Optimization of Image Guided Radiation Therapy Using
Limited Angle Projections

by

Lei Ren

Medical Physics Graduate Program
Duke University

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James T. Dobbins, III.

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John Kirkpatrick

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

2009
ABSTRACT

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Abstract

Digital tomosynthesis (DTS) is a quasi-three-dimensional (3D) imaging technique which reconstructs images from a limited angle of cone-beam projections with shorter acquisition time, lower imaging dose, and less mechanical constraint than full cone-beam CT (CBCT). However, DTS images reconstructed by the conventional filtered back projection method have low plane-to-plane resolution, and they do not provide full volumetric information for target localization due to the limited angle of the DTS acquisition.

This dissertation presents the optimization and clinical implementation of image guided radiation therapy using limited-angle projections.

A hybrid multiresolution rigid-body registration technique was developed to automatically register reference DTS images with on-board DTS images to guide patient positioning in radiation therapy. This hybrid registration technique uses a faster but less accurate static method to achieve an initial registration, followed by a slower but more accurate adaptive method to fine tune the registration. A multiresolution scheme is employed in the registration to further improve the registration accuracy, robustness and efficiency. Normalized mutual information is selected as the criterion for the similarity measure, and the downhill simplex method is used as the search engine. This technique was tested using image data both from an anthropomorphic chest phantom.
and from head-and-neck cancer patients. The effects of the scan angle and the region-of-interest size on the registration accuracy and robustness were investigated. The average capture ranges in single-axis simulations with a 44° scan angle and a large ROI covering the entire DTS volume were between -31 and +34 deg for rotations and between -89 and +78 mm for translations in the phantom study, and between -38 and +38 deg for rotations and between -58 and +65 mm for translations in the patient study.

Additionally, a novel limited-angle CBCT estimation method using a deformation field map was developed to optimally estimate volumetric information of organ deformation for soft tissue alignment in image guided radiation therapy. The deformation field map is solved by using prior information, a deformation model, and new projection data. Patients’ previous CBCT data are used as the prior information, and the new patient volume to be estimated is considered as a deformation of the prior patient volume. The deformation field is solved by minimizing bending energy and maintaining new projection data fidelity using a nonlinear conjugate gradient method. The new patient CBCT volume is then obtained by deforming the prior patient CBCT volume according to the solution to the deformation field. The method was tested for different scan angles in 2D and 3D cases using simulated and real projections of a Shepp-Logan phantom, liver, prostate and head-and-neck patient data. Hardware acceleration and multiresolution scheme are used to accelerate the 3D estimation process. The accuracy of the estimation was evaluated by comparing organ volume,
similarity and pixel value differences between limited-angle CBCT and full-rotation CBCT images. Results showed that the respiratory motion in the liver patient, rectum volume change in the prostate patient, and the weight loss and airway volume change in the head-and-neck patient were accurately estimated in the 60° CBCT images. This new estimation method is able to optimally estimate the volumetric information using 60-degree projection images. It is both technically and clinically feasible for image-guidance in radiation therapy.
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<th>Description</th>
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<tbody>
<tr>
<td>1-D</td>
<td>One-dimensional</td>
</tr>
<tr>
<td>2-D</td>
<td>Two-dimensional</td>
</tr>
<tr>
<td>3-D</td>
<td>Three-dimensional</td>
</tr>
<tr>
<td>4-D</td>
<td>Four-dimensional</td>
</tr>
<tr>
<td>AP</td>
<td>Anterior-posterior</td>
</tr>
<tr>
<td>API</td>
<td>Application program interface</td>
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<tr>
<td>CBCT</td>
<td>Cone-beam CT</td>
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<tr>
<td>CC</td>
<td>Cross correlation</td>
</tr>
<tr>
<td>CNR</td>
<td>Contrast to noise ratios</td>
</tr>
<tr>
<td>CS</td>
<td>Compressed sensing</td>
</tr>
<tr>
<td>CTV</td>
<td>Clinical target volume</td>
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<tr>
<td>DRR</td>
<td>Digitally reconstructed radiograph</td>
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<tr>
<td>DTS</td>
<td>Digital tomosynthesis</td>
</tr>
<tr>
<td>EPID</td>
<td>Electronic portal imaging device</td>
</tr>
<tr>
<td>FBP</td>
<td>Filtered back projection</td>
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<tr>
<td>GD</td>
<td>Image intensity gradient difference</td>
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<tr>
<td>GPU</td>
<td>Graphics processing unit</td>
</tr>
<tr>
<td>GTV</td>
<td>Gross tumor volume</td>
</tr>
<tr>
<td>IGRT</td>
<td>Image-guided radiation therapy</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Definition</td>
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<td>--------------</td>
<td>------------</td>
</tr>
<tr>
<td>kV</td>
<td>kiloVoltage</td>
</tr>
<tr>
<td>LAT</td>
<td>Lateral</td>
</tr>
<tr>
<td>mTRE</td>
<td>Mean target registration error</td>
</tr>
<tr>
<td>MV</td>
<td>Megavoltage</td>
</tr>
<tr>
<td>NMI</td>
<td>Normalized mutual information</td>
</tr>
<tr>
<td>OBI</td>
<td>On-board imager</td>
</tr>
<tr>
<td>PI</td>
<td>Pattern intensity</td>
</tr>
<tr>
<td>PSNR</td>
<td>Reconstructed pixel signal to noise ratio</td>
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<tr>
<td>PTV</td>
<td>Planning target volume</td>
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<tr>
<td>ROI</td>
<td>Region of interest</td>
</tr>
<tr>
<td>STDEV</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>TRE</td>
<td>Target registration error</td>
</tr>
<tr>
<td>TV</td>
<td>Total variation</td>
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Acknowledgements

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Dedication

To my wife Jia, for your endless support to my research and my life during my Ph.D. study. Thank you for offering me unconditional love and support throughout the course of this dissertation.
1. Introduction

1.1 Prelude

With the development of the kV on-board imager (OBI), cone-beam CT (CBCT) has become a valuable tool for image-guided radiation therapy (IGRT)\(^1\)\(^-\)\(^5\). However, due to its long acquisition time (~1 min), high imaging dose to the patient (2–9 cGy), and potential mechanical constraint (360° gantry rotation required)\(^6\), CBCT may not always be preferable for clinical use. Alternatively, digital tomosynthesis (DTS) is a quasi-three-dimensional (3-D) imaging technique which reconstructs images from a limited angle of projections with shorter acquisition time (<10 second), lower imaging dose (<1 cGy), and less mechanical constraint (<44° gantry rotation)\(^7\). These features could be extremely beneficial for imaging organs affected by respiratory motions and for those patient treatments when a full gantry rotation is mechanically impossible\(^8\)\(^-\)\(^11\). However, DTS images reconstructed by the conventional filtered back projection (FBP) method have low plane-to-plane resolution, and they do not provide full volumetric information for target localization due to the limited angle of the DTS acquisition. Therefore, it is not clear whether DTS can be used as an accurate and reliable tool for image guidance in radiation therapy.
1.2 Specific aims

The goal of this study is to investigate the feasibility of using DTS for patient rigid-body alignment and develop novel methods to improve the volumetric information in images reconstructed using limited-angle projections.

The specific aims are as follows:

Aim 1: Prove the feasibility of performing rigid-body registration between reference and on-board DTS images for patient positioning guidance in radiation therapy.

• Aim 1A: Develop an automatic rigid body registration method for image guidance using DTS images.

• Aim 1B: Investigate the accuracy and robustness of the automatic rigid body registration method.

Aim 2: Prove that the on-board limited-angle CBCT volume estimated by a deformable estimation method can provide accurate information about organ motion and soft tissue deformation.

• Aim 2A: Develop a new method to optimally estimate on-board CBCT from prior CT or CBCT using a deformable model based on on-board limited angle projections.

• Aim 2B: Compare the estimated on-board CBCT images with the on-board full rotation CBCT to evaluate the accuracy and robustness of this method.
### 1.3 Dissertation outline

The remainder of this dissertation is organized as follows:

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2. Background and clinical significance

2.1 Background introduction

2.1.1 Image guided radiation therapy (IGRT)

The tumor control probability for radiation therapy is proportional to the radiation dose delivered to the tumor, which is usually explained by a linear-quadratic model of cell killing. One of the important limiting factors in increasing the dose to the tumor is the radiation damage to the nearby healthy tissues. In addition to dose tolerance, the irradiated volume of normal tissue is a crucial parameter in the development of radiation induced toxicity. Traditionally, the irradiated volume covers the clinical target volume (CTV), which includes the gross tumor volume (GTV) and the area with microscopic disease surrounding the tumor. To ensure a sufficient coverage of the CTV, a margin is added to the CTV to compensate for daily positioning errors and internal organ motions, resulting in the planning target volume (PTV), to which the radiation dose is prescribed. To decrease the irradiated volume of nearby organs, it is necessary to decrease the PTV itself and thereby limit the volume of healthy tissue that is intentionally irradiated. Various radiation treatment techniques have been developed to precisely deliver highly conformal radiation to the target and minimize the radiation dose to normal tissues. One of the challenges for delivering conformal radiation is to accurately localize treatment target.
Recently image guided radiation therapy (IGRT) is introduced to improve the radiation deliver accuracy and precision. One important development in IGRT is to use in-room x-ray imaging techniques to guide radiation therapy treatment\textsuperscript{12,13}. The image guidance in IGRT is able to provide accurate information about patient positioning and organ motions, which can be used to correct positioning errors and control organ motion effects during the treatment. As a result, the radiation dose delivery accuracy is significantly improved, and correspondingly the PTV margins can be substantially reduced, leading to a substantial reduction in the volume of irradiated normal tissues. This reduction of the irradiated volume helps reduce the damage caused to the health tissues, allowing us to escalate the dose to the tumor to increase the tumor control probability\textsuperscript{14}.

2.1.2 Different imaging techniques used in IGRT

The imaging techniques used in IGRT include planar imaging techniques such as electronic portal imaging devices (EPID) and volumetric imaging techniques such as cone beam CT (CBCT).

EPID is the currently most widespread planar IGRT technology which was first described by Leong et al\textsuperscript{15}. The major advantage of this approach is the utilization of the actual treatment beam to ensure alignment of beam and target. In principle the imaging isocentre is identical to the treatment isocentre. In addition, the EPID can be used for
dose measurements, which is extremely useful in quality assurance and dosimetric treatment verification. However, the clinical application of EPID is limited due to the fact that it can’t provide 3D volumetric image information and it has poor soft tissue imaging contrast.

CBCT is a recently developed volumetric imaging technique for IGRT, which reconstructs tomographic images from a series of two-dimensional kV radiographs. These kV radiographs are acquired by the on-board imager (OBI) mounted on the gantry of the linear accelerator (Varian medical Systems, Palo Alto, CA). The same axis of rotation is shared between the kV imaging and MV treatment beams, and the central axis of the kV beam is oriented perpendicular to the treatment MV beam. For the current version of Varian OBI system, around 600-700 projections are acquired over a 360° scan angle within 1 min while the volumetric reconstruction proceeds in parallel. CBCT has become a powerful tool for IGRT because it is able to provide 3D volumetric images with good soft tissue contrast. However, CBCT may not always be preferable for clinical use due to its long acquisition time (~1 min), high imaging dose to the patient (2–9 cGy), and potential mechanical constraint (360° gantry rotation required).

Alternatively, digital tomosynthesis (DTS) is a quasi-three-dimensional (3D) imaging technique which reconstructs images from a limited angle of cone beam projections with shorter acquisition time (<10 second), lower imaging dose (<1 cGy), and less mechanical constraint (<44° gantry rotation). These features could be extremely
beneficial for imaging organs affected by respiratory motions and for those patient
treatments when a full gantry rotation is mechanically impossible. However, DTS
images reconstructed by the conventional FBP method have low plane-to-plane
resolution and do not provide full volumetric information for target localization due to
the limited angle of the DTS acquisition.

2.1.3 Image registration in IGRT

Image registration is an extremely important step in IGRT. The purpose of image
registration is to find the transformation (translation, rotation and preferably
deformation) that maps the daily image set onto the reference image set to obtain the
corresponding adjustments that are required to align the target volume and the
treatment beam as accurately as possible. The reference image set is usually generated at
the time of treatment planning and represents the ideal situation (that is, perfect
alignment of treatment beam and target volume). Image registration can be
accomplished manually or automatically. Compared with manual registration,
automatic registration is user independent and more efficient. Automatic registration
can be classified into two categories: rigid-body registration and deformable registration.
Rigid-body registration is used to register the rigid-body transformations between
reference and target images, which include translations along and rotations around
three axes in the Cartesian coordinate system. Deformable registration is used to register
the deformation between reference and target images. Specific automatic registration methods can be classified into feature based methods and intensity based methods\textsuperscript{19}. Feature based methods compare points, curves, or surfaces extracted as features in the image and determine the transformation between these features. These methods are usually fast and accurate, but they generally require manual feature extraction prior to the registration. Therefore, it is difficult to make feature based methods fully automatic. Intensity based methods directly use the image intensity values for registration, so they can be fully automated. These two categories of registration methods have been developed for the registration of various imaging modalities, including 2D radiographs, CT, and CBCT\textsuperscript{20-24}. However, none of them have been developed for the registration of DTS images.

In this study, we developed a hybrid multiresolution registration technique for automatic registration between reference and on-board DTS images. This technique uses a faster but less accurate static method to achieve an initial registration, followed by a slower but more accurate adaptive method to fine tune the registration. This approach is implemented in several stages, each using a higher resolution than the previous stage. Normalized mutual information is selected as the similarity measure, and the downhill simplex method is used as the search algorithm. This registration technique was tested using image data from an anthropomorphic chest phantom and also from eight head-and-neck cancer patients. The accuracy and robustness of the registration were
evaluated for two different DTS scan angles (44° and 22°) and two different region-of-interest (ROI) sizes. The necessity of using the fine tuning adaptive method was validated by comparing the registration results of the hybrid technique with the results of the static method.

2.1.4 Image reconstruction methods

2.1.4.1 Filtered back projection method

One conventional way to reconstruct the DTS images using OBI projections is the filtered back projection (FBP) method, which was described by Godfrey et al.9 FBP method is very efficient in terms of reconstruction time, but the DTS images reconstructed by the FBP method have low plane-to-plane resolution and do not provide full volumetric information for target localization.

2.1.4.2 Novel reconstruction methods using undersampled data

Several other image reconstruction methods have been developed to improve the image quality for reconstruction using undersampled projection data. One category of methods is based on the compressed sensing (CS) theory, and they have been implemented for image reconstruction from limited-views and limited-angle projection data.25-33 However, these methods generally require the sparseness prior of the image to be reconstructed which may not always be true for medical images. Another category of
methods uses deformable registration for image reconstruction. These methods were
developed only for 4D CT and 4D CBCT image reconstruction \cite{34-39}, and no such method
has been developed for limited-angle DTS reconstruction.

In this dissertation, a novel CBCT estimation method was developed to use a
deformation field map to optimally estimate volumetric information from limited-angle
projections. In this method, patients’ planning CT data or on-board CBCT data acquired
in a previous treatment session are used as prior information. After the initial rigid body
alignment of the patient using FBP based DTS images, the differences between the
patient’s new anatomy and prior anatomy are the deformation of internal organs and
soft tissues and the residual misalignment of bony structures. The patient’s new image
volume to be reconstructed is then considered as a deformation of the patient’s prior
image volume. Instead of directly solving the pixel values of the new image volume in
the reconstruction, we propose to solve the deformation field of the prior image volume
based on a deformation model and the new projection data acquired within a limited
angle span. The new on-board CBCT image is then obtained by deforming the prior CT
or CBCT image volume according to the solution to the deformation field.

2.2 Clinical significance

Based on the development in this project, limited-angle imaging can become a
valuable image guidance tool for IGRT. This new imaging technique has substantially
less imaging dose, shorter scan time and less mechanical constraint than full-rotation CBCT. Therefore, it can be used for patient positioning verification on a daily basis.
3. Hardware acceleration of DRR generation using the computer graphics card

A DRR is the simulation of a two-dimensional (2D) x-ray projection computed from conventional planning CT data. DRR generation is an important and time consuming step in both DTS image registration and image reconstruction. This chapter will focus on the acceleration of DRR generation using computer graphics card.

In general, DRR computation is a volume rendering process. Several volume rendering techniques have been applied for DRR computation. The most straightforward is the ray-casting algorithm, which is a simplified version of the ray-tracing without considering light reflection or scattering and only finds the intersection of a ray with all points of a volume/object. The core concepts of any ray-casting algorithm are to find the intersections of a ray with the voxels of the volume through which it passes and then to compute the integral of voxels’ gray values along each ray. Resulted images exhibit good image quality with simple implementation, but computation time is long. In order to accelerate this process, the improved version based on the shear warp factorization method was introduced. However, for clinical use it is still not sufficiently fast enough to meet the requirements for on-board image registration or image reconstruction. These algorithms have been implemented on specially designed hardware, such as ASIC chip (Terarecon Inc.) and FPGA board (Mercury Computer System Inc.). Real-time volume rendering performance was achieved, but developing algorithms on this hardware requires advanced computer
science proficiency which makes implementation impractical for most medical researchers.

Motivated by a fast-growing PC game industry, modern PC graphics hardware gained powerful computation capability by adopting the highly parallel structure previously owned by high performance hardware used in graphics workstations. It is now used in many engineering applications which require intensive computation, such as industry design and simulation. In addition, the application program interface (API) of these graphics hardware was standardized and well maintained to provide a convenient development environment for general-purpose users for quickly building their applications. In this study, a fast implementation of the ray-casting algorithm for DRR reconstruction was implemented on graphics hardware for accelerating the process of DTS reconstruction. To evaluate this new application, the performance and image quality of DRRs produced by the hardware and software methods and the RDTS images subsequently reconstructed from the hardware and software based DRRs were compared.
3.1 Graphics hardware fundamentals

![Diagram of graphics pipeline](image)

**Figure 1:** The standard graphics pipeline of GPU for display traversal

The processing pipeline of a graphics processing unit (GPU) is illustrated in Fig. 1. Initially, a 3D model consisting of several geometrical objects is established in a coordinate system specified by a standard graphics programming language such as OpenGL (Fig. 1 a). A set of vertices are used to define these geometrical objectives (Fig. 1 b). Complex objects are decomposed into several geometrical primitives, such as planar polygons via geometric processing (Fig. 1 c). Next, these planar polygons are converted...
to a 2D array of fragments (Fig. 1 d) via a rasterization operation. Then, a series of per-fragment operations are performed on these fragments to apply special effects such as light and texture. Among these operations, texture mapping is the most important step. A texture is an image stored in the texture memory of a GPU and it is associated with the polygon in user-specified transforms. During a per-fragment operation, texture pixels (texels) are mapped onto fragments (Fig. 1 e) via user-specified transforms. As a texel might not exist at a certain fragment position, interpolation is performed by fast hardwired circuitry. Once the texture mapping on fragments is accomplished, the texture mapped fragments are drawn on a frame buffer and later displayed on screen (Fig. 1 f).

To provide a convenient way of programming the graphics hardware, an API (consisting of hundreds of routines) is needed. This API acts as an interface between the high-level programming language and the specific device driver for the identified hardware. Currently, there are two important APIs for graphics hardware available: OpenGL and Direct3D. OpenGL is the API originally developed by Silicon Graphics industries. Since its introduction in 1992, it has become the industry’s most widely used and supported 2D and 3D graphics API. It is an open standard and extendible with an OpenGL extension. It can be used in different programming languages and on different platforms. Direct3D is a part of Microsoft’s DirectX API and it is only available for Microsoft Windows operating systems. The difference in functionality between OpenGL
and Direct3D is marginal. As opposed to OpenGL, Direct3D is not extendable and not an open standard. In this study, we use OpenGL for graphics hardware programming.

### 3.2 Ray-casting algorithm

The DRRs are produced by a ray-casting algorithm with the assumption that the volume is represented as a collection of points sampled at a grid. The value of a point is the linear attenuation coefficient of a material with distribution described by function \( \mu(x, y, z) \). A ray from a source located outside the object (with intensity \( Q_0 \)) traverses the object and reaches a 2D detector oriented at an angle \( \varphi \). The intensity collected in bin \((u, v)\) of the detector will be recorded as

\[
C^{0}_{\varphi}(u, v) = Q_0 \cdot e^{-\int_{0}^{t} \mu(t) \, dt}
\]  

where \( t \) is thickness variable of material defined along a ray and \( L \) is the distance between the source and the detector bin. By defining \( q_{\varphi}(u, v) = -\ln\left[C^{0}_{\varphi}(u, v) / Q_0\right] \), the transmission Eq. (1) can be rewritten as

\[
q_{\varphi}(u, v) = \int_{0}^{t} \mu(t) \, dt
\]  

It can be further approximated using a discretized form as

\[
q_{\varphi}(u, v) = \sum_{k=0}^{L/A} \mu(k \Delta t) \Delta t
\]
Here, $\Delta t$ is the step size varying across the slice. In a matrix form, Eq. (3) can be rewritten as

$$q_i^p = \sum_{j=0}^{N^3-1} \sum_{k=0}^{N^3-1} \mu_{jk} w_{ijk}, \quad i \in [0, K, N^D - 1]$$

( $N^D = N^{D_x} \times N^{D_y}$).

Here, $N^3$ is the total number of voxels contained in a CT slice and $N$ is the number of CT slices. $N^{D_x}$ and $N^{D_y}$ are the numbers of pixels along the X and Y dimensions of the detector. $w_{ijk}$ is the weight with which the object voxel $j$ (of value $\mu_{jk}$) contributes to detector pixel $i$ (with value $q_i^p$). These weights are determined by interpolation algorithms and integration rules.

### 3.3 Hardware implementation of ray-casting algorithm

In conventional 2D texture mapping, volume slices of a planning CT are stored as a stack of 2D images in the texture memory of a GPU, and processed slice-by-slice during volume rendering. Most new graphics hardware supports 3D texture mapping which allows a stack of 2D images to be stored as a 3D volume in texture memory. Thus, volume rendering can be accomplished at one time. In addition to fast volume rendering, 3D texture mapping utilizes trilinear interpolation instead of conventional bilinear interpolation for texture computation. It avoids the strip artifact on the final images introduced by 2D texture mapping due to the nonhomogeneous sampling along the slice.
plane during volume rendering. Graphics hardware with 3D texture mapping capability is strongly recommended and adopted in this study for the best volume rendering performance.

An on-board imager (OBI) is used to acquire x-ray images while the patient is on the treatment couch. It enables clinicians to obtain high-resolution x-ray images to pinpoint tumor sites and adjust patient positioning when necessary. To simulate the x-ray imaging process obtained by such a system, the setting of exact reconstruction geometry is needed. The center of the reconstructed object coincides with the origin of acquisition system (shared by both OBI and Linac system). The OBI system rotates within the plane (X-Y plane) perpendicular to the central axis (Z axis). The distance between the kV source and the central axis is defined by the source-to-axis distance, and the distance between the kV detector and the central axis is defined by imager-to-axis distance.

Similar to the classical ray-casting algorithm, the hardware algorithm simulates the physical process of cone-beam rays penetrating the volume containing the CT data and depositing the residual intensity on the plane of detector. The CT volume data with isotropic resolution in three dimensions were used as 3D texture. The value of each texel was saved in three color channels/components (red, green, and blue), which serves as $\mu_{ijk}$ in Eq. (4). The transparency value ($w_{ijk}$) of each texel is stored in an alpha channel which specify scale factor of the color components during a blending operation. The 3D
texture is set at isocenter and represented by the gray cube. To begin with, each parallel plane was converted to polygons via geometrical processing, then rasterized to 2D fragment. During a perfragment operation, the texels are mapped onto the 2D fragments via the predefined transformation in which the scan angle was taken into account. The texture mapping of each parallel plane performs the multiplication of $\mu_{jk}$ and $w_{ijk}$ for each pixel as it is conducted in the inner loop of Eq. (4). The texture mapped fragments were drawn on the frame buffer and later displayed on a screen. On the frame buffer, the incoming values of fragments composite with the values that already exist there. As the fragments corresponding to all parallel planes were composited, the DRR corresponding to the summation operation of the outer loop of Eq. (4) was accomplished.

### 3.4 Virtual extension of texture memory precision

In the graphic card, the CT volume was first loaded into a 3D texture map in the color channels of the graphic card. One color channel only has 8 bits, limiting the dynamic range of the data stored to be 0-255. To increase the dynamic range of the CT texture, we split the bits of each CT voxel into three parts and stored them in all three color channels of the graphic card. As shown in Fig 2, each CT voxel value was linearly scaled to the range 0-2047 (11 bits), and we stored the last four bits in the red channel, the next four bits in the green channel, and the left 3 bits in the blue channel. After the projection process, the projection pixel values generated in each color channel would be
shifted back to the original bit position and added together to recover the true projection pixel values.

Figure 2: Demonstration of the extension strategy for allowing high precision data stored in texture memory and deposited onto frame buffer.

After the loading of CT volume into the graphic card, the x-ray source position and the detector position were specified according to the real clinical setup, and the CT pose was adjusted to generate DRR at different angles. Each CT slice was then projected onto the detector plane according to the cone beam geometry, and the “attenuate” operator was used to combine the projections of all the slices to generate a DRR. The “attenuate” operator is an alpha blending mode, in which the projection of each slice is
divided by a constant and added together. To prevent the round-off errors caused by division in graphic card, we set the constant to be 1 so that the attenuate operator is just the sum of the projections of all the CT slices. The final projection image from graphic card was then loaded into the software and divided by the total slice number with double precision to generate DRR. To prevent overflow of the projection pixel values stored in the three color channels of the graphic card, we projected very 17 slices each time and added the resulted projection images together in software.

### 3.5 Results

A chest phantom was CT scanned with 1.25 mm slice thickness and in-slice pixel size of 0.94 mm. As 3D texture represents a volume with isotropic resolution in three dimensions, the original CT data were interpolated in the dimensions with low resolution. After the interpolation, the three orthogonal views of the CT volume to be loaded in 3D texture are shown in Figs. 3(a)–3(c). The central profiles along axial direction before interpolation (dot line) and after interpolation (solid line) are shown in Fig. 3(d), which indicated that there is no major interpolation error introduced. In addition, due to the limitation of GPU memory capacity, only part of CT volume as represented by the central cube of Figs. 3(a)–3(c) was loaded into texture memory. The central cube is 256×256×256 in size.
Figure 3: The (a) axial view, (b) coronal view, and (c) sagittal view of CT volume after interpolation along axial direction. (d) The central profile along axial direction before and after interpolation.
The total number of DRRs reconstructed was 660, which is equal to the number of projections obtained during scans using the OBI (covering 0°−360° with approximately 0.54° intervals). The DRRs reconstructed by the software and hardware methods in the anterior-posterior (AP) view are shown in Figs. 4(a) and 4(b). Another set of DRRs reconstructed by the software and hardware methods in the lateral (LAT) view are shown in Figs. 5(a) and 5(b). As the DRRs were obtained, their values were scaled to the same range (0–255). The central profiles of DRRs as indicated by the white lines are plotted in Figs. 4(c) and 5(c).
Visually, there is no major difference found between DRRs reconstructed using the two different methods. On the central profile plots, the minor noise introduced by the hardware method was observed. DRRs generated by the hardware method were subtracted from the ones generated by the software method. The difference images are shown in Figs. 4(d) and 5(d) in AP and LAT views. On average, the mean values and standard deviations of difference images are $-0.6\%\pm1.6\%$ for Fig. 4(d) and $1.0\%\pm0.9\%$ for Fig. 5(d). The correlation coefficients are 99.8% between DRRs of Figs. 4(a) and 4(b) and 99.9% between DRRs of Figs. 5(a) and 5(b).
Figure 6
DTS images were reconstructed from DRRs previously generated based on software and hardware methods. The DTS images were reconstructed in AP and lateral views with the setting of 311 planes (155 on either side of the isocenter), 0.5 mm plane spacing, and 0.5 mm in-plane pixel resolution. 80 of 660 DRRs (covering 40° scan angles) were used for DTS reconstruction. For reconstructing DTS images in AP view, the DRRs corresponding to the scan angles −20° to 20° were used. DRRs corresponding to the scan angles −250° to 290° were used for reconstructing DTS images in lateral view. The central slices of the DTS image sets for AP and lateral views using software-based DRRs are shown in Figs. 6(a) and 7(a) with their central profiles. The central slices of the DTS image sets for AP and lateral views using hardware-based DRRs are shown in Figs. 6(b) and 7(b) with their central profiles. There are visible noise observed on DTS images reconstructed using hardware-based DRR. As DTS images are obtained, their values were scaled to the same range (0–255). DTS images generated using hardware based DRRs were subtracted from those generated using software-based DRRs. Difference images are shown in Figs. 6(c) and 7(c) for AP and LAT views. On average, the mean values and standard deviations for the difference images are −6.4%±4.1% for the AP view and 5.5%±4.3% for the lateral view. The correlation coefficients are 98.7% for DTS.
images in the AP view as shown in Figs. 6(a) and 6(b) and 98.1% for DTS images in the lateral view as shown in Figs. 7(a) and 7(b). Two homogeneous regions of interest (ROIs) were chosen for evaluating contrast-to-noise ratios (CNRs) of the reconstructed DTS images. These ROIs were represented by square fields as shown in Figs. 6 and 7. Note that these squares only indicate the rough locations and areas of the ROIs. Below is the formulation used for computing CNR,

\[
\text{CNR} = \frac{\text{MEAN}(A) - \text{MEAN}(B)}{\text{MEAN}(B) \ast \text{STDEV}(B)}
\]  

(5)

MEAN(A) is the mean pixel value of ROI(A) which represents bone structure and MEAN(B) is the mean pixel value of ROI(B) which represents soft tissue. STDEV(B) is the standard deviation of pixel intensities in ROI(B). For DTS images shown in Figs. 6(a) and 6(b), CNRs are 0.027 and 0.025, and for DTS images shown in Figs. 7(a) and 7(b), CNRs are 0.048 and 0.034.

The noise introduced by the hardware-based DRR reconstructed process is further amplified by subsequent DTS reconstruction. For smoothing and noise suppression, a postprocessing median filter was applied. The filtered DTS images in AP and lateral views are shown in Figs. 6(d) and 7(d) with their central profiles. When subtracting the images in Fig. 6(d) from those in Fig. 6(a), the resulting mean values and standard deviations of the difference images were $-4.0\% \pm 2.8\%$. Similarly, when subtracting images in Fig. 7(d) from those in Fig. 7(a), the mean values and standard deviations of the difference images were $-1.4\% \pm 2.1\%$. 

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Figure 7
Figure 7: (a) DTS reconstructed in lateral view using DRR generated in the software method and its central profile. (b) DTS reconstructed in lateral view using DRR generated in the hardware method and its central profile. (c) The difference image between DTS of (a) and (b) and its central profile. (d) Postprocessed (b) by median filter and its central profile.

The correlation coefficients were 99.1% between Figs. 6(a) and 6(d) and 98.3% between Figs. 7(a) and 7(d). For the DTS image shown in Fig. 6(d), the CNR is 0.027, and for Fig. 7(d), it is 0.047. The total time needed to process 500 DTS slices by median filter is 1.5 min.

For reconstructing a set of 660 DRRs, the software method takes 189 min while the hardware method requires only 2.6 min. Based on this experimental result, it takes 0.23 s to reconstruct one DRR by the hardware method versus 17.18 s by the software method. With hardware acceleration, a set of 260 DRR images can be reconstructed within 1 min. In a temporary clinical trial, it only takes 15 s to generate 80 DRRs and another 2 min to reconstruct 100 DTS slices. Our next goal is to implement DTS reconstruction on hardware which makes total time for combined DRR and DTS reconstruction processes to be less than 1 min. The feasibility of this reconstruction algorithm was verified on several popular PC graphics cards including Nivida Quadro FX3500, Nivida Quadro FX1400, and ATI Radeon X1300, which were installed on a DELL precision workstation equipped with 3.20 GHz CPU (Intel Xeon) and 3.25 GB RAM. We believe that implementing this technique on general-purpose PC graphics hardware should be achievable.
3.6 Discussions

In this study, we have implemented a method for using common graphics hardware for accelerated reconstruction of DRRs, which are used for reference DTS image reconstruction. A substantial improvement of DRR reconstruction efficiency was achieved over the conventional software method. Nearly identical image quality was obtained using the hardware method. A minor difference is observed between central profiles of DRRs generated using software and hardware methods. The discrepancy may be negligible. With hardware-based DRR used for DTS reconstruction, there is an increased level of noise observed in the subsequently reconstructed DTS images. As indicated by CNRs, the influence on the visibility of anatomical structures is minor but not negligible. Such noise can be suppressed by using a median filter. The effectiveness of the median filter was demonstrated in Figs. 6(d) and 7(d) in which the CNRs increased to levels close to those of the DTS images reconstructed using the software-based DRRs as shown in Figs. 6(a) and 7(a). Since DTS is mainly used for target localization prior to radiation therapy, the minor loss of image contrast in exchange for a significant improvement in reconstruction efficiency would be acceptable.

The noise introduced by the hardware-based DRR reconstruction method is mainly caused by rescaling the value ranges of CT images to fit the limited bit size per pixel of the graphics hardware memory and the round-off error introduced by the
memory extension scheme. Such noise can be smoothed out by a median filter. Three ways were tested in different stages of DTS reconstruction. The first approach performed median filtering on DRR images. The second approach performed median filtering on DTS images. The third approach performed median filtering on both DRR images and DTS images. We found that the third approach was the most effective in suppressing noise but less time efficient. The image quality achieved by the second approach is closest to that of the third approach but more time efficient. The first approach is time efficient and smoothes out noise on DRR images but does not effectively suppress noise on final DTS images. Therefore, we adopted the second approach for noise suppression on DTS images for a balance between noise suppression and time efficiency.

Although there is an advantage to this hardware reconstruction method, certain limitations of hardware have to be considered. First, the maximum CT volume to be used was restricted by the physical size of GPU memory. Assuming there are 200 CT slices with thickness of 2.5 mm and in-slice pixel size of 1 mm, after interpolating volume data along the axial direction, the CT data will be $500 \times 512 \times 512$ in size with the same resolution in three dimensions. Considering that each texel is stored in four channels with size of 1 byte (8 bits), for storing whole volume data, the total memory to be allocated is $500 \times 512 \times 512 \times 4 \times 1 \text{ byte} = 500 \text{ Mbyte}$. Therefore, the CT data in this application easily reach the upper limit of memory size of the popular graphics
hardware which is usually equipped with 512 MB RAM. To overcome the memory limitation, advance graphics hardware with a large memory size is needed, but the hardware is more expensive. Alternatively, a virtual floating point texture memory can be created on CPU memory, but the hardware performance will be greatly compromised.

Second, the precision of texture memory was only 8 bits in each channel. If more bits are needed for storing data in high precision, the extension strategy as mentioned before can be used without any modification of graphics hardware. However, such extension has certain drawbacks. One problem is that although the compositing operation on the fragments is in float precision, the final precision is determined by the precision of frame buffer, which is in byte precision. Therefore, float precision resulting from the compositing process is rounded off on frame buffer. Another issue is that the compositied image on frame buffer needs to be read out after certain layers of fragments are composited to avoid overflowing of frame buffer. The read-out operation would add time to the DRR reconstruction. Therefore, an optimal read-out frequency should be determined for balancing time efficiency and image resolution. As graphics hardware design is progressing with miraculous speed with doubled performance of GPU every 6 months, it is reasonable to believe that the hardware restrictions mentioned above could be perfectly resolved in the near future.
3.7 Conclusion

A hardware-accelerated DRR reconstruction algorithm based on the principle of the ray-casting approach was implemented on PC graphics hardware with the support of a 3D texture mapping device. The subsequent DTS images were reconstructed from these hardware-based DRRs. The reconstruction efficiency of DRRs is substantially improved with the hardware method. A minor discrepancy between DRRs reconstructed using hardware and software methods was observed but determined to be negligible. This discrepancy could be amplified in the subsequently reconstructed DTS images. Noise in the reconstructed DTS images was effectively reduced using median filtering and the visibility of anatomical structures of these enhanced DTS images is similar to that which is achieved using the software-based DRR method. Hardware-based acceleration of DRR reconstruction was demonstrated to be an efficient method for reconstructing reference DTS images for target localization in radiation therapy.
4. Automatic registration between reference and on-board DTS images for rigid-body patient positioning

We previously developed a method for reconstructing reference DTS images from digitally reconstructed radiographs (DRRs) generated from planning CT data for registration with actual on-board DTS images reconstructed from the on-board projection images. A preliminary study showed that reference DTS is better than planning CT for registration with on-board DTS images due to the out-of-plane blurring effect. The analysis of the mutual information shared between reference and on-board DTS images indicated that under the right conditions, DTS registration could accurately detect rigid-body setup errors in radiation therapy. Unlike other image modalities, DTS images have high resolution in the reconstructed planes, but relatively low resolution along the plane-to-plane direction. This anisotropy of the resolution needs to be considered in developing the registration method for DTS.

In this study, we developed a hybrid multiresolution registration technique for automatic registration between reference and on-board DTS images. This technique uses a faster but less accurate static method to achieve an initial registration, followed by a slower but more accurate adaptive method to fine tune the registration. This approach is implemented in several stages, each using a higher resolution than the previous stage. Normalized mutual information is selected as the similarity measure, and the downhill simplex method is used as the search algorithm. This registration technique was tested using image data from an anthropomorphic chest phantom and also from eight head-
and-neck cancer patients. The accuracy and robustness of the registration were evaluated for two different DTS scan angles (44° and 22°) and two different region-of-interest (ROI) sizes. The necessity of using the fine tuning adaptive method was validated by comparing the registration results of the hybrid technique with the results of the static method.

4.1 Image acquisition

The planning CT data were acquired with a G.E. Lightspeed RT scanner (GE Healthcare, Waukesha, WI), and the on-board cone-beam projections were acquired by a kV on-board imager, which is mounted on the gantry of a Varian 21EX Clinac (Varian Medical Systems, Palo Alto, CA).

In the phantom study, an anthropomorphic chest phantom was used. Six reference metal balls of 2 mm diameter each were attached to the phantom in a non-coplanar fashion for localization purposes, as shown in Figure 8. The acquired planning CT image dimension was 512 × 512 × 351 with a voxel size of 0.94 × 0.94 × 1.25 mm, and the CBCT image dimension was 512 × 320 × 511 with a voxel size of 0.51 × 0.51 × 0.51 mm. On-board cone-beam projections were acquired approximately every 0.5° of gantry rotation, and the projection image size was 1024 × 768 with a pixel size of 0.388 × 0.388 mm. This projection image was then downsampled to be 512 × 384 with a pixel size of 0.776 × 0.776 mm for on-board DTS reconstruction.
In the head-and-neck cancer patient study, the planning CT image dimension was 512 × 512 × 150 with a voxel size of 0.98 × 0.98 × 2.5 mm, and the CBCT image dimension was 512 × 512 × 60 with a voxel size of 0.47 × 0.47 × 2.5 mm. The sampling frequency and the image size of the on-board cone-beam projections were the same as those in the phantom study.

4.2 Simulation of the patient setup deviation

The planning CT volume was first aligned with the on-board CBCT volume before the simulation of patient setup deviation. In the phantom study, 3D fiducial marker-based registration of the 6 non-coplanar reference metal balls attached to the phantom was used for the alignment. As shown in Figure 8, the metal balls were manually identified in CT and CBCT images, and the center of the mass of each ball was
calculated to determine its location. The 6-D rigid-body transformation relating the metal balls in the planning CT and on-board CBCT volumes was computed according to an algorithm described in the literature. The resulting transformation parameters were used to align the planning CT volume with the on-board CBCT volume. In the patient data study, 3-D mutual information based rigid-body registration between the CT and CBCT volumes was used for the initial alignment. The alignment was also manually adjusted by the physicist after the automatic registration.

After alignment between the planning CT and CBCT, setup deviations were simulated by translating and rotating the planning CT volume around its isocenter. Both single-axis and multiple-axis transformations were simulated in the planning CT volume. In the single-axis simulations, the planning CT volume was translated along, or rotated around, a single axis, while in the multiple-axis simulations, the planning CT volume was both translated along and rotated around all three axes. The values of the translational distances and the rotational angles in each multiple-axis simulation were set to be the same.

4.3 Reconstruction of reference and on-board DTS images

Reference DTS images are reconstructed from the DRRs generated from the planning CT data using the method described by Godfrey et al. We accelerated the
DRR generation process by implementing it in a 3D texture-map based volume-rendering process in the computer graphics card as explained in Chapter 3.\textsuperscript{20, 42, 43}

On-board DTS images are reconstructed from a subset of projection images from the CBCT by using a Feldkamp-type algorithm.\textsuperscript{44} The geometry of the on-board DTS reconstruction is shown in Figure 9. X is the lateral direction, Y is the superior-inferior direction, and Z is the anterior-posterior direction. The on-board x-ray tube rotates around the Y axis, and the detector is always opposite to the tube. Coronal on-board DTS slices are reconstructed from on-board projections within a limited scan angle that is symmetric to the Z axis, and sagittal on-board DTS slices are reconstructed from on-board projections within a limited scan angle that is symmetric to the X axis.

\textbf{Figure 9: Geometry of on-board DTS reconstruction}
Both reference and on-board DTS images have very high in-plane resolution, but relatively low resolution along the plane-to-plane direction due to the limited number of projections acquired. In this study, reference and on-board DTS images reconstructed in coronal view were used in the registration. The sizes of reference and on-board DTS images were both reconstructed to be $512 \times 320 \times 511$ with a voxel size of $0.51 \times 0.51 \times 0.51$ mm.

4.4 Registration between reference and on-board DTS images

We developed a hybrid multiresolution registration technique to automatically compare reference and on-board DTS images. This is an intensity based registration technique, which uses normalized mutual information as the similarity measure. This technique includes three major components: the static registration method, the adaptive registration method, and the multiresolution scheme. The static method is a direct and fast method for DTS registration, but it has relatively poorer registration accuracy for the out-of-plane rotations around the X and Y axes (defined in Fig. 9). The adaptive method has better registration accuracy especially for the out-of-plane rotations, but it is more time consuming than the static method. The hybrid method uses these two methods sequentially to achieve the optimal accuracy and efficiency. A multiresolution scheme is employed to improve the registration accuracy, robustness, and efficiency. The registration search engine is the Nelder-Mead downhill simplex method.
4.4.1 Similarity measure: normalized mutual information

Normalized mutual information is used as the standard to measure the similarity between reference and on-board DTS images because it has been widely applied in many image registration applications and has been proven to be accurate and robust. Formally, the normalized mutual information between reference and on-board DTS images is defined as:

\[
NMI(X;Y) = \frac{\sum_{x \in X} \sum_{y \in Y} p(x,y) \log_2 (p(x)p(y))}{\sum_{x \in X} \sum_{y \in Y} p(x,y) \log_2 p(x,y)}
\]  

(6)

where X and Y are the two sets of DTS images to be registered, p(x) and p(y) are the normalized histograms of X and Y separately, and p(x, y) is the normalized joint histogram of X and Y.

4.4.2 Registration methods

4.4.2.1 Static method

One direct and fast method for DTS registration is called the “static method.” The flow chart for this method is shown in Figure 10. The static method only reconstructs reference DTS images once from DRRs of the planning CT data, and then it manipulates the pose of the reference DTS images to match with the on-board DTS images. The anisotropic resolution of the reference DTS images doesn’t change during
the registration. The final registration results are the translations and rotations applied
to the reference DTS images that maximize the mutual information between the
reference and on-board DTS images.

**Figure 10: Flowchart of the static and adaptive methods for DTS registration**

The static method is a fast and easy way to register the two sets of DTS images
since it only involves 3D translations and rotations of the reference DTS images during
the registration. However, this method cannot correct the mismatch of the anisotropic resolution between the reference and on-board DTS images, which leads to large registration errors.

4.4.2.2 Adaptive method

To solve the resolution mismatch problem in the static method, the method called the “adaptive method” is proposed. The flow chart for this method is also shown in Figure 10. Instead of manipulating the pose of the reference DTS images, the adaptive method manipulates the pose of the CT data and regenerates DRRs and reference DTS images for each CT pose to match reference DTS with on-board DTS images. In this method, the anisotropic resolution of the reference DTS images is adaptively adjusted in each iteration of the registration to match with that of the on-board DTS images. The final registration results are the translations and rotations applied to the planning CT data that maximize the mutual information between the corresponding reference DTS images and the on-board DTS images.

The adaptive method is expected to exhibit better registration accuracy than the static method, especially in registering the out-of-plane rotations around X and Y axes. However, it is more time consuming than the static method due to the need to regenerate DRRs and reconstruct reference DTS images in each iteration loop of the registration.
4.4.2.3 Hybrid method

A hybrid method was developed to combine both the static and the adaptive methods in an efficient and accurate approach. In this approach, the static method is initially used to achieve a quick rough matching of the anatomical structures in the two sets of DTS images. This step leads to a rough estimate of the translational and rotational parameters, which are used as the starting point of the following adaptive method. The adaptive method is used afterwards to further fine tune these transformation parameters to achieve a more accurate matching of both the anatomical structures and the anisotropic resolutions of the two sets of DTS images. Since its starting point is close to the final convergence point, the adaptive method requires fewer iterations to converge to the final results, reducing the registration time significantly. Under this scheme, the hybrid method is able to achieve the same accuracy as the adaptive method and the similar efficiency as the static method.

4.4.3 Multi-resolution scheme

All the registration methods can be incorporated into a multiresolution scheme to improve their performance speed, robustness, and accuracy. Under this scheme, the registration is performed first at lower resolution levels by using the downsampled DTS images. After convergence, it proceeds at increasingly higher resolution levels, and
finally at full resolution level. In total three levels of resolution are employed in our study. The DTS volume is downsampled by a factor of 2 along each dimension for each lower level of resolution.

4.4.4 Registration search engine

The search engine used for maximization of normalized mutual information is the Nelder-Mead downhill simplex method, which is a commonly used nonlinear optimization algorithm. It is a numerical method for minimizing or maximizing an objective function in a multi-dimensional space, and it requires only function evaluations during the optimization. To minimize (or maximize) a function of N variables, the method is initialized with N+1 points, defining a non-degenerate simplex in the N-dimensional parameter space. The simplex adapts itself to the local landscape, and iteratively moves the vertices towards the final minimum (or maximum) of the function. In our study, the simplex is initialized with an initial starting point of the 6-D transformation parameters and with offsets around each transformation parameter. To prevent the algorithm from getting trapped at a local maximum, perturbations of ± 5° rotations and ± 5 mm translations along each axis are applied to the initial starting point in different trials. The registration result with the largest mutual information among all the trials is selected as the final result. The magnitude of these perturbations was determined based on the normal clinical setup deviations.
4.5 Evaluation methods

A widely used 3-D error measure for registration is the target registration error (TRE), which was proposed by Fitzpatrick et al.\textsuperscript{51,52} In our study, DTS registration accuracy is evaluated by calculating the mean target registration error (mTRE) proposed by van de Kraats et al.\textsuperscript{53} The mTRE is defined as:

\[
mTRE(P, T_{\text{reg}}, T_{\text{sim}}) = \frac{1}{k} \sum_{i=1}^{k} \left\| T_{\text{reg}} p_i - T_{\text{sim}} p_i \right\|
\]

(7)

where \( P = \{ p_i, i = 1, 2, ..., k \} \) is a fixed set of 3-D points uniformly distributed on a regular grid. \( T_{\text{reg}} \) is the registered transformation in the DTS images, and \( T_{\text{sim}} \) is the simulated transformation in the planning CT images. The mTRE is the average 3-D distance between the point \( p_i \) transformed with \( T_{\text{sim}} \) and the same point transformed with \( T_{\text{reg}} \). In our study, the 3-D points are sampled uniformly in a grid covering the volume being registered. The voxel size of the grid is 1 × 1 × 1mm.

The registration robustness is evaluated by calculating the capture range of the registration. A registration trial is considered successful if its mTRE is less than a preset threshold, which was 2mm in our study. The capture range is then defined as the range of the setup deviations over which the registration trials are all successful. The larger the capture range is, the more robust the registration is. The setup deviations were sampled every 2° and 2 mm for rotations and translations respectively for the capture range test.
The registration accuracy and robustness of the hybrid technique were investigated for two different DTS scan angles (44° and 22°) and two different ROI sizes by using image data from an anthropomorphic chest phantom and also from eight head-and-neck cancer patients. These tests were then repeated using the static method alone for comparison.

4.6 Results

4.6.1 Registration of simulated setup deviation in anthropomorphic chest phantom study

A simulated DRR of the anthropomorphic chest phantom and the corresponding on-board cone-beam projection image are shown in Figures 11(a) and 11(b) respectively. A coronal slice of the reconstructed reference DTS volume and the on-board DTS volume are shown in Figures 11(c) and 11(d) respectively.

4.6.1.1 Registration of the entire DTS volume

As shown in Figures 11(c) and 11(d), the entire DTS volume, which had an image size of 512 × 320 × 511 with a voxel size of 0.51 × 0.51 × 0.51 mm, was considered as a large ROI for registration.

The registration capture ranges of different methods using different scan angles are shown in Figure 12(a). For the hybrid method using a 44° scan angle, the average of the capture ranges was between -31 and +34deg for single-axis rotations and between -89 and +78mm for single-axis translations. The standard deviation of the capture ranges
was 25deg for the lower bound and 28deg for the upper bound for single-axis rotations, and 48mm for the lower bound and 41mm for the upper bound for single-axis translations.

Figure 11: Samples of a DRR, OBI projection, reference DTS images and on-board DTS images of the anthropomorphic chest phantom. (a) DRR, (b) the corresponding OBI projection image, (c) reference DTS slice, (d) the corresponding on-board DTS slice. Two different ROI sizes in DTS images were used for registration: the large ROI covers the entire reference and on-board DTS volume, while the small ROI covers the spinal cord volume, as shown in (c) and (d).
Figure 12
Figure 12: The registration capture ranges of both static and hybrid methods using different scan angles (44° and 22°) and different ROI sizes in the phantom study. Rx, Ry and Rz are single-axis rotations around X, Y, Z axes, which are defined in Fig. 9. Tx, Ty and Tz are single-axis translations along X, Y, Z axes. (a) The entire DTS volume was registered. (b) The ROI surrounding the spinal cord volume was registered.

The average, standard deviation, median, 90th percentile and maximum value of the mTREs are listed in Table 2.

Table 2: The average, standard deviation, median, 90th percentile and maximum of the mTREs of the hybrid method using a 44° scan angle in the phantom study.

<table>
<thead>
<tr>
<th></th>
<th>Single-axis (entire volume registered)</th>
<th>Multiple-axis (entire volume registered)</th>
<th>Single-axis (ROI registered)</th>
<th>Multiple-axis (ROI registered)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>1.0</td>
<td>1.0</td>
<td>0.7</td>
<td>0.9</td>
</tr>
<tr>
<td>STDEV</td>
<td>0.5</td>
<td>0.3</td>
<td>0.3</td>
<td>0.4</td>
</tr>
<tr>
<td>Median</td>
<td>1.1</td>
<td>1.0</td>
<td>0.6</td>
<td>1.0</td>
</tr>
<tr>
<td>90th percentile</td>
<td>1.8</td>
<td>1.4</td>
<td>1.2</td>
<td>1.4</td>
</tr>
<tr>
<td>Max</td>
<td>2.0</td>
<td>1.6</td>
<td>1.9</td>
<td>1.6</td>
</tr>
</tbody>
</table>

All values are in mm.

4.6.1.2 Registration of the ROI in DTS volume

As shown in Figures 11(c) and 11(d), the 68 × 143 × 21 mm spinal cord volumes in both reference and on-board DTS images were extracted as the smaller ROI to be registered.
The registration capture ranges of different methods using different scan angles are shown in Figure 12(b). For the hybrid method using a 44° scan angle, the average of the capture ranges was between -23 and +18 deg for single-axis rotations and between -33 and +43 mm for single-axis translations. The standard deviation of the capture ranges was 18 deg for the lower bound and 11 deg for the upper bound for single-axis rotations, and 21 mm for the lower bound and 19 mm for the upper bound for single-axis translations. The average, standard deviation, median, 90th percentile and maximum value of the mTREs are listed in Table 2.

**4.6.2 Registration of simulated setup deviation in head-and-neck cancer patient study**

Image data from eight head-and-neck cancer patients were used for the patient study. A simulated DRR of one patient and the corresponding on-board cone-beam projection image are shown in Figures 13(a) and 13(b) respectively. A coronal slice of the reconstructed reference DTS volume and the on-board DTS volume are shown in Figures 13(c) and 13(d) respectively.
Figure 13: Samples of a DRR, OBI projection, reference DTS image and on-board DTS image of a head-and-neck cancer patient. (a) DRR, (b) the corresponding OBI projection image, (c) reference DTS slice, (d) the corresponding on-board DTS slice. Two different ROI sizes in DTS images were used for registration: the large ROI covers the entire reference and on-board DTS volume, while the small ROI covers the spinal cord volume, as shown in (c) and (d).
4.6.2.1 Registration of the entire DTS volume

As shown in Figures 13(c) and 13(d), the entire DTS volume, which had an image size of $512 \times 320 \times 511$ with a voxel size of $0.51 \times 0.51 \times 0.51$ mm, was considered as the large ROI for registration.

The registration capture ranges of different methods using different scan angles are shown in Figure 14(a). For the hybrid method using a 44° scan angle, the average of the capture ranges was between -38 and +38 deg for single-axis rotations and between -58 and +65 mm for single-axis translations. The standard deviation of the capture ranges was 12 deg for the lower bound and 12 deg for the upper bound for single-axis rotations, and 14 mm for the lower bound and 15 mm for the upper bound for single-axis translations. The average, standard deviation, median, 90th percentile and maximum value of the mTREs are listed in Table 3.
Figure 14
Figure 14: The registration capture ranges of both static and hybrid methods using different scan angles (44° and 22°) and different ROI sizes in the head and neck cancer patient study. Rx, Ry, Rz, Tx, Ty and Tz are defined same as in Fig. 12. (a) The entire DTS volume was registered. Eight patients’ data were used for single-axis registration, and one patient’s data were used for multiple-axis registration. Error bars indicate standard deviation. (b) The ROI surrounding the spinal cord volume was registered using one patient’s data.

4.6.2.2 Registration of the ROI in DTS volume

As shown in Figures 13(c) and 13(d), the 80 × 79 × 34 mm spinal cord volumes in both reference and on-board DTS images were extracted as the smaller ROI for registration. The image data of one head-and-neck cancer patient were used for the registration test.

The registration capture ranges of different methods using different scan angles are shown in Figure 14(b). For the hybrid method using a 44° scan angle, the average of the capture ranges was between -18 and +25deg for single-axis rotations and between -35 and +39mm for single-axis translations. The standard deviation of the capture ranges was 2deg for the lower bound and 6deg for the upper bound for single-axis rotations, and 17mm for the lower bound and 21mm for the upper bound for single-axis translations. The average, standard deviation, median, 90th percentile and maximum value of the mTREs are listed in Table 3.
Table 3: The average, standard deviation, median, 90\textsuperscript{th} percentile and maximum of the mTREs of the hybrid method using a 44\textdegree{} scan angle in the head and neck cancer patient study

<table>
<thead>
<tr>
<th></th>
<th>Single-axis (entire volume registered)</th>
<th>Multiple-axis (entire volume registered)</th>
<th>Single-axis (ROI registered)</th>
<th>Multiple-axis (ROI registered)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average</td>
<td>1.4</td>
<td>1.4</td>
<td>1.4</td>
<td>1.5</td>
</tr>
<tr>
<td>STDEV</td>
<td>0.4</td>
<td>0.4</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>Median</td>
<td>1.4</td>
<td>1.4</td>
<td>1.4</td>
<td>1.5</td>
</tr>
<tr>
<td>90th percentile</td>
<td>1.8</td>
<td>1.8</td>
<td>1.7</td>
<td>1.7</td>
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<tr>
<td>Max</td>
<td>2.0</td>
<td>1.9</td>
<td>1.9</td>
<td>2.0</td>
</tr>
</tbody>
</table>

All values are in mm.

4.6.3 Registration of real patient setup deviation in head-and-neck cancer patient study

Real patient setup deviations of 10 head-and-neck cancer patients were registered using the hybrid multi-resolution method. The region surrounding the spinal cord was used as ROI in the registration. Both coronal and sagittal DTS images reconstructed using different scan angles (20 and 40 deg) were evaluated. The automatic registration between CT and CBCT images was used as the gold standard to evaluate the registration accuracy. The results for the registration errors are shown in table 4 and table 5.
**Table 4: Errors of automatic DTS registration using 10 different patients’ data**

<table>
<thead>
<tr>
<th></th>
<th>DTS40-coronal</th>
<th>DTS20-coronal</th>
<th>DTS40-sagittal</th>
<th>DTS20-sagittal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertical (mm)</td>
<td>-0.8 (0.3)</td>
<td>-0.9 (0.5)</td>
<td>-0.3 (0.3)</td>
<td>-0.1 (0.7)</td>
</tr>
<tr>
<td>Longitudinal (mm)</td>
<td>-0.2 (0.5)</td>
<td>-0.2 (0.8)</td>
<td>0.4 (0.3)</td>
<td>0.4 (0.4)</td>
</tr>
<tr>
<td>Lateral (mm)</td>
<td>0.4 (0.4)</td>
<td>0.5 (0.7)</td>
<td>0.2 (0.4)</td>
<td>0.2 (0.3)</td>
</tr>
<tr>
<td>Pitch (°)</td>
<td>-0.1 (0.7)</td>
<td>-0.3 (1.2)</td>
<td>-0.1 (0.4)</td>
<td>-0.1 (0.8)</td>
</tr>
<tr>
<td>Roll (°)</td>
<td>0.1 (0.5)</td>
<td>0.1 (0.5)</td>
<td>0.0 (0.9)</td>
<td>0.1 (1.5)</td>
</tr>
<tr>
<td>Yaw (°)</td>
<td>-0.1 (0.7)</td>
<td>-0.1 (1.0)</td>
<td>0.1 (1.0)</td>
<td>0.3 (1.0)</td>
</tr>
</tbody>
</table>

The numbers in the parenthesis are standard deviations.

**Table 5: Errors of automatic DTS registration using five treatment fractions’ data from one patient**

<table>
<thead>
<tr>
<th></th>
<th>DTS40-coronal</th>
<th>DTS20-coronal</th>
<th>DTS40-sagittal</th>
<th>DTS20-sagittal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertical (mm)</td>
<td>-0.6 (0.1)</td>
<td>-0.4 (0.2)</td>
<td>-0.1 (0.2)</td>
<td>0.0 (0.7)</td>
</tr>
<tr>
<td>Longitudinal (mm)</td>
<td>0.2 (0.3)</td>
<td>-0.3 (0.6)</td>
<td>0.6 (0.1)</td>
<td>0.6 (0.2)</td>
</tr>
<tr>
<td>Lateral (mm)</td>
<td>0.2 (0.6)</td>
<td>0.2 (0.6)</td>
<td>-0.2 (0.5)</td>
<td>0.0 (0.6)</td>
</tr>
<tr>
<td>Pitch (°)</td>
<td>0.1 (0.2)</td>
<td>0.2 (0.4)</td>
<td>0.0 (0.2)</td>
<td>0.0 (0.2)</td>
</tr>
<tr>
<td>Roll (°)</td>
<td>0.4 (0.3)</td>
<td>0.1 (0.2)</td>
<td>-0.5 (0.3)</td>
<td>-0.7 (0.9)</td>
</tr>
<tr>
<td>Yaw (°)</td>
<td>0.3 (0.5)</td>
<td>0.9 (0.5)</td>
<td>0.0 (0.2)</td>
<td>0.3 (0.2)</td>
</tr>
</tbody>
</table>

The numbers in the parenthesis are standard deviations.
4.7 Discussions

4.7.1 Selection of the similarity measure

Figure 15: The registration capture ranges of the hybrid method using a 44° scan angle, a large ROI covering the entire DTS volume and four different similarity measures in the phantom study. The similarity measures compared are cross-correlation (CC), pattern intensity (PI), gradient difference (GD) and normalized mutual information (NMI). Rx, Ry, Rz, Tx, Ty and Tz are defined same as in Fig. 12.

Initially, we tested four commonly used similarity measures using the phantom data to determine the most reliable and accurate similarity measure for the DTS registration. The similarity measures tested include normalized mutual information (NMI), cross correlation (CC), pattern intensity (PI) and image intensity gradient...
difference (GD). Details about the definition of these similarity measures can be found in a paper by Penney et al. The registration capture ranges for all the four similarity measures using the hybrid method and a $44^\circ$ scan angle are shown in Figure 15. Normalized mutual information has the largest registration capture range among all the four similarity measures. Therefore, normalized mutual information is selected as the similarity measure for 3-D-3-D DTS registration.

### 4.7.2 Comparison between the static method and the hybrid method

The registration results in Figures 12 and 14 show that the hybrid method for both $44^\circ$ and $22^\circ$ scan angles generally has much larger capture ranges than the static method in registering the out-of-plane rotations around X and Y axes, but similar capture ranges as the static method in registering the in-plane rotation around Z axis and the translations along all three axes. The reason is explained as following.

When the planning CT volume has rotations around X or Y axes relative to the on-board CBCT volume, the reconstructed reference and on-board DTS volumes have different high resolution planes inside the volume. Both the alignment of the anisotropic resolution and the alignment of the geometry affect the mutual information between the reference and on-board DTS images. In the static method, the reference DTS volume is directly rotated and translated, keeping its high resolution planes relatively unchanged. When the geometry of the reference and on-board DTS images is aligned, their high
resolution planes are misaligned. This misalignment decreases their mutual information and sometimes leads to an incorrectly located global mutual information maximum point. This phenomenon results in larger registration errors. On the other hand, in the adaptive method, the coronal reference DTS images are regenerated for each CT pose, so the high resolution planes in reference DTS images are adjusted adaptively. When the geometry of the reference and on-board DTS images is aligned, their high resolution planes are also aligned, making their mutual information the global maximum. As a result, the adaptive method is able to register the rotations with better accuracy. This improvement of registration accuracy leads to substantial increase of the registration capture ranges since the capture range is determined based on the registration accuracy.

When the planning CT volume only has in-plane rotation around the Z axis or translations along three axes, the reconstructed reference and on-board DTS volumes have the same high resolution planes initially. No resolution mismatch problem exists to affect the registration accuracy of the static method. Therefore, the static method has similar accuracy and capture ranges as the hybrid method.

4.7.3 Effects of the scan angle

As shown in Figures 12 and 14, the decrease of the scan angle from 44° to 22° mainly reduced the capture ranges for the out-of-plane rotations around the X and Y axes. For the static method, the decrease of capture ranges for smaller scan angles arises
because a smaller scan angle leads to more severe anisotropy of the DTS resolution and therefore more severe effects of resolution mismatch in the registration of out-of-plane rotations. The degradation of the accuracy of the static method leads to a worse starting point for the following adaptive method, so the accuracy of the adaptive method is degraded accordingly. As a result, the accuracy of the hybrid method is degraded and its capture range is reduced.

4.7.4 Effects of the ROI size

As shown in Figures 12 and 14, registration of a smaller ROI surrounding the spinal cord volume has smaller capture ranges than registration of the entire DTS volume. This is because less information is available for registration in the smaller ROI volume.

4.7.5 Asymmetry of the capture range

As shown in Figure 12 and 14, the capture range along each axis is not symmetric relative to 0. This asymmetry is due to the limitation of the downhill simplex method. To verify this, we simulated 40mm and -40mm translational setup deviations along X axis separately in the CT volume of the phantom, and then applied different translations along the X axis to the corresponding reference DTS images to match with the on-board DTS images. The normalized mutual information between reference and on-board DTS
images versus the amount of translations for 40 and -40mm setup deviations are plotted in Figures 16a and 16b respectively. Both NMI curves have a sharp peak at the true alignment location. When the starting point of the searching algorithm falls into a region where NMI increases as the point moves away from the global maximum peak, such as the points 80 and 0 in Figures 16a and 16b respectively, the algorithm is led away from the global maximum peak and the registration trial fails. On the other hand, when the starting point falls into a region where NMI increases as the point moves toward the global maximum peak, such as the points 0 and -80 in Figures 16a and 16b respectively, the algorithm is led toward the global maximum peak and the registration trial succeeds. In our study, the starting point of the searching algorithm is always at 0, so the registration trial succeeds for 40mm translational setup deviation, but fails for -40mm translational setup deviation, causing the registration capture range to be asymmetric.

Although perturbations of ± 5° rotations and ± 5 mm translations along each axis are applied to the starting point to prevent the algorithm from being trapped in a local maximum, they are not large enough for the large setup deviations simulated here. To solve this problem, we can add more perturbations to the starting point, but the registration efficiency will be degraded significantly.
Figure 16: Normalized mutual information between reference and on-board DTS images versus the amount of translations along X axis applied to the reference DTS images during the registration of 40 or -40mm translational setup deviations along X axis. (a). Registration of 40mm translational setup deviation along X axis. Registration trial succeeds when the search starting point is at 0, but fails when the search starting point is at 80. (b) Registration of -40mm translational deviation along X axis. Registration trial succeeds when the search starting point is at -80, but fails when the search starting point is at 0.
4.8 Conclusions

We developed a hybrid multiresolution registration technique to automatically register reference DTS images with on-board DTS images to guide patient positioning in radiation therapy. This technique was tested using image data from both an anthropomorphic chest phantom and eight head-and-neck cancer patients. The average capture ranges in single-axis simulations with a 44° scan angle and a large ROI covering the entire DTS volume were between -31 and +34 deg for rotations and between -89 and +78 mm for translations in the phantom study, and between -38 and +38 deg for rotations and between -58 and +65 mm for translations in the patient study. Decreasing the DTS scan angle mainly affected the registration accuracy and the robustness for the out-of-plane rotations. Decreasing the ROI size from the entire DTS volume to the volume surrounding the spinal cord caused the decrease of the registration capture ranges. Results also showed that the hybrid registration technique had much larger capture ranges than the static method alone in registering the out-of-plane rotations.

In summary, this pre-clinical study shows that the hybrid multiresolution registration technique using DTS images is an accurate and reliable tool for 3-D image guidance in the head and neck treatment. Our next step is to implement this registration technique in a real clinical setup for daily image guidance. To achieve that, we need to improve the speed of the registration algorithm to make the total registration time
within the clinical time constraint. This goal can be achieved by using hardware acceleration, parallel computing and algorithm optimization.
5. Novel limited-angle CBCT estimation method using a deformation field map

In Chapter 4, we showed that registration between reference and on-board DTS images reconstructed by the filtered back projection (FBP) method is able to provide accurate rigid body alignment of the patient’s bony structures. However, DTS images reconstructed by the conventional FBP method have low plane-to-plane resolution, and they do not provide full volumetric information about organ deformation for soft tissue alignment.

In this chapter, we developed a novel method to optimally estimate on-board CBCT images from limited-angle projections using a deformation field map. In this method, patients’ on-board CBCT data acquired in a previous treatment session are used as prior information. After the initial rigid body alignment of the patient using FBP based DTS images, the differences between the patient’s new anatomy and prior anatomy are the deformation of internal organs and soft tissues and the residual misalignment of bony structures. The patient’s new image volume to be reconstructed is then considered as a deformation of the patient’s prior image volume. Instead of directly solving the pixel values of the new image volume in the reconstruction, we propose to solve the deformation field of the prior image volume based on a deformation model and the new projection data acquired within a limited angle span. The new on-board CBCT image is then obtained by deforming the prior CT or CBCT image volume according to the solution to the deformation field.
5.1 2D estimation method

This new estimation method is demonstrated as follows in 2D cases, and it can be extended to 3D using a similar approach. The size of all the images studied is defined to be n*n. The deformation field is represented by \( D_k(i, j), \quad k = 1, 2, \quad i, j = 1 \text{ to } n \), where \( k=1, 2 \) stand for the two directional components of the deformation field along x and y axes respectively, and \( i \) and \( j \) stand for the 2D index of the deformation field at each image pixel. The new CBCT image to be estimated is represented by \( I_{\text{new}} \), and the prior planning CT or CBCT image volume is represented by \( I_{\text{prior}} \). Then \( I_{\text{new}} \) can be expressed as a function of \( D \) and \( I_{\text{prior}} \) as follows:

\[
I_{\text{new}} = I_{\text{new}}(D, I_{\text{prior}})
\]

Specifically, each pixel value in \( I_{\text{new}} \) is interpolated from \( I_{\text{prior}} \) according to the deformation field \( D \) using bilinear interpolation. The equation for calculating the pixel value at \((i, j)\) in the new CBCT image is as follows:

\[
I_{\text{new}}(i, j) = I_{\text{prior}}(i + D_1(i, j), j + D_2(i, j))
\]

In image estimation, the data fidelity constraint needs to be met, which means the projections of the image \( I_{\text{new}} \) should match with the projection data acquired. This constraint can be expressed by the following equation:

\[
P \cdot I_{\text{new}}(D, I_{\text{prior}}) = Y
\]
where $P$ is the system matrix to describe the x-ray projection measurements, and $Y$ is the projection data acquired. Since only projections within a limited scan angle are acquired, there are not enough equations in Eq. (10) to solve for the deformation field $D$.

Therefore, we added another constraint called the energy constraint. The 2D bending energy of the deformation field is defined as follows:

$$E(D) = \int \int \left( \left( \frac{\partial^2 D}{\partial x^2} \right)^2 + 2 \left( \frac{\partial^2 D}{\partial x \partial y} \right)^2 + \left( \frac{\partial^2 D}{\partial y^2} \right)^2 \right) dx \, dy,$$

(11)

In a discrete version, Eq. (11) becomes:

$$E(D) = \sum_{k=1}^{2} \sum_{i=1}^{n} \sum_{j=1}^{n} \left( \left( \frac{\partial^2 D_k(i, j)}{\partial x^2} \right)^2 + 2 \left( \frac{\partial^2 D_k(i, j)}{\partial x \partial y} \right)^2 + \left( \frac{\partial^2 D_k(i, j)}{\partial y^2} \right)^2 \right),$$

(12)

The energy constraint requires the deformation field $D$ to have the minimum bending energy. Based on these two constraints, the limited-angle CBCT estimation problem is converted into the following constrained optimization problem:

$$\min_D (E(D)), \ s.t. \ P \bullet I_{new}(D, I_{prior}) = Y$$

(13)

The above constrained problem can be further converted into the following unconstrained optimization problem:

$$\tilde{D} = \arg \min_{D} \ f(D) = \arg \min_{D} \left( \mu \ast E(D) + \left\| P \bullet I_{new}(D, I_{prior}) - Y \right\|_2^2 \right)$$

(14)

where $f(D)$ is the objective function to be minimized, and $\mu$ is the relative weight of the bending energy. A nonlinear conjugate gradient (CG) method is used as the
optimizer to solve the optimization problem in Eq. (14). The gradient of the objective function \( f(D) \) can be calculated as follows:

\[
\nabla f(D) = \mu \nabla E(D) + 2P^* \cdot (P \cdot I_{new}(D, I_{prior}) - Y) \cdot \nabla I_{new}(D, I_{prior})
\]

where \( P^* \) is the Hermitian of the projection matrix \( P \). The starting point of the deformation field is set to be zero and the initial value of the relative weight \( \mu \) is set to be \( 1.0 \times 10^{-7} \). After every 100 iterations, the relative weight \( \mu \) is increased by a factor of 10 and the deformation field solved is used as the starting point of the next 100 iterations. A total of \(~500\) iterations are used in the optimization. After the deformation field \( D \) is solved, the new CBCT image \( I_{new} \) is obtained by deforming the prior image \( I_{prior} \) based on Eq. (9). The diagram of this new limited-angle CBCT estimation method is shown in Fig. 17.
5.2 3D estimation method

The 2D estimation algorithm was implemented in 3D using a similar approach, and the computer graphics card was used to accelerate the 3D estimation process.

5.2.1 Algorithm

This new estimation method is implemented in 3D. The size of all the images studied is defined to be \( n \times n \times n \). The deformation field is represented by \( D_m(k, j, i), \quad m = 1, 2, 3, \quad k, j, i = 1 \Lambda n \), where \( m = 1, 2, 3 \) stand for the three
directional components of the deformation field along x, y and z axes respectively, and k, j, and i stand for the 3D index of the deformation field at each image pixel. The new CBCT image to be estimated is represented by $\tilde{CBCT}_{new}$, and the prior planning CT or CBCT image volume is represented by $I_{prior}$. Then $\tilde{CBCT}_{new}$ can be expressed as a function of $D$ and $I_{prior}$ as follows:

$$\tilde{CBCT}_{new} = CBCT_{new} (D, I_{prior})$$

(16)

Specifically, each pixel value in $\tilde{CBCT}_{new}$ is interpolated from $I_{prior}$ according to the deformation field $D$ using trilinear interpolation. The equation for calculating the pixel value at $(k, j, i)$ in the new CBCT image is as follows:

$$\tilde{CBCT}_{new} (k, j, i) = I_{prior} (k + D_1 (k, j, i), j + D_2 (k, j, i), i + D_3 (k, j, i))$$

(17)

In the limited-angle CBCT estimation, the data fidelity constraint needs to be met, which can be expressed by the following equation:

$$P \cdot CBCT_{new} (D, I_{prior}) = Y$$

(18)

where $P$ is the system matrix to describe the x-ray projection measurements, and $Y$ is the projection data acquired. Another constraint we used to solve the deformation field is the energy constraint, which requires the deformation field to have the minimum deformation energy. We used the free form energy defined by Lu et al. as the deformation energy. The formula of the free form energy is as follows:
\[ E(D) = \sum_{k=1}^{n} \sum_{j=1}^{n} \sum_{i=1}^{n} \left( \left( \frac{\partial D_m(k,j,i)}{\partial x} \right)^2 + \left( \frac{\partial D_m(k,j,i)}{\partial y} \right)^2 + \left( \frac{\partial D_m(k,j,i)}{\partial z} \right)^2 \right) \] (19)

Based on these two constraints, the limited-angle CBCT estimation problem is converted into the following unconstrained optimization problem:

\[ \tilde{D} = \arg \min_{\forall D} f(D) = \arg \min_{\forall D} \left( \mu \cdot E(D) + \left\| P \cdot CBCT_{new}(D,I_{prior}) - Y \right\|_2^2 \right) \] (20)

where \( f(D) \) is the objective function to be minimized, and \( \mu \) is the relative weight of the deformation energy. A nonlinear conjugate gradient (CG) method is used as the optimizer to solve the optimization problem in Eq. (20). After the deformation field \( D \) is solved, the estimated new CBCT image \( CBCT_{new} \) is obtained by deforming the prior image \( I_{prior} \) based on Eq. (17).

5.2.2 Hardware acceleration

This 3D estimation algorithm requires forward projection and back projection of the 3D volume in each iteration. The forward projection process which generates digital reconstructed radiographs (DRR) is the most time consuming process in each iteration loop. We implemented this process in the computer graphics card to accelerate the speed. By using the three color channels in the graphics card, we are able to extend the data storage range to 0-2047 (11bit). For limited-angle CBCT estimation using simulated
projections of the new CBCT image, both $I_{\text{prior}}$ and the new CBCT images are linearly scaled to 0-2047 data range before the generation of DRRs and simulated new projections. For CBCT estimation using real cone-beam projections, the image intensity values of the DRRs need to match with the image intensity values of the real projection images in the estimation process. To achieve that, we first linearly scale the gray values of the $I_{\text{prior}}$ into 11bit range by using the following formula:

$$I'_{\text{prior}} = \left( I_{\text{prior}} - I_{\text{prior}}^{\text{min}} \right) / \left( I_{\text{prior}}^{\text{max}} - I_{\text{prior}}^{\text{min}} \right) \times 2047$$  \hspace{1cm} (21)$$

The scaled image volume $I'_{\text{prior}}$ is loaded into the three color channels in the computer graphics card. The image volume is then resliced into 256 slices and projected onto the detector plane slice by slice based on the cone-beam geometry. The DRR of $I'_{\text{prior}}$ is generated according to the following formula:

$$\text{DRR}' = \frac{1}{256} \sum_{i=1}^{256} P_i'$$  \hspace{1cm} (22)$$

where $P_i'$ is the projection of the $i^{th}$ slice of $I'_{\text{prior}}$. Since the projection process is a linear process and DRR' is taking the average of all the projection, the DRR of the original $I_{\text{prior}}$ and the DRR' generated by hardware have the same relationship as defined in Eq. (21). Therefore, the DRR of $I_{\text{prior}}$ can be calculated according to the following equation:

$$\text{DRR} = \text{DRR}' / 2047 \times (I_{\text{prior}}^{\text{max}} - I_{\text{prior}}^{\text{min}}) + I_{\text{prior}}^{\text{min}}$$  \hspace{1cm} (23)$$
5.2.3 Multi-resolution scheme

A multi-resolution is used to improve the speed, robustness and accuracy of the estimation algorithm.

Figure 18: Multi-resolution scheme employed in the estimation algorithm: the CBCT\textsubscript{prior} image is downsampled into different levels, the estimation process proceeds from the coarsest resolution level to the full resolution level, at each level the starting point of the deformation field is obtained by expanding the deformation field solved from the previous lower resolution level.

As shown in Fig. 18, the CBCT\textsubscript{prior} image is downsampled into different resolution levels. The estimation process is performed first at the coarsest resolution level, and the starting point of the deformation field is set to be zero. After convergence, the algorithm proceeds to higher resolution levels, and finally at full resolution level. At each higher resolution level, the starting point of the deformation field is obtained by
expanding the deformation field solved from the previous lower resolution level. Linear interpolation is used to expand the deformation field. In our study, three levels of resolution are employed in the scheme, and the CBCT<sub>prior</sub> image volume is downsampled by a factor of 2 along each dimension for each lower resolution level.

5.2.4 Limited-angle CBCT estimation using real projection images

5.2.4.1 Bowtie correction of real cone-beam projection images

A bowtie filter was mounted on the on-board kV source during the cone-beam CT scan of the patient. To compensate for the filtration by the bowtie filter, we acquired a blank scan with the bowtie filter attached using the same kV and mAs setup as in the patient scan. Then the projection image Y used in Eq. (18) is calculated as follows:

\[ Y = -\log(\text{raw patient projection image}) - (-\log(\text{raw blank scan projection image})) \]  \hspace{1cm} (24)

5.2.4.2 Prior CBCT image reconstruction

To make the DRRs of the deformed CBCT<sub>prior</sub> image match with the new projection images in the estimation algorithm, we need to make the DRRs of the original CBCT<sub>prior</sub> image match with the prior projection images. Therefore, we used an iterative method, instead of FBP method, to reconstruct the patient CBCT<sub>prior</sub> image.

To solve for the CBCT<sub>prior</sub> image, the data fidelity constraint needs to be met. This constraint is expressed in the following equation:
\[ P \cdot \text{CBCT}_{\text{prior}} = Y \]  

(25)

where \( P \) is the projection matrix, and \( Y \) is the prior cone-beam projection images acquired. Another constraint we used is the total variation (TV) constraint. The total variation of a 3D image volume \( I \) is defined as follows:

\[
TV(I) = \sum_{k=1}^{n} \sum_{j=1}^{n} \sum_{i=1}^{n} \left( \frac{\partial I(k,j,i)}{\partial x} \right)^2 + \left( \frac{\partial I(k,j,i)}{\partial y} \right)^2 + \left( \frac{\partial I(k,j,i)}{\partial z} \right)^2
\]

(26)

The total variation constraint requires the \( \text{CBCT}_{\text{prior}} \) image to have the minimum total variation, which is used to smooth the image while preserving the edge information. By combining these two constraints, we converted the CBCT reconstruction problem into the following unconstrained optimization problem:

\[
\text{CBCT}_{\text{prior}} = \arg \min_{\forall \text{CBCT}_{\text{prior}}} f\left( \text{CBCT}_{\text{prior}} \right) = \arg \min_{\forall \text{CBCT}_{\text{prior}}} \left( \mu \cdot TV\left( \text{CBCT}_{\text{prior}} \right) + \left\| P \cdot \text{CBCT}_{\text{prior}} - Y \right\|_2^2 \right)
\]

(27)

where \( f\left( \text{CBCT}_{\text{prior}} \right) \) is the objective function to be minimized, and \( \mu \) is the relative weight of the total variation. A nonlinear conjugate gradient method is used as the optimizer. In total around 600 projections acquired over a 360° scan angle are used for reconstruction, and the CBCT image reconstructed using FBP method is used as the starting point of the optimization. The initial value of the relative weight \( \mu \) is set to be zero, and after 3 iterations \( \mu \) is set to be 1000.
5.3 Evaluation methods

In 2D estimation, the accuracy of this novel method was quantitatively evaluated by calculating the errors of both organ volume and pixel values estimated. The organ volume and pixel values in the new full-rotation CBCT image $\text{CBCT}_{\text{new}}$ were used as the truth. The relative error of the organ volume in the estimated limited-angle CBCT image or the prior image $I_{\text{prior}}$ was calculated as follows:

$$\text{Relative error of organ volume} = \frac{|V_{\text{new}} - V_{0}|}{V_{0}} \times 100\%$$

(28)

where $V$ was the organ volume contoured in the estimated limited-angle $\text{CBCT}_{\text{new}}$ or $I_{\text{prior}}$ image, and $V_{0}$ was the organ volume contoured in the full-rotation $\text{CBCT}_{\text{new}}$ image. The error of the pixel values estimated was estimated by the pixel signal-to-noise ratio (PSNR), which is defined as follows:

$$\text{PSNR}(X,Z) = 10 \log_{10} \frac{\sum \sum X_{i,j}^2}{\sum \sum (X_{i,j} - Z_{i,j})^2} (dB)$$

(29)

where $X$ is the full-rotation $\text{CBCT}_{\text{new}}$ image, and $Z$ is the estimated limited-angle $\text{CBCT}_{\text{new}}$ or $I_{\text{prior}}$ image. The numerator describes the signal strength of the new full-rotation CBCT image and the denominator represents the pixel value estimation error.

In 3D estimation, the accuracy of the estimation algorithm was quantitatively evaluated by calculating the similarity between the limited-angle $\tilde{\text{CBCT}}_{\text{new}}$ and the full-
rotation $CBCT_{new}$ and the PSNR of the limited-angle $CBCT_{new}$. Specifically, the similarity was evaluated by the cross correlation (CC) and mutual information (MI) between the two sets of images. Cross correlation is defined as follows:

$$CC(X, Y) = \frac{\sum_{k=1}^{n} \sum_{j=1}^{n} \sum_{i=1}^{n} (X(k, j, i) - \text{mean}(X))(Y(k, j, i) - \text{mean}(Y))}{\sqrt{\left(\sum_{k=1}^{n} \sum_{j=1}^{n} \sum_{i=1}^{n} (X(k, j, i) - \text{mean}(X))^2\right) \left(\sum_{k=1}^{n} \sum_{j=1}^{n} \sum_{i=1}^{n} (Y(k, j, i) - \text{mean}(Y))^2\right)}}$$

(30)

where $X$ and $Y$ are the limited-angle $CBCT_{new}$ and the full-rotation $CBCT_{new}$ images respectively. Mutual information is defined as follows:

$$MI(X, Y) = \sum_{y \in Y} \sum_{x \in X} p(x, y) \log \frac{p(x, y)}{p(x) \cdot p(y)}$$

(31)

where $X$ and $Y$ are the limited-angle $CBCT_{new}$ and the full-rotation $CBCT_{new}$ respectively, $p(x)$ and $p(y)$ are the normalized histograms of $X$ and $Y$ separately, and $p(x, y)$ is the normalized joint histogram of $X$ and $Y$.

In 2D estimation, this estimation algorithm was tested using a Matlab Shepp-Logan phantom, liver and head-and-neck patient data. The image size in all the tests was set to be 256*256. Projections simulated around every 0.5 degree over 60 to 90 degree scan angles from the new full-rotation CBCT image $CBCT_{new}$ were used for the estimation. In 3D estimation, this method was tested using liver, prostate and head-and-neck patient data. The estimated CBCT image size in all the tests was set to be
256*256*256. Simulated cone-beam projections were used in the estimation of liver and prostate patient data. Both simulated projections and real cone-beam CT projection images were used in the estimation of head-and-neck patient data. Projections were sampled around every 0.5 degree over 30 to 60 degree scan angles.

5.4 Results

5.4.1 2D estimation results

5.4.1.1 Shepp-Logan phantom

In the Shepp-Logan phantom test, three tumors of different sizes were simulated at different locations in the prior CBCT image $CBCT_{\text{prior}}$, and they were simulated to experience tumor shrinkage in the new full-rotation CBCT image $CBCT_{\text{new}}$, as shown in Fig. 19(a) and 19(b). The $CBCT_{\text{new}}$ estimated from 60 and 90 degree projections are shown in Fig. 19(c) and 19(d), respectively. The FBP based DTS image reconstructed from 90 degree projections is shown in Fig. 19(e) for comparison. The PSNR for estimated 60-deg and 90-deg $CBCT_{\text{new}}$ images and the $CBCT_{\text{prior}}$ image are shown in Table 6. The deformation field solved using 90-degree projections is overlaid onto the prior CBCT image in Fig. 20.
Figure 19: Estimation of limited-angle CBCT of Shepp-Logan phantom with 60 to 90 degree scan angles. (The three tumors simulated are indicated by the red arrows.) a) the prior CBCT image $CBCT_{prior}$ b) the new full-rotation CBCT image $CBCT_{new}$ c) estimated 60-deg $CBCT_{new}$ d) estimated 90-deg $CBCT_{new}$ e) FBP based 90-deg DTSnew.

Table 6: PSNR for the estimated limited-angle CBCT images and the prior CBCT image in the Shepp-Logan phantom study

<table>
<thead>
<tr>
<th></th>
<th>Estimated 90-deg $CBCT_{new}$</th>
<th>Estimated 60-deg $CBCT_{new}$</th>
<th>Prior CBCT image $CBCT_{prior}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSNR (dB)</td>
<td>35.7</td>
<td>34.3</td>
<td>18.3</td>
</tr>
</tbody>
</table>
5.4.1.2 Liver patient data

In the liver patient test, the 4D CT images of a liver patient at the exhale and inhale phases were used to simulate two extreme cases for soft tissue deformation in prior CBCT and new full-rotation CBCT images, as shown in Fig. 21(a) and 21(b). The $\tilde{CBCT}_{\text{new}}$ estimated from 60 and 90 degree projections are shown in Fig. 21(c) and 21(d),
respectively. The FBP based DTS image reconstructed from 90 degree projections is shown in Fig. 21(e) for comparison.

Figure 21: Estimation of limited-angle CBCT of liver patient data with 60 to 90 degree scan angles. (The contours of the liver are shown as red lines in the images.) a). the prior CBCT image CBCTprior  b). the new full-rotation CBCT image CBCTnew c). estimated 60-deg CBCTnew d). estimated 90-deg CBCTnew e). FBP based 90-deg DTSnew.

The deformation field solved by the new method using 90 degree projections is overlaid onto the prior CBCT image in Fig. 22. To evaluate the organ volume estimation error, the liver was contoured in CBCT images (as shown in Fig. 21). The relative error of the liver volume reconstructed is calculated according to Eq. (28), and the error of the
pixel values estimated is evaluated by PSNR as defined in Eq. (29). The results are shown in Table 7.

Figure 22: Deformation field (red arrows) solved by the new estimation method overlaid onto the prior CBCT image in the liver patient study. (90-degree scan angle was used)

Table 7: The relative error of the liver volume and the PSNR for the estimated limited-angle CBCT images and the prior CBCT image in the liver patient study

<table>
<thead>
<tr>
<th></th>
<th>Estimated 90-deg $\tilde{CBCT}_{\text{new}}$</th>
<th>Estimated 60-deg $\tilde{CBCT}_{\text{new}}$</th>
<th>Prior CBCT image $CBCT_{\text{prior}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative error of the liver volume (%)</td>
<td>2.3</td>
<td>3.4</td>
<td>16.2</td>
</tr>
<tr>
<td>PSNR (dB)</td>
<td>28.8</td>
<td>23.5</td>
<td>15.4</td>
</tr>
</tbody>
</table>
5.4.1.3 Head-and-neck patient data

In the head-and-neck patient test, different days’ CBCT images of a head-and-neck patient were used as prior CBCT and new full-rotation CBCT images, as shown in Fig. 23(a) and 23(b). The $\tilde{CBCT}_{\text{new}}$ estimated from 60 and 90 degree projections are shown in Fig. 23(c) and 23(d), respectively. The FBP based DTS image reconstructed from 90 degree projections is shown in Fig. 23(e) for comparison. The angulations of the bony structures in CBCT images were evaluated by calculating the angle alpha between the neck bone and the horizontal line, as shown in Fig. 23. Results showed that the bony structure in the new full-rotation CBCT image has 8.1 degree counter clockwise rotation relative to the bony structure in the prior CBCT image. In $\tilde{CBCT}_{\text{new}}$ estimated from 60 and 90 degree projections, this rotation has been accurately reconstructed with 0.0 degree error. The difference image between full-rotation $\tilde{CBCT}^{\text{new}}$ and $\tilde{CBCT}^{\text{prior}}$ and the difference image between full-rotation $\tilde{CBCT}^{\text{new}}$ and 60-deg $\tilde{CBCT}^{\text{new}}$ are shown in Fig. 24(a) and 24(b), respectively.
Figure 23: Estimation of limited-angle CBCT of head-and-neck patient data with 60 to 90 degree scan angles. The angulations of the bony structures in CBCT images were evaluated by calculating the angle alpha between the neck bone and the horizontal line. a). the prior CBCT image CBCT\textsubscript{prior} b). the new full-rotation CBCT image CBCT\textsubscript{new} c). estimated 60-deg CBCT\textsubscript{new} d). estimated 90-deg CBCT\textsubscript{new} e). FBP based 90-deg DTS\text sub{new}. 
Figure 24: Difference images in the head-and-neck patient study. a). the difference image between the new full-rotation CBCT image $CBCT_{\text{new}}$ and the prior CBCT image $CBCT_{\text{prior}}$. b). the difference image between the new full-rotation CBCT image $CBCT_{\text{new}}$ and the estimated 60-degree CBCT $\tilde{CBCT}_{\text{new}}$ image.

Table 8: PSNR for the estimated limited-angle CBCT images and the prior CBCT image in the head-and-neck patient study

<table>
<thead>
<tr>
<th></th>
<th>Estimated 90-deg $\tilde{CBCT}_{\text{new}}$</th>
<th>Estimated 60-deg $\tilde{CBCT}_{\text{new}}$</th>
<th>Prior CBCT image $CBCT_{\text{prior}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSNR (dB)</td>
<td>25.1</td>
<td>24.2</td>
<td>12.5</td>
</tr>
</tbody>
</table>

The deformation field solved using 90-degree projections is overlaid onto the prior CBCT image in Fig. 25. The deformation field also shows a counter clockwise rotation of the bony structure in the prior CBCT image. The PSNR for the estimated 60-deg and 90-deg $\tilde{CBCT}_{\text{new}}$ images and the $CBCT_{\text{prior}}$ image are shown in Table 8. The estimated 60-deg and 90-deg $\tilde{CBCT}_{\text{new}}$ images have much higher PSNR than the
\( \text{CBCT}_{\text{prior}} \) image, which suggests that the limited-angle \( \text{CBCT}_{\text{new}} \) image is not retaining much the incorrect anatomical information in the \( \text{CBCT}_{\text{prior}} \) image.

Figure 25: Deformation field (red arrows) solved by the new estimation method overlaid onto the prior CBCT image in the head-and-neck patient study. (90-degree scan angle was used)

5.4.2 3D estimation results

5.4.2.1 Liver patient data (simulated projections)

As shown in Fig. 26, the 4D CT images of a liver patient at the exhale and inhale phases were used to simulate two extreme cases of soft tissue deformation in prior CBCT and new CBCT images. Projections simulated from the \( \text{CBCT}_{\text{new}} \) image were used.
for limited-angle CBCT estimation. As indicated by the arrows and dashed lines in Fig. 26, motion of the liver and diaphragm is estimated accurately in 30-deg and 60-deg $CBCT_{\text{new}}$ images. The PSNR of the $CBCT_{\text{prior}}$, 30-deg and 60-deg $CBCT_{\text{new}}$ images are 13.0, 15.1 and 16.9 respectively. The cross correlation between $CBCT_{\text{new}}$ and $CBCT_{\text{prior}}$, 30-deg and 60-deg $CBCT_{\text{new}}$ images are 0.806, 0.896 and 0.928 respectively.

Figure 26: Estimation of limited-angle CBCT images of liver patient data. The 4D CT images of a liver cancer patient at the exhale and inhale phases were used as prior CBCT and new CBCT images. Projections simulated from the CBCTnew image were used for limited-angle CBCT estimation. The first row is the axial view, the second row is the coronal view, and the third row is the sagittal view.
5.4.2.2 Prostate patient data (simulated projections)

Figure 27
Figure 27: Estimation of limited-angle CBCT images of prostate patient data. Different days’ CBCT images of a prostate patient were used as the prior CBCT and new CBCT images. Projections simulated from the CBCTnew image were used for limited-angle CBCT estimation. a). the prior CBCT image CBCT\textsubscript{prior}, b). FBP based 60-deg DTS\textsubscript{new}, c). estimated 30-deg CBCT\textsubscript{new} d). estimated 60-deg CBCT\textsubscript{new} e). the new full-rotation CBCT image CBCT\textsubscript{new}.

Different days’ CBCT images of a prostate patient were used as the prior CBCT and new CBCT images. Projections simulated from the CBCT\textsubscript{new} image were used for CBCT estimation. As indicated by the arrows in Fig. 27, the rectum volume change in the CBCT\textsubscript{new} image is reconstructed in estimated 60° CBCT\textsubscript{new} images. The PSNR of the CBCT\textsubscript{prior}, estimated 30° and 60° CBCT\textsubscript{new} images are 12.0, 17.7 and 20.6 respectively. The cross correlation between CBCT\textsubscript{new} and CBCT\textsubscript{prior}, estimated 30° and 60° CBCT\textsubscript{new} images are 0.825, 0.909 and 0.928 respectively.

5.4.2.3 Head-and-neck patient data (simulated projections)

Different days’ CBCT images of a head-and-neck patient were used as prior CBCT and new CBCT images. Projections simulated from the CBCT\textsubscript{new} image were used for CBCT estimation. As indicated by dashed lines and arrows in Fig. 28, the patient’s weight loss and airway volume change from CBCT\textsubscript{prior} to CBCT\textsubscript{new} have been estimated in the 30° and 60° CBCT\textsubscript{new} images. The PSNR of the CBCT\textsubscript{prior}, the 30° and 60° CBCT\textsubscript{new} images are 10.2, 14.8 and 17.7 respectively. The cross correlation between CBCT\textsubscript{new} and CBCT\textsubscript{prior}, 30° and 60° CBCT\textsubscript{new} images are 0.904, 0.960 and 0.979 respectively.
Figure 28
Figure 28: Estimation of limited-angle CBCT images of head-and-neck patient data. Different days’ CBCT images of a head-and-neck patient were used as the prior CBCT and new CBCT images. Projections simulated from the CBCT\textsubscript{new} image were used for limited-angle CBCT estimation. a). the prior CBCT image CBCT\textsubscript{prior}, b). FBP based 60-deg DTS\textsubscript{new}, c). estimated 30-deg CBCT\textsubscript{new} d). estimated 60-deg CBCT\textsubscript{new} e). the new full-rotation CBCT\textsubscript{new} image.

5.4.2.4 Head-and-neck patient data (real projections)

In this test, different days’ CBCT images of a head-and-neck patient were used as prior CBCT and new CBCT images, as shown in Fig. 31(a) and 31(c). Real cone-beam projection images are used for CBCT estimation. Blank scans with the full fan bowtie attached to the kV source are acquired. The projection image and a line profile in the projection image are shown in Fig. 29(a) and 29(b), respectively. These blank scan projection images are then used to correct the bowtie effects in the raw patient projection images, as explained in 5.2.4.1.
Figure 29: Blank cone-beam CT scan with the full fan bowtie attached to the kV source. a). the raw projection image. b). a line profile in the raw projection image (the location of the profile is indicated by the yellow line in the projection image).

The CBCT\textsubscript{prior} image is reconstructed using the iterative method explained in 5.2.4.2. The DRR of the reconstructed CBCT\textsubscript{prior} image and the raw projection image are shown in Fig. 30. As shown in the two line profiles, the intensity values of the pixels in DRR match with the intensity values in the raw projection image very well.
Figure 30: Comparison between the DRR of the reconstructed CBCT\textsubscript{prior} image and the raw projection image. (a). DRR of the reconstructed CBCT\textsubscript{prior} image. (b). Raw projection image of the patient’s prior anatomy after bowtie correction. (c). line profile in the DRR image (indicated by the yellow line). (d). line profile at the same location as in (c) in the raw projection image.
Figure 31
Figure 31: Estimation of limited-angle CBCT images of head-and-neck patient data. Different days’ CBCT images of a head-and-neck patient were used as the prior CBCT and new CBCT images. Real cone-beam projection images were used for CBCT estimation. a). the prior CBCT image $\text{CBCT}_{\text{prior}}$, b). FBP based 60-deg DTS$_{\text{new}}$, c). estimated 60-deg CBCT$_{\text{new}}$ d). the new full-rotation CBCT$_{\text{new}}$.

As indicated by the dashed lines and arrows in Fig. 31, the patient’s weight loss and airway volume change from CBCT$_{\text{prior}}$ to CBCT$_{\text{new}}$ have been reconstructed in the estimated 60° CBCT$_{\text{new}}$ images. The PSNR of the CBCT$_{\text{prior}}$ and estimated 60° CBCT$_{\text{new}}$ images are 10.1 and 14.2 respectively. The cross correlation between CBCT$_{\text{new}}$ and CBCT$_{\text{prior}}$, estimated 60° CBCT$_{\text{new}}$ images are 0.893 and 0.950 respectively.

5.5 Discussion

Results show that this new CBCT estimation method can obtain volumetric information about both soft tissue deformation and rigid body misalignment of bony structures using 60-degree projections, which are only 1/6 of the projections acquired in a full CBCT scan. This implies a substantial reduction of the imaging dose and time for daily image-guidance in the patient treatment. The deformation field solved during the reconstruction can be used as deformable registration results for tumor localization and dose tracking. Potentially, this method can also be applied for 4D CT, 4D CBCT and 4D DTS image estimation when patients’ prior images are available.

To our knowledge, this is the first time deformable registration has been combined with limited angle image estimation. Under this scheme, a series of other
limited-angle CBCT estimation methods can be developed by introducing other
defformation models into the estimation process, such as contour based and control point
based deformation models. These models can further reduce the degrees of freedom in
the estimation and therefore can potentially further reduce the scan angle and the
number of projections needed to obtain the volumetric information.

Since patient prior information is used in this new CBCT estimation method, the
estimated new CBCT images are subject to the influence of the prior images. The degree
of influence is determined by the scan angle, number of projections, and the
optimization algorithm. Our results show that estimation using 60° projections sampled
around every 0.5° can has reasonable control of the influence of prior images and
generates patients’ new anatomical information in the estimated CBCT images.

5.6 Conclusions

We developed a novel 3D limited-angle CBCT estimation method to estimate
CBCT images using a deformation field map. This method was evaluated for 30° and
60° scan angles using both simulated and real projection images of liver, prostate and
head-and-neck patients. Results show that this method is able to estimate 3D patient
volume information using a 60° scan angle and it is feasible for daily image guidance in
radiation therapy.
6. Summary and future work

This dissertation has focused on optimizing and implementing image guided radiation therapy using limited-angle projections. Results suggest that the hybrid multiresolution registration technique using 44° FBP based DTS images is an accurate and reliable tool for 3-D rigid-body patient alignment in image guided radiation therapy. Results also show that the novel limited-angle CBCT estimation method is able to estimate 3D patient volumetric information using a 60° scan angle, which provides patient deformation information for soft tissue alignment.

The main contributions of this work include:

- Acceleration of DRR generation process using computer graphics card. This work has been published in Medical Physics.

- Development of a hybrid-multiresolution automatic rigid-body registration algorithm for patient positioning using DTS. This work has been published in Medical Physics.

- Development of a novel limited-angle CBCT estimation method using prior information and a deformation model to recover the volumetric information. This work has been published as a Medical Physics Letter in Medical Physics.

Future work includes a larger clinical trial to evaluate the efficacy of using automatic DTS registration for different sites’ patient positioning and the accuracy and robustness of the novel CBCT estimation method for estimating 3D patient anatomy.
change. Other deformation models can also be introduced into the novel CBCT estimation method to further reduce the number of projections needed to reconstruct patient 3D volume. Application of this novel estimation method in 4-D CT, 4-D CBCT or 4-D DTS is also a promising direction to be investigated.
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1. “A Novel Digital Tomosynthesis (DTS) Reconstruction Method Using a Deformation Field Map”
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2. “A Novel Digital Tomosynthesis (DTS) Reconstruction Method Using Prior Information and a Deformation Model”
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2. “A Hybrid Multiresolution Method for Automatic Registration Between Reference and On Board Digital Tomosynthesis”
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