simulated white noise signal shows as a flat spectrum in the FFT; after filtration, the simulated noise shows the same spectral characteristics as the real experimental data. The Gaussian fit shows good agreement with the shape of the FFT curve, and suggests a good choice for modeling the noise transfer function. A characteristic white spectrum is seen in the FFT of the dark fields (electronic noise). Note also that the magnitude of the electronic noise is also much less than the Poisson component.

5.2.3. Noise transfer function

The image quality maps described above are first order predictions using a simplified parallel ray model and correction factors. Results describing the measurement of the transfer function $g$ for explicitly modeling the effect of detector specific correlations in the noise in fan-beam geometry as defined in Eq. (5.2) are discussed below.
Figure 5-7 shows the average magnitude of the FFT for a measured flood field (1 mAs) fitted with a Gaussian curve. As shown, the fit agrees well with the measured data and is used to model the magnitude of the FFT of the transfer function $g$ required in Eq. (5.2). Figure 5-7 also shows the amplitude of the FFT of a simulated white noise field before and after convolution with $g$. Agreement of the simulated and real noise distributions gives confidence that the modeled transfer function accurately characterizes the correlations in the noise. The form of the normalized transfer function was also found to be consistent for different flood fields suggesting that the relative shape of $g$ is not dependent on the magnitude of the incident fluence. Comparison of the variance of the white noise field prior to and after convolution with $g$ yielded a value of 2.12 for the proportionality constant $b$. The same result for $b$ was found regardless of the magnitude of the white noise distribution. Also shown in Figure 5-7 is the average magnitude of the FFT of electronic noise (from acquired dark field data). Note that the FFT for the electronic noise is approximately flat across frequency bins. The transfer function was therefore assumed to be unity for the electronic noise, and the proportionality constant is also assumed to be 1 in that case.

5.2.4. High resolution, fan-beam variance predictions and measurements

Figure 5-8 shows a comparison of the reconstructions of the cylinder using synthesized FFMCT projections versus a reconstruction using an unmodulated beam and using a 1.25 mAs tube current setting. The FFMCT reconstruction shows better image quality within the prioritized region of interest for the FFMCT case, with reduced quality elsewhere, following closely with the predicted image quality map.

A variance map for the high resolution data is shown in Figure 5-9 (a), with the corresponding SNR distribution also shown in Figure 5-9 (b). Note that the SNR distribution follows closely with the first-order approximation using the parallel ray geometry shown in Figure 5-5, suggesting the estimates used in the optimization method were reasonable. The range of SNR values observed also agreed with the expected range based on the upper and lower limits of image quality observed over the range of tube current settings available. Measurements of the variance within the regions indicated in Figure 5-9 (a) were made using the reconstructed data shown in Figure 5-8 (b). Results indicated agreement well within 5% between the predicted and
experimental results. A comparison of the results of variance measurements compared to the predicted values for these regions is shown in Table 5-5.

<table>
<thead>
<tr>
<th>Location</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predicted (cm^{-2} x 10^{-4})</td>
<td>3.2219</td>
<td>21.095</td>
<td>6.2962</td>
</tr>
<tr>
<td>Actual (cm^{-2} x 10^{-4})</td>
<td>3.3136</td>
<td>21.0486</td>
<td>6.3366</td>
</tr>
<tr>
<td>% Difference</td>
<td>2.8</td>
<td>0.2</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Figure 5-8: (a) Reconstruction of data acquired using a 1.25 mAs tube current setting. (b) Reconstruction of data using synthesized modulated projections, where the tube current setting ranged from 0.4 – 4 mAs. The bottom right corner in the modulated projection data set illustrates the predicted SNR distribution. Colour washed regions in (a) correspond to regions of high and intermediate image quality predicted in the FFMCT case for visual comparison.
5.2.5. Study Limitations

Advantages of the approach used for creating modulated projections in this study are that it allows for testing a modulation approach prior to construction of the modulator, and secondly that it allows for testing under idealized circumstances which can be treated as a benchmark for future studies; note that since no collimator was used, no correction was required for either beam hardening or scatter contributions from the collimator which could be modelled separately.

Limitations of this study were principally with inaccuracies with respect to the scatter effects from the object itself since the modulated projections were synthesized from a series of individual projections rather than using an actual modulator. Typically, one would expect that reduction of fluence outside some region of interest would reduce the scatter-to-primary ratio within that region, which could not be observed when synthesizing FFMCT projections in the manner indicated. However, this issue was circumvented by utilizing a small cylinder, and collimating to the central plane, which is expected to have greatly reduced scatter contribution. Potential artifacts due to abrupt scatter to primary ratio changes in the field of view\textsuperscript{41} were therefore also avoided using this technique. Using a small cylinder also permitted the

Figure 5-9: (a) Variance distribution predicted using the Eq. derived by Zhu et. al. The mean variance in regions A, B and C were compared to the actual measured variance in the experimental data and found to agree well within 5%. (b) Predicted ratio of water signal to noise.
simplification of using a parallel beam model for noise propagation. Larger objects will likely require more accurate noise propagation models explicitly included in the optimization method, such as the one derived by Zhu et al. for fan-beam geometry. Larger objects would also require a more advanced dose estimation method, and scatter correction strategies. Another important limitation of the experimental method implemented should also be highlighted here. As described in detail above, noise correlations between pixels are described by the transfer function, $g$. However, since each FFMCT projection is synthesized from 11 different projections, this assumption is violated between subregions of pixels acquired at different mAs settings since they are independent measurements and would not be subject to the same correlations. However, given that each bin in the modulation profile represents 8 pixels in the high resolution projection, and that several bixels of the same mAs setting may be grouped together in any given projection, the local transfer characteristics may still be modeled well, explaining the good agreement between experimental and predicted outcomes.

5.3. Conclusion

The outcomes of this study further support that FFMCT could potentially be applied with success in real clinical CT systems, provided that a suitable method for modulation be found. Results show superior management of dose for achieving local high SNR performance in the presence of both high and low contrast materials.
Chapter 6
Remaining Challenges and Future Work

6.1. Key Outcomes

6.1.1. FFMCT

This thesis investigates the use of x-ray fluence field modulation for dose and noise optimization in CT. The framework developed includes defining an image quality plan based on a patient model, followed by a search for a fluence modulation profile that will deliver the defined image quality objectives. This search was carried out in the studies presented by defining a cost function with weighted image quality and dosimetric terms and attempting to minimize it via simulated annealing by iteratively changing the modulation profile. Simulations using uniform and anthropomorphic phantoms support the hypothesis that regionally varying image quality prescriptions (e.g., defined low and high image quality ROIs) with better uniformity within prioritized ROIs may be achieved with substantially better management of dose using FFMCT. Though an ideal modulator is desirable, more simplistic dynamic modulator designs may still reap significant benefits over current static modulator approaches. FFMCT experiments using projection data acquired on a laboratory cone-beam CT unit further suggests that extension from theory to practice is feasible.

6.1.2. Impact

Based on the LNT model, reductions in dose translate linearly to reduced risk of cancer. Since different organs have different sensitivities to radiation, effective dose is the preferred and more
relevant indicator of impact on overall lifetime attributable risk of cancer. Relatively, the average decrease in effective dose was on the order of the differences in absolute dose observed for the thoracic imaging tasks evaluated. Decreased individual cancer risk from CT scans utilizing FFMCT could therefore be on the order of 20-50% depending on the imaging task and application compared to doses in conventional practice with similar image quality. Results also suggest that local dose reduction to radiation sensitive tissue could also be achieved in some instances without sacrificing the image quality objective, principally when the low dose and high image quality ROIs do not overlap. This result suggests that a further reduction in effective dose may be possible for the same absolute dose to the patient, increasing the overall benefit to risk ratio. Application of fluence field modulation in CT could therefore have a profound impact on patient care as the utility of the images would increase substantially while achieving much more effective management of the radiation dose due to imaging.

6.2. Limitations, Challenges and Future Directions

6.2.1. System Modeling

While the examples shown utilize a filtered-backprojection approach for reconstruction it is noted that other reconstruction methods could be explored provided that relationships between image quality and fluence are available. Some recent developments in noise predictors\(^\text{48,49}\) for statistically based iterative methods indicate that FFMCT could also be applied to non-linear reconstruction methods. Further, though a planar, parallel-ray geometry was assumed in the optimization, the framework is equally valid for alternative methods and/or geometries, including region-of-interest (ROI) imaging with backprojection of locally filtered projections\(^\text{37}\), and inverse geometry CT\(^\text{61,62}\). As shown in Chapter 5, accurate noise models also require modeling of the detector noise properties, which is an important factor in the evaluation of FFMCT in real systems. Other image quality and/or noise metrics such as the noise power spectrum\(^\text{79}\) (NPS) should also be considered in future studies.

In the studies presented, a simplified dose model with no simulation of x-ray scatter was employed. Given the substantial level of dose attributed to backscatter at CT energies, the inclusion of scatter in the models is likely necessary for more accurate dose prediction. However, reduced fluence to the surrounding volumes outside of ROIs suggests that the
backscatter to the target high image quality regions would be reduced significantly for the given scenarios\textsuperscript{36}; as a result, a higher level of dose reduction would be anticipated there without loss of SNR, depending upon the degree of modulation in neighbouring regions. Conversely, the remaining scatter contribution from high SNR ROIs to the surrounding volume may be non-trivial, suggesting that dose reduction near the target high SNR ROIs may be overestimated using the present models. Further, no modeling of beam hardening was included since the assumption was a monoenergetic beam. These effects should be studied by the introduction of a more complete dose model in future simulations. It is also recognized that moving from theory to practice would require consideration of other practical factors, including appropriate patient positioning.

6.2.2. Patient Modeling

Throughout this work, the approach presented has relied on a previous CT scan as an \textit{a priori} patient model for optimizing modulation profiles to meet image quality prescriptions. Of course, in many instances a previous CT scan has never been performed on the patient, or may not be available for the region of interest considered. An alternative approach could rely on a population based model adapted to the general size and shape of the patient; one could envision orthogonal 2D scout scans assisting in this modeling approach. However, since this method would largely rely on patient averages, it risks incorrectly compensating for patient specific anatomy. Another method could acquire a low dose prior CT scan to provide the patient model. Recall that in this work all optimizations were performed on low resolution images, which when applied to the high resolution counterparts, exhibited similar performance. These results suggest that a very low dose CT scan could adequately provide the \textit{a priori} knowledge required to accurately model the patient. Further, the low dose scan could potentially be incorporated into a “two exposure” technique as defined in Chapter 4. In lieu of an \textit{a priori} model, one could also consider a near real time technique where the choice of modulation is predicted based on a previous set of projections, such as suggested by Szczykutowicz et al.\textsuperscript{80} This technique has the advantage of providing patient specific modulation profiles in near real time in order to meet target signal values at the detector and more uniform noise properties across the image. The disadvantage of this approach is that it may not reap some of the benefits that may be afforded by optimization using \textit{a priori} knowledge, such as placing a higher priority on dose reduction for
tissues that are more radiation sensitive, or adjusting weights to tolerate greater noise non-uniformity if the tradeoff allows further significant dose reduction. Further investigations into these techniques will influence the effectiveness of FFMCT as well as its feasible translation into clinical practice.

6.2.3. On the Simplifying Assumptions Used in this Work

As discussed in various contexts above and in previous chapters, a number of simplifying assumptions have been made in the evaluation of the potential benefits of FFMCT in simulation. These assumptions simplified the optimization task and allowed for a more straightforward analysis of the results, where relatively few, yet physically fundamental, factors governed the outcome. The inherent trends observed, such as to changes in weights in the cost function, are expected to underlie increased levels of complexity, and can be useful in the design of further investigations that attempt to parse out the impact of other physical factors.

The goal of Chapter 5 was to remove a number of the simplifying assumptions made by considering the application of FFMCT to data acquired using an experimental CT system employing a realistic system geometry (e.g., fan-beam), and subject to non-idealities (e.g., additive electronic noise, noise correlations, imperfect detector, polychromatic beam). The results supported the observations made in simulation, providing strong evidence that the approach for FFMCT is robust in application to real CT systems and should yield similar benefits. Of the remaining assumptions, scatter and beam-hardening are the two largest physical factors that require further investigation. Background behind how these particularly relevant factors impact CT and the associated challenges posed to FFMCT are discussed in detail below.

6.2.4. Beam Hardening

The most common method for reconstruction in CT utilizes the filtered backprojection reconstruction method, which implicitly relies on an assumption of a monochromatic x-ray energy source. Though CT x-ray sources are polychromatic in nature, the beam can be approximately modeled as a monochromatic source with a single “effective energy”, defined such that the attenuation characteristics of the polychromatic beam are similar to that of a monochromatic beam of the given effective energy.
This model would be accurate if the spectrums of the incident beam and the exit x-ray beams were the same. However, when an object attenuates a polychromatic x-ray beam, the lower energies of the beam tend to be preferentially absorbed; this phenomenon, called “beam-hardening”, results in a spectrum exiting the object with a higher average energy than the beam that entered it. The discrepancy between the expected result using an effective energy approximation and the actual result is largest at regions that have been more highly attenuated, but also depend on the specific properties of the attenuating tissues. Beam hardening corrections to account for these differences are common practice in CT.

Physical modulators that use a strategy of partially attenuating the beam will inherently harden the beam to different degrees depending on the amount of attenuation observed. Given that the material properties of the attenuator are known and that an estimate of the patient anatomy is obtained from the initial reconstruction, post-processing corrections for beam hardening may be possible for accommodating the introduction of beam hardening from physical modulators. The patient model could also be used to explicitly model beam hardening in the optimization algorithm. It is interesting to note, however, that rather than introducing greater artifacts into the reconstruction without correction, the partial attenuator approach may actually serve to reduce some of the beam hardening artifacts induced by the patient. This effect may be observed since the attenuator could act to “pre-harden” portions of the beam that are incident on weakly attenuating regions of the patient; the end result is a beam that may have more uniform spectral properties across the detector. Alternatively, as discussed in Chapter 4, using a binary approach where the collimator positions define where the beam is either “on” or “off” could be used. In this case, a series of exposures with the collimators in different positions can be combined to form a single modulated projection as in the two exposure case of Chapter 4. Since the fluence that arrives at the detector has not been attenuated by the modulator, there is no additional beam hardening presented by the modulation system and conventional beam-hardening corrections that consider only the patient should be applicable.

6.2.5. Influence of Scatter on Image Reconstruction in FFMCT

In conventional CT, the ideal projection would measure only the portion of the primary x-ray beam that passed through the patient without interaction with the tissues along the way. In
general, however, scattered X-rays from the patient also arrive at the detector, contaminating the measurement of primary fluence. The fluence measured at the detector, \( N' \) can be described as

\[
N'(..) = N(..) + S(\xi)
\]

(6.1)

where \( N \) is the desired primary contribution and \( S \) is the additive undesired scatter component. The contribution of scatter to the measured signal is often characterized as a low frequency additive component where the contribution is largest near the centre of the projection and gradually reduces in magnitude near the periphery of the detector. When left uncorrected, the impact of scatter on conventional CT images is typically observed as “cupping” artifacts, where the reconstructed values are lower than would be expected, and where the greatest discrepancy is near the centre of the imaged object. In other words the attenuation coefficients of the object are underestimated due to a greater fluence arriving at the detector than expected.

As demonstrated by Szczykutowicz et al.\(^{41}\), the effects of uncorrected scatter may be much more pronounced in FFMCT images than in conventional CT. Unlike the primary beam, the amount of scattered radiation impinging at a given detector position \( \xi \) does not vary linearly with the corresponding modulation factor applied to the incident beam at that position, but instead continues to observe more gradual changes across the detector. During the log processing step of the projection, therefore, the modulation factors do not cancel for the scattered component as they do for the primary component (see Eq. (2.2)). The processing step including the scatter component can be described mathematically as\(^{41}\)

\[
\ln\left( \frac{N'(\xi, \mathbf{m})}{m(\xi)N(\xi)} \right) = -\ln\left( \frac{m(\xi)N + S(\xi, \mathbf{m})}{m(\xi)N(\xi)} \right) = -\ln\left( \frac{N}{N^o(\xi)} + \frac{S(\xi, \mathbf{m})}{m(\xi)N^o(\xi)} \right) .
\]

(6.2)

If the modulation profile is high frequency in nature, but the scatter component is not, this equation suggests that the second term in the natural logarithm will introduce high frequency components into the processed projection. These high frequency changes can manifest themselves as streaks, or where occurring at the same location in each projection such as with the 16 bin scenario in Chapter 4, as dominant ring artifacts\(^{41}\). Feasible implementation of FFMCT therefore requires an accurate and effective scatter correction method. The most accurate correction methods generally utilize Monte Carlo techniques; though typically slow, increased computing power, and faster algorithms\(^{81-83}\) may allow Monte Carlo predictions to be made on a
reasonable order of time (e.g., minutes or seconds) for practical implementation. Given that the approach for FFMCT already incorporates some *a priori* information in order to optimize modulation profiles, such modeling of the scatter profiles could potentially be explicitly included into the optimization algorithm and cost function. Alternatively, some research\(^{41,84}\) suggests that modulation patterns that are high frequency in nature may actually be useful for the characterization and correction of scatter; methods that have been proposed that rely on such primary modulation patterns have considered parsing the scatter from the primary fields in the Fourier domain\(^{84}\), and directly solving for the scatter component where high gradients are known to be present in the unprocessed projection data\(^{41}\).

6.2.6. Compensator Approaches

Chapter 4 examined the inclusion of possible physical constraints directly in the optimization algorithm. Such approaches are currently used in the field of IMRT, where fluence patterns for dose delivery are constrained by the shape and design of beam-shaping collimator leaves and optimized via direct machine parameter optimization (DMPO)\(^{85}\). A similar multi-leaf collimation approach for altering fluence patterns might also be applicable to FFMCT. Current MeV CT scanners for example, are already equipped with multi-leaf collimation for dose delivery application. The results of Chapter 4 suggest that other proposed methods for modulation including multi-source scanners and the “electronic bowtie”\(^{61}\), dynamic moving apertures\(^{45}\), and sliding wedges\(^{41}\) may also potentially be implemented. Moreover, the results suggest that the presented framework could be used to find optimal exposure levels for TCM using existing fixed compensators, including bowtie and fixed window type filters (by imposing the compensator method as a constraint on the modulation profile).

Though the use of simple modulators may still reap benefits over conventional techniques, physical confounding factors that may be introduced by the modulator design, including beam-hardening\(^{86-91}\) and changes to scatter profiles\(^{92-98}\), were left unexplored in this work (see discussion in Sections 6.2.4 and 6.2.5). Comparing the relative severity of these effects for different methods of modulation may ultimately influence their relative feasibility. For example, as mentioned above, partial attenuators may introduce significant beam hardening, while a multi-source electronic bowtie, or a multi-leaf collimator (used to completely block the beam with varied leaf positions) may potentially avoid changing the incident energy spectrum. Further
study is required to evaluate the impact of changes to beam characteristics introduced by fluence field modulation and the use of attenuators.

Another factor influencing feasibility is the relative speed of modulation mechanisms. Given the very fast rotation speeds of CT scanners today, the modulator must be able to dynamically change the incident fluence profile for hundreds of projections within a fraction of a second, or otherwise introduce a tradeoff with respect to imaging time which may not be desirable or feasible depending on the application. Recent work examining the speed requirements of dynamic collimators for ROI imaging has shown that the speed requirements on the motion of those collimators can be significantly reduced by moving them closer to the source. This placement would reduce the speed requirements of the modulator but would also increase the requirement on accuracy of the positioning. Given that nanoscale positioning accuracy is now available (e.g., using piezoelectric motors), this latter requirement may not be a limiting factor.

6.2.7. Measurement of the Incident Fluence Field

An implicit assumption of the approach for FFMCT presented is that an accurate measure of the incident fluence field is available. In other words, the error in the reference incident field is considered to be minimal or insignificant. In practice, one generally measures the fluence with no object in place as a reference for the incident fluence profile. Similarly, one possible mechanism for FFMCT might be running the FFMCT scan without the patient in the field of view. However, this method is not very practical since the scanning time for each patient would effectively be doubled, substantially increasing the duty cycle of the units. Additionally, in conventional CT a small portion of the detector outside of the patient field of view is often used to track variations of the average fluence output of the source per projection in order to account for tube fluctuations that may occur during the scan. However, this approach is not readily applicable to FFMCT in general, since fluence fluctuations measured at the detector periphery are no longer representative of changes to the incident fluence at other locations across the field of view. Creative investigation into alternative methods for measuring (or reliably predicting) the post modulation, pre-patient, fluence fields is therefore another necessary area for future research and practical implementation of FFMCT.
6.2.8. Image Quality Prescription

Though the results of these studies show greatly enhanced control over defining the noise characteristics in the reconstructed images, limitations were also observed with respect to how steep changes can occur between low and high image quality regions, and to what degree arbitrary values can be prescribed. Due to these limitations, appropriate selection of weights in the cost function was found to be very important for the prioritization of different regions or subregions.

An important open question is whether prescribing uniform image quality is preferable over prescribing image qualities based on a minimum tolerance (or a compromise between these two metrics). Though uniform image quality is desirable, some non-uniformity in prioritized regions may be tolerable and provide more favourable outcomes in terms of dose. Recent investigations into the impact of non-stationarity of noise on the observer, quantified in terms of a detectability index, may be readily applicable to choosing criteria best-suited to the task. Of interest for further study is therefore the inclusion of various metrics and/or their relative weights as well as incorporation of more advanced metrics such as detectability index and changes to the optimization approach accordingly. Such investigations may invoke observer studies to explore the relative benefits in image quality of different approaches.

Evaluations of high resolution images with added anomalies also indicated that small perturbations will not change the output modulation profile greatly. This outcome is important in situations where multiple scans are made to observe changes in anatomy. Future work should explore the limits of this assumption, for example, when tracking a surgical tool which would introduce very high contrast changes to the image.

6.2.9. Risk Based Optimization

One finding of particular interest in this study was the ability to redistribute dose within the patient while achieving the same or similar image quality objectives. Introducing prioritized regions for low dose had an overall weak change to the absolute dose to the patient, but a more significant change to the distribution of dose within the phantom. This finding motivates the substitution of dose in the cost function with effective dose, a measure found to be more directly associated with the lifetime attributable risk of cancer. Consideration of effective dose may
inherently reveal a greater benefit for some procedures than consideration of absolute dose. In particular, tasks where the target is less radiation sensitive (e.g., heart) than surrounding organs (e.g., lung) may find an overall greater benefit in terms of risk reduction using FFMCT.

6.2.10. Beyond Dose Reduction

Other potential imaging benefits can be recognized for FFMCT that were not demonstrated here, but may also be subject for future study. For example, the dynamic range of flat panel detectors may be challenged in exposure conditions that are well outside the detector’s linear range (i.e., the detector is both saturated and under-exposed in the same scan)\textsuperscript{32}. While bowtie filtration reduces these effects, FFMCT would allow for patient specific changes in exposure levels to compensate for dynamic range constraints. In addition, the scatter to primary ratio in cone-beam CT scans is expected to reduce significantly within target high quality regions because of the reduced exposure levels to the surrounding volume. The resulting improvements in image quality could greatly enhance the utility of cone-beam CT scans, extending their use beyond conventional image guidance and allowing for such things as tracking disease progression throughout the course of radiation therapy.
References


## Appendix A

### FFMCT Optimization Improvements over Original Algorithm (Graham 2006)

<table>
<thead>
<tr>
<th>Original Simulated Annealing (Graham 2006)</th>
<th>Improved Simulated Annealing (Bartolac 2012)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimization on low resolution object (64 x 64)</td>
<td>Optimization on low resolution object (64 x 64) with capacity to translate to high resolution data</td>
</tr>
<tr>
<td>A priori information required by algorithm based on cylindrical uniform water phantom</td>
<td>A priori information based on model of actual patient or phantom (i.e., includes varied attenuation coefficients)</td>
</tr>
<tr>
<td>Assumed symmetry in object and quality plan</td>
<td>No assumption of symmetry in object or plan</td>
</tr>
<tr>
<td>Optimization over 90 projections</td>
<td>Optimization over 192 projections (with capacity to interpolate to more)</td>
</tr>
<tr>
<td>Scaling (Object Size) and Noise Model Errors present (non-Poisson model employed, incorrect filter)</td>
<td>Corrections made to errors in geometry and noise modeling</td>
</tr>
<tr>
<td>Relative Dose estimates based on integral over input fluence</td>
<td>Absolute voxel to voxel dose estimates based on collision kerma and mass absorption coefficients of object from National Institute of Science</td>
</tr>
<tr>
<td>Computation time on the order of 8-10 hours</td>
<td>Computation on the order of 20 minutes by:</td>
</tr>
<tr>
<td></td>
<td>• Optimizing Initialization Pars based on heuristics</td>
</tr>
<tr>
<td></td>
<td>• Optimizing in stages, beginning with very low resolution modulation profile, ending with full resolution</td>
</tr>
<tr>
<td></td>
<td>• Improving Neighbour Generator – constrained the selection of new solution to certain projections, focused regions, and constrained resolution</td>
</tr>
<tr>
<td></td>
<td>• Increasing computing power (~2x faster)</td>
</tr>
<tr>
<td></td>
<td>Low resolution approximation with satisfactory results can be achieved in 2-3 minutes.</td>
</tr>
<tr>
<td>Noise Model restricted to Parallel Ray (Kak &amp; Slaney)</td>
<td>Noise Model extended to Fan Beam (Zhu et. al.)</td>
</tr>
<tr>
<td>No provisions for constraints</td>
<td>Various options for constrained cases built in to the neighbour generator</td>
</tr>
</tbody>
</table>
## Appendix B

**Impact of Weight Changes on the Optimization Outcome**

<table>
<thead>
<tr>
<th>Change</th>
<th>$w_q$</th>
<th>$w_d$</th>
<th>$W_q(r)$</th>
<th>$W_d(r)$</th>
</tr>
</thead>
</table>
| Increase | - Integral dose increases  
- Noisier modulation profile (increase iterations to compensate)  
- Solution more closely approaches prescribed noise distribution |
| | - Integral dose decreases  
- Modulation profile smoother  
- Trends to higher variance values than prescribed |
| | --Minor change in total dose outcome  
- Distribution in dose may change significantly  
- Greater agreement with prescribed parameters where $W_q$ higher; less uniform, less conformity elsewhere |
| | (See Chapters 3 and 5 for examples of varied local weight on image quality) |
| | - Minor Change in total dose outcome  
- Dose distribution changes, lower where higher $W_d$  
- Local increase in $W_d$ may sacrifice noise prescription there (if high) or bring closer to value (if low) |
| | (See Chapter 3 for example) |
| Decrease | - Integral dose decreases  
- Modulation profile smoother  
- Trends to higher variance values than prescribed |
| | - Integral dose increases  
- Noisier modulation profile (increase iters to compensate)  
- Solution more closely approaches prescribed noise distribution |
| | - Minor change in total dose outcome  
- Dose distribution may change  
- Lesser agreement with prescribed parameters where $W_q$ decreased; greater conformity to prescribed values elsewhere |
| | (See Chapters 3 and 5 for examples of varied local weight on image quality) |
| | - Minor Change in total dose outcome  
- Dose distribution changes, higher in higher image quality regions  
- Local decrease in $W_d$ in high priority image quality ROI may bring solution closer to prescribed value there |
| | (See Chapter 3 for example) |
Appendix C

Summary of Relevant Contributions

a. Articles published in refereed journals:

b. Other refereed contributions (* indicates presenting author for presentations):
Copyright Acknowledgments

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