Estimation of patient setup errors in radiation therapy using portal imaging

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Abstract

In all radiation therapy a correct patient setup with reference to the treatment machine is important, since setup errors result in deviations from the planned treatment. The precision of the patient setup is even more crucial in Intensity Modulated Radiation Therapy (IMRT) since the dose distributions conform well to the intended target volume in the patient. To verify the patient position on the treatment couch, Portal Images (PIs) recorded during treatment can be compared to Digitally Reconstructed Radiographs (DRRs). DRRs are generated from the treatment planning CT-data. It is assumed that the patient setup error can be correctly represented by a 3D rigid transformation. Several intensity-based, fully automatic image registration algorithms have been implemented. These methods all use the Powell-Brent optimization procedure and the similarity of different images is determined using the correlation coefficient. The accuracy of the methods was tested in simulations with real patient CT-data and they all performed well. Of particular interest is the semi-2D3D-θ method, which determines the full transformation without a large number of time consuming DRR generations. The achieved accuracy was better than 0.3 mm and 0.4° using the CT-data of a prostate patient. The method requires relatively short time which makes it a possible candidate in offline adaptive radiotherapy.
Acknowledgements

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1 Introduction

1.1 Radiation treatment and IMRT

There are generally three ways of treating cancer: surgery, chemotherapy and radiation therapy. Depending on the size, shape and location of the tumor, and the aim of therapy one or several of these treatments are used.

This thesis focuses on radiation therapy. Radiation therapy works by damaging the DNA chain of the cell, thus impairing its ability to reproduce [1]. The biological effects of radiation can be divided into two groups, direct and indirect effects. The direct effects occur when the radiation interacts with the DNA-chain and thereby causes a biological effect. Indirect effects occur when radiation produces secondary electrons, which subsequently create radicals. These are highly reactive and break bonds in the DNA-chain. The biological effects can of course occur both in healthy tissue and in the cancer cells [2]. The goal is to achieve an acceptable compromise between normal tissue complications and damage to the cancer cells. To reduce damage of normal tissue, as little dose as possible should be delivered to it. Also, normal tissue is more likely to repair the damages caused by radiation than tumor tissue is. This fact is exploited by fractionating the treatment. A small part of the total dose (a fraction) is delivered daily for an extended period of time, thus giving the normal tissue time to recover between treatments [1].

When a patient has been diagnosed with cancer and radiation has been chosen as means of treatment, the radiation therapy treatment consists of the following five steps [3]: establishing the aim of treatment, acquiring patient data for treatment planning, treatment planning, treatment execution and follow-up.

(i) Aim of treatment

The aim of the radiation treatment can be twofold. Either the aim is to cure the patient, so called radical treatment, or the aim is to relieve symptoms and increase quality of life, so called palliative treatment. In the first case, both the gross tumor and areas susceptible to spread have to be irradiated. Short term complications are accepted if the patient can be cured, but long term effects should be avoided. This implies that all tumor cells should have a high probability of being included in the target. In palliative treatment, the long term effects are not important since the patients have short life expectancy. However, short term complications must be avoided [2].
(ii) Acquisition of patient data
The next step is to gather patient data, generally computed tomography (CT) data but possibly also nuclear magnetic resonance and other images, to use in the treatment planning. The CT data has two major advantages: it is 3D and therefore volumes can easily be delineated and it contains information about the density of different regions, thus providing the basis for dose calculations. The CT data can therefore be used to produce a 3D dose plan. It is therefore important that the patient is placed in a position identical to that in the treatment machine so that the patient geometry in the treatment planning data resembles the geometry of the patient at the treatment machine as much as possible [2] [3]. Other methods, not based on images, can also be used to gather important information about tumor growth rate and radiation sensitivity.

(iii) Planning the treatment
In planning the treatment, the target volume – containing the tumor and other areas that need to be irradiated – as well as the organs at risk (OAR) have to be defined and delineated in the CT data. To deal with inaccuracies, margins are generally added to the target volume. The goal is to deliver enough dose to the target while sparing the OARs. In this thesis, only external radiation therapy is regarded (internal radiation therapy, brachytherapy, is another form of radiation therapy where radiation sources are implanted in the patient). External radiation therapy will inevitably deposit dose in surrounding tissue. One way of reducing the dose level in healthy tissue is to deliver it from several different angles. This will result in the irradiation of more healthy tissue, but the dose delivered to it will be lower. Usually, the beam angles are selected beforehand, based on experience. A prostate patient for instance is generally treated with 5 beams whereas a head-and-neck patient is treated with 7-9 beams. Coplanar treatments where the head of the radiation delivery machine, the gantry, is moved in a circle centered on the isocenter are most common, although a non-coplanar treatment is also feasible. During the treatment, the patient is usually positioned so that the isocenter coincides with the center of the target.

In conformal radiation therapy the shape of the beam cross section is shaped to conform to the shape of the target. In intensity modulated radiation therapy (IMRT) not only the shape of the cross section but also the intensity across it, the fluence profile, is modulated to achieve an even better dose distribution. These distributions are characterized by steep gradients and can conform even to concave-shaped targets. In IMRT so called inverse treatment planning is used. A desired dose distribution is prescribed, and fluence profiles that produce a distribution as close as possible to the prescribed distribution are then derived in an optimization process.

To sum up, the treatment planning involves the selection of a treatment delivery method and gantry angles, and the calculation of dose distributions. A simulation is also performed as a part of the treatment planning. The patient is placed in a room with a treatment simulator, an x-ray machine with a geometry identical to the therapy system. The patient is positioned according to the treatment plan and fixation devices, skin marks and lasers are used to tune the setup and make it reproducible. Images of the patient are recorded at the simulator to confirm the correct treatment setup.
**Treatment execution**

When the treatment planning is finished the actual treatment execution starts. As mentioned earlier, the treatment is divided into fractions for a curative treatment. Usually the dose is delivered in approximately 30 fractions. This means that the setup of the patient has to be reproduced a large number of times and it must repeatedly be verified that the treatment is in accordance with the plans. It is common practice to control the setup more rigorously in the first couple of fractions to determine if the setup procedure is stable. A Portal Imaging Device (PID) can be used during the treatment to confirm the setup of the patient. These are usually electronic (so called Electronic Portal Imaging Devices or EPIDs) and are placed opposite the gantry on the other side of the couch. The detector rotates together with the gantry. The treatment beam is used similar to an x-ray source and an image of the patient can be recorded.

![Schematic image of an EPID](image)

In IMRT, where the dose distributions conform well to the target volume, the correct setup is of great importance. In Adaptive radiation treatment (ART) measurements during each fraction can be used to adjust the rest of the treatment. This would yield a plan better suited to the individual patient resulting in lower dose to healthy tissue and OARs [5]. This can be done either offline, between the different fractions, or online while the patient is still in the treatment room.

**Follow-up**

The follow-up consists of recording the tumor response as well as the normal tissue reactions. The follow-up can continue several years after the treatment [3].
1.2 The purpose of the thesis

As mentioned earlier, IMRT is sensitive to setup errors. Small errors can have a large effect since the expected dose distribution varies substantially over the target volume and surrounding tissue. A small error in setup can result in a higher dose than expected to organs at risk and a lower dose to the tumor itself. This results in a treatment that deviates from the intended treatment. Setup errors occur due to difficulties in positioning the patient correctly at each fraction. Other errors arise because of organ motion and deformation of soft tissue. Such errors are not considered in this thesis. The use of a portal imaging device to examine the patient setup was mentioned earlier. Such a device uses the treatment beam like an x-ray source and can detect the transmitted high energy photons of this beam. The images recorded by the EPID during the treatment can then be compared to images recorded with known patient setup. Digitally Reconstructed Radiographs (DRRs) are such images. A DRR is a simulated projection image generated from CT-data, and the viewing angle of the DRRs is defined in relation to this data. The procedure of matching different images to each other is called image registration.

The aim of this thesis is to model the response of an EPID, generate DRRs that can be used in image registration and simulate the image registration of 3D CT-data to 2D portal images. In this thesis, the transformation between desired and actual patient geometry is assumed to be rigid and the goal is to implement a registration method that determines all parameters of such a transformation (3 translations and 3 rotations). The method should be fast and accurate enough to be used in offline adaptive radiation therapy.

1.2.1 ORBIT Workbench

The methods and algorithms described in this thesis have been implemented in C++ as a part of ORBIT Workbench. ORBIT is a general software framework for solving optimization problems in radiation therapy and is the result of years of research at Karolinska Institutet. It is the main product of RaySearch Laboratories. ORBIT Workbench is a version of ORBIT used for research and development of product prototypes. It contains code to represent patients and radiation treatments. It also contains algorithms to calculate dose distributions and solve IMRT problems. As a part of this study, ORBIT Workbench has been extended with algorithms to generate DRRs and perform image registration.
2 Background

The following section gives an introduction to important concepts and ideas regarding setup errors and setup error determination in radiation therapy. A short introduction to medical x-ray imaging is given as well as an outline of the work performed in this thesis.

2.1 Setup errors

The patient setup error is defined as the difference between the intended and the actual position of the patient. Generally, the errors are divided into random, interfractional errors (deviations between different fractions) and systematic errors. The sizes of typical translational setup errors for various regions are presented in Table 2.1.

<table>
<thead>
<tr>
<th>Region</th>
<th>Standard deviation systematic error (mm)</th>
<th>Standard deviation random error (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head and neck</td>
<td>1.6 - 5</td>
<td>1.1 - 2.5</td>
</tr>
<tr>
<td>Prostate</td>
<td>1.0 - 4</td>
<td>1.2 - 3.5</td>
</tr>
<tr>
<td>Pelvis</td>
<td>1.1 - 5</td>
<td>1.1 - 5</td>
</tr>
</tbody>
</table>

Table 2.1. Standard deviation of the random and systematic error of different regions. The values are taken from Hurkmans et al.[6] and have been compiled by Camilla Forsgren, RaySearch Laboratories. The table shows the rounded off values of this compilation.

The data in Table 2.1 refers to translation along the cranial-caudal (c-c), the anterior-posterior (a-p) or the medial-lateral (m-l) axes (see Figure 2.1). These axes are defined in the following way: cranial-caudal is the axis from the head to feet, medial-lateral is the axis from the left to the right side of the patient and anterior-posterior is the axis from the backside to the front side. There is some evidence that the translational setup errors in the pelvic region are larger in the cranial-caudal and the anterior-posterior direction, than in the medial-lateral direction, but the data is not conclusive [6].

Hurkmans et al states that good clinical practice, including the use of immobilization devices and portal imaging verification, should produce setup
errors (both systematic and random) smaller than 2 mm for head-and-neck patients, smaller than 2.5 mm for prostate treatments and setup errors smaller than 3 mm for pelvic treatments.

The data on rotational errors is not as exhaustive as the data on translational errors. Table 2-2 shows the rotational setup errors for 30 prostate patients, examined by Remeijer et al [7].

<table>
<thead>
<tr>
<th>Axis</th>
<th>Standard dev systematic error (°)</th>
<th>Standard dev random error (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cranial-Caudal</td>
<td>0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Anterior-Posterior</td>
<td>0.8</td>
<td>0.5</td>
</tr>
<tr>
<td>Medial-Lateral</td>
<td>0.9</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Table 2-2. Rotational setup error around the principal axes for 30 prostate patients examined by Remeijer et al [7].

The results show that the rotations generally were larger around the m-l axis, and that nearly 20% of the rotations around this axis were larger than 2°. For the c-c and a-p axes, the corresponding value was 1.4% and 5.8% respectively. A knee support was used to minimize rotations of the pelvis. Apparently, the rotations for prostate patients are generally fairly small. It has however been shown that some patients have setup errors as large as 7° rotation of the pelvis bone. [8]. The possibility of rigid fixation of the head ought to imply that there are only small rotations when considering head-and-neck patients.

2.2 Imaging

Medical images are of course an important tool in setup error determination. X-rays can be used to produce 2D projective images as well as 3D computed tomography data. Portal images collected during treatment are projection images similar to x-ray images and Digitally Reconstructed Radiographs (DRRs) are simulated projection images derived from CT-data which in turn also is recorded using x-rays. This section describes the basic theory behind projection photon imaging and computed tomography.

2.2.1 X-ray imaging

In x-ray imaging, photons are transmitted through the patient and recorded by a detector. On their way through the patient, the photons either pass without interaction or are scattered or absorbed. The interaction process between x-ray and patient can be described as a linear attenuation of the x-rays.

The magnitude of attenuation depends on what media the x-ray beam passes through; different tissues have different attenuation coefficients, \( \mu \). This difference in attenuation between different tissues gives rise to contrast in the x-ray image. Consider the left block in Figure 2-2. \( I_i \) is the incoming photon fluence (in this case entering a homogenous block with thickness \( x \) and attenuation coefficient \( \mu \)) and \( I_o \) is the photon fluence exiting the block unaffected.
According to Beer’s law, the relationship between $I_{in}$ and $I_{out}$ is [9, p 61]

$$I_{out} = I_{in} e^{-\mu x} \quad (2.1)$$

Now consider the right block in Figure 2-2. This block consists of two different kinds of materials, with different attenuation coefficients $\mu_1$ and $\mu_2$. If $\mu_1 < \mu_2$, less photons will be transmitted through the center of the block than through the other parts. If a detector is placed behind the block to record an image, this difference in number of transmitted photons will give rise to contrast in the recorded image. Using the notation from Figure 2-2, contrast $C$ is defined as

$$C = \frac{I_1 - I_2}{I_1} \quad (2.2)$$

The attenuation coefficient for a certain material varies with the energy of the photons. The coefficient decreases as the energy increases, meaning that the number of interactions between photons and tissue decreases as the energy increases. The difference in attenuation coefficient between different materials also decreases as energy increases.
In Figure 2-3, the relationship between attenuation coefficient and energy for cortical bone and soft tissue is shown. As can be seen, low photon energy yields a better contrast in the image, since the difference between attenuation coefficients are larger. In diagnostic imaging, the photon energy is in the range of 17-150 keV [10, p 24] depending on what part of the body is examined. There is a trade off between contrast in the image and dose received by the patient.

2.2.1.1 Portal images

Patient setup can be examined with the help of portal images (PIs). The portal image is recorded during the treatment session and the treatment beam is used as photon source. The image is recorded by an Electronic Portal Imaging Device (EPID). In therapy, the photons are more energetic than diagnostic x-ray imaging photons. The beams are usually in the range of 5 to 20 MV, which corresponds to a mean photon energy between about 1.5 and 7 MeV. As mentioned above, the difference in attenuation coefficient between different materials is small at these energies and the images suffer from low contrast. However, the image data can be manipulated to improve general contrast and visibility of certain features. Modern detectors, such as amorphous silicon EPIDs, add little noise and display images well [12]. Other factors also contribute to the poor quality of PIs, such as the size of the photon source and the position of the detector.

Figure 2-4. An EPID portal image of a pelvis obtained from Södersjukhuset. The square on the etched pelvis on the right shows the approximate area displayed on the left. The vertical stripe in the PI is a carbon fiber beam that supports the couch. It should have been removed before the image was recorded.
2.2.2 Scatter and noise

The linear attenuation model describes the amount of primary radiation that passes through the patient when radiated with photons. The rest of the energy is either absorbed or scattered (Figure 2-5). Scattered photons can still reach the detector and contribute to the recorded image, thus distorting it. However, in megavoltage imaging, scattering is less of a problem than in diagnostic kilovoltage imaging, since the fraction of the total fluence reaching the detector that is due to scattered rays decreases considerably with increasing energy [12].

An important concept in determining the quality of an image is the signal-to-noise ratio. It is defined as follows:

\[
\text{SNR} = \frac{\text{image signal}}{\text{noise}}
\]  

(2.3)

The SNR increases with increasing fluence detected but decreases as the photon energy increases. Therefore, good image quality (i.e. high SNR) in PIs usually results in a high dose delivered to the patient. Typically, a dose of about 10 cGy is delivered when recording a PI with good SNR [12]. Noise can also appear in the image due to different statistical fluctuations during the readout of the signal recorded by the detector [13].

2.2.3 Computed Tomography

In computed tomography (CT), the body of the patient is divided into planar, parallel slices. The CT data consists of a stack of 2D images where each image represents a slice. Each slice is irradiated with kilovoltage photons and the photon beam is always parallel to and contained within the slice. Projection x-ray images of the slice are recorded from a multitude of angles.
Projections must be recorded over at least 180° without any large gaps in between. Usually, projections are recorded over 360° of the slice to reduce artifacts in the reconstructed data. The number of projections needed is governed by the sampling theorem. Assuming a full set of projections, the two-dimensional attenuation coefficient distribution of the slice (in practice, a 2D image grid) can be reconstructed [10, p109].

A common method of reconstruction is convolution and backprojection [14]. As suggested by the name, the method consists of a convolution step, in which the data from each projection is filtered with a high-pass filter (a ramp function in Fourier space) to avoid losing high spatial frequencies in the reconstructed image. The filtering is followed by a backprojection step, where the filtered projection is backprojected onto the 2D image grid. The result of each projection angle is summed to yield the final attenuation distribution. The information about the attenuation is stored in Hounsfield units (HU), also called CT number, and is defined as [9, p 232]

\[
H_U = \frac{\mu_{\text{tissue}} - \mu_{\text{water}}}{\mu_{\text{water}}} \times 1000
\]  

(2.4)

where \( \mu \) is the attenuation coefficient. The values range from -1000 HU (air) to approximately +3000 HU. The HU can be converted back to the attenuation coefficient. It should be noted that there are differences between CT-scanners in how the attenuation data is stored.

2.3 Outline of the work: DRRs and image registration

In order to determine if the patient is positioned properly during treatment, portal images recorded at the time of treatment are often used. In many cases, the portal images are simply inspected by a physician to ensure the proper position of the patient. They can also be compared to images corresponding to known patient setup, for instance DRRs.

The procedure of aligning two images is referred to as image registration. In our case, 2D projective data (the portal image) should be aligned to the 3D CT-data used in the treatment planning. This is called 2D3D registration [15]. A 2D3D registration method can either consider only in-plane rotation and translation (three degrees of freedom) in which case the method is said to be two-dimensional (2D). The method can also be 3D and consider both in-plane and out-of-plane rotations and translations (six degrees of freedom). An out-of-plane rotation is defined as a rotation around an axis parallel to the imaging plane. It has been shown that an out-of-plane rotation smaller than 3° does not produce important differences in a projective image [7]. 3D methods usually match at least two different PI/DRR-pairs at the same time to increase accuracy, although in theory one image pair should be sufficient to determine all six degrees of freedom. In that case, the accuracy in translation along the viewing axis will be poor.

Figure 2-7 outlines the work performed in this thesis. The work can be divided into two parts. One part involves the generation of DRRs, and the other part involves determining setup errors with the aid of these DRRs and portal images. Figure 2-7 describes the process of 2D3D registration and lists the most important concepts.
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Figure 2-7. A schematic description of the process of 2D3D registration.

The portal image is the floating image and the DRR is the reference image generated with known setup. In the present work, which is a simulation study, the portal image will also be a DRR. In order to compare the reference and floating image, some kind of similarity measure has to be used. They are generally divided into two groups: feature- and intensity-based, and are assumed to be at an extreme point when the images are aligned. Lately, gradient-based registration methods have been developed which match projections of volumetric data gradients with x-ray image gradients [16] [17]. The optimizer provides a way of finding transformations that yield a better and better match between the floating images and the reference images.

2.3.1 Digitally Reconstructed Radiographs

From CT-data gathered at the planning of the treatment, Digitally Reconstructed Radiographs (DRRs) can be generated. A DRR is a simulated photon projection image and is basically a 2D projection of the CT-data. The DRR can be calculated for high energy photons (MV-DRR) thus changing its appearance compared to an x-ray image to become more similar to a portal image. A DRR, which represents the intended patient setup, can then be compared to a portal image to evaluate the actual setup.

The CT-data is recorded using kV-photons, and each voxel value corresponds to the attenuation in that part of the patient. These values can be translated to the corresponding attenuation coefficient for higher energy photons. The image quality of a MV-DRR will be worse compared to a kV-DRR, and more similar to a real PI.

2.3.1.1 Ray tracing

A common and straightforward way of generating DRRs is by so called ray tracing, or ray casting. The DRR is computed considering each pixel individually and a ray is traced between the virtual radiation source and each pixel in the image plane, traversing the CT-data.
In a non-homogeneous block containing a discrete distribution of attenuation coefficients (like the CT-data), the transmitted primary fluence can be calculated by integration of the linear attenuation coefficient along the ray. This is done using the equation:

\[ I_{\text{out}} = I_{\text{in}} r^{-2} e^{-\sum \mu_i d_i} \]  
(2.5)

where \( I_{\text{in}} \) is the incident fluence, \( r \) is the distance between the source and the pixel, \( i \) is a traversed voxel, \( \mu_i \) is its attenuation coefficient and finally \( d_i \) is the distance traversed in the voxel [18]. The factor \( r^{-2} \) is due to the inverse square law, which states that the fluence falls off as the square of the distance to the source. The ray tracing algorithm has to determine which voxels that are traversed, the points where the ray enters and exits the voxel and the distance between those points.

The amount of CT-data, the number of voxels, is large. Needless to say, these calculations are time consuming. When matching DRRs and PIs, several DRRs have to be calculated. It is therefore of great importance that these calculations are time efficient. Other ways of generating DRRs have been developed to reduce the time of image generation (see for instance LaRose [19] or Russakoff et al [20]).

### 2.3.2 Notation

\( I \) and \( J \) are intensity distributions, where \( J \) refers to the intensity distribution of the floating image (representing the actual position of the patient including setup errors) and \( I \) is the intensity distribution of the reference image. The images map points in the image to an intensity value:

\[ I : x_i \in \Omega_i \mapsto I(x_i) \]  
(2.6)

where \( \Omega_i \) is the domain, or field-of-view, of the image. In the registration, only those pixels that share the same field of view should be used to calculate the similarity measure:

\[ \Omega_{ij}^T = \left\{ x \in \Omega_i \mid T^{-1}(x) \in \Omega_j \right\} \]  
(2.7)

where \( T \) is the transformation describing the setup error.
2.3.3 Transformation

The transformation $T$ is assumed to be rigid and composed of three translations and three rotations. It is also assumed to be global, meaning that it applies to the entire patient volume. It is possible to look at special features, for instance a vertebra, and assume that the rigid transformation only applies to that feature, in which case it would be local. The transformation is defined as the transformation of coordinates from the treatment coordinate system (where the portal image is recorded) to the CT data coordinate system. A point $p$ with coordinates $(x_{\text{data}}, y_{\text{data}}, z_{\text{data}})$ in the data coordinate system is the transform $T$ of the coordinates $(x_{\text{treat}}, y_{\text{treat}}, z_{\text{treat}})$ in the treatment coordinate system:

$$(x_{\text{data}}, y_{\text{data}}, z_{\text{data}}) = T((x_{\text{treat}}, y_{\text{treat}}, z_{\text{treat}}))$$

The CT-data should be centered on the data coordinate system’s origin to make rotations of the system more natural [21].

2.3.4 Feature-based similarity measures

In the feature-based methods, natural landmarks or fiducial markers\(^1\) are identified in both the reference and in the floating image. The methods usually involve a segmentation step, where the interesting features are extracted from both floating and reference image and then compared and matched. Due to the low contrast in PIs, the segmentation step introduces inaccuracies in the measurement. The segmentation is often manual or semiautomatic, requiring some kind of user interaction. Segmentation can also be performed in the CT-data, where volumes with high attenuation coefficients are extracted (presumably bony features) and projected onto a 2D image [22].

2.3.5 Intensity-based similarity measures

Intensity-based methods on the other hand do not include a segmentation step. Instead, the intensity (grey-level values) at corresponding pixels in the floating image and the reference image is compared. These methods use all the available information in the images throughout the registration process [15]. To be precise, $I(x)$ and $J_T(x)$ are compared, where $x$ is a spatial coordinate, $T$ is the transformation and $I$ and $J$ the previously mentioned intensity distributions. There are several intensity-based similarity measures: correlation coefficient, mutual information, pattern intensity, correlation ratio, entropy and other. Correlation ratio and correlation coefficient have both been used successfully when comparing megavoltage PIs and MV-DRRs [4].

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\(^1\) A fiducial marker is a radio opaque marker inserted at a known position of the patient’s body. It provides an easily located landmark that can be used to determine the patient setup.
2.3.5.1 Correlation coefficient
The correlation coefficient assumes a linear relationship between each pixel in $I$ and $J$. It has been shown to work well even if there are contrast and brightness differences between the images, as well as with noise [23]. The correlation coefficient is calculated with the formula [24]

$$CC(T, I, J) = \frac{\sum_{x \in \Omega} (I(x) - \bar{I})(J(x) - \bar{J})}{\sqrt{\sum_{x \in \Omega} (I(x) - \bar{I})^2} \cdot \sqrt{\sum_{x \in \Omega} (J(x) - \bar{J})^2}}$$

(2.8)

where $\bar{I}$ and $\bar{J}$ are the mean values of $I$ and $J$. The correlation coefficient is equal to one for a perfect match and lower for worse matches.

2.3.5.2 Other similarity measures
- **Correlation ratio**
  Another similarity measure that works well when comparing PIs and MV-DRRs is the correlation ratio (CR). CR also considers the nearby intensities. These convey spatial information, since a certain tissue type never is represented by a single intensity value [25]. CR assumes a functional relationship between the image intensities.
- **Mutual information**
  Mutual Information is a popular intensity-based similarity measure. The strength of this measure is its applicability to a wide range of problems, since this measure doesn't assume a particular (linear or functional) relationship between intensity distributions [21], it only assumes that there is a relationship. For instance, it has been successfully used when matching CT-data with MR-data (Magnetic Resonance data).

2.3.6 Optimization
The optimization problem will be formulated as a minimization problem, meaning that the function to be minimized, the objective function, should have its minima at a perfect match of two images. The correlation coefficient (CC) is equal to one for a perfect match and lower for worse matches, meaning that the objective function will actually be $1 - CC$.

The problem can then be formulated in the following way:

$$T = \arg \min_T \left(1 - CC(T, I, J)\right)$$

(2.9)

Since the transformation $T$ has six parameters that need to be determined, this will be a minimization in six dimensions. In the majority of previous studies, non-gradient based methods have been used. This is mainly because the gradient of the objective function can be difficult, if not impossible, to derive. The downside of these methods is that they require more function evaluations than gradient based methods. In intensity-based image registration the function evaluation usually involves generating new DRRs. This is time consuming and therefore it is important to keep the number of function evaluations as low as possible. Another option of course, is to use a method that doesn’t have to generate new DRRs in each function evaluation.
2.3.7 Previous studies

Below follows a short presentation of a selection of previous studies. The studies presented have been selected based on their relevance and applicability to the work performed in this study. The results of the studies are presented in different ways, making the comparison between different studies difficult. All studies contain simulation tests similar to the tests performed in this work. One of these studies also includes a clinical test. A clinical test however has a problem of determining the true initial setup error. The registration simulations on the other hand have a correct answer. Thus, the methods can be seen as being verified by dependent data in the sense that there is a “correct answer”, one particular DRR that corresponds to the initial setup.

2.3.7.1 Lemieux et al [26]

The study performed by Lemieux et al were the first suggesting the use of an iterative registration procedure with rendering of DRRs at each new transformation of the CT data; a full 3D registration procedure. Diagnostic radiographs were matched to DRRs of a head phantom. This method also involves a hierarchical approach where the resolution of the images to be registered was increased during the registration process. The CT-data used had a voxel size of 0.67 · 0.67 · 1.5 mm³. The initial errors had a mean discrepancy of 5 mm in the translational directions and a mean discrepancy of 5.1º around the m-l axis, 3.8º around the c-c axis and 2.7º around the a-p axis. The results are presented as the average distance and standard deviation in millimeters between each point in a set of points in its desired position and the corresponding point transformed by the acquired transformation. The test points were spread inside a sphere with a 75 mm radius. After performing the registrations, the tests points deviated from their intended position with an average distance of 0.52 mm (± 0.14 mm).

2.3.7.2 Sarrut and Clippe [4]

This is an interesting study since it compares MV-DRRs with PIs using different intensity based similarity measures. A special method was used to render DRRs. It involves the precomputation of approximately 225 DRRs from different angles. Only rigid transformations of the patient pose were considered and the registration is 3D. The CT-data used had a voxel size of 0.93 · 0.93 · 5 mm³. The size of the initial setup errors is not presented in the paper. The results are presented in the same way as in Lemieux et al. However, only the average (and not the standard deviation) is presented. The authors refer to this as the RMS error. The test points were again spread out inside a sphere with a 75 mm radius. In the simulated experiments, with DRRs playing the role of the PIs, the performed registrations had a median RMS error of 0.45 mm. The entire registration procedure was performed in approximately 30 s. A clinical experiment was also performed with real PIs, where the correct pose was first assessed by a radiation oncologist. The registrations had a median RMS error of 1.7 mm, which is of course worse than in the simulation tests.

2.3.7.3 Gilhuijs et al [27]

This study describes an automatic procedure of determining the patient setup. The method is fast (the whole procedure takes approximately 2 minutes). The method adjusts the CT data to “maximize the distance through bone in the CT data along lines between the focus […] and bony features in the transmission images” and involves the delineation of bone in the transmission images. The transmission images in this case can be either PIs or simulator images. The initial setup errors had a SD of 3 mm in translation and 3º
in rotation. The registration results in simulation experiments has an accuracy of approximately 1 mm in each translational direction and 1º in each rotational direction.

### 2.3.7.4  Birkfellner et al [28]

In this study, a conventional full 3D method is compared to a new method called the 5+1 method, which requires less iterations and hence less DRR generations. This method evaluates 5 degrees of freedom using a full 3D technique, and determines the last degree of freedom (rotation around the central beam axis) through a 2D/2D procedure. In the study, only one beam was used, something which reduces the accuracy of the method. The initial setup was allowed to vary in the interval ± 10 mm and ± 5º. The full 3D method had an average accuracy of 1.0 ± 0.6(º) and 4.1 ± 1.9(mm) while the 5+1 method had an accuracy of 1.0 ± 0.7(º) and 4.2 ± 1.6(mm). The results of the two methods are similar, but the 5+1 method required only a third of the time needed by the full 3D method to reach registration.

The so called RMS error used in the first two studies, also called Target Registration Error (TRE) is a way of representing the accuracy of a registration method mostly used in point-based registration. In this study however, the results are presented as rotation error around rotation axes and displacement error along the displacement directions (in the same way as the two last studies) since this fully describes the 3D registration error.
3 Methods and materials

3.1 Implementation of DRR generation

The following section describes the methods and algorithms behind the generation of DRRs.

3.1.1 The reference coordinate system

Several coordinate systems are used to describe the treatment setup. The main coordinate system, the reference coordinate system, is the one defined relative to the ideal, expected position of the patient. It is defined as depicted in Figure 3-1 and the patient is positioned to have its isocenter in the origin. This definition does not conform to the DICOM standard, where the coordinate system is rotated 180° around the x-axis in Figure 3-1. There is also one coordinate system associated with the beam and one coordinate system associated with the actual position of the patient. All coordinate systems are defined relative to the reference coordinate system.

3.1.2 The PI detector

The response of a state-of-the-art EPID was modeled in the present work. PortalVision aS500 is an amorphous silicon (aSi) detector with dimensions ~ 40x30 cm² and 512x384 pixels. According to Herman et al [Herman] amorphous silicon detectors come close to being ideal image receptors that add little noise and display the image well. The aS500 EPID has been investigated and described in several studies, both regarding the effects of backscattering from the detector (for instance [29][30]) and the use of the EPID for dosimetric verification (for instance [31][32]). The pixels have a width of 0.784 mm. An amorphous silicon detector detects the radiation indirectly which means that the photons are first transformed to visible light. The EPID has a 1 mm layer of copper covering a scintillating layer (in this case Gd₂O₂S:Tb). In the copper layer, the high energy photons produce secondary electrons which in turn produce visible photons in the scintillating layer. The actual composition and parts of the detector is unknown (i.e. not revealed by the manufacturer). The response of the detector is linear with energy fluence (within ± 2 % of ideal linearity) [32].
### 3.1.3 Generating DRRs

The CT-data and its orientation relative to the source and the detector are needed before the generation of a DRR can start. The fluence at each pixel is calculated in order to derive a grey level value. The calculation was performed using the equations

\[
I(d_w) = I_0 r^{-2} e^{-\mu_w d_w} \\
(3.1)
\]

\[
d_w = \frac{1}{\rho_w} \sum \rho_v d_v \\
(3.2)
\]

where \( I \) is the fluence at the pixel, \( I_0 \) is the primary fluence at some point, \( r \) is the distance between that point and the pixel, \( \mu_w \) is the attenuation coefficient in water and \( d_w \) is the \textit{water-equivalent distance} between the source and the pixel. \( \rho_w \) is the density of water, \( \rho_v \) is a voxel traversed by a ray traced from the source to the pixel, and \( \rho_v d_v \) is the distance traversed in the voxel.

The algorithm for DRR generation and ray tracing is summarized in the following steps:

1. A ray is traced between the source and center of each pixel in the detector.
2. The CT-number in each traversed voxel is transformed to density using a calibration curve for the specific CT-scanner.
3. The water-equivalent thickness of the patient along the ray is calculated according to (3.2).
4. The fluence in the isocenter plane is known. The inverse square law, where \( r \) is the distance between the pixel and the point where the ray intersects the isocenter plane, gives the fluence at the detector.
5. The fluence \( I \) is calculated according to (3.1).
6. When the energy fluence at each pixel has been derived, the values are transformed into appropriate grey level values.

The transformation from CT-number to density depends on the specific CT-scanner. The spread of photon energies within the beam is ignored, and all photons are assumed to have the same energy. The linear absorption theory only calculates primary energy fluence, and the contribution of scattered photons to the image is also ignored (the consequences of this is discussed further in the following section).

Each image has 256 different grey levels. The windowing of the image, deciding which energy fluence value that corresponds to the highest grey level and which corresponds to the lowest grey level, had to be performed prior to registration.

In the implementation it is possible to select photon energy as well as different source – detector distance (SDD). It is also possible to select the pixel size and whether or not the CT-data should be interpolated prior to DRR-generation.
3.1.4 Contribution from scatter and noise

It could be useful to calculate secondary radiation contributions to the reference images since this would make the registration simulation more similar to a real PI registration. However, when generating the DRRs, secondary radiation was not regarded due to the following. A short distance between the patient and the detector should produce noisier images, since more secondary radiation reaches the detector. However, the distance between the source and the detector has been shown not to have that effect on EPID image quality. In fact, patient generated scatter has been found to have an insignificant effect on EPID image quality except in extreme situations with very large patient thicknesses and very small distances between patient and detector [12] [29]. Most of the noise is produced by scatter in the detector itself. Therefore it seems unnecessary to calculate the contribution of secondary radiation from the patient to the image.

The easiest way of simulating the contribution of scatter in the reference image, both from patient and detector, is by simply adding random noise. In reality, the contribution of secondary radiation is not necessarily uniform across the image, but the approach should work well when examining how well the registration algorithm works when there are differences in grey scale value between the reference and the floating image.

3.2 Image registration algorithms

The following section describes the methods and algorithms used in image registration.

3.2.1 The optimization

The optimization procedure is a vital instrument in the registration process. The Powell-Brent method was used in this thesis. This method does not require calculations of the gradient of the objective function. It instead requires a larger number of evaluations of the objective function.

The Powell-Brent method has behaved robustly in other studies [4][21] although the risk of getting trapped in local minima is high. By down-sampling the images, local minima can be avoided and at the same time the computational time is decreased [21], although that has not been implemented here. The generation of new DRRs is a part of evaluating the objection function in some of the registration methods. Therefore a large number of evaluations seriously effects the time needed to perform the match.

In short, the Powell-Brent method is a conjugate direction set method. The function is minimized along an initial direction using methods for one dimensional minimization, and then minimized along another direction and so on, until optimum is reached. The trick is choosing the directions, so that minimization along one direction doesn’t spoil the previous minimizations. So called conjugate directions have this property. The directions $u$ and $v$ are said to be conjugate if they have the property

$$ u \cdot A \cdot v = 0 $$

where $A$ is a symmetric matrix. The optimization procedure and the implementation used here are described in detail in Press et al [33], from which the following description has been obtained.
Powell initially came up with a procedure to derive $N$ mutually conjugate directions in an $N$-dimensional space without information about the gradient of the objective function:

1. Use the basis vectors as initial search directions $u_i, i = 0, \ldots, N-1$
2. Save the starting position as $P_0$
3. For $i = 0, \ldots, N-1$ move $P_i$ to the minimum along direction $u_i$ and call this point $P'_i$
4. For $i = 0, \ldots, N-2$ set $u_i \leftarrow u_{i+1}$
5. Set $u_{N-1} \leftarrow P_N - P_0$
6. Move $P_n$ to the minimum along direction $u_{N-1}$ and call this point $P_0$
7. Repeat steps 2 to 6 until the function stops decreasing

Powell proved that $k$ iterations of steps 2 – 6 will produce a set of search direction $u_i$ whose last $k$ members are mutually conjugate. A problem with this procedure however, is that the search directions tend to become linearly dependent meaning that the method only finds a minimum in a subspace of the initial $N$-dimensional space (that is, it doesn’t find the right extreme point). This can be dealt with in several ways. In the original procedure described above the direction $u_0$ is always discarded, which means that information about conjugate directions is thrown away. Instead of indiscriminately discarding the $u_0$ direction, another procedure is employed. The basic idea of this modified version is to still accept $P_N - P_0$ as a new direction, but instead of discarding $u_0$, the direction along which the objective function made its largest decrease is thrown away. Chances are that this direction is a major part of $P_N - P_0$ and by discarding it, the risk of linear dependence building up is decreased. A few other rules are also used to determine if it could be better not to add a new direction at all.

To perform the minimization in one dimension of the objective function $f$, Brent’s method is used. First the minimum is bracketed by two points $a < c$ and a third point $b$ in-between is evaluated to ensure that

$$f(a) > f(b) < f(c) \quad (3.3)$$

The method then proceeds by fitting a parabola to these three points and the function is evaluated at the minimum abscissa $c$ of this parabola. Depending on the value of $f(c)$, $c$ is substituted into the triplet $[a \ b \ c]$ so that the condition (3.3) is still satisfied. Brent’s method will switch to golden section search if the parabolic interpolation isn’t working.

### 3.2.2 2D2D registration

As a first step, two 2D images are registered to evaluate the optimization method and similarity measure. The optimization procedure determines the three parameters $(t_x, t_y, \theta)$ of the in-plane transformation between the images, $T_{12}$. 

20
Two DRRs are generated, one reference DRR with a known setup error in the CT-data and one floating DRR with the expected position of the CT-data (that is, without setup error). The optimization procedure reaches registration of the images by iteratively changing the parameters to find the match. This method does not require any generation of new DRRs during registration (Figure 3-2).

3.2.2.1 Objective function
In this 2D2D case, the overlapping points are assumed to share the same field-of-view when the objective function is evaluated. Hence, the similarity measure should only be calculated for those points. Each new set of \((t_x, t_y, \theta)\) tried by the optimization procedure defines a 2D transformation between the images. The overlapping points of the rotated floating image and the reference image are easy to find. Nearest neighbor interpolation is used and the correlation coefficient is calculated. New parameter values, and hence new overlapping field-of-views, are tried until a satisfactory registration is reached.

3.2.3 2D3D registration
The next step is to retrieve the full 3D setup error. A rigid transformation has six degrees of freedom. The parameterization of the setup error could be done in several ways. The most straightforward way, the one used here, is translation in the x, y and z-direction \((t_x, t_y, t_z)\) and rotation about x-axis \((\theta_x)\), the y-axis \((\theta_y)\) and the z-axis \((\theta_z)\). The x-, y- and z-axes are axes of the reference coordinate system (Figure 3-1).

As mentioned earlier, a 2D3D registration method is a method that aligns spatial data to projective data [15], for instance CT-data to PIs. The 2D3D method implemented as part of this study (referred to as the full 2D3D method or simply the 2D3D method) is straightforward. At least two different gantry angles are used to obtain the setup error. Each reference image is compared to a DRR generated with known setup error. A reference image and its corresponding floating image are referred to as an image pair. An optimal match is again determined using the Powell-Brent method. Since one new DRR per gantry angle has to be generated at each evaluation of the objective function this is a time consuming method. This method was first presented by Lemieux et al [26].
3.2.3.1 Objective function for several image pairs
Evaluating the correlation coefficient for more than one image pair could be done in several ways. For instance, the correlation coefficient of each image pair could be linearly combined. Another way, advocated by Sarrut and Clippe [4] and used in this thesis, is to simultaneously calculate the correlation coefficient of all the image pairs. Instead of only including pixels from one image pair, the calculation is performed including the pixels with overlapping field of view from all image pairs. In the 2D3D method, the images in an image pair are assumed to share the same field of view. Therefore, the correlation coefficient is evaluated for all pixels in all images.

3.2.4 Semi-2D3D registration
Clearly, simply matching the two images in the 2D2D method doesn’t yield enough information about the 3D transformation of the setup error. However, it would be advantageous if it were possible to avoid generating a new DRR in each evaluation of the objective function, as in the 2D3D method. It should be possible to exploit the fact that rotations which are out-of-plane for one gantry angle might be in-plane for another. By performing a 2D2D registration for several gantry angles, all parameters could be derived. In coplanar treatments, the z-axis is always parallel to the imaging plane and hence \( \theta_z \) is not possible to determine by 2D2D registration.

The main idea of this method is to convert the 3D transformation suggested by the optimization procedure into a 2D transformation (in-plane rotations and translations) for each gantry angle \( \alpha \):

\[
T(t_x, t_y, t_z, \theta_x, \theta_y, \theta_z) \Rightarrow T_{ix}(t_{ix}, t_{iy}, \theta_i) \tag{3.4}
\]

The out-of-plane parts for each angle are ignored. If only coplanar treatments are regarded, the parameter \( \theta_i \) must be determined some other way. This method, when the parameters \( t_x, t_y, t_z \) and \( \theta_x \) and \( \theta_y \) can be determined through 2D2D matching of several image pairs, is referred to as the semi-2D3D method. If non-coplanar treatments are performed, \( \theta_z \) could also be estimated using this method, although that has not been evaluated in this thesis.

The method can also be used iteratively, with the result of one optimization used as starting point for another, with a new set of reference DRRs generated at the next starting point.

3.2.4.1 Retrieving in-plane rotations and translation
The derivation of \( T_{ix}(t_{ix}, t_{iy}, \theta_i) \) is based on the assumption that all rotations are small. The rotation of the rigid body can be described by a rotation matrix \( R \). The rotation of angle \( \theta_x \) around the x-axis is represented by the matrix

\[
R_x = \begin{bmatrix}
1 & 0 & 0 \\
0 & \cos \theta_x & -\sin \theta_x \\
0 & \sin \theta_x & \cos \theta_x 
\end{bmatrix} \tag{3.5}
\]

and the rotation \( \theta_y \) and \( \theta_z \) around the y- and z-axis respectively, are represented by the matrices
If the body is rotated an angle $\theta_x$ around the x-axis and then $\theta_y$ and $\theta_z$ around the y- and z-axis, the rotation matrix $R$ of the composite rotation is the product of the rotational matrices of each rotation: $R = R_x(\theta_x)R_y(\theta_y)R_z(\theta_z)$. Assuming small angles, the matrix $R$ can be written as

$$R(\theta_x, \theta_y, \theta_z) = \begin{bmatrix} 1 & -\theta_z & \theta_x \\ \theta_z & 1 & -\theta_y \\ -\theta_x & \theta_y & 1 \end{bmatrix}$$ \hspace{1cm} (3.6)$$

The rotation of a rigid body can also be characterized by an angle of rotation $\omega = (\omega_x, \omega_y, \omega_z)^T$ and $R$ can also be written in the following way according to Rodrigues’ formula:

$$R(\omega) = I + \sin\|\omega\| \left[ S(\omega) + O(\|\omega\|^2) \right]$$ \hspace{1cm} (3.7)$$

where 

$$S(\omega) = \begin{bmatrix} 0 & \omega_z & -\omega_y \\ -\omega_z & 0 & \omega_x \\ \omega_y & -\omega_x & 0 \end{bmatrix}$$

and $I$ is the identity matrix.

For small angles, $R(\omega)$ can be approximated by

$$R(\omega) \approx I + S(\omega)$$ \hspace{1cm} (3.8)$$

Comparing (3.7) to (3.8) shows that for small angles

$$\omega = (-\theta_x, -\theta_y, -\theta_z)^T$$ \hspace{1cm} (3.9)$$

The in-plane rotation $\theta_i$ for a certain gantry angle is the inner product of $\omega$ and the normal to the image plane (see Figure 3-3). Similarly, the in-plane translation $(t_{i,x}, t_{i,y})$ is the projection of $(t_x, t_y, t_z)$ on the image plane (again see Figure 3-3). The translation in the image plane has to be scaled by the factor $\frac{SDD}{SID}$ where $SDD$ is the source-detector distance and $SID$ is the source-isocenter distance.
3.2.4.2 Objective function

The correlation coefficient is calculated for all gantry angles simultaneously, similarly to the 2D3D method, but only for those parts of the images that presumably share the same field-of-view, as in the 2D2D case. The overlapping part of each image pair is determined by \( T_{||,\omega} \).

3.2.5 Semi-2D3D-\( \theta_z \) registration

The method described above can be used to determine all those rotations that are in-plane to at least one of the detector planes. However, as stated earlier, setup error rotations around the rotational axis of the gantry are always out-of-plane to all detector planes in coplanar treatment and can therefore not be determined with this approximate method. To retrieve this last rotation, a 2D3D registration has to be performed. However, the optimization only has to be performed on one variable (\( \theta_z \)), so instead of using the Powell-Brent optimization method (optimization in several dimensions), only the line search method (optimization in one dimension) is used. The registration is performed in the following steps:

1. Semi-2D2D registration to determine \( t_x, t_y, t_z, \theta_x \), and \( \theta_y \)
2. 2D3D registration to determine \( \theta_z \) (keeping the other variables fixed as determined in step 1.)

These steps can then be repeated until a satisfactory result is reached. This method, which combines the semi-2D3D method with the full 2D3D method, is referred to as the semi-2D3D-\( \theta_z \) method.

3.3 Test protocol

In the tests presented in this thesis, no registrations with real PIs were performed. Instead, the tests consisted entirely of simulated data, where DRRs were registered to other DRRs generated from the same CT-data. This approach makes it possible to compare the different methods.

The CT-data from two different patients were used to evaluate the DRR algorithm and the registration methods, one head-and-neck patient and one prostate patient. The
specification of the CT-data is displayed in Table 3-1. The larger part of the tests was performed on the prostate patient. The CT-data was linearly interpolated in the \( \zeta \) direction prior to use in order to yield smoother-looking DRRs.

<table>
<thead>
<tr>
<th></th>
<th>Prostate</th>
<th>Head/Neck</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of pixels</td>
<td>X: 512</td>
<td>512</td>
</tr>
<tr>
<td></td>
<td>Y: 512</td>
<td>512</td>
</tr>
<tr>
<td></td>
<td>Z: 67</td>
<td>89</td>
</tr>
<tr>
<td>Pixel dimensions (mm)</td>
<td>X: 0.9</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>Y: 0.9</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>Z: 3.0</td>
<td>3.0</td>
</tr>
</tbody>
</table>

*Table 3-1. Specifications of the CT-data sets used in the tests.*

As previously stated, the EPID detector that was modeled had an effective detector area of approximately 30 x 40 cm\(^2\). In the registration simulations no full-sized DRRs were generated, only smaller DRRs (256 x 192 pixels) with the same pixel size as the \(aS\)00 EPID, with an area (in the imaging plane) of approximately 20 x 15 cm\(^2\). There is no reason why smaller DRRs could not be registered to larger PIs. It corresponds to extracting a region of interest in the DRR and matching it to the PI. The images were mainly generated with a photon energy of 6 MeV (approximately equivalent to a 18 MV beam). A source-detector distance of 140 cm was used in all tests.

In some tests, random noise was added to the reference images to simulate the contribution by noise and scatter to the image recorded by the EPID. The pixel value was allowed to vary within a certain range for all pixels. The most common interval was \( \pm 25 \) grey levels but the interval \( \pm 50 \) was also tried in one instance. Unless otherwise stated, the \( \pm 25 \) grey level interval is used. As mentioned earlier, there are 256 grey levels.

![Figure 3-4](image)

*Figure 3-4. The distribution of the initial setup error parameter \( t_x \) in one of the tests. The parameter was allowed to vary in the range \(-3, 2\) cm.*

Generally, the tests of the registration methods consisted of performing several registrations with different, random, setup errors within a certain interval (see Figure...
The setup errors were generated with a random number generator. The size of the translations is measured in the isocenter plane. For each test, the initial error distribution is represented by the standard deviation of the distribution.

The results are displayed in tables and the data are given as absolute average value and standard deviation of the error in registration, that is, the difference between the estimated setup error and the initial setup error for all parameters. Of course, the difference should be as small as possible.

In all registration tests, mismatches that were easy to detect by looking at the obtained objective function value were removed before calculating mean error and standard deviation. (The value should be close to 0, so if a value of 0.7 is obtained, it is clearly a mismatch.) No absolute value of the objective function has been determined to indicate that the registration resulted in a mismatch. Instead, it was determined by comparing the different values obtained for a particular test. Note that a mismatch is defined as not reaching a low enough objective function value, and not as achieving a bad registration result.

The semi-2D3D, semi-2D3D-θ, and the full 2D3D registrations were all performed with the same abortion criteria in the optimization. All registration methods start by assuming no setup error. To improve the performance of the optimization procedure, the search was restricted to ±30 mm in translation and ±26° (0.5 radians) of rotation.

A summary of the most important registration tests is presented below.

### 3.3.1 2D2D tests

The 2D2D registration method was evaluated in three different tests. Two gantry angles, 0° and 90°, and both test patient data sets were used.

- **Test 1.** The aim was to evaluate the general performance of the registration algorithm. There was no out-of-plane rotation in the floating image. 20 random setup errors per gantry angle and patient, in the range ± 20 mm in translation and ± 11.4° (0.2 radians) in rotation, were generated and tested.

- **Test 2.** The aim in this case was to evaluate the performance when noise had been added in the reference DRR. There was still no out-of-plane rotation in the floating image. The setup errors were in the same range as in test 1. Two different noise levels: ±25 grey levels per pixel and ±50 grey levels per pixel were tested and only the prostate patient was used.

- **Test 3.** In this case, the general behavior in the presence of out-of-plane rotation in the floating image was investigated. The setup errors were in the range ±10 mm in translation and ±5.7° (0.1 radians) in rotation.

### 3.3.2 Semi-2D3D tests

The semi-2D3D method was evaluated in a similar way as the 2D2D method. The tests were mainly performed on the prostate patient data with three gantry angles: 0°, 45° and 90°. If nothing else is mentioned, coplanar treatment is assumed, in which case θz cannot be determined.

- **Test 4.** The aim was to evaluate the performance of the algorithm when the setup error contains no rotation around the cranial-caudal axis. Several different setup error ranges were tested (presented as different test cases), the largest one being
± 20 mm in translation and ± 11.4° (0.2 radians) in rotation. 50 different random setup errors per test case were generated.

- Test 5. The method was also used iteratively, with the result of one optimization used as starting point for another, with new DRRs generated at the new starting point. This was tested both with and without cranial-caudal rotation in the setup error. Setup errors in the range ± 20 mm in translation and ± 11.4° (0.2 radians) in rotation were used. 25 different random setup errors per test case were generated.

3.3.3 Semi-2D3D-$\theta_z$ and full 2D3D

The semi-2D3D-$\theta_z$ method was evaluated with the 0°, 45° and 90° gantry angles. During the 2D3D part of registration, only the 0° and 90° gantry angles were used. The method was run in five steps:

1. semi-2D3D to determine all parameters except $\theta_z$
2. 2D3D to determine cranial-caudal rotation ($\theta_z$)
3. semi-2D3D (as step 1)
4. 2D3D (as step 2)
5. semi-2D3D (as step 1)

The result of each step is used as input for the next step. The result after each step is displayed in the result table. Each test included 25 different registrations with random initial setup errors.

- Test 6. The general performance of the method was tested with initial setup errors in the range ± 10 mm in translation and ± 5.7° (0.1 radians) in rotation and in the range ± 20 mm in translation and ± 11.4° (0.2 radians) in rotation.

The full 2D3D method was not evaluated extensively. Instead, some tests were performed as a comparison to the semi-2D3D-$\theta_z$ method. This was done to compare the time required for each method. These tests included 10 different registrations (due to the long time needed by the full 2D3D method). The result after step 5 of the semi-2D3D-$\theta_z$ is presented in the result table.

- Test 7. Semi-2D3D-$\theta_z$ was tested and compared to the full 2D3D method. The initial setup error was in the range ± 15 mm in translation and ± 5.7° (0.1 radians) in rotation. It was performed both for the prostate patient and the head and neck patient, both with and without noise.
4 Results and discussion

4.1 DRRs

First, the performance of the DRR-generation algorithm was examined. Only a few real PIs are available as reference (Figure 4-1). In Figure 4-1, the DRR (on the right) has been generated with the CT-data interpolated from $0.9 \times 0.9 \times 3$ mm$^3$ voxels to voxels of the size of $0.9 \times 0.9 \times 1.5$ mm$^3$. The DRR still shows the voxels of the CT-data. Otherwise the contrast and general appearance of the two images are similar. Note the dark area in both images which is the bladder. The visibility of low density passages is enhanced in MV photon projection images, since the subject contrast of bone is reduced to a larger extent then the subject contrast of low density regions [12]. Figure 4-2 shows the same DRR as in Figure 4-1 generated with different CT-data interpolation.

The time needed to generate the 256 x 192 pixel image in Figure 4-1 was 15 seconds. In Alakuijala et al, a DRR with 192 x 192 pixels take 3 seconds to generate. However that was done on CT-data with 48 slices consisting of 256 x 256 pixels, which should be compared to the CT-data used here, with 67 slices with 512 x 512 pixels. If we assume that both these CT-volumes cover the same patient volume, our CT-data contains more than 5 times as much data. The conclusion of this is that the DRR generation can be considered to perform as expected regarding time consumption.
4.2 Registration tests

The tests performed to investigate the registration methods have been described earlier and the results are presented below. The smallest shift in the CT-data that can be detected by the objective function is limited by the pixel size. The pixel size in the isocenter plane is 0.56 mm which means that translations of the CT-data smaller than ±0.28 mm cannot be detected. The smallest detectable in-plane rotation was ±0.2°.

4.2.1 Evaluation of the 2D2D-method

4.2.1.1 Test 1 – General Performance

The result of test 1 is displayed in Table 4-1. Even though the initial setup errors could be large, there was only one mismatch in one test case. The mismatch occurred as a result of large initial translational setup error (The initial setup error is measured in the isocenter plane, so a translation of 20 mm corresponds to a translation of 28 mm in the image plane). Note that the 90° gantry angle of the prostate patient produces good results even though the contrast in those images is low (see Figure 4-4) and few features are distinguishable.

<table>
<thead>
<tr>
<th>Patient, gantry angle</th>
<th>Mean error and standard deviation</th>
<th>Mismatches/Registrations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>x (mm)</td>
<td>y (mm)</td>
</tr>
<tr>
<td>Prostate, 0°</td>
<td>0.0 ± 0.2</td>
<td>0.1 ± 0.2</td>
</tr>
<tr>
<td>Prostate, 90°</td>
<td>0.0 ± 0.1</td>
<td>0.1 ± 0.2</td>
</tr>
<tr>
<td>Head/Neck, 0°</td>
<td>0.0 ± 0.6</td>
<td>0.1 ± 0.3</td>
</tr>
<tr>
<td>Head/Neck, 90°</td>
<td>0.1 ± 0.4</td>
<td>0.1 ± 0.6</td>
</tr>
</tbody>
</table>

Table 4-1: Mean error and standard deviation of error, only in-plane rotations and translations with standard deviation 12 mm in translation and 6.2° in rotation.
4.2.1.2 Test 2 – Noise

Table 4-2 displays the result of test 2. In the ± 25 case, the results are comparable to the no noise case (see Table 4-1) for all parameters except in the x-direction from the 90° gantry angle. The 90°, ± 50 – case differs a lot from the no noise case. Again, this is probably due to the low contrast of those images (especially along the x-axis), which is further degraded by the added noise (see Figure 4-3). In fact, it is surprising that the 90°, ± 25 – case works well. Note also that the results are good in the 0°, ± 50 – case.

<table>
<thead>
<tr>
<th>Patient, gantry angle, noise interval</th>
<th>Mean error and standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>x (mm)</td>
</tr>
<tr>
<td>Prostate 0°, ± 25</td>
<td>0.0 ± 0.3</td>
</tr>
<tr>
<td>Prostate 90°, ± 25</td>
<td>0.7 ± 1.0</td>
</tr>
<tr>
<td>Prostate 0°, ± 50</td>
<td>0.0 ± 0.3</td>
</tr>
<tr>
<td>Prostate 90°, ± 50</td>
<td>3.0 ± 4</td>
</tr>
</tbody>
</table>

Table 4-2. Mean error and standard deviation of error, only in-plane rotations and translations with standard deviation 12 mm in translation and 6.6° in rotation. Noise has been added to the floating image. “± 25” refers to the interval of grey levels, within which the random noise was allowed to fluctuate for each pixel. No mismatches, 20 registrations per gantry angle.

4.2.1.3 Test 3 – Out-of-plane rotation

The results (Table 4-3) are somewhat difficult to interpret. No clear mismatches could be found. The setup error was allowed to be in the interval ±10 mm in translation and ± 5.7° in rotations in this case and the results show that a fairly good match is found in all cases except in the 0° head-and-neck case. These results seem to confirm that out-of-plane rotations smaller than 3° don’t distort the image significantly. The result in the 0° head-and-neck case could be due to the somewhat blurry appearance of those images, but it is surprisingly bad compared to the results in Table 4-1.

<table>
<thead>
<tr>
<th>Patient, gantry angle</th>
<th>Mean error and standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>x (mm)</td>
</tr>
<tr>
<td>Prostate 0°</td>
<td>0.7 ± 1.4</td>
</tr>
<tr>
<td>Prostate 90°</td>
<td>0.1 ± 0.7</td>
</tr>
<tr>
<td>Head/Neck 0°</td>
<td>1.3 ± 3.1</td>
</tr>
<tr>
<td>Head/Neck 90°</td>
<td>0.3 ± 1.1</td>
</tr>
</tbody>
</table>

Table 4-3. Mean error and standard deviation of error in presence of out-of-plane rotations and translations. Setup errors with standard deviation 7 mm, 4.5°. No mismatches.

The conclusion of these tests is that the 2D2D registration works well for in-plane rotations and translations and that it behaves fairly well also in the presence of out-of-plane rotations. The objective function also works when noise is added to the floating image.
Figure 4-3. DRRs of the prostate patient generated from a 90° gantry angle. Noise interval ± 25 is displayed on top and ± 50 below. Note the poor contrast and absence of distinguishing features.
4.2.2 Evaluation of the semi-2D3D method

4.2.2.1 Test 4 – General performance

Several tests with different setup error ranges were performed to examine the general performance of the semi-2D3D method. The results are shown in Table 4-4. No rotation around the cranial-caudal axis was present.

<table>
<thead>
<tr>
<th>Test case, setup error stdv</th>
<th>Translation (mm)</th>
<th>Rotation (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>m-l</td>
<td>a-p</td>
</tr>
<tr>
<td>a) 6 mm 3.4°</td>
<td>0.0 ± 0.2</td>
<td>0.3 ± 0.9</td>
</tr>
<tr>
<td>b) 12 mm 2.9°</td>
<td>0.1 ± 0.3</td>
<td>0.1 ± 1.7</td>
</tr>
<tr>
<td>c) 6 mm 5.8°</td>
<td>0.1 ± 0.3</td>
<td>0.0 ± 1.1</td>
</tr>
<tr>
<td>d) 11 mm 5.8°</td>
<td>0.1 ± 0.4</td>
<td>0.1 ± 2.0</td>
</tr>
<tr>
<td>e) 6 mm noise ± 25</td>
<td>0.0 ± 0.2</td>
<td>0.3 ± 1.1</td>
</tr>
</tbody>
</table>

Table 4-4. Mean and standard deviation of error in registration, no rotation around the cranial-caudal axis. All tests were performed with 3 gantry angles: 0°, 45° and 90° on a prostate patient. 50 registrations per test.

Note that the difference in result when random noise is added to the floating images is very small (test cases a) and e)). Test case a) was repeated once using only the 0° and 90° gantry angles and once using the 0° and 72° gantry angles. The difference in result was negligible. When test case a) was repeated with gantry angles 0°, 120°, and 240° the results for translation in the a-p direction was improved significantly, to 0.1 ± 0.3 mm, indicating that this is actually a better choice of gantry angles. The results for rotation around the m-l axis also improved to 0.2 ± 0.3. This is probably due to the fact that the problematic 90° gantry angle, which results in poor contrast images (see Figure 4-3), is avoided. Note that no obvious mismatches could be found in the tests in Table 4-4.

An important conclusion of Table 4-4 is that smaller initial setup errors result in better registration results (compare test case a) with test case d)). Also, the registrations in test case a) required slightly less time then those in test case d), 2.8 minutes as opposed to 3 minutes, indicating that a better starting guess leads to faster registration.

The poor result in the anterior-posterior direction could again be due to the lack of distinguishing features in the DRRs from the 90° gantry angle (Figure 4-4). This conclusion is supported by the results in Table 4-5 where test case a) and b) were repeated for the head-and-neck patient. These DRRs have a better contrast from the 90° gantry angle (Figure 4-4 again). The a-p translational direction does not display much larger error than the other translational directions in the registrations performed on this patient. This is also supported by the fact that other gantry angles (0°, 120° and 140°) produced a better result in the a-p direction.
<table>
<thead>
<tr>
<th>Test case, setup error stdv</th>
<th>Translation (mm)</th>
<th>Rotation (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>m-l</td>
<td>a-p</td>
</tr>
<tr>
<td>a) ± 6 mm, ± 2.9°</td>
<td>0.1 ± 0.5</td>
<td>0.1 ± 0.4</td>
</tr>
<tr>
<td>b) ± 11 mm, ± 2.9°</td>
<td>0.3 ± 1.0</td>
<td>0.2 ± 0.6</td>
</tr>
</tbody>
</table>

Table 4-5: No rotation around the cranial-caudal axis. All tests were performed with 3 gantry angles: 0°, 45° and 90° on a head-and-neck patient. 50 registrations per test.

Figure 4-4: DRRs generated from a 90° gantry angle of prostate (top) and head-and-neck patient (below). Hardly any features are visible in the pelvis case.
The progress of optimization for one semi-2D3D registration is displayed in Figure 4-5. Note that it does not converge towards 0. This is because there are still out-of-plane components in the setup error for all gantry angles, despite the lack of c-c rotation. The progress of optimization for a larger initial setup error converges towards a larger value, since there are larger out-of-plane rotations present in such a setup.

![Figure 4-5. Progress of optimization for the semi-2D3D method. Note that the objective function does not converge towards 0.](image)

4.2.2.2 Test 5 - Iteration

Test 4 d) was performed again but with fewer registrations, this time to examine the results with the semi-2D3D method performed twice. In the second iteration, new DRRs are generated at the position reached by the first iteration. The results are displayed in Table 4-6. There is an obvious improvement between the first and the second iteration when there is no rotation around the cranial-caudal axis.

<table>
<thead>
<tr>
<th>Test case d)</th>
<th>Translation (mm)</th>
<th>Rotation (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>m-l</td>
<td>a-p</td>
</tr>
<tr>
<td>Iteration 1, no c-c rot</td>
<td>0.1 ± 0.4</td>
<td>0.2 ± 2.3</td>
</tr>
<tr>
<td>Iteration 2, no c-c rot</td>
<td>0.0 ± 0.3</td>
<td>0.2 ± 0.9</td>
</tr>
<tr>
<td>Iteration 1, c-c rot</td>
<td>6.9 ± 14.3</td>
<td>0.2 ± 4.3</td>
</tr>
<tr>
<td>Iteration 2, c-c rot</td>
<td>4.0 ± 9.3</td>
<td>1.3 ± 5.4</td>
</tr>
</tbody>
</table>

Table 4-6. Tests with the semi2D3D method performed twice. Setup errors with standard deviation 6.4° and 11 mm. In the case with c-c rotation, it was kept in the same range as the other rotations (i.e. a standard deviation of 6.4°).

Table 4-6 also shows the same test in the presence of cranial-caudal rotation. There is no improvement between the first and the second iteration in the presence of these large out-of-plane rotations and in several parameters the result is actually worse after the second iteration. Clearly, the semi-2D3D method does not work well in the presence of large c-c rotations.
Figure 4-6 shows the progress of optimization for the iterated semi-2D3D method without c-c rotation. The step in the curve illustrates the drop in objective function value as new DRRs are generated at the position reached by the first iteration.

![Figure 4-6. Progress of optimization for iterated semi-2D3D method. Note the step in the curve at the start of the second semi-2D3D iteration.](image)

4.2.3 Evaluation of the semi-2D3D-θz method

4.2.3.1 Test 6 – General performance

The semi-2D3D-θz method was developed to improve the performance of the semi-2D3D method when c-c rotations are present. In Table 4-7 and Table 4-8 the results of the five-step semi-2D3D-θz evaluation (described in section 3.3.3) are shown. In Table 4-7, the initial setup errors were smaller than in Table 4-8. After all five steps, the results are good in both cases. However, when the rotations are large the failure rate is high. There were 6 mismatches in the 25 registrations performed which have all been removed from the result. Closer inspection of the mismatches showed that they occurred when the setup error had large rotational parts around more than one axis, although some registrations succeeded with such initial errors. Table 4-7 also shows the relative time consumption of the different steps.
### Table 4-7. Setup errors with standard deviation 3.5° and 6 mm. 25 registrations.

<table>
<thead>
<tr>
<th></th>
<th>Translation (mm)</th>
<th>Rotation (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>m-l</td>
<td>a-p</td>
</tr>
<tr>
<td>step 1.</td>
<td>0.1 ± 0.3</td>
<td>1.5 ± 2.7</td>
</tr>
<tr>
<td>step 2.</td>
<td>0.4</td>
<td>-</td>
</tr>
<tr>
<td>step 3.</td>
<td>0.1 ± 0.3</td>
<td>0.2 ± 0.6</td>
</tr>
<tr>
<td>step 4.</td>
<td>0.3</td>
<td>-</td>
</tr>
<tr>
<td>step 5.</td>
<td>0.1 ± 0.3</td>
<td>0.0 ± 0.2</td>
</tr>
<tr>
<td>Final result</td>
<td>1.0 ± 0.3</td>
<td>0.0 ± 0.2</td>
</tr>
</tbody>
</table>

Prostate. No obvious mismatches.

The method seems to work well and achieve good results. When the setup errors are small, the results are good already after step 4, but larger initial errors also require a fifth step. Again, the results seem to confirm that out-of-plane rotations smaller than 3° don’t distort the image significantly.

Figure 4-7 and Figure 4-8 shows how the parameter error changes as the optimization proceeds. Figure 4-7 shows a mismatch whereas Figure 4-8 shows the progress in a match. Note that the individual error in a parameter might increase even though the objective function value decreases.
Figure 4-7. Parameter error in step 1 of the semi-2D3D-θz method of a mismatch. The dotted lines represent translational parameters and the solid lines represent rotational parameters.

Figure 4-8. Parameter errors in step 1 of the semi-2D3D-θz method.

4.2.3.2 Test 7 – Comparing Semi-2D3D-θz and full 2D3D
Ten registrations were performed with the full 2D3D and with the semi2D3D-θz method. Both methods were also used with noise in the floating image. The rotations were kept in the range ± 5.7° (standard deviation of ~ 3.4°) and the translations in the range ± 15 mm (standard deviation of ~ 8 mm). This interval can be considered realistic according to the setup errors reported in chapter 2.1, but on the larger side.
<table>
<thead>
<tr>
<th>Test case, setup error range</th>
<th>Translation (mm)</th>
<th>Rotation (°)</th>
<th>Mean time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>m-l</td>
<td>a-p</td>
<td>c-c</td>
</tr>
<tr>
<td>semi2D3D-θ, after step 5</td>
<td>0.0 ± 0.1</td>
<td>0.0 ± 0.2</td>
<td>0.0 ± 0.1</td>
</tr>
<tr>
<td>semi2D3D-θ, noise after step 5</td>
<td>0.1 ± 0.2</td>
<td>0.0 ± 0.3</td>
<td>0.1 ± 0.2</td>
</tr>
<tr>
<td>full 2D3D</td>
<td>0.5 ± 0.8</td>
<td>0.0 ± 0.5</td>
<td>0.1 ± 0.7</td>
</tr>
<tr>
<td>full 2D3D, noise</td>
<td>0.4 ± 0.6</td>
<td>0.4 ± 0.9</td>
<td>0.2 ± 0.6</td>
</tr>
</tbody>
</table>

Table 4-9. The result of ten registrations on prostate patient. No mismatches.

The semi2D3D-θ method actually performs better than the full 2D3D method in determining the translational error and it is of course much faster. However, the optimization procedure has been adjusted to make the semi-2D3D method perform well and all settings have been the same for both methods. It is possible that the optimization procedure could be tuned to suit the full 2D3D method better, or that the termination criteria could be adjusted to force the 2D3D method to reach better results. That would of course require even more time. It is the DRR generations in the full 2D3D method that takes time. The optimization procedure in itself requires little time.

The progress of optimization for one full 2D3D registration (without noise in the floating image) is shown in Figure 4-9 and displays a nice convergence towards 0 which is the optimal value of the objective function. Figure 4-10 shows how the error in each parameter decreases as the optimization proceeds. Note again that certain parameter errors increase even though the objective value decreases.
4.2.4 Remarks

For online correction of setup, when the patient is still in the treatment room awaiting treatment, the semi2D3D-θ method is too slow. There are other faster methods developed mainly for computer aided surgery but also for radiation therapy. These methods include some sort of precomputation step where either DRRs are generated beforehand [4][34] or the CT-data is processed in some other way to make the DRR generation faster [19]. It is feasible to perform a semi-2D3D registration online to evaluate the setup. It would require approximately 2 minutes assuming that the DRRs
have been precomputed. If the initial setup error is fairly small, the accuracy should be about the same as after step 1 in Table 4-7. This kind of accuracy might not be sufficient even for a rough estimate. The semi2D3D-θ method would have the benefit of requiring little precomputation and also not require storage of large additional amounts of data.

On the other hand, if off-line registration is performed, where the setup of the patient is checked after treatment, an accurate but slow 2D3D technique might suffice. On the other hand, the semi-2D3D-θ method produces accurate results comparable to, or in this case, better than the results of a 2D3D method in a much shorter time which makes it a good alternative to full 2D3D registration. It would also increase the possibilities of performing offline setup verification for a large number of patients each day.

4.3 Future work

It could be of interest to further develop some parts of this study. The DRR generation algorithm could be changed in order to speed up the registration process. The algorithm employed here is straightforward and correct, but slow. Other methods, for instance antialiased splatting [35] or generating DRRs with the aid of a Transgraph [19] are faster. Another interesting approach is to exploit the functionality of modern off-the-shelf graphics cards with hardware acceleration to map 3D objects on a 2D surface [19].

Further, only one similarity measure, correlation coefficient, was used in the registration methods. Correlation ratio has also worked well when comparing MV-DRRs and PIs, and that could be verified. Also, other optimization procedures than the Powell-Brent method, for instance the downhill simplex method, could be investigated. Similarly to Powell-Brent, it doesn’t require calculations of the gradient. It could also be interesting to examine the results with the help of the Target Registration Error measure previously mentioned. It should also be of interest to implement a hierarchical optimization, where the images are first down-sampled and matched. A new registration is then performed, where the resolution is increased.

It could also be interesting to look at ways to deal with mismatches of the semi-2D3D-θ method. Even though the error rate of the semi-2D3D-θ method was low when the initial errors were kept within a realistic range (Table 4-9 and Table 4-10) the error rate was high when the setup errors were large (Table 4-8). This could be dealt with in different ways. A first step must be to automatically determine what objective function value corresponds to a mismatch. This could be done by performing a large number of tests and determine a limiting value. Of course, this value would be different when there is more noise in the floating image and perhaps also when treating different body regions. Once a semi-2D3D-θ registration has failed, the problem could be dealt with by performing a fixed number of iterations of the full 2D3D method and then use the result as a starting point for a new try with the semi-2D3D-θ method. Another option is to perform a full 2D3D method until a specific objective function value has been reached before switching to the semi-2D3D-θ method. This would of course increase the registration time considerably. Also, a hierarchical registration approach, where the resolution of the image is changed during the registration, could help avoid these mismatches.

4.4 Conclusion

The aim of this thesis has been to simulate the generation of portal images and study treatment setup verification by the registration of portal images to DRRs. Three different
registration methods have been implemented; simple 2D2D registration of two images to
determine in-plane setup errors, full 2D3D registration and the approximate semi-2D3D
method in combination with 2D3D registration (the semi-2D3D-$\theta_z$ method) to
determine the 3D setup error. The 2D2D method confirmed that the similarity measure
and optimization procedure work well. It also gives good results when noise is added to
the simulated PIs. This was confirmed by the tests of the other methods, which also
performed well.

It is important to remember that this is only a simulation study. The verification of how
well a method works is based on dependent data. Both the simulated PI and the DRRs
are based on the same CT-data which means that there is a “correct” position to reach by
the registration algorithm. Therefore, the results must be considered to represent the best
possible accuracy of the method. Previous studies have shown that the clinical
measurements are worse than simulation results, but it is also difficult to determine the
actual initial setup error in such measurements.

The accuracy of the semi-2D3D-$\theta_z$ method and the fact that it is relatively fast makes it a
possible candidate in offline adaptive radiotherapy. The simplicity of the semi-2D3D-$\theta_z$
method and its good results call for further investigation and development.
References


