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**On radiotherapy
dose verification
with a flat-panel imager**

Leah Nicole McDermott

On radiotherapy dose verification with a flat-panel imager

ACADEMISCH PROEFSCHRIFT

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aan de Universiteit van Amsterdam
op gezag van de Rector Magnificus
prof. dr. J.W. Zwemmer

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to Mum & Dad

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1

General Introduction

1.1 Introduction

The incidence of cancer in Europe is increasing, due to life-style changes and an aging population. The good news, however, is that mortality rates are decreasing, for a number of reasons.⁹ In 1985 the '*Europe Against Cancer*' programme was established to monitor the number of deaths due to cancer and promote ways to achieve a reduction. The target was a 15% lower mortality rate by the year 2000. In 2003 a study was performed to establish whether this ambitious goal was achieved.¹⁹ Overall mortality due to cancer was reduced by 10% (averaged over 25 countries). In the Netherlands the reduction was 14%. The results varied between countries according to demographics, cancer incidence and treatment strategies. The main reasons for the decrease were raising public awareness, early detection strategies and improved treatment techniques.

Radiotherapy is one of the main treatment methods for cancer in the western world. Of cancer patients receiving conventional treatment (as opposed to alternative medicines), 40% are cured with radiotherapy (alone or in combination with other treatments) in the European Union.⁹ Other curative treatments include surgery (49%) as well as chemotherapy and hormone therapy (11%). The goal of external beam radiotherapy is to stop proliferation of cancer cells through irradiation, with the advantage that the treatment is non-invasive. This is achieved by delivering multiple radiation beams through the target region within the patient. By increasing the target dose, the probability that the cancer cells are destroyed is increased. Dose escalation is, however, limited by the probability of complications resulting from delivering extraneous dose to healthy tissue. To this end, a vast amount of research activity in radiotherapy today is geared towards delivering higher dose prescriptions as accurately as possible.

1.2 Advances in radiotherapy

Recent advances in dose delivery and treatment planning have made it possible to treat patients with highly conformal dose distributions that are 'sculpted' to the shape of complex target volumes, while avoiding neighbouring healthy tissue. A common method in recent years is three-dimensional conformal radiotherapy (3D-CRT), whereby the beams are shaped by the use of a multileaf collimator (MLC).

The MLC is a mechanically controlled shaping device, located inside the head of the accelerator (Figure 1.1). Typical MLCs consist of a series of 80 to 120 metallic leaves, 0.25 to 1.0 cm wide. The leaves can be positioned individually, to create irregularly shaped projections on the target volume, while blocking parts of the beam in order to reduce the dose delivered to surrounding healthy tissue.

Figure 1.1 A linear accelerator ("linac") used to treat patients with radiotherapy. (a) treatment couch on which the patient lies, (b) head of the linac and source of mega-volt (MV) photon beams, (c) flat-panel imager (electronic portal imaging device), acquires MV images for position and dose verification of the patient, (d) kilo-volt (kV) photon source for cone-beam computer tomography (CBCT) and (e) flat panel imager, used to acquire kV images.

A new technique was introduced in the early 90s into clinical practice called intensity-modulated radiotherapy (IMRT). With IMRT, the intensity over the beam cross-sectional area is varied, instead of flat, enabling better control of the dose distribution. IMRT beams are modulated by either delivering a sequence of sub-fields (segmented IMRT) or continuously moving the leaves during irradiation (dynamic IMRT). The advantage of dynamic IMRT is that in principle, the delivered dose distribution is better able to match the planned distribution. Segmented IMRT, on the other hand, may compromise the intended distribution by delivering the field as a number of discrete sub-fields. By increasing the number of small segments this compromise is reduced.

Quality assurance (QA) of the MLC is more straightforward when using segmented IMRT since only the position of the leaves needs to be correct. For dynamic IMRT, quality assurance becomes more complicated as both the position and speed of the leaves have to be controlled accurately.

When IMRT was first introduced, segment shapes were defined by the planner, and the weight of each segment was computer optimised. The user would prescribe a number of dose criteria for regions of interest (ROI), such as minimum dose limits for target volumes and maximum dose limits for organs at risk (OAR). The optimisation procedure was based on iteratively minimising a cost function. This approach was developed further to become what is now known as inverse planning, whereby the user sets dose criteria for ROIs. For inverse planning, the desired dose distribution is optimised by allowing variable number, shape and relative weight of segments. To this end, typically fluence profiles are optimised for each beam direction by minimising a cost function.^{15,20} The process of sequencing transforms the optimised profile into a number of segments that can be delivered by the MLC either as part of, or after, the optimisation process. Better dose distributions are achieved by automatically optimising multiple degrees of freedom.

Alongside IMRT and inverse planning, the use of multi-modality imaging techniques such as computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) has improved the accuracy with which the perceived tumour volume and organs at risk can be delineated for planning treatments. Tumour identification, however, still remains one of the weakest links in the radiotherapy planning chain and further improvements are necessary.

Furthermore, radiotherapy departments are rapidly moving towards image-guided radiotherapy verification (IGRT). IGRT uses imaging devices located in the treatment room to accurately determine the position of targets and healthy tissue, calculate deviations from the planned position and apply corrections to ensure the prescribed dose is delivered to the right location over the course of treatment.

IGRT has been advanced by the development of imaging modalities, such as cone-beam CT (CBCT), a CT scanner integrated with the linac enabling acquisition of patient images (2, 3 or 4D), while the patient is positioned on the treatment couch for set-up verification (Figure 1.1). The number of fractions checked is usually a balance between the workload available and set-up accuracy required. Combined with immobilisation techniques, IGRT serves to minimise the effects of set-up errors and organ motion. Such improvements in treatment planning, patient set-up and dose delivery have enabled radiation oncologists to prescribe higher doses for better control of the disease. The advantages of dose escalation, however, are thwarted if the dose is not delivered to the patient as planned due to errors or large uncertainties. QA, therefore, has become one of the big challenges in radiotherapy.

1.3 Dose verification in radiotherapy

Ideal verification of radiotherapy would ensure the dose distribution delivered to the patient at the time of treatment corresponded to the planned treatment, and do this as efficiently as possible. With the introduction of advanced irradiation techniques and IGRT, verification of the radiation dose delivered to patients has become increasingly important, since the advantages gained are compromised when errors occur.

Improved treatment techniques that serve to reduce cancer mortality rates, however, are often so complicated that ensuring accurate dose delivery is more challenging. Nowadays dose verification is usually performed pre-treatment, by delivering the planned fields to an object called a phantom, consisting of material with tissue- or water-equivalent density. Various detectors are used within phantoms to verify the planned dose at either points, lines, planes or volumes. Point detectors include ionisation chambers, diodes and thermoluminescent dosimeters (TLDs). Two-dimensional dosimetry devices have also been proposed based on ionisation chamber or diode arrays or matrices.^{57,63,134}

While good agreement has been reported at specific points or along profiles, they have limited resolution (0.7 to 1.4 cm grid spacing) and require additional set-up time. Radiographic film is commonly used as a 2D detector.

^{22,23,26,39,56,72,141} It has the advantage of high resolution, however measurement time is extensive because each film must be developed and digitised before it can be analysed. Furthermore, it is difficult to achieve an absolute dose calibration because of the dependence of the film response on photon energy.³⁹ This means that the film response is also a function of depth and field size for a specific photon beam. As medical departments strive to digitise medical data,¹⁰³ film processors are becoming more scarce and alternative devices will be required for radiotherapy dosimetry.

Radiochromic film has several advantages over radiographic film; no developing is required so variations introduced by the film processing step are eliminated, it is insensitive to visible light, allowing for ease of handling¹¹⁶, and the film is fabricated from low-atomic number materials¹⁰⁶, so it does not influence the radiation beam to the same degree as silver-based film. On the other hand, radiochromic film still has limitations: it is relatively expensive, has a large relative variation in film uniformity up to $\pm 6\%$ and there is a strong polarisation effect, requiring care in film orientation during readout.¹¹⁰ Like radiographic film, radiochromic film still needs to be digitised and converted to dose, which both take time.

Finally, various forms of gel have been proven viable dosimeters, being the only real volumetric dosimeter currently commercially available. A number of research groups has reported good results comparing planned and measured dose distributions in 3D.^{29,105,137} While being able to directly measure the dose distribution in 3D is an advantage, this method is limited by the complicated preparation and analysis procedure required.

A major limitation with methods restricted to phantoms is, of course, that it is not possible to determine the dose distribution inside the patient during treatment.

1.4 EPIDs

Electronic portal imaging devices (EPIDs) were originally developed for patient set-up verification, i.e. to replace film for localisation of patient anatomy with respect to the radiation field edge. An EPID is like a large, digital x-ray camera, equipped to the linac as shown in Figure 1.1. Various types of EPIDs have been developed, based on different optical and x-ray detector systems. These include EPIDs based on a camera with a scintillator screen,⁸⁵ scintillation crystal-photodiode detector,¹²⁰ and scanning liquid-filled ionisation chamber.¹²⁶

Amorphous silicon electronic portal imaging devices (*a*-Si EPIDs) became commercially available in 2000.³ They consist of an x-ray converter, light detector, electronic acquisition system for receiving and processing the resulting digital image. *A*-Si imagers have the advantage of high resolution and good image quality, and require less patient dose for the same image quality, compared to other types of EPIDs.

Not long after EPIDs were established to replace film for patient position verification, it was realised they could also be used for dose verification. In the case of *a*-Si EPIDs, photons that pass through the patient interact with the detector screen and are converted to visible light. The light signal measured at each pixel can be related to the dose distribution inside the patient or phantom. Compared with other dosimetry devices, EPIDs have the advantage of being already fixed to the linac without the need for additional hardware. As many radiotherapy departments have invested in portal imagers for set-up verification in recent years (and will continue to do so in the coming years), it is attractive if the same device can be used for absolute dose verification as well.

EPID measurements are simple to perform with minimum set-up requirements, they can be repeated easily and digital data is obtained immediately, unlike films that require additional time for developing and digitising. EPID images can be immediately converted to absolute dose images, whereas each film batch requires a new calibration, involving additional measurements.⁴⁰ Also recording, storage and archiving of QA measurements becomes more efficient when images are acquired digitally.

There are a number of ways to use EPIDs to verify a plan prior to treatment. Some studies have used the detector placed inside a phantom.^{33,84} Other studies converted EPID images to dose images at the detector plane, in some cases behind a phantom.^{24,42,48,60,73,87,95,129} Alternatively, EPID images were used to reconstruct the dose in a plane within the patient or phantom^{2,11,45,65,94,115,131}. Of these studies, some have explored the possibility of using an *a*-Si EPID for dose verification of IMRT fields.^{2,24,42,94,115,131} A back-projection algorithm (described in chapter 5 of this thesis) forms the basis of the EPID dosimetry program in our department. The transmission signal measured at the level of the EPID is used to reconstruct the dose either inside a phantom or the patient.

The current method reconstructs the dose in a single plane, intersecting the isocentre, perpendicular to the beam axis and parallel with the EPID detector plane. For phantom measurements, the phantom is positioned isocentrically so that this plane intersects the middle of the phantom for all gantry angles.

The reason for choosing this method is that the reconstructed dose distribution can be directly compared with either the corresponding planned dose distribution or that measured with other dosimetry devices. By using a simple dose reconstruction method, the QA system is completely independent of the treatment planning system (TPS). Additional motivation for back-projecting the EPID signal is that it allows for verification of the dose *in vivo*, i.e. determining the dose inside the patient during treatment. Furthermore, the dose can be determined in 3D by back-projecting the calibrated signal to multiple planes. *In vivo* and/or 3D dose verification are not possible with methods that use the TPS (or an alternative algorithm) to predict the EPID dose and compare it with the planned dose at the imager plane.

1.5 Purpose of this thesis

Radiotherapy today needs a verification device that can provide a check of the delivered dose as accurately and efficiently as possible. To this end, the *a*-Si EPID has been identified as a potential candidate dosimeter. Its dosimetric characteristics and use in the clinic, however, have not been thoroughly explored previously. The aim of this study was to develop techniques for the verification of radiotherapeutic dose delivery using an *a*-Si EPID. The four main objectives were to;

- investigate the dosimetric characteristics of the *a*-Si EPID detector;
- develop an algorithm that determines the 2D dose distribution within a phantom or patient, based on *a*-Si EPID images of treatment fields, both prior to and during radiotherapy;
- develop and test clinical protocols for the verification of patient plans with an EPID, both prior to and during radiotherapy, and
- analyse the results of using *in vivo* dosimetry in the clinic; to obtain an overview of the nature and extent of differences found between measured and planned dose distributions, and develop strategies to distinguish clinically relevant errors from non-clinically relevant discrepancies.

2

Dose-response and ghosting effects of an *a*-Si EPID

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Medical Physics 31 (2) 2004

Abstract

The purpose of this study was to investigate the dose-response characteristics, including ghosting effects, of an amorphous silicon-based electronic portal imaging device (*a*-Si EPID) under clinical conditions. EPID measurements were performed using one prototype and two commercial *a*-Si detectors on two linear accelerators; one with 4 and 6 MV and the other with 8 and 18 MV x-ray beams. First, the EPID signal and ionisation chamber measurements in a mini-phantom were compared to determine the amount of build-up required for EPID dosimetry. Subsequently, EPID signal characteristics were studied as a function of dose per pulse, pulse repetition frequency (PRF) and total dose, as well as the effects of ghosting. There was an over-response of the EPID signal compared to the ionisation chamber of up to 18%, with no additional build-up layer over an air gap range of 10 to 60 cm. The addition of a 2.5 mm thick copper plate sufficiently reduced this over-response to within 1% at clinically relevant patient-detector air gaps (>40 cm). The response of the EPIDs varied by up to 8% over a large range of dose per pulse values, PRF values and number of monitor units. EPID response showed an under-response at shorter beam times due to ghosting effects, which depended on the number of exposure frames for a fixed frame acquisition rate. With an appropriate build-up layer and corrections for dose per pulse, PRF and ghosting, the variation in the *a*-Si EPID response can be reduced to well within $\pm 1\%$.

2.1 Introduction

Electronic portal imaging devices (EPIDs) were originally designed and developed for the purpose of geometric verification of patient set-up during treatment. However, their use has been increasingly extended to also obtaining dosimetric information of the radiation treatment, either by pre-treatment verification or by means of *in vivo* dosimetry. Despite the obvious advantages of an on-line, 2D EPID dosimetry system, extensive clinical use has been limited for a number of reasons. The use of EPIDs in the clinic for set-up verification is still limited worldwide, and there has been little support from vendors to invest extensively in dosimetric applications. Verification of the dose in 2D or 3D in the patient is complicated, which is especially significant if portal dosimetry is to be used as an independent check of the treatment planning system. Furthermore, most departments will have limited resources for the development of software required for portal dosimetry.

There are various possible approaches to portal dosimetry. One is to calculate the dose at the plane of the detector behind the phantom or patient. This usually requires development of in-house algorithms to predict the portal dose image (PDI), since this option is not yet widely available in commercial treatment planning systems. An alternative approach is to take the PDI and predict the dose in a plane in the phantom or patient, since it is often more interesting to know and verify the dose in the target volume than at the EPID plane. This approach has been applied using an algorithm to back-project the PDI to the mid-plane^{11,14,65} or to reconstruct the patient dose based on convolution / superposition methods, back-projecting the fluence measured with the EPID.⁷⁹

Applications of portal dosimetry have been reported mainly for the type of EPIDs based on a liquid-filled (Li-Fi) ionisation chamber matrix^{11,14,36,59,65,123} the CCD camera-based EPID^{28,48,60,96,114,130} and a solid-state based EPID.⁴⁵ These studies compared the PDI with various combinations of film and ionisation chamber measurements. The accuracy in dose prediction of 3% for most of these studies has usually been limited to point doses on the central beam axis, low dose gradient regions and / or use of homogeneous phantoms.

More recently, amorphous silicon (a-Si) based EPIDs have been developed with excellent image quality, relatively high optical transfer efficiency, large imaging area and high resistance to radiation damage.^{5,5,86} Moreover, the response of the a-Si EPID has an excellent long-term signal reproducibility of 0.5% (1 SD), as observed in our department.⁶⁶

Use of the a-Si EPID has also been extended to dose determination in recent years.^{33,42,42,43,43,73,73} A reported advantage of the a-Si EPID is its linear dose-response relationship, whereby a simple calibration factor may be applied to convert the EPID signal to absolute dose. A number of these studies have reported a linear signal better than 1%, for various commercial types of a-Si pane

In addition to quantifying the EPID dose-response relationship, it is important to determine the amount of build-up layer required, as in any dosimetric system applied to high energy photon beams. EPIDs are typically designed today with an intrinsic 1 mm copper (Cu) plate covering the phosphor layer, used to absorb low energy, scattered radiation which would otherwise reduce the image contrast. This Cu plate also provides some build-up to convert primary x-rays into Compton electrons.⁶ Two reasons for using additional build-up material for portal dosimetry are 1) to ensure measurements are made beyond dose maximum and 2) to attenuate scattered radiation from the patient. The latter is especially relevant at small patient-detector air gaps (< 40 cm), in which case the scatter contribution from the irradiated volume (of a phantom or patient) to the EPID dose may be considerable.^{92,138,138} Yeboah and Pistorius¹³⁸ investigated the dependence of the EPID dose-response on scatter from a phantom using Monte Carlo calculations for a copper-phosphor portal imaging screen. They found a broad peak in the photon spectra at low energies (50-100 keV) and observed a high sensitivity of the imager for low energy photons. Previous authors have reported on the need for additional build-up layer material such as polystyrene (PS),^{12,73,73} stainless steel⁹⁶ and Cu^{90,90,92} for EPID dosimetry applications. As suggested by Partridge *et al.*,⁹² a sharp rise in the mass attenuation coefficient of Cu below 500 keV indicates that this material should preferentially filter out low energy photons.

Other reported phenomena in imaging are ghosting effects, namely image lag and change in sensitivity or gain. These may be distinguished as separate effects,⁹³ reportedly primarily due to trapped charge in the photodiodes.^{108,136,136} Image lag is a signal delay, so charge generated in one image frame is read out in subsequent frames, adding an offset to the signal in subsequent recorded frames or images.¹⁰⁸ Previous reports have studied image lag by measuring the residual signal in the dark field, lasting in the order of minutes following beam off.^{89,89,93,136,136,140,140}

The extent of the image lag has been found to be highly dependent on the number of frames read out, or acquired, as opposed to an explicit dependence on the time of irradiation. Therefore one would expect a change in the influence of ghosting on the response for alternative or irregular frame acquisition rates. If the frame acquisition rate is fixed, the two parameters, beam time and number of frames, can be said to be interchangeable. Another type of ghosting, while also related to charge trapping, has been associated with a change in gain (or sensitivity). During exposure, the charge stored in deep trapping states alters the electric field strength within the photodiode bulk and interface layers. This will consequently change the sensitivity of the *a*-Si layer.^{89,90,90} Gain ghosting is multiplicative, influencing read out of both the signal at the time of exposure and any delayed signal. Properties of, and corrections for, both image lag and change in gain have been investigated for normal portal imaging applications of *a*-Si detectors in the above mentioned studies. However, the effect has not yet been reported in terms of *a*-Si portal dosimetry, where both types of ghosting will influence the measured dose-response relationship.

To use the EPID for dosimetry, ideally the absolute response of the EPID should be determined, i.e. the signal of the EPID per unit dose from photons, yielding an energy dependent dose-response curve. This is impractical however, because the output of the accelerator is not mono-energetic. More importantly, the purpose of this study was to calibrate the measured portal signal against dose in air, approximated by the dose measured with an ionisation-chamber in a mini-phantom at the EPID plane. This calibration would then later be used with a back projection algorithm to determine the dose within the phantom or patient.

This work extends previous *a*-Si EPID investigations to include all relevant parameters that change under clinical conditions, such as dose, dose per pulse and pulse repetition frequency (PRF). Therefore the objectives of this study were to investigate the amount and type of material required as a build-up layer for dosimetry and the dose-response characteristics, including ghosting effects, of the *a*-Si EPID.

2.2 Methods & Materials

The type of EPID used throughout all experiments is an amorphous silicon flat panel-type imager (Elekta iViewGT). It has a 41x41 cm² detection area (1024x1024 pixels), a touch guard, a 1 mm Cu build-up layer, a phosphor screen and a hydrogenated *a*-Si:H photodiode array. Further details regarding similar types of imagers can be found in an overview by Antonuk.⁴

An EPID image is defined as the stored signal – this may be the signal integrated or averaged over all or a specific number of frames. A frame is defined as the signal from one readout of the entire panel. For this study, an acquisition mode was used whereby a frame is taken every 285 ms during acquisition and 2 pre- and 2 post-beam frames are added to ensure that dose from partially irradiated frames at beam-on and beam-off are included. An average of all frames is then stored as a raw image, I_{raw} , or alternatively, it is also possible to store all individual frames, as required for parts of this study. All images are processed to correct for individual pixel sensitivity and offset. The processed image I_{proc} is then

$$I_{proc} = \frac{I_{raw} - I_{dark_dyn}}{I_{flat} - I_{dark}} \quad (2.1)$$

where I_{flat} is an open flood-field image encompassing the sensitive area of the detector and I_{dark} is a dark field image (i.e. acquired without irradiation) which serves as an offset correction. An arbitrary scaling factor of 8192 is included to be able to store the signal data in 16-bit format. The calibration images (I_{flat} and I_{dark}) are typically acquired when the EPID is installed or any changes in set-up are made. I_{dark_dyn} is a new dark field acquired prior to image acquisition. This updated dark field compensates for any dependence on ambient temperature or radiation history in the signal.

Reference dose measurements were performed with an ion chamber (Semiflex 0.125 cm³, PTW Freiburg) and electrometer (Keithley #617). The reference dose (D_{ref}) was measured at dose maximum in a polymethylmetacrylate (PMMA) mini-phantom, with a diameter of 4.0 cm for 4, 6 and 8 MV and 5.0 cm for 18 MV. The effective point of measurement was at the depth of dose maximum for each energy.

The mini-phantom was placed at the same source-surface distance (SSD) as the imager touch guard surface (with a touch guard approximately 3 cm above the scintillator screen) such that the effective point of measurement for both detectors was reproducible and similar. For some measurements it was necessary to compare reference and EPID dose-rate signals during irradiation, in these cases a p-type diode (Scanditronix Medical AB, Uppsala, Sweden) positioned on the EPID was used as a reference detector. All ionisation chamber and diode measurements were relative, except those concerned with dose per pulse, whereby absolute dose to water was determined in the mini-phantom (with corrections for measuring in a PMMA medium). The EPID signal (S_{EPID}) was calculated by multiplying the average pixel value of 20x20 central pixels from I_{proc} by the number of frames acquired (stored in the image file header). The EPID response (R_{EPID}) was then defined as the ratio of the EPID signal and the reference dose.

$$R_{EPID} = \frac{S_{EPID}}{D_{ref}} = \frac{I_{proc} \times (\# frames)}{D_{ref}} \quad (2.2)$$

Measurements were made using two detectors (based on the same design) mounted on two linear accelerators, with photon beams of 4 and 6 MV (Elekta SL-15i, with EPID A) and 8 and 18 MV (Elekta SL-20i, with EPID B), respectively. A number of measurements was repeated using a prototype a-Si flat panel device (RID 1640 AF2, Perkin Elmer Optoelectronics, EPID X). This imager has the advantage of mobility and is similar in design to the commercially available EPIDs. However, EPID X has a different type of amplifier, producing 1/3 of the output signal of EPIDs A or B. When attached to the linear accelerator, SSD of all EPIDs (to the surface of the touch guard) was fixed at 156.9 cm. EPID X (which did not have a touch guard) was placed at 161.0 cm when the SSD was not varied, to ensure the sensitive areas of both panels were at a comparable SSD.

2.2a *Build-up layer and air gap*

In this part of the study, R_{EPID} was measured over the maximum possible air gap range of 10 - 60 cm, defined as the distance between the table exit surface on which the phantom is placed and the surface of the EPID (Figure 2.1). This was performed for two different build-up layer materials, Cu and polystyrene (PS). To compare the influence of these two build-up materials, the thickness of each layer was chosen according to approximate equivalent density thicknesses: 22.0 mm of PS and 2.5 mm Cu. Comparison of the two build-up layer materials of these particular thicknesses were chosen as they were similar to the layer thicknesses used in other studies measuring the dose-response of an *a*-Si EPID. The additional layer (PS or Cu) was positioned on top of the imager touch guard. A polystyrene slab-geometry phantom was used in all cases, with a thickness of 15 cm for the 4 and 6 MV beams and 35 cm for the 8 and 18 MV beams, which are typical patient thicknesses for these energies. The EPID response was measured with a 15x15 cm² field, 100 monitor units (MUs) at a PRF of 400 Hz. The air gap was varied by changing the height of the table on which the phantom was placed.

In addition to determining the influence of the material used, the required thickness of the build-up layer was also studied. The response, R_{EPID} was measured as a function of air gap with additional build-up layers of 1.0, 2.5 (as above) and 5.0 mm Cu for the 4 and 6 MV photon beams (EPID A). For 8 and 18 MV (EPID B), the response was measured with only 2.5 and 5.0 mm Cu layers, since at least 2.5 mm Cu build-up was required for measuring beyond dose maximum.

2.2b *Dose-response relationships*

The EPID response was determined by varying dose delivery parameters at the position of the detector in various ways. Physical properties of the beam that were modified included variation in dose per pulse, PRF and total dose. All measurements were made with open fields and an additional 5.0 mm Cu build-up layer. First, R_{EPID} was measured at different SSDs ranging from 85 to 334 cm, to vary the dose per pulse from 0.08 to 1.40 cGy/pulse.

To allow such a large SSD range, the gantry was rotated 90 degrees and the EPID was detached. The detector was then positioned at successive source-surface distances, keeping the detector plane perpendicular to the beam direction at each measurement position.

The SSD range was limited by the distance from the linac head to the opposing wall of the treatment room. To avoid changes in the EPID lateral scatter dose component, the field size was adjusted, maintaining a constant effective field size at the sensitive layer of the detector of $20 \times 20 \text{ cm}^2$. All beams were delivered with 100 MUs at the maximum PRF for each energy (200 Hz for 4 and 18 MV, 400 Hz for 6 and 8 MV). In this part of the study, EPID B was used at both machines to compare the dose per pulse dependence of all four energies with EPID X.

Figure 2.1 Schematic diagram of the experimental set-up for the air gap measurements.

Secondly, R_{EPID} was measured by varying the dose-rate setting at the treatment machine, effectively changing the beam PRF from 13 to 400 Hz for each energy, except 4 and 18 MV which have a maximum PRF of 200 Hz. The change in response was measured in two ways – first delivering a series with varying number of MUs, keeping the beam time constant at 50 s, followed by a second series delivering a constant dose of 100 MUs, which varied the beam time.

Finally, R_{EPID} was measured by varying the total dose delivered using a fixed PRF over a range of 5 to 1000 MUs at maximum dose-rate setting for each energy. Dose-response measurements were performed with EPID A for 4 and 6 MV, EPID B for 8 and 18 MV and EPID X for all energies, unless otherwise specified.

2.2c Ghosting

Two sets of measurements were made using EPID A with 6 MV photon beams delivered at PRFs of 400, 200, 50 and 25 Hz. In the first set, the beam time was kept constant (12 s) and the total dose (number of MUs) was correspondingly varied. In the second set, the total dose was kept constant (100 MUs) and the beam time was varied. Instead of storing an average image for each beam, the signal from each frame was recorded during and after irradiation. The decay of the signal was measured over time following beam-off.

Prompted by results from studying the signal decay, another set of measurements was performed to investigate the cumulative effect of ghosting over all frames, both during and after irradiation. Images were acquired for a series of beams ranging from 5 to 1000 MUs, at 2 PRFs (400 and 200 Hz), for 8 and 18 MV photon beams with EPID B. All frames were stored (every 285 ms) while simultaneously recording the relative dose rate with a diode as a reference detector. Measurements were continued following beam-off, until the EPID signal dropped below 0.1% of the maximum signal during exposure.

The results for R_{EPID} as a function of PRF (for varying beam time) and number of MUs were expressed as a function of beam time and combined to determine a beam time dependence relationship for the EPID response. A fit was made of the data set to then use as a "ghosting correction" for response measurements as a function of PRF and number of MUs. The time of each irradiation was determined from the number of frames (read every 0.285 s) acquired for each image.

2.3 Results

The reproducibility of ionisation chamber, diode and EPID signal readings, was $\pm 0.5\%$ (1 SD). In each set of response measurements, R_{EPID} was normalised to the maximum value, except for the PRF measurements, where results were normalised to 200 Hz, the maximum PRF common to all energies.

2.3a Build-up layer and air gap

Figure 2.2 presents data for the variation in R_{EPID} over an air gap range of 10 to 60 cm with two different build-up materials, copper (Cu) and polystyrene (PS), for 4 and 6 MV beams. The over-response at smaller air gaps (relative to the reference detector distance of 60 cm) can be attributed to a change in the number of photons scattered from the phantom to the EPID. This over-response is reduced from 16% to 12% for 4 MV and from 12% to 8% for 6 MV when a Cu build-up layer is used compared with an equivalent density thickness of PS.

Figure 2.2 Variation in EPID response with air gap for additional build-up layers of polystyrene (dashed line) and copper (solid line) with EPID A for 4 and 6 MV. The response is normalised at the maximum air gap (60 cm), assuming negligible scatter contribution from the phantom to the detector at this air gap.

R_{EPID} is presented in Figure 2.3 over a range of air gaps for different thicknesses of the Cu build-up layer. The response curves increase at small air gaps for 4, 6 and 8 MV beams. This over-response was minimised by using an additional 5.0 mm Cu build-up layer, especially at lower beam energies. Results for the minimum clinically relevant air gap of 40 cm are given in Table 2-1. At this air gap, the greatest reduction in the over-response was found using the thickest Cu layer (5.0 mm) and the lowest beam energy (4 MV), where the over-response was reduced from 2.2% to 0.1%. At 18 MV, the response remains within 1% over the entire air gap range, independent of the Cu build-up layer thickness. The response for an air gap of at least 40 cm was within the limits of accuracy of 1% for all energies with an additional 5.0 mm Cu build-up layer, and less than 1.1% with 2.5 mm Cu.

Table 2-1 EPID over- or under-response at an air gap of 40 cm for each energy, normalised to the value measured at a 60 cm air gap. No measurements were performed for 8 and 18MV with thicknesses less than 2.5 mm, since electron equilibrium is not obtained at the sensitive area of the detector.

Energy (MV)	+ 0 mm Cu	+ 1.0 mm Cu	+ 2.5 mm Cu	+ 5.0 mm Cu
4	2.2%	1.1%	1.1%	0.1%
6	2.1%	1.1%	0.7%	0.1%
8	-	-	0.7%	-0.2%
18	-	-	-0.1%	-0.6%

2.3b Dose-response relationships

For EPID B (measured at 4, 6, 8 and 18 MV), R_{EPID} is not constant as a function of dose per pulse, with a change in response up to 8% relative to SSD = 100 cm, over the dose per pulse range (Figure 2.4a). For measurements with EPID X (Figure 2.4b), the variation in response over the investigated range of dose per pulse values is within 4%. The response curves show no clear dependence on beam energy. This implies corrections of the EPID response are needed based on the dose per pulse, which would require knowledge of the thickness of the attenuating medium (e.g. phantom, patient or wedge) for a fixed source-EPID distance. The gradient of the response curves for both EPIDs is steeper at low dose per pulse values (< 0.5 cGy / pulse to the reference detector). This corresponds to a reduction in measured dose of over 70%.

Figure 2.3 Variation of EPID response with air gap for various Cu build-up layer thicknesses - EPID A for the 4 MV (a) and 6 MV (b) beams and EPID B for the 8 MV (c) and 18 MV (d) beams. The response is normalised at the maximum air gap (60 cm) for all energies.

Figure 2.4 EPID response as a function of dose per pulse, decreased by moving the detector away from the source (85-334 cm). The field size, number of MUs and PRF was kept constant for beam energies of 4 MV, 6 MV, 8 MV and 18 MV. Results for the commercial EPID B (a) and prototype EPID X (b) are normalised to the maximum dose per pulse for each energy (filled marker).

The EPID response as a function of PRF is given in Figure 2.5 for 13 to 400 Hz. For the commercial EPIDs (A and B), R_{EPID} falls by 6% with constant beam time (Figure 2.5a) and 5% for constant number of MUs (Figure 2.5b). Both curves show a sharper decrease in response at lower PRF values, independent of beam energy. Results for the prototype EPID (X) show less variation in R_{EPID} over the same range, with the response remaining within 2% for constant beam time (Figure 2.5c) and constant number of MUs (Figure 2.5d). Since the PRF is always known prior to treatment, it is a simple correction to apply if beams are delivered at a PRF other than that at which the EPID is calibrated.

Finally, R_{EPID} was also found to vary as a function of number of monitor units for all four energies and both EPID-types, as shown in Figure 2.6. Relative to the maximum dose (1000 MUs), the under-response was up to 5% over the entire dose range for the commercial EPID and 6% for the prototype EPID. The EPID response curve is very similar for both EPID types. The response varied by 3% for beams of 5 to 100 MUs, which was the range of MUs where the response gradient was steepest. This suggested either a beam time or dose dependence of the EPID response, which prompted further investigation.

Figure 2.5 EPID response as a function of PRF for 4 MV, 6 MV, 8 MV and 18 MV. EPIDs A and B with the same beam time (50 s) are given in (a), the same number of MUs (100 MUs) in (b). Corresponding curves for EPID X are given in (c) and (d). Results are normalised at 200 Hz, the maximum PRF for 4 MV.

2.3c Ghosting

The signal of the dark field following irradiation is presented in Figure 2.7. All data is normalised to the maximum irradiated signal. The series in which the beam time was kept constant (12 s, Figure 2.7a), the decay was very similar for all curves. In the following series for irradiations of equal dose (100 MUs, Figure 2.7b), the decay in the image signal was faster for shorter beam times. This suggests that the decay rate of the EPID signal depends primarily on beam time, and not on dose or PRF.

Figure 2.6 EPID response as a function of dose for varying number of monitor units with EPIDs A, B and X, for 4 MV, 6 MV, 8 MV and 18 MV. The maximum possible PRF was used for each energy.

Figure 2.7 Post-irradiation ghosting effects: curves for PRFs of 50, 100, 200 and 400 Hz, with a 6MV beam. The relative signal is given following irradiations of the same beam time (12 s) with varying dose (a) and of the same dose (100 MUs) with varying beam times (b). Results indicate ghosting in the signal after irradiation may be said to depend on beam time, and not dose or dose-rate (PRF).

Figure 2.8a shows the dose rate signal as measured by the EPID and diode, acquired simultaneously during and following irradiation. Results are given for 1000 MUs delivered with an 8 MV photon beam at maximum PRF (400 Hz). The signal of each frame is normalised to the signal at 100 s, at which the signals have reached a stable value. Comparing EPID and diode dose rates, the EPID takes approximately 40 s to reach within 0.5% of its maximum value, whereas the diode signal is within this range after only 8 s. The three curves in Figure 2.8b represent an ideal, constant response, the measured response (R_{EPID}), and also a corrected measured response, $R_{\text{EPID+lag}}$. This corrected response includes the integrated image lag signal measured after beam-off (as shown in Figure 2.7).

Figure 2.8 EPID and diode signal throughout irradiation with 1000 MUs (a). Signal measurements are normalised to the stable signal at 100 s. The slow rise in EPID signal (line + dots) compared to the diode signal (open circles) partially accounts for the EPID's under-response at shorter irradiation times. In (b), if the 'missing signal' is compensated by adding the lag signal measured in the dark field after beam off, the measured response, R_{EPID} (closed squares) should approach that of an ideal linear detector (dashed line). The result is a slightly improved response, $R_{\text{EPID+lag}}$ (open diamonds).

The measured response varies up to 5%, while the corrected response is only improved by at most 1.5%, with up to 3.5% remaining below the ideal case. Therefore the post-beam signal is not enough to account for the slower rise in EPID signal, compared with the reference detector at beam-on (Figure 2.8a). This suggests the ghosting effect is more than only image lag, and an alternative correction method is required based on the irradiation time.

To determine a ghosting correction factor, $G(t)$, an exponential fit was made for the normalised R_{EPID} as a function of beam-on time (Figure 2.9). The function was accurate for all energies and dose rates measured to within 0.5% for beam-on times greater than 2 s, corresponding to 5 MUs at a maximum PRF value of 400 Hz. The correction function applied took the form of a triple-exponential,

$$G(t) = A_0 - A_1 \exp(-r_1 t) - A_2 \exp(-r_2 t) - A_3 \exp(-r_3 t) \quad (2.3)$$

where A_0 to A_3 were fitted coefficients (1.000, 234.3, 0.036, -0.026) and r_1 to r_3 were the fitted decay rates (7.8, 0.46, 0.034 s) of the combined ghosting effects. Modelling the curve with up to 3 time constants was necessary to match measured data to within 0.5%.

Figure 2.9 Fit of the EPID response as a function of beam time. The symbols mark the measured response for 5 to 1000 MUs delivered at two PRF settings, with 8 MV photon beams. The fit is accurate to within 0.5% for irradiation times greater than 2.0 s. The filled symbols mark the normalisation points.

The corrected response of the EPID, R_{EPID_G} , was then determined by the EPID signal (S_{EPID}), the reference dose (D_{ref}) and the ghosting correction factor $G(t)$, based on the exposure time determined from the number of frames acquired:

$$R_{EPID_G} = \frac{S_{EPID}}{D_{ref} \times G(t)} \quad (2.4)$$

The ghosting correction was applied to all EPID A and B response measurements involving varying exposure times (examples are given in Figure 2.10). For all energies, R_{EPID_G} as a function of the number of MUs was effectively linear within $\pm 1\%$ of the measured dose (4 and 18 MV data are shown in Figure 2.10a). For the response as a function of PRF, the dependence on beam time is removed and both curves representing R_{EPID_G} overlap (Figure 2.10b), indicating a true PRF dependence. The effect of the correction was similar for all energies. Without the correction, the under-response at lower PRF values is partly compensated by the increased response due to ghosting at longer beam times.

Figure 2.10 The EPID response with and without corrections for ghosting effects. For varying number of monitor units (a), the original response for 4 and 18 MV (solid lines) is shown with the corrected response (dashed lines), which is constant to within $\pm 1\%$. For varying PRF (b), the corrected response for varying beam time (dashed line) overlaps the response for constant beam time measurements i.e. apart from PRF dependence, with a ghosting correction the detector is linear. Response curves were similarly improved for all time-varying measurements. For clarity, results for only a few energies are shown.

2.4 Discussion

Properties of the *a*-Si EPID were investigated in this study for the purpose of understanding the EPID response behaviour, prior to calibration for patient treatment evaluation. Whether the dose is to be compared at the portal plane, or a back-projection method is applied, the dose-response characteristics and ghosting effects should be well understood for EPID dosimetry. Applying an adequate build-up layer for *a*-Si EPID dosimetry applications is important for three reasons: 1) to absorb low-energy electrons before reaching the EPID sensitive layer which would reduce image quality, 2) to ensure electron equilibrium at the sensitive layer of the detector during dosimetry and 3) to minimize the additional photons scattered from the patient and measured by the EPID. For each of these issues, the thickness of build-up required depends on the energy applied, but not necessarily in the same way. Measurements from this study highlighted the benefits of using Cu instead of PS build-up for absorption of patient scatter at small air gaps. At lower, scattered photon energies, the photoelectric effect dominates. Its cross section is dependent on the atomic number ($\tau \propto Z^3$), which becomes negligible at energies above 100 keV. The inclusion of a higher *Z* material absorbing layer such as copper meant more scattered photons were absorbed than with the equivalent density thickness of polystyrene. It is also worth noting that the copper plate was more convenient than polystyrene as build-up layer material because it occupied less volume (limited by the presence of the touch guard) within the panel for the same effective path length.

There was an apparent, minor trend for the measurements presented in Figure 2.3 of the air gap which gave the minimum response to decrease with increasing energy, i.e. the minimum response was at the largest air gap for 4 and 6 MV, and at mid-range air gaps for 8 MV and 18 MV. This could be due to two opposing effects. At smaller air gaps, the phantom is further from the source and the dose to the phantom is reduced by the $1/r^2$ law. The secondary photons are scattered over a broader angle, so fewer low energy photons per unit phantom volume reach the centre of the detector. On the other hand, the total scattering volume is larger and the exit plane is closer to the EPID. This increases the scatter to primary ratio of photons reaching the EPID.

The rate at which each of these effects increases or decreases the amount of scatter from the phantom detected by the EPID depends on the beam energy and Cu build-up layer thickness. However, detailed Monte Carlo calculations modelling this particular experiment would be required to fully understand the observed results. With a 5.0 mm additional Cu build-up layer, the over-response of the EPID due to patient scatter was almost completely eliminated.

This was especially true for lower energies where the over-response was generally higher. However, adding 2.5 mm or 5.0 mm –thick Cu layers (area = 41x41 cm², Cu density = 8.9 g/cm³) increases the load on the EPID-arm by either 3.7 kg or 7.5 kg, respectively. For 8 and 18 MV, 2.5 mm Cu was sufficient build-up thickness, and the weight was considered acceptable for clinical use. Additional fatigue calculations would be required to justify the extra load on the EPID-arm. Another potential constraint to the build-up layer was reduced image quality. While the intrinsic build-up layer of 1 mm Cu is used to reduce blurring due to low energy scattered electrons, adding too much Cu may generate an excess amount of scatter and have the opposite effect. Partridge *et al.* indicated that there is no significant effect on the spatial resolution of this type of panel by adding 3 to 4 mm Cu.⁹³ Line spread function measurements made to study the effect of adding 5.0 mm Cu on image quality at our institution showed negligible deterioration (data not shown). Qualitative checks involving blind tests to distinguish bony anatomy in a Rando-Alderson head phantom were also performed by a radiation technologist. Though the images made with additional Cu build-up layer could be distinguished, it was found the slight reduction in image quality was not significant for patient treatment set-up verification.

The EPID response was different for both EPID types when the dose per pulse and the PRF were varied. This may be related to differences in design of the EPIDs used for this study, primarily in the types of amplifiers each type uses. Wischmann *et al.* have attributed the amplifier as a major source of non-linearity in the EPID signal, though some corrections to the gain are applied to both EPIDs, this might be one possible explanation.¹³⁶ For both dose per pulse and PRF, the dose per frame is varied, however we have no physical explanation for the observed EPID response variation.

While they are linear by design (as long as the photodiodes are not saturated), it is possible that various amplifiers will have different sensitivities over the same signal level range. These results emphasise the need for a unique investigation of the dose-response characteristics for any type of EPID used for dosimetric applications. While dependence of the EPID response on PRF may only amount to a few percent, it is important to be aware of the characteristic curves for each imager applied for dosimetric applications.

Corrections for PRF would rarely be required for the EPIDs used in this study, since beams delivered at a PRF other than the maximum (at which the EPID is calibrated) are rare in the clinic, and the PRF would have to be reduced by a factor of 3 (which is very rare) before the EPID response will change by more than 2% (Figure 2.5).

Dose per pulse dependence with varying SSD was recently investigated by Greer and Popescu⁴² and found to be linear within 1%, this was consistent with the results of this study, however it was over a smaller range and a detector from a different manufacturer was used. The dose per pulse dependence of the EPID signal is significant for dosimetry because not only is it dependent on SSD, which is usually fixed, but also on the attenuation of the beam (i.e. the thickness of the phantom, patient or wedge). According to the response curve determined in this study (Figure 2.4), the signal response drops significantly at dose per pulse values below 0.5 cGy/pulse. This is similar to the attenuation of an 18 MV photon beam by a 40 cm thick phantom (lateral field) or by a 60° wedge. Therefore in most clinical situations, the dose per pulse dependence is closer to within 3% for both types of EPID (excepting beams with thick wedges). However, the variation of dose per pulse based on attenuator thickness would still need to be determined for full calibration of the EPID. This is because of the spectral change induced when the dose per pulse is reduced by an attenuating medium, especially for higher Z materials such as that of wedges.

The dose-response as a function of number of MUs was similar for both EPID types. In clinical cases, most treatment prescriptions lie within the range of 20 – 300 MUs, the steeper part of the response curve (Figure 2.6). IMRT fields are an exception to this, with step-and-shoot segments down to 3 MUs not uncommon. If beams are prescribed with segments ranging from 5 to 50 MUs, for example, the EPID response will vary by 3% if no corrections for ghosting effects are applied. One solution would be to continue reading out the charge in the dark field following exposure and include this in the integrated EPID signal. However it is not often clinically practical to continue acquiring images after irradiation (especially between segmented fields given in quick succession), and in any case, our measurements showed the method does not sufficiently account for the signal missed in the first 40 s of irradiation. An alternative solution proposed in this report involves determining a fit of the response curve as a function of beam time.

Since previous studies have shown that ghosting effects depend on the number frames acquired,^{93,108,108} and in all our studies the frame acquisition rate is fixed, the time and number of frame parameters may be considered equivalent. This is then applied as a universal correction for ghosting effects of all images acquired, independent of the beam energy, PRF setting or number of monitor units. This suggests the solution is especially ideal for verifying segmented IMRT fields, despite the fact that it is not derived from a theoretical or physical basis. Most importantly, the pragmatic approach is a simple means of ensuring the calculated dose based on EPID measurements, once corrected for PRF and ghosting, is approximately linear with reference dose within 1%.

2.5 Conclusions

The response of the *a*-Si EPID was found to vary by up to 18% over an air gap range of 10 to 60 cm. This variation was reduced to within 1% for clinically relevant air gaps (> 40 cm) with an additional 2.5 mm Cu build-up layer on the EPID during dosimetric applications. The measured EPID response was significantly dependent on the type of imager used, even between imagers based on a similar design. For the commercial EPID used in this study, the signal for varying PRF and dose per pulse is non-linear over the range measured, with maximum variation in response up to 8%. For clinically relevant ranges, a small correction would be required for these settings at the time of treatment. Non-linearities up to 6% also persist for total dose measurements (varying MUs) for both EPID-types over the applied energy range. This was explained by the combined ghosting effects of image lag and changing sensitivity. Ghosting effects are found to depend on the number of acquired frames, not on the dose or PRF, within the range measured. Modelling the change in response as a function of beam time is a successful, pragmatic correction to obtain a constant dose-response within $\pm 1\%$ up to 1000 MUs.

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3

Comparison of ghosting effects for three commercial a-Si EPIDs

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Abstract

Many studies have reported dosimetric characteristics of amorphous silicon electronic portal imaging devices (EPIDs). Some studies ascribed a non-linear signal to gain ghosting and image lag. Other reports, however, state the effect is negligible. This study compared the signal-to-monitor unit (MU) ratio for three different brands of EPID systems. The signal was measured for a wide range of monitor units (5-1000), dose-rates and beam energies. All EPIDs exhibited a relative under-response for beams of few MUs; giving 4 to 10% lower signal-to-MU ratio relative to that of 1000 MUs. This under-response is consistent with ghosting effects due to charge trapping.

3.1 Introduction

Dosimetry with portal imagers is becoming increasingly popular, offering the potential for multi-dimensional dose verification. There are currently three brands of amorphous silicon electronic portal imaging devices (a-Si EPIDs) commercially available: Elekta *ViewGT* (Elekta, Crawley, United Kingdom), Varian *aS500/1000* (Varian Medical Systems, Palo Alto, California, United States) and Siemens *OptiVue 500/1000* (Siemens Medical Solution, Concord, California, United States).

Before using such a device for dose verification, it is necessary to first determine its dosimetric characteristics. Signal-to-dose ratios have been measured for these types of detectors, and found to be non-constant.^{77,135} A lower signal-to-MU ratio was reported for relatively short irradiation times, up to 10% lower than that of longer irradiation times for the Elekta EPID. The source of the deviation was attributed to image lag and gain ghosting effects. ‘Image lag’ is due to charge trapped in the photodiode bulk modulus or at the surface. Trapped charge read out in subsequent frames results in an off-set of the EPID signal. ‘Gain ghosting’ refers to the change in gain, or pixel sensitivity, due to the trapped charge, which alters the electric field strength in the bulk or surface of the photodiode layer. The extent of both effects (image lag and gain ghosting) will depend on both the panel design and the exposure time. Trapping in the bulk layers effectively involves the “direct capture of charge at defect energy levels in the gap and is followed by the slow release over a broad range of time constants.”¹⁰⁸ In particular, the design and manufacture of the diode layer will influence the density of trapping states, and hence influence the way charge is trapped at the diode level. Various reports have investigated image lag and gain ghosting properties of indirect flat panel detectors in further detail.^{89,93,108,136}

When using the EPID as a dosimeter, both image lag and gain ghosting effects combine to influence the dose per frame read out by the detector.⁷⁷ According to our previous study, frames within the first few seconds of irradiation ‘missed dose’. The longer the irradiation time, the smaller the relative deficit (proportional to the integrated dose over all frames). The EPID signal per frame persisted in the seconds following beam off, gradually decreasing, indicating image lag. When this ‘lag’ (dark signal) was added to the integrated dose, there was still a deficit.

This was attributed to gain ghosting effects. For the purposes of MU dependence, and for remainder of this report, we refer to the combination of gain ghosting and image lag as 'ghosting'. Ghosting effects can cause problems for EPID dosimetry if the imager signal is assumed to be linear with accumulated dose. Discrepancies will arise when the treatment exposure time differs from calibration exposure times.

Other studies, however, have reported a linear dose-signal relationship within 2%.^{42,43,73,82,122,131} All of these studies used the Varian EPID, which has a different scintillator from the Elekta and Siemens detectors. The EPID signal for these studies was measured over different dose ranges, energies and dose-rate settings compared to measurements with the Elekta EPIDs. Dosimetric characteristics for the Siemens EPIDs have not yet been reported. Non-linearity due to energy spectrum and dose/frame changes, or differences in acquisition software, can also influence the dosimetric characteristics.^{33,77,93,135} The purpose of this study was to compare the signal-to-monitor unit (MU) ratio for a comparable (wide) dose range, for all three a-Si EPID brands.

3.2 Methods & Materials

Six a-Si EPIDs were investigated in this study: two Elekta panels (iView GT) from the Netherlands Cancer Institute, Amsterdam, The Netherlands, one Varian panel (aS500) at the Rigshospitalet, Copenhagen, Denmark, another Varian panel (aS500) at The Royal Marsden Hospital, London, United Kingdom, and two Siemens panels (OptiVue 500 and 1000) at the Maastricht University Hospital, Maastricht, The Netherlands. Commercial acquisition software used to acquire images for the Varian and Siemens EPIDs. In-house software, on the other hand, was used to acquire images with the Elekta EPIDs. This software is very similar to the commercially available acquisition software provided by Elekta for the iView-GT detector.²¹ The active detection areas and image resolutions of each panel are given in Table 3-I. The Varian aS1000 was not tested in this study, the difference between this panel and the aS500 is a higher resolution (1024×768 pixels), with the same active area and acquisition software.

Ghosting effects are known to depend on exposure time,⁹³ which is linked to the dose-rate for a given dose. The Elekta and Siemens frame acquisition rates are constant, both ~3.5 frames per second (fps). The Varian acquisition rate depends on the linac pulse rate, which was ~ 4.5 to 7.5 fps for the dose-rates measured in this study. One of the differences between the two Varian panels tested in this study was that different versions of Varian's PortalVision software were used to acquire images. The earlier version (v6.1.03, 'Varian A') employs a reset every 64 frames to move the frame buffer content to the CPU, creating a dead-time of 0.28 s, or loss of 1 to 2 image frames (depending on the frame rate).⁴² More recent versions of the software do not have this dead-time.

For each panel, images were acquired for a series of open square fields, irradiated with 5, 10, 20, 50, 100, 200, 500 and 1000 MUs, integrated over all frames. Various dose-rate and photon beam energies settings were tested, according to the available settings for each linac on which the panels were mounted. For the Elekta and Varian detectors, 8 series were measured (A and B EPIDs, each with 2 dose-rate/beam energy combinations, each series measured twice). For the Siemens detectors, 6 series were included. 'Siemens A' was measured with 2 dose-rate/beam energy combinations, and 'Siemens B' with 4 dose-rate/beam energy combinations. Details regarding panel properties, beam parameters and image acquisition parameters are summarised in Table 3-1. Measurements with the Elekta panel were performed first, with field size 20×20 cm² and SDD=160 cm. Measurements with subsequent detectors could not be made with the same parameters because the dimensions of the panels and the SDDs (and hence effective field size at the detector) varied at other clinics. All fields were much larger than the central region of interest (ROI) selected for analysis (by more than a factor of 8), to avoid any field edge effects.

The results were expressed as the EPID signal divided by the number of MUs and then normalised to the ratio at 1000 MUs. It should be noted that only individual, non-segmented square fields were investigated to be able to compare the EPIDs without introducing too many variables. The implications of ghosting effects for IMRT fields (segmented or dynamic) fall outside the objectives of this study.

Table 3-1 Details of the imagers and acquisition parameters for each set of a-Si EPID measurements. A signal-to-MU curve was acquired for each EPID on the central axis of square fields, 5 to 1000 MUs, at the dose-rate settings and beam energies indicated. The value of the signal for each measurement was the average pixel value of the central region of interest (ROI) of each detector.

	Elekta A	Elekta B	Varian A	Varian B	Siemens A	Siemens B
EPID	Elekta iViewGT	Elekta iViewGT	Varian aS500	Varian aS500	Siemens OptiVue 500	Siemens OptiVue 1000
Institute	Netherlands Cancer Institute	Netherlands Cancer Institute	Rigs-hospitalet	Royal Marsden	Maastricht University Hospital	Maastricht University Hospital
	Amsterdam	Amsterdam	Copenhagen	London	Maastricht	Maastricht
Acquisition software	in-house*	in-house*	PortalVision v6.1.03	PortalVision v6.1.11	Coherence Therapist Workspace 1.0.657	Coherence Therapist Workspace 1.0.657
Active area	41×41 cm ²	41×41 cm ²	40×30 cm ²	40×30 cm ²	41×41 cm ²	41×41 cm ²
Image resolution	1024×1024	1024×1024	512×384	512×384	512×512	1024×1024
Field size (at isocentre)	20×20 cm ²	20×20 cm ²	10×10 cm ²	10×10 cm ²	10×10 cm ²	10×10 cm ²
SSD	160 cm	160 cm	145 cm	145 cm	150 cm	150 cm
Central ROI	0.8×0.8 cm ²	0.8×0.8 cm ²	1.6×1.6 cm ²	1.6×1.6 cm ²	0.5×0.5 cm ²	0.5×0.5 cm ²
Series measured:						
beam energy & (dose-rate, MU/min)	4 MV (250) 6 MV (500)	8 MV (200) 8 MV (400)	6 MV (300) 6 MV (500)	6 MV (100) 6 MV (400)	6 MV (300) 10 MV (500)	6 MV (50) 6 MV (300) 10 MV (50) 10 MV (500)

*NB The in-house software used with the Elekta EPIDs is very similar to the commercially available acquisition software provided by Elekta for the iView-GT detector.

3.3 Results

Figure 3.1 shows an average of the series measured for each of the three a-Si EPID brands. For the Varian EPID, only 4 series using ‘Varian B’ were included in the average (2 dose-rate/beam energy combinations, each series measured twice). The measurements with ‘Varian A’ were not included here because it uses a different acquisition software, however it is presented separately. All series exhibited a lower signal-to-MU ratio for shorter irradiation times. This is consistent with previous reports suggesting that ghosting effects depend on exposure and/or acquisition time.^{77,93} For irradiations of more than 200 MUs, the ratio for each detector was constant to within $\pm 1.5\%$, i.e. the response is effectively linear with dose. Below 200 MUs, the average signal-to-MU ratio decreases 4% for the Elekta panels, and 5% for the Varian and Siemens panels.

Figure 3.1 Signal-to-MU ratios for Elekta, Varian and Siemens a-Si EPIDs, averaged over 2 to 3 dose-rate settings for different energies, with 1 or 2 detectors for each brand. All points are normalised at 1000 MUs. One outlying series, Varian A, used a different acquisition mode and was therefore excluded for this figure. The standard deviations at each point were less than 1.4%, and are shown as error bars (± 1 SD). Different scintillators employed by different brands will exhibit slight variation in ghosting effects, however there is a consistent under-response for fields of fewer MUs for all three brands.

Error bars represent ± 1 standard deviation (SD). The relative average SD was 0.3% and the maximum was $\pm 1.4\%$. As expected, the results averaged over the largest range of dose-rate/beam energy combinations had the largest SD, i.e. the Siemens dose-rate settings, ranging from 50 to 500 MU/min, with beam energies of 6 and 10 MV. A variation in the signal-to-MU ratio could be due to variation in the design and manufacture of the *a*-Si layer, (as used by different brands), or read out of the electronics, leading to different number of charge particles trapped and/or read out in the bulk modulus or interface of the photodiode layer. In addition to physical differences, different image acquisition parameters (e.g. trigger levels) will also influence the EPID signal differently at various exposure times.

Signal-to-MU ratios measured at different beam energies and dose-rate settings for each detector are also shown in Figure 3.2. For each detector type, the MU dependence was similar (within $\pm 1.4\%$) for all energies and dose-rate settings, except below 10 MUs for the Varian A and B EPIDs. For the EPID using the earlier version of PortalVision (Varian A), the signal-to-MU curve dropped by 1% between 50 MUs (43 frames) and 100 MUs (95 frames), for both dose-rates. The discontinuity in the curve was due to the reset occurring every 64 frames and so resulted in a dead-time during acquisition if more than 64 frames were acquired (Figure 3.2). The data for both Varian A series were subsequently corrected for the missing signal due to dead-time and are also given in Figure 3.2. The difference in signal ratio between 5 and 1000 MUs is clearly much greater for the corrected Varian A than Varian B. The reason was not investigated further for this study, however it can be assumed differences in image acquisition, panel design and variation in read out electronics are possible reasons for the differences between the two sets of measurements in Figure 3.2.

Due to non-linearity of linac monitor signal, the Siemens EPID signals measured with 5 MUs, 6 MV and 300 MU/min were corrected based on relative dose values measured with an ionisation chamber. The linac output used for all other series was also checked and found to be linear, so no corrections were necessary.

Figure 3.2 EPID signal-to-MU ratios, separated for Elekta, Varian and Siemens detectors. Two panels (A and B) for each brand were tested and normalised at 1000 MUs. The curves are similar for all but one series. For the EPID using the earlier version of PortalVision (Varian A, 'x'), there is a 1% 'drop' in the curve, between 50 MUs and 100 MUs, for both dose-rates. This discontinuity is due to a dead-time introduced while frames are being stored, occurring every 64 frames. The data for both Varian A series are also presented, correcting for the missing signal (*).

Two series were also measured with the 'Siemens B' EPID at very low dose-rate settings of 50 MU/min. The relative signal-to-MU ratio at smaller number of MUs (0.96 at 5 MUs) was not as low as for the higher dose-rate settings (0.93 at 5 MUs, same EPID, same beam energies). This dose-rate dependence is consistent with ghosting behaviour. Since ghosting depends on the exposure time and not on dose, slower dose-rates will result in an EPID signal with a much weaker MU dependence. This is because a lower nominal dose-rate setting at the linac will result in a lower dose per frame rate.

At lower dose per frame rates, an equilibrium can be achieved much faster between the amount of charge that is trapped, and the amount that is read out. So at very low dose-rates, there would be no ghosting effect. The range of dose-rate settings for the Elekta and Varian panels was not large enough to see this effect. It should be noted that although all measurements were normalised to the respective EPID signals at 1000 MUs, there was variation in the EPID signal at this normalisation point for different dose-rates of the order of a few percent (for the same detector brand, linac and energy). This difference could be best illustrated with additional data at multiple dose-rate settings for each detector, linac and energy combination, however this is beyond the scope of this technical note.

3.4 Conclusions

Signal-to-MU ratios for all EPIDs tested showed a dependence on the number of MUs delivered, independent of the manufacturer. This dependence indicated that charge trapping, resulting in ghosting effects, influences the *a*-Si EPID response to dose. Therefore it is important to be aware of the resulting relative under-response at shorter irradiation times. The similarity of the results for all detectors tested suggested that the acquisition time dependence, or ghosting effect, is a fundamental property of indirect detection *a*-Si-based EPIDs. The small differences between the signal-to-MU ratio for the three manufactures was likely to be due to differences in panel design and acquisition software. Variation between curves of the same manufacturer may be due to a combination of dose-rate and energy dependence, both influencing the dose delivered per frame. Errors of 4-10% at the centre of the field are likely to influence EPID dosimetry measurements if the imager is applied over a wide range of irradiation times, by varying dose or dose-rate, to single fields without corrections.

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4

The long-term stability of amorphous silicon flat-panel imaging devices for dosimetry purposes

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Abstract

This study was carried out to determine the stability of the response of amorphous silicon (a-Si)-flat panel imagers for dosimetry applications. Measurements of the imager's response under reference conditions were performed on a regular basis for four detectors of the same manufacturer. We found that the ambient temperature influenced the dark field, while the gain of the imager signal was unaffected. Therefore, temperature fluctuations were corrected for by applying a 'dynamic' dark-field correction. This correction method also removed the influence of a small, irreversible increase of the dark-field current, which was equal to 0.5% of the dynamic range of the imager and was probably caused by mild radiation damage to the a-Si array. By applying a dynamic dark-field correction, excellent stability of the response over the entire panel of all imagers of 0.5% (1 SD) was obtained over an observation period up to 23 months. However, two imagers had to be replaced after several months. For one imager, an image segment stopped functioning, while the image quality of the other imager degraded significantly. We conclude that the tested a-Si EPIDs have a very stable response and are therefore well suited for dosimetry. We recommend, however, applying quality assurance tests dedicated to both imaging and dosimetry.

4.1 Introduction

Various quality assurance (QA) protocols for electronic portal imaging devices (EPIDs) exist, but they generally do not include recommendations for dosimetry applications.^{49,70,99,100} We have recently developed a dedicated QA programme to verify the long-term stability of liquid-filled matrix ionisation (LiFi)-type EPIDs.⁶⁷ In that study, it was shown that several factors influence the reproducibility of the EPID response (e.g. ambient temperature, radiation damage, warm-up time). For LiFi-EPIDs, a temperature dependence of about 1%/°C, and a decrease in response of approximately 4% per year was found.⁶⁷ Similarly, the effect of these factors needs to be well characterised for new types of EPIDs prior to their use for dosimetry purposes. Knowledge about the environmental influences or long term change in response are important to develop QA procedures and allow implementation of correction procedures to compensate for these effects. For instance, for LiFi-EPIDs it was shown that correction for temperature and age can result in a reproducibility better than 1% (1 SD) over a period up to two years.⁶⁷

Amorphous-silicon (*a*-Si) EPIDs were installed in our department in January 2002. These imagers are flat-panel, indirect detectors and their dose-response characteristics have been investigated. The only short-term (i.e. within one day) deviations in response that we observed for these imagers could be well explained by image persistence, which has been quantitatively described by McDermott *et al.*⁷⁷ The long-term (i.e. day to day) stability however, has not previously been investigated in a systematic way. For a different type of *a*-Si EPID utilising direct detection of photons, a maximum deviation of 1% of the response over a period of two months has been reported.³³

Our purpose in this study was first to determine the long-term stability of the response of the *a*-Si EPIDs used in our department. Secondly, the temperature dependence and long-term drift were investigated for this type of EPID. The third aim of this study was to refine the procedure required for accurate EPID dosimetry, which was described in a previous paper,⁶⁷ using *a*-Si EPIDs.

4.2 Methods & Materials

4.2a *The imagers used in this study*

Four *a*-Si EPIDs (Elekta iView-GT, Elekta Oncology Systems, Crawley, UK), which are routinely used in our clinic for set-up verification, were investigated in this study. These imagers are indirect detectors, i.e. a phosphorous scintillation layer is used to convert incident radiation to optical photons.⁴⁹ A copper plate of 1 mm thickness, placed on top of the scintillation layer, is provided by the vendor as build-up material to enhance image quality. The optical photons are detected by an array of coupled amorphous silicon photodiodes and thin film transistors.⁴ The imagers have a sensitive area of 41x41 cm² (1024x1024 pixels, 400 μ m pitch). In order to reduce the required data storage capacity, the acquired images are stored with a resolution of 512x512 pixels. The *a*-Si array is read out using 16 amplifier chips, eight for each half of the imager. In this way, 16 image segments can be defined, each with an individual response (Figure 4.1). Imagers *A*, *B* and *C* are mounted on linear accelerators producing photon beams of 4 and 6 MV, 8 and 18 MV, and 6 and 18 MV, respectively. All imagers were positioned at a fixed focus-detector distance of approximately 157 cm. Imager *B*₁ was replaced after 7.5 months by imager *B*₂ because one of its amplifier chips stopped functioning. Because imagers *B*₁, *B*₂ and *C* are used in 18 MV photon beams, an additional copper plate of 2.5 mm was mounted with screws on top of the existing 1.0 mm copper plate covering the detector area, within the imager encasement. This extra build-up was added to obtain electron equilibrium for 18 MV photon beams at the scintillation layer during dosimetry.⁷⁷ No additional build-up material was used for imager *A*.

4.2b *Calibration of the imagers*

A full calibration of the imagers is performed in two steps. In order to optimise the image quality for patient position verification, a so-called *image calibration* is performed, similar to the procedure previously described for the LiFi-EPIDs.^{49,67} For the *a*-Si EPIDs however, we found that it is not necessary to correct for variations in response at gantry angles other than 0°, and calibration images are only acquired at 0°.

Furthermore, the image calibration is not only performed after installation of the imager (static calibration set), but it is partly updated just prior to image acquisition to correct for image persistence from previous irradiations.¹⁰⁸ For this purpose dark-field images are acquired continuously every 30 s the EPID is not irradiated. The most recent dynamic dark-field image taken just prior to irradiation, I_D^{dyn} , is then used to correct the acquired images, in combination with the flood and dark-field image acquired during image calibration:

$$I_{corr}^{dyn} = \frac{I_{raw} - I_D^{dyn}}{I_F - I_D} \cdot 8192 \quad (4.1)$$

in which I_F and I_D are the flood and dark-field images, taken during the image calibration procedure, and I_{raw} and I_{corr}^{dyn} are the uncorrected and corrected images, respectively. The factor 8192 has been introduced to maintain sufficient accuracy when the pixel values of the images are stored as short integers. Details concerning the different calibration images are recorded in the image header of the corrected portal image to prevent loss of information. For routine clinical use, the dynamic dark-field correction is sufficient to improve the image quality, and is carried out automatically. In this study however, the images were also re-processed using

$$I_{corr}^{stat} = \frac{I_{raw} - I_D}{I_F - I_D} \cdot 8192 \quad (4.2)$$

in order to compare the stability of the *a*-Si EPIDs after either a dynamic dark-field correction or a ‘static’ dark-field correction.

A more detailed *dosimetric calibration*^{12,65} is required for EPID dosimetry. For the reproducibility experiments in this study, however, the signal of the *a*-Si EPIDs is assumed to be proportional to the dose delivered to the imagers.^{42,77} For consistency with the other EPID types which were already present in our institute, all image acquisition, manipulation, and analysis was performed using software developed in our institution. The Elekta software however, uses the same procedure as described by equation 4.1.

4.2c Tests performed in this study

To test the overall long-term reproducibility of the response, portal images of 10x10 cm² and 20x20 cm² fields were initially acquired twice a week at all beam energies. After a number of months however, the results showed that the response of the imagers was very stable, therefore the images were acquired less frequently, i.e. once a week. Each image was acquired using beams of 100 monitor units (MUs), corresponding to a dose to water at the position of the imager of approximately 40 cGy.

All data analysis was performed using the images which were stored after image acquisition with a resolution of 512x512 pixels. For various tests, the signals of the pixels within several regions of interest were averaged to analyse the measurements. The ambient temperature was also measured with a mercury thermometer just prior to each EPID measurement. The thermometer was located in the treatment room with the EPID, in order to determine the temperature dependence of the imager response. Furthermore, the output of the linear accelerators was measured just prior to image acquisition with a calibrated Farmer-ionisation chamber (NE Technology Limited, NE2571), which was positioned in a rectangular polystyrene slab phantom, in combination with an electrometer (Keithley, 615). These data were subsequently used to correct the EPID signal for output variations of the accelerator. The variation in the ionisation chamber measurements was less than 0.1% (1 SD), which shows that the ionisation chamber measurements are representative of the accelerator output during the EPID measurements.

The average value of the central 5x5 pixels was used to determine the central response of the imagers. In order to assess potential differences in response between the sixteen image segments which may occur for this type of imager, the average signal of 102x32 pixels within each image segment (Figure 4.1) was calculated. Subsequently, these values were normalized to the average value at the central 5x5 pixels, and the standard deviation of the normalized values was calculated.

Figure 4.1 Gain image of imager B_2 showing 16 individual image segments. This image was calculated by subtracting the flood and dark-field images which were obtained shortly after installation of this imager.

The observed variations in response and dark-field signal were correlated with both temperature and time using multiple regression analysis. To verify the analysis of the change in the dynamic dark-field signal independently, additional measurements were performed with imager B_1 placed in a laboratory room. By turning the heating facility on or off, a larger ambient temperature range could be achieved than would be possible in a treatment room with climate control. The temperature dependence of the dark-field of EPID B_1 was measured over a period of 13 days without irradiating the imager to determine the temperature dependence more thoroughly. For this purpose, the ambient temperature was measured using a thermocouple. In addition, the temperature of the imager was measured using two thermocouples attached to centre of the 1 mm copper plate, on top of the scintillation layer (i.e. the touch guard was removed). All three thermocouples were calibrated before and after the measurement using a mercury thermometer placed next to them, resulting in an accuracy better than 0.5 °C.

4.3 Results

The variation of the output of all linear accelerators during this study observed over a period of 5 to 23 months was smaller than 1% (1 SD). If the dynamic dark-field correction was used, the variation in response of all four a -Si EPIDs at the central pixel region was approximately 0.5% (1 SD) (Table 4-I). These variations were not correlated with the ambient temperature (data not shown).

When the same set of images was processed retrospectively with a static dark-field, both the systematic deviation and the random variation increased noticeably, up to several percent depending on the observation period (Table 4-I).

Table 4-I Mean and standard deviation of the difference Δ between the average EPID signal of the central 5x5 pixels during the period of observation and that of the first measurement. The values in brackets represent one standard deviation. Δ^{dyn} and Δ^{stat} represent the values obtained after dynamic or static dark-field correction, respectively. All measurements were corrected for fluctuations of the accelerator output.

EPID	Period (months)	Δ^{dyn}	Δ^{stat}
A	Jan.02-Dec.03 (22.9)	-0.3% (0.5%)	2.4% (2.1%)
B ₁	Apr.02-Nov.02 (7.5)	0.0% (0.5%)	1.7% (1.5%)
B ₂	Nov.02-Dec.03 (11.0)	0.2% (0.5%)	-2.2% (1.2%)
C	Aug. 03-Dec.03 (4.1)	-0.2% (0.4%)	-0.1% (0.4%)

As an example, these data have been plotted for imager A (Figure 4.2a). The difference between these corrections originates from the change of the dynamic dark-field signal. Two features can be observed: a general increase of the dynamic dark-field signal over the period of observation, as well as a correlation with the ambient temperature (Figure 4.2b). For all imagers, it was found that the dynamic dark-field signal changes linearly with both time and the ambient temperature fluctuation ΔT (see Appendix).

The temperature dependence of the dark-field of EPID B₁ was measured in a laboratory room over a period of 13 days *without* irradiating the imager. Various temperature cycles were observed during this period, as well as a warm-up period of one day. In this period, the ambient temperature ranged from 19.7°C to 25.3°C, while the temperature at the central position of the imager surface after warm-up ranged from 32.1°C to 37.2 °C. The observed dark-field signal could be accurately described by a 2nd degree polynomial, using either the surface or ambient temperature as the explanatory variable (see Appendix). However, the best results were obtained when the EPID surface temperature was used and these have been plotted in Figure 4.3.

Figure 4.2 (a) Reproducibility of the detector signal of the central 5x5 pixels observed with imager A with static (open symbols) and dynamic (closed symbols) dark-field correction over a period of 23 months; (b) corresponding dynamic dark-field signal (closed symbols) showing the combined effects of ambient temperature fluctuations (open symbols) and a time trend. The solid line represents a fit using the factors presented in Table 4-II.

Figure 4.3 The dark-field signal of imager B_1 during several temperature cycles, plotted as a function of the EPID surface temperature. The solid line represents a fit obtained with the factors presented in Table 4-III.

For all imagers, the difference in response of the sixteen image segments relative to the average value at the central 5x5 pixels was less than 0.5% (1 SD), and did not display a discernable time trend. Remarkably, this was also the case for imager B_2 during the last month before replacement when its image quality degraded significantly. In this period the borders between the various image segments became visually enhanced and hampered normal clinical use of the imager (Figure 4.4).

Although four borders are situated in the central pixel region, the standard deviation of the central 5x5 pixels values within each image slightly increased, but it was still less than 0.5% (1 SD) when the imager was replaced.

Figure 4.4 Images of a 20x20 cm² radiation field acquired with imager B₂. Image (a) was obtained in the first month after installation of this imager, and image (b) just before its replacement after 11 months of use. Both images were processed using an unsharp mask filter to enhance artefacts in the images. Image processing clearly enhances the few new bad pixels that appeared after 11 months, the borders between the individual image segments in image (b) that appear due to problems with the electronics, as well as the field edges in both images.

4.4 Discussion

The excellent reproducibility of the response of the imagers used in this study is achieved by applying a dynamic dark-field obtained just prior to image acquisition. This method is a partial image re-calibration, which only corrects for the change of the dark-field signal, while the original flood-field calibration image is left unchanged. In addition to the temperature induced variations, an irreversible increase of the dynamic dark-field signal was observed. This increase is presumably related to (mild) radiation damage of the *a*-Si array, because the largest increase of the dynamic dark-field signal is located at the centre of the array, which is irradiated most frequently (data not shown). The excellent reproducibility of these *a*-Si EPIDs shows that the actual dose-response (i.e. the imager signal per unit dose after dynamic dark-field correction) of this type of *a*-Si EPID is independent of room temperature fluctuations and radiation history.

The residual variation in both the actual EPID response and the dark-field signal (after multiple regression analysis using time and temperature as fit factors) over a measurement period up to almost two years is negligible for all imagers. Therefore, we can safely conclude that no other factors influence the imager response on time scales longer than a few days. The only deviations in response that we observed on shorter time scales were due to image persistence which can be corrected for as described by McDermott *et al.*⁷⁷ The most important advantage of the dynamic dark-field correction, compared to frequent dosimetric re-calibration of the imager, is that it can be applied automatically. Furthermore, dynamic dark-field correction eliminates the temperature dependence of the response of *a*-Si EPIDs, while re-calibration of the imager would only remove the drift of the imager response.

The annual increase of the dark-field signal is approximately 0.5% of the total dynamic range of the imager of 65536 counts. Since at most 30% of the total dynamic range of the imager is effectively used during clinical use of our imagers, we can safely conclude that this increase of the dark-field signal will not noticeably influence the useful lifetime of the *a*-Si EPIDs. However, the increase of the dark-field signal of imager A is significantly smaller than that of imagers B_1 and B_2 (Table 4-II). The larger degradation observed for imagers B_1 and B_2 may be related to the production of neutrons at the higher photon beam energies at which they are used.

The temperature dependence of the dynamic dark-field signal of the newer imager B_2 was significantly smaller than those of imagers A and B_1 (Table 4-II). This difference may be intrinsic and related to differences in EPID construction, but no details about differences are available. However, the difference between the dependence of the dark-field signal on the ambient and EPID surface temperature (Table 4-III) indicates that the environmental setting of the imager (air-conditioning and housing of the imager) also influences the temperature dependence.

For imager B_1 , one image segment stopped functioning after 7.5 months, while for imager B_2 , the image quality degraded and was no longer acceptable for patient position verification after 12 months. The degradation was characterized by a small, unilateral gradient super-imposed on top of the signal over each image segment.

Table 4-II Multiple regression analysis of the variation of the dynamic dark-field signal observed for the imagers A, B₁, and B₂ using the fluctuations of the ambient temperature ΔT , and time as explanatory variables. The constant represents the dark-field signal which was already present at the start of the measurements. Full scale is 65536 counts.

Variable	Value	p-value	95% confidence interval		Units
EPID A: $r^2 = 0.93$; residuals = 34 Counts (1SD)					
ΔT	46	<< 0.01	33	58	Counts/°C
time	246	<< 0.01	230	262	Counts/year
constant	4501	<< 0.01	4488	4515	Counts
EPID B ₁ : $r^2 = 0.93$; residuals = 30 Counts (1SD)					
ΔT	58	<< 0.01	34	82	Counts/°C
time	502	<< 0.01	439	565	Counts/year
constant	3697	<< 0.01	3675	3719	Counts
EPID B ₂ : $r^2 = 0.99$; residuals = 11 Counts (1SD)					
ΔT	13	<< 0.01	7	18	Counts/°C
time	445	<< 0.01	431	460	Counts/year
constant	4119	<< 0.01	4113	4127	Counts

This resulted in a step-wise change in sensitivity at the borders between image segments, and a strong visual enhancement of these borders (Figure 4.4b). This gradient occurred in the same direction in which the pixels in each row are read out, which suggests that either one of the electronic amplifiers or a multiplexer had become unstable. Because an image re-calibration did not improve the image quality either, the imager response seemed to change from minute to minute. However, a quantitative analysis showed that the relative response of the various image segments had not changed more than 0.5% (1 SD).

Similarly, the standard deviation of the EPID signal at the central pixel region, in which four image segments participate, was only 0.5% (1 SD) before the imager was replaced. Due to the spatial frequency of the artefacts, the degradation of the image quality only caused a problem for use of the EPID for patient position verification, while EPID dosimetry would not have been hampered. The most practical method for identifying image degradation of a-Si EPIDs at an early stage is to regularly inspect the image quality visually after image processing with a dedicated filter (e.g. an unsharp mask¹⁰) and use a fixed level and window setting of the image viewer.

Table 4-III Multiple regression analysis of the variation of the dynamic dark-field signal observed for imager B₁, using the fluctuations ΔT of either the ambient temperature or the EPID surface temperature as explanatory variables. The constant represents the dark-field signal which was already present at the start of the measurements. Full scale is 65536 counts.

Variable	Value	p-value	95% confidence interval		Units
<i>T</i> = ambient temperature: $r^2 = 0.98$; residuals = 10 Counts (1SD)					
ΔT	38.4	<< 0.01	38.0	38.8	Counts/°C
$(\Delta T)^2$	0.9	<< 0.01	0.7	1.1	Counts/year
Constant	3827	<< 0.01	3826	3827	Counts
<i>T</i> =EPID surface temperature: $r^2 = 1.00$; residuals = 4 Counts (1SD)					
ΔT	46.8	<< 0.01	46.6	47.0	Counts/°C
$(\Delta T)^2$	3.4	<< 0.01	3.3	3.5	Counts/year
Constant	3825	<< 0.01	3825	3825	Counts

The dosimetric stability of the *a*-Si EPIDs used in this study is very similar or better than other types of EPID.^{31,41,42,67} However to achieve such a good long-term stability, LiFi-EPIDs require a correction for both the temperature dependence and the drift of the response, which can not be obtained using dynamic dark-field correction.⁶⁷ A limited number of studies have been performed concerning the variation in response of video-based EPIDs over a time period of 2 months. Both studies report a variation in response of 0.5% (1 SD), and a drift ranging from 0.5% to 2.5%.^{31,41} For the *a*-Si EPIDs of another vendor, a variation in response of 0.8% (1 SD) over a period of 1 month has been reported¹⁶, and a drift depending on the beam quality up to 4% over a period of 5 months.⁸²

The methods and results presented in this study may be used in combination with the procedures and recommendations in the previous study to develop a QA programme for accurate dosimetry. Both studies show that temperature dependence and time trends of the imager response are important factors influencing the long-term reproducibility of both imager types. It may be expected that the response of other EPID types will show some temperature dependence and time trends, as observed for the *a*-Si- and LiFi-EPIDs. However, the magnitude and mechanisms of these effects may be different, and may thus require different correction procedures.

Furthermore, (small) differences between individual imagers, differences in environmental settings, and differences in imager irradiation (beam quality, and the frequency at which the EPID is exposed), will influence these factors.

Therefore, it is necessary to perform long-term stability tests for each EPID, especially if a high accuracy is required. For *a*-Si-EPIDs, the development of a QA programme is largely simplified compared to other imager types because the temperature dependence and drift can be automatically removed by dynamic dark field correction. However, the apparent sensitivity of the electronics for radiation damage indicates that a more frequent inspection of the image quality is required. In this study, all image acquisition, manipulation, and analysis of these images were performed using in-house developed software, for practical reasons (consistency in networking with older imagers). However, for the Elekta imager it is not difficult to access the raw pixel data, since the images are stored in the lossless JPEG compression standard. Furthermore, dynamic dark field correction is standard in the Elekta software.

4.5 Conclusions

The reproducibility of the *a*-Si EPIDs at the central pixel region was excellent: 0.5% (1 SD) over a period up to 23 months. In addition, the difference in response of the 16 imager segments corresponding to separate amplifier chips, was smaller than 0.5% (1 SD) for all imagers. This result proves that the gain of the tested *a*-Si EPIDs does not depend on radiation history or temperature fluctuations. Use of a dynamic dark-field correction in the processing of all images was sufficient to eliminate virtually all variation of the imager response. Because the change of the dark-field signal of all imagers used in this study can be fully explained by radiation history and temperature fluctuation, there are no other factors influencing the response of this type of EPID. In spite of the excellent reproducibility results, instability in the individual image segments and overall degradation in image quality still rendered two imagers inadequate for normal clinical use (i.e. patient set-up verification) and had to be replaced. This degradation however, did not noticeably influence the reproducibility of the EPID response. Because clinical decisions will be made based on dosimetric data obtained with these imagers, adequate routine QA is essential.

This study reports a thorough QA procedure which systematically monitors and corrects for short- and long-term variation in the EPID signal. Using these methods, a stable EPID signal was achieved and faults were detected, which will improve the accuracy of these EPIDs for dosimetry.

Appendix : Statistical analysis of the data

Multiple regression analysis of the dynamic dark-field signal of imagers A , B_1 and B_2 was applied to distinguish between temperature dependence and time trends. A smaller time trend was obtained for imager A compared to those obtained for imagers B_1 and B_2 , while a significantly smaller temperature dependence was found for imager B_2 than for imagers A and B_1 (Table 4-II). For imager C , too few data were available to obtain meaningful fit results.

After its replacement, the temperature dependence of the dark-field signal of imager B_1 was again measured *without* irradiating the imager to verify the analysis of the change in dynamic dark-field signal (Table 4-III). For this purpose, the dark-field signal, the ambient temperature and the surface temperature of the imager were measured over 13 days. The temperature dependence that was obtained from these measurements was slightly different compared to that obtained from the long-term reproducibility measurements during clinical use of this imager. This difference could be caused by environmental differences (e.g. air-conditioning).

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5

Accurate two-dimensional IMRT verification using a back-projection EPID dosimetry method

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Abstract

The use of electronic portal imaging devices (EPIDs) is a promising method for the dosimetric verification of external beam, megavoltage radiation therapy – both pre-treatment and *in vivo*. In this study, a previously developed EPID back-projection algorithm was modified for IMRT techniques and applied to an amorphous silicon EPID. By using this back-projection algorithm, two-dimensional dose distributions inside a phantom or patient are reconstructed from portal images. The model requires the primary dose component at the position of the EPID. A parameterised description of the lateral scatter within the imager was obtained from measurements with an ionisation chamber in a mini-phantom. In addition to point dose measurements on the central axis of square fields of different size, we also used dose profiles of those fields as reference input data for our model. This yielded a better description of the lateral scatter within the EPID, which resulted in a higher accuracy in the back-projected, two-dimensional dose distributions. The accuracy of our approach was tested for pre-treatment verification of a five-field IMRT plan for the treatment of prostate cancer. Each field had between six and eight segments and was evaluated by comparing the back-projected, two-dimensional EPID dose distribution with a film measurement inside a homogeneous slab phantom. For this purpose, the γ evaluation method was used with a dose-difference criterion of 2% of dose maximum and a distance-to-agreement criterion of 2 mm. Excellent agreement was found between EPID and film measurements for each field, both in the central part of the beam and in the penumbra and low-dose regions. It can be concluded that our modified algorithm is able to accurately predict the dose in the mid-plane of a homogeneous slab phantom. For pre-treatment IMRT plan verification, EPID dosimetry is a reliable and potentially fast tool to check the absolute dose in two dimensions inside a phantom for individual IMRT fields. Film measurements inside a phantom can therefore be replaced by EPID measurements.

5.1 Introduction

The challenge of external beam radiotherapy for cancer treatment is to irradiate the tumour with a high dose, while the surrounding healthy tissue suffers as little as possible radiation damage. Due to the increasing complexity of nearly all steps in modern radiotherapy, the demand for a thorough verification of the dose delivered to the patient has also increased, either pre-treatment or *in vivo*.

For pre-treatment verification various treatment parameters, such as beam energy, number of monitor units, and (multileaf) collimator settings, have to be verified to ensure the correct dose delivery to a patient. These parameters can be used to calculate a dose distribution within a phantom. A variety of methods is available to check the absolute dose at specific points, which is usually done with ionisation chamber measurements, and to verify relative dose distributions, e.g. by film measurements in specific planes or by gel dosimetry in three dimensions.²⁹ *In vivo* dose verification is often done by placing dosimeters, such as diodes, thermoluminescent dosimeters, or metal oxide semiconductor field effect transistors (MOSFETs), on the skin of patients or inside patients to derive the dose at specific points within the patient (see review³⁸).

These measurements are very labour intensive and yield merely a limited amount of information; often, the dose is only determined at a single point. One would like to have an alternative method to verify dose delivery in two or, preferably, three dimensions. EPID dosimetry is a very promising approach for this purpose. EPIDs - electronic portal imaging devices - are widely used for set-up verification during radiotherapy. These devices are easy to use and data acquisition is fast. Many types of EPIDs combine good reproducibility of the response,^{31,41,42,66,67} the possibility to measure dose distributions in two dimensions with high spatial resolution, and a digital format of the images.

Basically, there are two approaches to EPID dosimetry and in principle both are suitable for pre-treatment verification and *in vivo* dosimetry. In the “forward approach”, the measured (and sometimes processed) portal image is compared to a predicted dose or photon fluence *at the plane of the EPID*, which is calculated with the treatment planning system (TPS) or an independent algorithm.^{28,48,60,73,76,87,95-97,122}

In the “backward approach”, portal images are used to reconstruct the dose *within the patient or phantom*.^{11,45,65} This back-projection method makes it possible to directly compare the calculated with the delivered dose distribution in the patient or phantom. While the dose is verified in only one plane with the forward approach, three-dimensional dose reconstruction is potentially possible with the back-projection method.^{45,65,91}

Variations on these approaches have also been described in the literature. In a “hybrid” method, McNutt *et al.*^{80,81} treat the EPID as part of an extended volume and use a convolution/superposition algorithm to predict a portal dose image. The primary energy fluence is then iteratively adapted until predicted and measured portal dose distributions agree. Finally, the converged primary energy fluence is back-projected and convolved with the dose deposition kernel yielding the dose distribution within the patient or phantom in three dimensions. In the pre-treatment verification method of Warkentin *et al.*,¹³¹ EPID images are acquired *without* a phantom in the beam and these EPID images are deconvolved with a (two-component) “dose-glare” kernel for the EPID to yield the two-dimensional primary fluence. This fluence is then convolved with a phantom dose-deposition kernel to yield the dose distribution in a solid-water phantom; for absolute dosimetry, cross-calibration with an ionisation chamber is performed. However, this method cannot be applied for *in vivo* dosimetry purposes.

Our back-projection method has been described for liquid-filled matrix ionisation chamber EPIDs,^{11,65} but is also applicable to other types of EPIDs. The calibration of the EPID for back-projection dosimetry consists of two parts. First, a dosimetric calibration is needed to establish the dose-response relationship by relating EPID pixel values to dose values at the position of the imager. Secondly, the parameters for the back-projection algorithm have to be determined to enable the conversion from the dose at the EPID position to the dose inside the patient or phantom.

This is done by applying correction procedures for the scatter component of the dose within the EPID and the scatter from the patient or phantom to the EPID. Furthermore, the scatter component within the patient or phantom, in combination with the attenuation of the beam, is accounted for to obtain the total dose at specific points in the patient or phantom.

In our back-projection approach,^{11,65} the relationship between the EPID signal and the “real dose” (defined as the dose measured with a calibrated ionisation chamber) has, until now, been derived from data only on the central axis. As a consequence, the errors in dose reconstruction at off-axis positions are usually larger than those on the central axis. This is relevant since the treatment outcome does not only critically depend on the dose delivered to the tumour (usually close to the isocentre), but also on the dose delivered to normal tissue. Moreover, sensitive anatomical structures are often close to the location of steep dose gradients within the patient. Therefore it is essential to improve the accuracy of the method in the penumbra region and outside the field. This especially applies to IMRT fields, which may have many steep dose gradient/penumbra regions, spread throughout the target volume and organs at risk.

The purpose of this study was to improve and evaluate the accuracy of the back-projection method for verifying two-dimensional dose distributions in phantoms irradiated with intensity-modulated beams. The back-projection method was originally developed for a liquid-filled matrix ionisation chamber EPID;^{11,65} we adapted the algorithm and applied it to an amorphous silicon (*a*-Si) EPID. The aim of this study was also to reveal how well the EPID back-projection method compares with the *de facto* “gold standard” film dosimetry procedure for pre-treatment IMRT verification.

There are currently three *a*-Si EPID systems commercially available for portal imaging: the PortalVision aS500 by Varian Medical Systems (Palo Alto, CA, USA), the BEAMVIEW TI by Siemens Medical Solutions (Erlangen, Germany), and the iViewGT by Elekta (Crawley, UK). The panels for both Siemens and Elekta EPIDs are manufactured by PerkinElmer (Fremont, CA, USA). Depending on the hard- and software used, the dosimetric properties of the various *a*-Si EPID systems may differ. The basic dosimetric properties of *a*-Si EPIDs have been reported for both the Varian Portal Vision aS500^{42,43} and the Elekta iViewGT^{66,77} systems.

An Elekta *a*-Si EPID was used for our study; however, while parameter details may vary, the principles underlying the (improved) back-projection algorithm outlined here are also valid for other types of EPIDs.

5.2 Methods & Materials

5.2a Accelerator and EPID

The measurements were done using an 18 MV photon beam of an SL20i linear accelerator (Elekta, Crawley, UK). The accelerator was equipped with a multileaf collimator (MLC), consisting of 40 leaf pairs with a projected leaf width at the isocentre of 1 cm.⁵⁴ For all measurements described in this paper the gantry angle was set to 0°.

A PerkinElmer RID 1680 AL5/Elekta iViewGT *a*-Si EPID was used for all measurements. This imager has a 1 mm thick copper plate on top of the scintillation layer. An extra 2.5 mm thick copper plate was mounted directly on top of the standard plate (replacing the aluminium cover plate) both as additional build-up material and to absorb scattered low-energy photons from the phantom or patient; this modification has negligible impact on image quality.⁷⁷ The EPID has a sensitive area of 41x41 cm². In this paper, the axis of an EPID image parallel to the plane of gantry rotation is called *x*, the axis perpendicular to it, *y*.

Images were acquired using in-house developed software^{66,77} (a similar image acquisition is possible with the commercially available Elekta software). In the acquisition mode used, EPID frames are acquired every 285 ms and stored in a buffer. When the signal of a frame increases above a set threshold (“beam-on” trigger), the image acquisition is started. When the signal of a frame drops below the threshold (“beam-off” trigger), the image acquisition is stopped. The signal of all frames between beam-on and beam-off is averaged; two pre-beam-on and two post-beam-off frames are included in the average to make sure that no signal before the beam-on trigger and after the beam-off trigger is missed, which is especially important for segments having a small number of monitor units. This raw EPID image is processed with flood-field and (dynamic) dark-field images to optimize the image quality for patient position verification. (Note that dynamic dark-field images are continuously acquired every 30 s the EPID is not irradiated.⁶⁶

Therefore, all segments of one field will usually have the same dynamic dark field, whereas segments of different fields will have different ones.) The processed image is then stored, with the number of frames in the image header. Consequently, in a multiple-segment field, one image is obtained per segment.

The EPID images were recorded at a resolution of 512x512 pixels, yielding an effective pixel size of 0.05 cm in the isocentre plane. When we mention in this study the “central pixel value” or “central pixel dose” of the EPID, we refer to the “average pixel value” or the “average pixel dose” of a region of 9x9 pixels at the centre of the EPID.

The distance between the accelerator target and the touch-guard of the EPID was approximately 157 cm. To accurately estimate the effective source-detector distance (SDD), i.e. the distance from the target to the “imaging” layer of the EPID, we placed a thin brass plate with well-known dimensions in the isocentre plane perpendicular to the beam axis. The plate was irradiated with a field larger than the plate, and the plate’s dimensions in the portal image were measured. From this experiment we concluded that for this accelerator the effective SDD of the *a*-Si EPID is 160.0 cm $\pm$ 0.5 cm.

5.2b Calibration of the EPID and the back-projection algorithm

Several steps are necessary to reconstruct the dose in the phantom or patient from the pixel values of the EPID. By multiplying the acquired (frame-averaged) EPID image by the number of frames, the time-integrated EPID signal is obtained (knowledge of the delivered number of monitor units is not necessary). The resulting response of the *a*-Si EPID has been shown to be linear with dose,^{42,43} although a small ghosting effect remains, which is mainly a function of the number of exposed frames.^{77,93}

In this study, no correction for ghosting was made. Note that the flood-field calibration corrects both for variations in pixel sensitivity and non-flatness of the flood field. For dosimetry purposes, the latter is an “over-correction” and needs to be “factored out”. This is achieved by using the so-called sensitivity matrix, which is determined experimentally.³⁷

Our original implementation of the back-projection algorithm has been described in detail elsewhere.^{11,65} Briefly, for *dose reconstruction*, i.e. relating pixel values in the EPID images with absolute dose values in the phantom or patient, we have to account for

- the dose-response of the EPID,
- the lateral scatter within the EPID,
- the scatter from the phantom or patient to the EPID,
- the attenuation of the beam by the phantom or patient,
- the distance from the radiation source to the EPID plane and to the dose-reconstruction plane,
- the scatter within the phantom or patient.

In order to determine the necessary parameters, EPID images of square fields of several sizes are recorded, with and without a polystyrene slab phantom of several thicknesses in the beam. In this study, we used field sizes of 3, 4, 5, 6, 8, 10, 15 and 20 cm. The phantoms were between 11 and 49 cm thick; this thickness range was chosen to encompass more than sufficiently “typical patient thicknesses” for 18 MV photon beams. For the phantom measurements an isocentric set-up [SAD (source-axis distance) set-up] was used.

Ionisation chamber measurements are used as reference data to fit the model parameters for steps (i), (ii), and (vi). In the original algorithm, the reference dose is only determined at a single *point* on the central axis. In this study, the method was extended by using dose *profiles* (instead of point dose measurements alone) as a reference in step (ii) to account more accurately for the lateral scatter within the EPID. This was done as follows.

After the conversion of the EPID pixel values into dose values according to the dose-response relation, the resulting image is called dose image D^{EPID} . The portal dose image PD^{EPID} , which is the dose image *after* correction for lateral scatter in the EPID, is obtained by

$$PD_{ij}^{\text{EPID}} = D_{ij}^{\text{EPID}} \otimes^{-1} K_{ij}^{\text{EPID},1} \otimes K_{ij}^{\text{EPID},2} \quad (5.1)$$

with

$$K_{ij}^{\text{EPID},1} = c_{\text{DR}} \begin{cases} c_1 \cdot \frac{e^{-\mu_1 \cdot r_{ij}}}{r_{ij}^2} & \text{for } r_{ij} \neq 0 \\ 1 & \text{for } r_{ij} = 0 \end{cases} \quad (5.2)$$

$$K_{ij}^{\text{EPID},2} = \frac{c_2}{2\pi\sigma^2} e^{-\frac{r_{ij}^2}{2\sigma^2}}$$

where $K^{\text{EPID},1}$ and $K^{\text{EPID},2}$ are EPID scatter correction kernels. $\otimes$ and $\otimes^{-1}$ denote the convolution and deconvolution operator, respectively.

Every pixel in the EPID image is referred to by its indices i and j . r_{ij} is the distance of a pixel ij from the central axis. c_1 , μ_1 , c_{DR} , c_2 and σ are the kernel parameters. In the original method only the first kernel was applied.⁶⁵ This was sufficient when only point measurements were used as reference input data in the model. We introduced the second kernel to improve the agreement for dose profiles at the plane of the EPID, in order to arrive at a more accurate dose reconstruction - especially in the penumbra region, which is important for IMRT fields.

Convolution and deconvolution operations were performed in the frequency domain using the fast Fourier transform in two-dimensions for computational speed. In order to prevent wrap-around effects, the EPID images were first padded with zeros at all edges. With this procedure it is assumed that the dose at the edges of the imager is negligible. For this reason, profiles for the largest field size (20x20 cm²) were not taken into account.

The dose reconstruction is done per acquired EPID image, i.e. per segment (or per field for non-segmented fields). Note that for every image behind the phantom or patient, one additional image is required without the phantom or patient in the beam to estimate its transmission. In order to summarize the back-projection method and to elucidate the extensions of the method, the details are given in the Appendix.

For all profile measurements a small ionisation chamber (Semiflex 0.125 cm³, PTW-Freiburg, Freiburg, Germany) was used in combination with an electrometer (Keithley Instruments Inc., Ohio, USA).

This ionisation chamber has an inner diameter of approximately 5 mm. For profile measurements at the level of the EPID, the ionisation chamber was located in a cylindrical PMMA mini-phantom (diameter 4 cm, build-up 3 cm for an 18 MV photon beam), which was placed in an empty water-phantom (PTW-Freiburg, Freiburg, Germany) for accurate positioning in two dimensions. However, with the water-phantom the ionisation chamber in the mini-phantom could not be moved to SDDs much larger than 140 cm; the profiles were therefore measured at an SDD of 140 cm and their coordinates were scaled to the actual EPID level of 160 cm (for absolute dose determination, the ionisation chamber in the mini-phantom was set up without the water-phantom at an SDD of 160 cm at the central axis).

Dose profiles in the full-scatter water-phantom [source-surface distance (SSD) = 90 cm] were measured with the ionisation chamber at 10 cm depth. For absolute dosimetry, the Semiflex ionisation chamber was calibrated under reference conditions (at 10 cm depth in a 20 cm thick polystyrene slab phantom with SSD = 90 cm, 200 monitor units, 10x10 cm² field) against a calibrated Farmer-type ionisation chamber (NE 2571 0.6 cm³, NE Technology Ltd, Reading, UK).

An approach to use film dosimetry (see §5.2c) instead of ionisation chamber measurements as a reference method to estimate the parameters for the second EPID kernel, $K^{\text{EPID},2}$, was also studied. Measurements with film should be done under full-scatter conditions and therefore the method presented so far had to be adapted.

First, all parameters for the back-projection algorithm (see Appendix) were estimated using only reference values on the central axis, i.e. only kernel $K^{\text{EPID},1}$ was used at the EPID level. Then, the dose profile in the x-direction of a 10x10 cm² field was taken from a film measurement at 10 cm depth in a 20 cm thick polystyrene slab phantom at an SSD of 90 cm. This profile was used as a reference for the reconstructed EPID mid-plane dose profile for that field in order to adjust the parameters for the second kernel $K^{\text{EPID},2}$; we will call the “film-adjusted” second kernel $K^{\text{EPID},\tilde{2}}$. In principle, this approach should be iterated, i.e. after $K^{\text{EPID},\tilde{2}}$ is fit for the first time, all earlier steps in the parameter estimation for the back-projection procedure should be repeated.

Then $K^{\text{EPID},\tilde{2}}$ should be fit for the second time etc., until all parameters for the back-projection algorithm have converged. However, because introducing $K^{\text{EPID},\tilde{2}}$ is only a small modification, affecting mainly the penumbra region, we omitted the iteration process and used the first fit result for $K^{\text{EPID},\tilde{2}}$.

In this paper, all presented results for EPID dose reconstruction inside a phantom were obtained for an isocentrally positioned polystyrene slab geometry phantom (20 cm thick, SSD = 90 cm). In principle, the dose is reconstructed in the radiological mid-surface of the phantom. Due to the simple geometry and set-up of the phantom, this plane coincides both with the geometrical mid-plane of the phantom and a plane through the isocentre.

5.2c Film dosimetry

For the film measurements EDR2 films (Eastman Kodak Company, Rochester, NY, USA) were used. The film was placed perpendicular to the beam axis at 10 cm depth in the polystyrene slab geometry phantom (20 cm thick, SSD = 90 cm), i.e. the film was located at the plane to which the EPID dose was back-projected.

The films were processed using a Kodak X-OMAT 3000 RA film processor and digitized with a Lumiscan 75 film scanner (Lumisys Inc., now part of Eastman Kodak Company). The digitized images were corrected for background and by linear scaling for geometric distortion in both the film-feeding direction of the scanner and the direction perpendicular to it. The resolution of the scanned images was 0.1 mm in both directions. The images were smoothed using a running average filter with a size of $0.5 \times 0.5 \text{ mm}^2$ for noise reduction and for making the effective film image resolution approximately equal to the EPID pixel size at the isocentre.

The sensitometric curve of the film (pixel values of the film versus absolute dose) was determined by irradiating films with a different number of monitor units (0, 25, 50, 75, 100, 150, 200, 250, 300, 350) for a field size of $10 \times 10 \text{ cm}^2$. The absolute dose at the film position was determined with the calibrated Farmer-type ionisation chamber. The sensitometric curve was fit using a fourth-order polynomial (rms = 1.08), which was then used to convert film pixel values into absolute dose. Good dosimetric results can be obtained with this method.²⁷

5.2d *Pre-treatment verification: EPID versus film*

In order to assess the accuracy of our method for pre-treatment verification, we used a clinical step-and-shoot IMRT plan for a prostate cancer treatment generated with our TPS (Pinnacle V7.4, Philips Medical Systems, Eindhoven, The Netherlands). This plan consisted of five fields, and each field had between six and eight segments; the total number of segments was 37. In order to avoid under-exposure of the EDR2 films, the original number of monitor units for each field was multiplied by a factor 5 to reach optimal dose values.

With the EPID, one image was acquired for each segment with the phantom in the beam and one image for each segment without the phantom in the beam (per-segment image acquisition and storage also allows verification of MLC leaf positions). The back-projection to the mid-plane was also done separately for each segment. The two-dimensional mid-plane dose distributions of all segments of each field were then summed to obtain the total mid-plane dose of that specific field. The film was irradiated simultaneously with the corresponding EPID image acquisition for each field, to prevent (small) differences in MLC leaf (re-)positioning and accelerator output variations. For comparison of the two dose distributions, the field edges of the (summed) EPID mid-plane dose image and of the film dose image were first matched for each field - since both measurements were performed simultaneously, the field edges had to agree. Then, profiles of EPID and film dose distributions were compared and a γ evaluation⁶⁹ was performed in two dimensions.

5.2e *γ evaluation*

The γ index is a useful tool to compare dose distributions that have both low- and high-dose gradient regions.⁶⁹ It combines a dose-difference criterion with a distance-to-agreement criterion. A γ index smaller/larger than unity means that both distributions agree/disagree for that point with respect to the chosen criteria. In this study, the two-dimensional dose distributions measured with EPID and with film were compared. The γ index was calculated for every pixel of the EPID image. We used 2% of the maximum dose as dose-difference criterion and 2 mm as distance-to-agreement criterion.

During the determination of the parameters for the back-projection algorithm (see §5.2b), the same method was used for the comparison of EPID dose profiles with dose profiles measured with an ionisation chamber. The optimization of the parameters of EPID scatter kernel $K^{\text{EPID},2}$, c_2 and σ (see equation 5.2), was done as follows. For each EPID-ionisation chamber profile pair (i.e. for each field size) a “ γ profile” was calculated over the length of the EPID profile and from this γ profile a mean γ index was computed. The average (over all field sizes) of the mean γ indices was minimized in the fit procedure.

An overall shift for all ionisation chamber dose profiles was allowed in the fit to be able to correct for (small) positioning errors of the ionisation chamber/mini-phantom and of the EPID. This shift was found to be smaller than 0.2 cm.

5.3 Results

5.3a Scatter in the EPID

In Figure 5.1, central axis dose values of square fields of different size are shown. These were determined at the position of the EPID without a phantom in the beam, both with an ionisation chamber in a mini-phantom and with the EPID (dose values before and after EPID scatter correction are shown). The ionisation chamber data were used as reference values for the (primary) portal dose. If no scatter correction was performed for the EPID, the EPID curve was steeper than the one for the ionisation chamber. When the reference curve was used to fit the scatter kernel $K^{\text{EPID},1}$, the maximum difference between EPID and ionisation chamber measurements became smaller than 0.2% (see Figure 5.1).

Figure 5.1 Dose values on the central axis of square fields measured with an ionisation chamber in a mini-phantom (open circles) and determined with the EPID (lines) using an 18 MV photon beam. Measurements were performed without a phantom in the beam at an SDD of 160 cm. The dotted line represents the central pixel dose of the EPID before scatter correction, D^{EPID} , normalized to the ionisation chamber measurement of the $10 \times 10 \text{ cm}^2$ field. After deconvolution with the scatter kernel $K^{EPID,1}$ the portal dose at the EPID, PD^{EPID} , is derived (solid line).

As in previous studies, ionisation chamber and EPID data were only fit and compared on the central axis so far. In Figure 5.2a we compare dose *profiles* measured with an ionisation chamber in a mini-phantom with those determined with the EPID after the first scatter correction with the deconvolution kernel $K^{EPID,1}$. As could be expected from the results shown in Figure 5.1, the agreement was very good for the central axis region, but became worse in the penumbra and in the tails of the profiles. Generally, the EPID dose profiles showed a steeper dose fall-off in the penumbra than the ionisation chamber data due to blurring of the measurement by the ionisation chamber.

Figure 5.2 Dose profiles of square fields determined with an ionisation chamber in a mini-phantom (dashed lines) and with the EPID (solid lines) for an SDD of 160 cm using an 18 MV photon beam. Measurements were done without a phantom in the beam. The profiles were taken through the central axis in the x -direction. The distances in the figure refer to the isocentre plane. (a) only the first scatter kernel $K^{\text{EPID},1}$ was applied to the EPID dose image; (b) both scatter kernels $K^{\text{EPID},1}$ and $K^{\text{EPID},2}$ were applied to the EPID dose image. For clarity of representation, only one half of each profile is shown; the profiles are approximately symmetric.

In Figure 5.2b, EPID profiles are again compared with ionisation chamber profiles, but now both EPID scatter kernels, $K^{\text{EPID},1}$ and $K^{\text{EPID},2}$, were applied. Compared to Figure 5.2a, the agreement improved considerably and was very good for both the absolute dose and for the shape of the profiles, although some discrepancy remained in the penumbra regions. The profiles for all field sizes were fit simultaneously and therefore the result is a compromise. The average of the mean γ indices of all profiles decreased from 0.4 to 0.2 by using an additional kernel $K^{\text{EPID},2}$. The kernel parameters were $c_1=4.0 \cdot 10^{-5}$, $\mu_1=0.011 \text{ cm}^{-1}$, $c_{\text{DR}}=1.2$ for $K^{\text{EPID},1}$ and $c_2=1.0$, $\sigma=0.41 \text{ cm}$ for $K^{\text{EPID},2}$. Both EPID scatter kernels are displayed in Figure 5.3. The parameters for the film-adjusted second kernel $K^{\text{EPID},\tilde{2}}$ are presented as part of the next section.

Figure 5.3 Kernels for the correction of the scatter within the EPID: deconvolution kernel $K^{EPID,1}$, convolution kernel $K^{EPID,2}$ and “film-adjusted” convolution kernel, $K^{EPID,2\sim}$. These kernels are radial symmetric; here profiles are shown along a line through the centre of the detector. The kernels were normalized to their maximum value.

5.3b Mid-plane dose

In Figure 5.4, mid-plane dose profiles of square fields of different size measured with an ionisation chamber in a full-scatter water-phantom are shown together with mid-plane dose profiles reconstructed from EPID images. For Figure 5.4a, the EPID reconstruction was done using only one kernel, $K^{EPID,1}$, to correct for the lateral EPID scatter (see Figure 5.2a). For the EPID profiles shown in Figure 5.4b, both EPID scatter kernels, $K^{EPID,1}$ and $K^{EPID,2}$, were applied (see Figure 5.2b). Note that no extra fitting of parameters was performed for the mid-plane dose profiles. After the EPID scatter kernels $K^{EPID,1}$ and $K^{EPID,2}$ were determined, as described in §5.2b, the remaining parameters for the back-projection method were estimated in each case using values on the central axis only (see Appendix). The agreement of the mid-plane dose profiles, especially in the penumbra region, clearly improved by using a better fit at the level of the EPID. The discrepancy on the central axis was smaller than 1%.

Overall, the profiles from reconstructed EPID images of square fields agreed with the ionisation chamber measurements within the 2%/2 mm γ -criteria both in the centre and in the penumbra of the fields; in small parts of the profile tails, the maximum dose difference was approximately 3% of dose maximum.

Figure 5.4 Dose profiles of square fields in an 18 MV photon beam measured with an ionisation chamber at 10 cm depth in a water-phantom at an SSD of 90 cm (dashed lines) and reconstructed in the mid-plane from EPID images behind a 20 cm thick polystyrene slab phantom at the same SSD (solid lines). The profiles were taken through the central axis in the x-direction. The lateral scatter within the EPID was corrected (a) with only the first scatter kernel $K^{EPID,1}$, (b) with both scatter kernels $K^{EPID,1}$ and $K^{EPID,2}$. For clarity of representation, only one half of each profile is shown; the profiles are approximately symmetric.

In Figure 5.5 we compare the mid-plane dose profile of a 10x10 cm² field determined with film and other methods: (1) the ionisation chamber measurement shows a shallower penumbra than the film; (2) when only EPID kernel $K^{EPID,1}$ is used, the reconstructed EPID dose profile has a steeper penumbra than the film, and deviations exist especially in the shoulders and tails of the profiles; (3) when kernel $K^{EPID,\tilde{2}}$ is determined to fit the EPID profile measurement to the film (with parameters $c_2=1.0$, $\sigma=0.38$ cm, displayed in Figure 5.3), the best agreement is obtained: shoulder and tail regions agree very well, however, there is still some discrepancy in (the upper part of) the penumbra region. Note that due to $K^{EPID,\tilde{2}}$ the penumbra for the EPID has broadened.

Figure 5.5 Dose profiles of a $10 \times 10 \text{ cm}^2$ field of an 18 MV photon beam at 10 cm depth in a 20 cm thick polystyrene slab phantom at an SSD of 90 cm. The profiles were taken through the central axis in the x-direction. Film (black solid line) is compared with other methods (other lines): (1) ionisation chamber, measured in a corresponding water-phantom, (2) EPID, reconstructed using only the first EPID kernel $K^{\text{EPID},1}$, (3) EPID, reconstructed using EPID kernels $K^{\text{EPID},1}$ and “film-adjusted” kernel $K^{\text{EPID},2}$. For clarity of representation, the profiles are shifted in the x-direction and only a part of each profile is shown; the profiles are approximately symmetric.

In Figure 5.6 we compare the reconstructed EPID mid-plane dose image of a $10 \times 10 \text{ cm}^2$ field with a film measurement in the homogeneous slab phantom using the γ evaluation method with the 2%/2 mm criteria. The γ histogram shows the distribution of γ indices. Over an area of $14 \times 14 \text{ cm}^2$ (which approximately represents the area within the 3% isodose line), 99.8% of the pixels satisfied the chosen criteria with a maximum γ index of 1.12. When the pixels with dose values smaller than 10% of the maximum dose were disregarded, all points satisfied the chosen γ criteria and the maximum γ index was 0.96.

5.3c Pre-treatment IMRT verification: EPID versus film

A clinical step-and-shoot IMRT plan was delivered to a 20 cm thick polystyrene slab phantom. Figure 5.7 shows the results for one field consisting of eight segments as an example. The mid-plane dose distribution for this field, which was reconstructed from EPID images, is shown in Figure 5.7a and illustrates the typical intensity modulation of the fields.

In Figure 5.7b y -profiles from the reconstructed EPID mid-plane dose image and from the film dose image are shown, demonstrating very good agreement. The γ index distribution for the comparison of EPID and film measurements is presented in Figure 5.7c, and shows agreement within the 2%/2 mm γ criteria. In the area of 14x14 cm² only a few pixels had a γ index larger than unity with a maximum of 1.09. In Figure 5.8, γ histograms for all five IMRT fields are shown. The histograms were calculated for a 14x14 cm² square, which amply encompasses each field. All γ distributions had a mean value below 0.4. Nearly all γ indices were below unity. The percentages of pixels with γ indices above unity were 0.04%, 0.03%, 0.05%, 0.01%, and 0.14% with maximum γ indices of 1.09, 1.15, 1.19, 1.15, and 1.47 for fields A, B, C, D, and E, respectively.

5.4 Discussion

5.4a Scatter in the EPID

In the back-projection algorithm, we need the primary dose component at the level of the EPID. We used an ionisation chamber in a mini-phantom at the EPID position as a reference detector, because in this way only the primary dose component is measured.^{32,124} Within the EPID, mainly lateral x-ray scatter takes place, but also optical photon scatter occurs.¹³¹ For these reasons, the uncorrected EPID has a steeper field size dependent response than the ionisation chamber in a mini-phantom³⁶ (see Figure 5.1). Note that the EPID was normalized to the ionisation chamber measurement of the 10x10 cm² field. This point was chosen arbitrarily and the normalization factor is compensated by the fit parameter c_{DR} of kernel $K^{EPID,1}$ (see equation 5.2). The EPID images are corrected with kernel $K^{EPID,1}$, which describes the overall scatter effect, i.e. both the “dosimetric scatter” (x-rays) and the “glare” (optical photons). After correction of the EPID images with kernel $K^{EPID,1}$, the average pixel dose agreed with the ionisation chamber measurement within 0.2%. However, the EPID dose profiles deviated in the region of the “horns” from the profiles measured with the ionisation chamber in a mini-phantom. Moreover, the EPID profiles had a steeper penumbra (see Figure 5.2a).

Figure 5.6 Two-dimensional γ evaluation for a $10 \times 10 \text{ cm}^2$ field of an 18 MV photon beam comparing the reconstructed EPID mid-plane dose at 10 cm depth in a 20 cm thick polystyrene slab phantom at an SSD of 90 cm to a film measurement at the same depth. The γ criteria are 2% of the maximum dose for the dose difference and 2 mm for the distance-to-agreement. (a) γ index distribution. (b) Histogram of the γ indices over the displayed area of $14 \times 14 \text{ cm}^2$.

Figure 5.7 Comparison of EPID and film dose distributions inside a phantom for pre-treatment verification of an IMRT field consisting of eight segments using an 18 MV photon beam. The 20 cm thick polystyrene slab phantom was located at an SSD of 90 cm. The EPID dose was reconstructed at a depth of 10 cm. The film measurement was done at the same depth simultaneously with the EPID measurement. (a) Two-dimensional dose distribution derived with the EPID, isodose lines are shown. The vertical line in the dose distribution indicates the position of the y-profiles shown in panel (b), EPID as solid line, film as dashed line. (c) Two-dimensional γ distribution of EPID versus film. A dose-difference criterion of 2% of the maximum dose and a distance-to-agreement criterion of 2 mm were used.

Figure 5.8 Histograms of the γ indices of all IMRT fields for an area of $14 \times 14 \text{ cm}^2$ encompassing each field. The histogram of field A corresponds to the γ distribution shown in Figure 5.7c.

These differences may have (at least) the following causes: (i) the (dimensions of the) ionisation chamber, (ii) the size of the mini-phantom, and (iii) the increased low-energy response of the EPID.

- Compared to the EPID, the ionisation chamber has a lower spatial resolution due to volume averaging effects.⁶² Moreover, in principle a gas-filled ionisation chamber itself is not a good instrument to determine the dose in the penumbra, because of the lack of electron equilibrium in this region.^{18,62}
- The mini-phantom is used to measure the primary dose component. On one hand the diameter of the mini-phantom has to be large enough that lateral electron equilibrium is achieved, on the other hand it has to be small (“mini”) with respect to the field size, so that negligible side scatter takes place.^{32,124}
- Amorphous silicon EPIDs are known to have an over-response to low-energy photons.^{51,52,73,76,92,138} The distribution of low-energy photons reaching the EPID is in principle field size and position dependent (when there is a patient or phantom in the beam, it also depends on the exact patient or phantom geometry). Due to the shape of the flattening filter, low-energy photons contribute relatively more to the energy spectrum off-axis. However, this effect was reduced by adding a 2.5 mm extra copper plate to the detector (see §5.2a). This copper plate also reduces the effect of low-energy photons scattered from the phantom or patient on the EPID under our measurement conditions, i.e. at an SDD of 160 cm for the EPID and hence with a large air gap between EPID and phantom or patient.

All effects were combined in one additional *empirical* kernel, $K^{\text{EPID},2}$, at the level of the EPID, and we forced the EPID dose profiles to agree with the data from the ionisation chamber in a mini-phantom. From Figure 5.2a it is obvious that this kernel had to exhibit a blurring effect. For this purpose a Gaussian convolution kernel was chosen as it is a commonly used and well-understood blur function, though other functions might work equally as well. At the level of the EPID the agreement is excellent (see Figure 5.2b). The validity of the assumptions of our dose-reconstruction algorithm (as detailed in the Appendix) was tested after the back-projection into the mid-plane of the phantom (discussed below).

5.4b Mid-plane dose

After accounting for scatter from the phantom to the EPID, for attenuation of the beam by the phantom, and for scatter within the phantom, the mid-plane dose was reconstructed. Profiles of square fields back-projected from EPID images were compared with those measured with an ionisation chamber that was located in a full-scatter water-phantom to measure the total dose (see Figure 5.4). When only kernel $K^{\text{EPID},1}$ was used to correct the EPID scatter, the penumbras of the EPID mid-plane dose profiles were steeper than those of the ionisation chamber (see Figure 5.4a). This is reasonable considering the pixel size of the EPID (0.5 mm in the isocentre plane) and the inner diameter of the Semiflex ionisation chamber (5 mm), limiting the resolution for profile measurements. However, the agreement improved by using a combination of two kernels to correct (mainly for the lateral scatter within) the EPID (see Figure 5.4b). The profiles of square fields down to $3 \times 3 \text{ cm}^2$ were well reproduced with the EPID considering both absolute dose and shape.

We investigated the effect of using film instead of ionisation chamber data on the reconstruction of a mid-plane dose profile (see Figure 5.5). Also with film a steeper penumbra was measured than with the ionisation chamber. Nevertheless, the overall disagreement between ionisation chamber and film is quite small. If one reconstructs the dose from EPID images using only kernel $K^{\text{EPID},1}$, even a steeper penumbra is obtained with the EPID than with film - however, with obvious differences in shoulders and tails. Adjusting the EPID dose reconstruction to the film data with kernel $K^{\text{EPID},\tilde{2}}$ improved the agreement at the cost of the penumbra region. This is the result of the fitting procedure: fewer points contribute in the penumbra region relative to shoulders and tails. The parameters for $K^{\text{EPID},\tilde{2}}$ were very similar to those of kernel $K^{\text{EPID},2}$ determined with the ionisation chamber reference (see Figure 5.3). Therefore, the respective mid-plane profiles are virtually indistinguishable.

Although the pixel size of the EPID is effectively 0.5 mm in the isocentre plane, the reference data for the EPID profiles were measured with a small ionisation chamber (Semiflex) with an inner diameter of the measuring volume of approximately 5 mm. Kernel $K^{\text{EPID},2}$ was based on these reference data, so in practice the resolution of the reconstructed EPID images is approximately 5 mm. We are aware of the limitations of this ionisation chamber to measure dose in steep dose gradient regions such as in the penumbra. Nevertheless, this ionisation chamber was our reference detector of choice for the measurement of the reference profiles, because this ionisation chamber is also used in our hospital to collect the data for the commissioning of our TPS. Therefore, all planned dose distributions will have this “ionisation chamber effect.” In a clinical pre-treatment situation, one wants to verify that the delivered dose agrees with the planned dose, i.e. we aim for consistency between measurements and calculations. Therefore, in our opinion, fitting kernel $K^{\text{EPID},2}$ in the described way is a reasonable approach. If one chooses film as a reference detector, the procedure can be adopted as described in §5.2b.

The *de facto* gold-standard for two-dimensional dosimetry in many institutions is radiographic film. With film the dose inside a phantom can be measured independently. The film was scanned with a resolution of 0.1 mm. The scanned film images were smoothed using a running average filter with a size of $0.5 \times 0.5 \text{ mm}^2$. This procedure removes noise from the film images, which is important since the γ distribution would be underestimated with noise in the dose distribution.⁶⁸ In Figure 5.6, by comparing the dose distributions from EPID and film for a $10 \times 10 \text{ cm}^2$ field, we demonstrated that our back-projection method agreed very well with film dosimetry.

5.4c IMRT verification

As a test for a clinical pre-treatment verification situation, an IMRT plan was delivered to the homogenous slab phantom and the EPID reconstruction was compared to film dosimetry. Again, excellent agreement was obtained for all fields (see Figures 5.7 and 5.8). In our hospital, 3% and 3 mm are currently used as criteria for the γ evaluation for pre-treatment verification of IMRT prostate plans. We like to emphasize that the $10 \times 10 \text{ cm}^2$ field and the five IMRT fields completely satisfied those criteria.

In this paper, however, we have chosen to use 2% and 2 mm to assess the limitations of our back-projection method (one can easily “translate” from 2%/2 mm to 3%/3 mm by scaling the γ index with a factor 1.5). Even for 2%/2 mm criteria, the agreement is excellent, with only a very small percentage of points not satisfying those criteria.

The γ histogram for the 10x10 cm² field shows a slightly worse distribution of γ values than the histograms for the IMRT fields (Figure 5.6b versus Figure 5.8). The main reason is the nature of the γ evaluation method: combining a dose-difference with a distance-to-agreement criterion will usually result in smaller γ indices for a modulated field compared to a more flat field. Note that this effect is intended in the γ evaluation method, because points of two dose distributions are said to agree when at least one of the criteria is satisfied.

It can be argued that the film dose image should be smoothed with an “ionisation chamber like” response kernel. In that approach, one would exclude potential differences between EPID and film dose distributions that are due to resolution/averaging effects. We would like to note that when a broader averaging kernel is used for the film image (e.g. 5x5 mm², making the effective film resolution equal to the diameter of the ionisation chamber), the dose distributions of EPID and film for the 10x10 cm² field and the five IMRT fields agree within the 2%/2 mm γ criteria, but the γ distributions improve only slightly due to the somewhat better agreement in the penumbra region. For the 14x14 cm² square region of interest, more than sufficiently encompassing each field, the percentages of pixels with γ indices above unity and the maximum γ indices (given in brackets) decrease to 0.05% (1.02) for the 10x10 cm² field and 0.02% (1.06), 0% (0.89), 0% (0.92), 0% (0.88), 0.09% (1.23) for the five IMRT fields A, B, C, D and E, respectively (compare to §5.3b and §5.3c). An opposite effect, however, is the noise reduction by the large kernel, which increases the γ values.⁶⁸ This is reflected by the increase of the mean γ index from 0.34 to 0.39 for the 10x10 cm² field and from 0.31 to 0.38 on average for all IMRT fields.

The time required to perform a field-by-field dose verification of a five-field prostate plan with 37 segments as described in this study - either by EPID or by film - is estimated. Note that the original number of monitor units for each field was multiplied by a factor 5 to reach optimal dose values for measurements with the EDR2 films. The delivery of those five fields takes approximately 15 min. Handling, developing and scanning of the films take approximately 15 min, yielding 30 min for the whole film measurement and processing procedure. In case of a more sensitive film, for which the monitor unit scaling would not be necessary, we would need $3 \text{ min} + 15 \text{ min} = 18 \text{ min}$.

In a clinical pre-treatment verification, the dose determined with the EPID is compared with the TPS dose calculation and therefore the scaling of the monitor units can be omitted. However, for EPID dosimetry, the whole plan has to be delivered twice, because the images without the phantom in the beam also have to be acquired. This yields in total $2 \times 3 \text{ min} = 6 \text{ min}$ for the EPID measurements. Moreover, with EPID dosimetry, the result is immediately available. This is particularly advantageous for *in vivo* dosimetry of a series of fractions, where the images without a patient in the beam have to be acquired only once, which implies that if this is done prior to treatment, the result is immediately available after each fraction. Overall, EPID and film dosimetry take approximately 10 min and (at least) 20 min, respectively, for a field-by-field dose verification of the five-field prostate plan.

The back-projection algorithm enables accurate, simple and potentially fast field-by-field IMRT pre-treatment verification *inside* a phantom. Therefore, the EPID can replace film for this purpose. In the future it might become more important to have an alternative method to film dosimetry, as the processing facilities for radiographic films in many hospitals may disappear because of the digitization of radiography.

Due to the excellent agreement between reconstructed and actual dose values in the phantom, our EPID dosimetry method could potentially be extended to *in vivo* verification. For this application, however, the position and geometry of the patient should also be known. The accuracy of two-dimensional dose reconstruction considerably improves when contour information is used for the attenuation correction. This information can usually be obtained from the planning CT scan.⁶⁵

So far no inhomogeneity corrections are implemented in the model. In general, this will lead to lower accuracy in the dose reconstruction for situations where inhomogeneities, such as air cavities, are present, for example in an anthropomorphic phantom or patient. However, under certain circumstances, the dose can be reconstructed accurately (in three dimensions) despite the inhomogeneity, for instance in the case of two (almost) opposing beams for a breast cancer treatment.⁶⁵

As for any quality assurance protocol, it has to be decided in each institute whether EPID dosimetry is necessary and - if yes - for what purpose it should be used. This will determine the required accuracy and hence complexity, of the dose-reconstruction method. In our opinion, EPID dosimetry as described in this work is valuable for finding (even relatively small) errors in the whole “radiotherapy treatment chain” - from planning to actual delivery.

From our own experience, EPID dosimetry is particularly useful when a new TPS is tested, or when a new treatment technique such as IMRT is implemented and standard verification procedures such as point dose measurements with an ionisation chamber or independent monitor unit calculations are inadequate. As described in this study, a homogeneous slab geometry phantom is sufficient for field-by-field verification with high accuracy to check various aspects of the dose calculation and plan delivery.

When the same algorithm is used for the dose reconstruction as for the original planning dose calculation, one has to be aware that the dose delivery verification is not fully independent.⁹¹ Our back-projection method is completely independent of the TPS. The calibration and correction procedures are straightforward. Deriving all calibration and correction parameters for this algorithm is certainly more labour intensive than if only the dose at the level of the EPID is verified.^{28,48,60,73,76,87,95-97,122} However, in the latter case the TPS or an independent algorithm is needed to calculate the dose at the EPID level. Commissioning the TPS or the independent algorithm for that task also involves some effort - if it is possible with a particular TPS at all. Moreover, by reconstructing the dose field-by-field with the back-projection method in two dimensions *inside* the phantom at different distances from the accelerator target, a three-dimensional dose reconstruction is feasible, either field-by-field or for all fields together.

This approach has already been demonstrated for conformal breast cancer treatments.⁶⁵

A pre-requisite for three-dimensional dose reconstruction is that the back-projection also works accurately for other phantom thicknesses. In order to have an indication if this is really the case, the IMRT field analyzed in Figure 5.7 was also delivered to an isocentrically aligned homogeneous slab geometry phantom with a thickness of 30 cm instead of 20 cm. Comparison against a film measured simultaneously, showed again excellent agreement. The γ index distribution was comparable to Figure 5.7c (data not shown). Our current efforts are directed to further develop our modified algorithm for the three-dimensional verification of IMRT fields inside phantoms.

5.5 Conclusions

We have shown that the improved back-projection algorithm can be applied to an a-Si EPID and provides an accurate method to verify the dose of IMRT fields in two dimensions inside a homogeneous slab phantom. The algorithm performs well both in the centre of a field (target volume), in the penumbra(s) and in the tails of the dose distributions. This is important for IMRT treatments with potentially many steep dose gradients and for situations where organs at risk are located close to the target volume. The EPID is an accurate and potentially fast alternative to film for field-by-field pre-treatment verification of IMRT inside a phantom.

Appendix: Description of the back-projection algorithm

This appendix summarizes the details of the back-projection algorithm. Most of the elucidations and equations can also be found in previous papers^{11,13,65} (and references therein). They are given here for a complete description with our extensions for the benefit of the reader. We will start with the description of the back-projection algorithm after the image calibration,^{66,77} and the sensitivity matrix correction;³⁷ these issues will not be discussed. When we mention in this appendix *patient*, this also refers to *phantom*.

5.5a Dose-response function

The dose D_{ij}^{EPID} at a certain pixel ij of the EPID consists of two parts: the portal dose PD_{ij}^{EPID} of radiation reaching the EPID directly and the scatter part Sc_{ij}^{EPID} of (lateral) scatter within the EPID. Therefore:

$$D_{ij}^{\text{EPID}} = PD_{ij}^{\text{EPID}} + Sc_{ij}^{\text{EPID}} \quad (5.1A)$$

In order to measure dose with the EPID, we first have to relate dose values with pixel values, i.e. we have to determine the dose-response function, f_{DR} , of the EPID:

$$PV_{ij}^{\text{EPID}} = f_{\text{DR}}(D_{ij}^{\text{EPID}}) \quad (5.2A)$$

PV_{ij}^{EPID} is the time-integrated pixel value at a certain pixel ij of the EPID after flood-field, (dynamic) dark-field and sensitivity corrections.^{37,66,77}

We assume that the dose-response function f_{DR} is equal for all pixels of the EPID. (In order to keep the notation general, we use f_{DR} , instead of an explicit linear function for *a*-Si EPIDs.)^{42,43}

Note that D^{EPID} (see equation 5.1A) cannot directly be obtained nor can a reference value be measured to determine f_{DR} absolutely. Instead, we use an ionisation chamber in a mini-phantom^{32,124} to measure the dose in air on the central axis (CAX), providing a reference value $PD_{\text{CAX}}^{\text{ref}}$ for the portal dose PD^{EPID} (see equation 5.1A).

This is done for the reference field size (typically 10x10 cm²) at the SDD of the EPID for several numbers of monitor units without a phantom in the beam. Under the same conditions, EPID images are acquired. Therefore, we can determine the *relative* dose-response function, $f_{\text{DR}}^{\text{rel}, 10 \times 10 \text{cm}^2}$, by fitting a function to relate EPID pixel and dose values:

$$\langle PV_{ij}^{\text{EPID}} \rangle_{\text{cROI}} \approx f_{\text{DR}}^{\text{rel}}(PD_{\text{CAX}}^{\text{ref}, 10 \times 10 \text{cm}^2}) \quad (5.3A)$$

The data are determined as a function of the number of monitor units. The brackets $\langle \rangle_{\text{cROI}}$ represent the average over a small central region of interest (cROI) of the EPID at the central axis. Typically, the cROI is defined as a region around the central axis of approximately $0.5 \times 0.5 \text{ cm}^2$ (projected into the isocentre plane).

5.5b Scatter within the EPID

In our algorithm, the scatter component is modelled as the convolution of the portal dose with a scatter kernel $\tilde{K}^{\text{EPID}}$:

$$Sc_{ij}^{\text{EPID}} = PD_{ij}^{\text{EPID}} \otimes \tilde{K}_{ij}^{\text{EPID}} \quad (5.4A)$$

Therefore, with equation 5.1A:

$$\begin{aligned} D_{ij}^{\text{EPID}} &= PD_{ij}^{\text{EPID}} + PD_{ij}^{\text{EPID}} \otimes \tilde{K}_{ij}^{\text{EPID}} = PD_{ij}^{\text{EPID}} \otimes [\delta(r_{ij}) + \tilde{K}_{ij}^{\text{EPID}}] \\ &= PD_{ij}^{\text{EPID}} \otimes K_{ij}^{\text{EPID},1} \end{aligned} \quad (5.5A)$$

with

$$K_{ij}^{\text{EPID},1} = \delta(r_{ij}) + \tilde{K}_{ij}^{\text{EPID}} \quad (5.6A)$$

$\delta(r_{ij})$ represents the δ -function and r_{ij} is the distance of a pixel ij from the central axis. As the (primary) portal dose at the position of the EPID is needed for our back-projection algorithm, we have to deconvolve the dose image with the scatter kernel:

$$PD_{ij}^{\text{EPID}} = D_{ij}^{\text{EPID}} \otimes^{-1} K_{ij}^{\text{EPID},1} \quad (5.7A)$$

We introduce the scatter kernel $K^{\text{EPID},1}$ with the following model:

$$K_{ij}^{\text{EPID},1} = c_{\text{DR}} \begin{cases} c_1 \cdot \frac{e^{-\mu_1 \cdot r_{ij}}}{r_{ij}^2} & \text{for } r_{ij} \neq 0 \\ 1 & \text{for } r_{ij} = 0 \end{cases} \quad (5.8A)$$

c_1 , μ_1 and c_{DR} are the kernel parameters. c_{DR} is a dose-response correction factor for the EPID, which has to be introduced because in equation 5.7A it is assumed that the dose

D^{EPID} has been determined absolutely, which is not the case (see §5.6a). The δ -function from equation 5.6A is implemented here as the term for $r_{ij} = 0$.

To experimentally derive the parameters c_1 , μ_1 and c_{DR} for the EPID scatter kernel $K^{\text{EPID},1}$, square fields of different size are measured with the EPID without a phantom in the beam and averaged over the central region of interest. Then the dose is measured in air on the central axis with an ionisation chamber in a mini-phantom^{32,124} for the same field sizes at the same SDD. These ionisation chamber measurements are then used as reference data for the portal dose PD :

$$\langle PD_{ij}^{\text{EPID}}(fs) \rangle_{\text{cROI}} \approx PD_{\text{CAX}}^{\text{ref}}(fs) \quad (5.9A)$$

The data are determined as a function of field size fs . By adjusting the kernel parameters c_1 , μ_1 and c_{DR} (see equation 5.8A), the portal dose PD^{EPID} (see equation 5.7A) is fit to the reference data, and the kernel $K^{\text{EPID},1}$ is obtained for a specific EPID-photon beam energy combination.

The portal dose image PD^{EPID} can now be calculated for any field size and shape. However, for an accurate two-dimensional dose reconstruction within a patient with our back-projection model, we do need an accurate description of the portal dose image over the whole field, including the penumbra region.

To assess and improve the accuracy in two dimensions, profiles are also measured with the ionisation chamber in the mini-phantom under the same conditions using the scanning mechanism of a water-phantom. As the profiles from EPID portal dose images are steeper in the penumbra region than the ionisation chamber profiles, the portal dose image is convolved with a second kernel $K^{\text{EPID},2}$.

For this purpose, a Gaussian is chosen as a commonly used and well-understood blur function, though other functions may work equally as well:

$$PD_{ij}^{\text{EPID}} = D_{ij}^{\text{EPID}} \otimes^{-1} K_{ij}^{\text{EPID},1} \otimes K_{ij}^{\text{EPID},2} \quad (5.10A)$$

with

$$K_{ij}^{\text{EPID},2} = \frac{c_2}{2\pi\sigma^2} \cdot e^{-\frac{r_{ij}^2}{2\sigma^2}} \quad (5.11A)$$

with the kernel parameters c_2 and σ . For fitting the parameters of $K^{\text{EPID},2}$ a suitable method for comparing EPID with ionisation chamber dose profiles has to be used (e.g. the γ evaluation method).⁶⁹

Instead of profile measurements with the ionisation chamber in a mini-phantom at the EPID level, film measurements under full-scatter conditions (at 10 cm depth in a 20 cm thick polystyrene slab phantom with SSD = 90 cm) can be used as an alternative reference to estimate the parameters for the second EPID kernel $K^{\text{EPID},2}$. The parameters of this “film-adjusted” second EPID kernel, $K^{\text{EPID},\tilde{2}}$, are determined by fitting the reconstructed EPID mid-plane dose profile(s) to the corresponding film measurement(s).

5.5c Scatter from patient to EPID

The portal dose image PD^{EPID} behind a patient includes a component $Sc^{\text{patient} \rightarrow \text{EPID}}$ due to scatter from the patient to the EPID:

$$PD_{ij}^{\text{EPID}} = Pr_{ij}^{\text{EPID}} + Sc_{ij}^{\text{patient} \rightarrow \text{EPID}} \quad (5.12A)$$

Pr^{EPID} is the primary portal dose, which results from radiation coming directly from the radiation head of the accelerator,^{32,124} and is required for our back-projection method. The primary portal dose is obtained by subtracting the scatter contribution from the portal dose:

$$Pr_{ij}^{\text{EPID}} = PD_{ij}^{\text{EPID}} - Sc_{ij}^{\text{patient} \rightarrow \text{EPID}} \quad (5.13A)$$

In order to estimate the scatter contribution, we first calculate the total transmission image T^{total} by dividing the portal dose image with a patient in the beam by the portal dose image without a patient in the beam and use equation 5.12A for the separation into a primary and a scatter contribution:

$$\begin{aligned}
 T_{ij}^{\text{total}} &= \frac{PD_{ij}^{\text{EPID, with patient}}}{PD_{ij}^{\text{EPID, without patient}}} = \frac{Pr_{ij}^{\text{EPID, with patient}} + Sc_{ij}^{\text{patient} \rightarrow \text{EPID}}}{PD_{ij}^{\text{EPID, without patient}}} \\
 &= T_{ij}^{\text{primary}} + \frac{Sc_{ij}^{\text{patient} \rightarrow \text{EPID}}}{PD_{ij}^{\text{EPID, without patient}}}
 \end{aligned} \tag{5.14A}$$

T_{ij}^{primary} is the “primary transmission”, i.e. the transmission, when no scatter from the patient would reach the EPID, and is given by:

$$T_{ij}^{\text{primary}} = T_{ij}^{\text{total}} - \frac{Sc_{ij}^{\text{patient} \rightarrow \text{EPID}}}{PD_{ij}^{\text{EPID, without patient}}} \tag{5.15A}$$

Note, that T^{total} depends on field size, but T^{primary} has to be field size independent by definition. This fact is used to assess the scatter contribution $Sc^{\text{patient} \rightarrow \text{EPID}}$ as follows. The total transmission T^{total} is experimentally determined as a function of field size fs , by irradiating a phantom of “reference thickness” (typically 20 cm) with square fields of different size. For very small field sizes, there is negligible scatter from the phantom to the EPID. Thus, in the limit of zero field size, the total transmission T^{total} equals the primary transmission T^{primary} . The values of the total transmission T^{total} averaged over the cROI, $\langle T_{ij}^{\text{total}} \rangle_{\text{cROI}}$, are plotted as a function of field area, fs^2 , and extrapolated to zero field size. By adjusting $Sc^{\text{patient} \rightarrow \text{EPID}}$ in equation 5.15 using a model explained below, T^{primary} at the cROI is fit for all field sizes to the zero-field-size limit of T^{total} at the cROI:

$$\langle T_{ij}^{\text{primary}}(fs^2) \rangle_{\text{cROI}} \approx \lim_{fs \rightarrow 0} \left[\langle T_{ij}^{\text{total}}(fs^2) \rangle_{\text{cROI}} \right] \tag{5.16A}$$

i.e. the right side of this equation is a constant and the left side has to be made equal to that constant for all field sizes to achieve the field size independence of T^{primary} . The field *area* is used as the independent variable instead of the field *size*, because the scatter-to-primary ratio for the scatter from the phantom to the EPID, and therefore also T^{total} (see equation 5.14A), increases for small field sizes and for large air gaps approximately linearly with the field *area*.¹¹⁹

For our data, a second order polynomial appeared sufficient for a reasonable fit of $\langle T_{ij}^{\text{total}} \rangle_{\text{cROI}}$ and the extrapolation to zero field size.

The scatter from the patient to the EPID is modelled as a convolution of the portal dose image with a scatter kernel $K^{\text{patient} \rightarrow \text{EPID}}$:

$$Sc_{ij}^{\text{patient} \rightarrow \text{EPID}} = PD_{ij}^{\text{EPID, with patient}} \otimes K_{ij}^{\text{patient} \rightarrow \text{EPID}} \quad (5.17A)$$

In principle, the primary portal dose P_r^{EPID} should be used here instead of the portal dose $PD^{\text{EPID, with patient}}$, suggesting an iterative approach.^{46,114} However, for relatively large air gaps and a copper plate filtering (scattered) low-energy photons (as in our set-up), the scatter contribution is small and the portal dose itself can be used in good approximation. The parts of the image without the patient in the beam are excluded from the scatter computation. As kernel we choose a constant:

$$K_{ij}^{\text{patient} \rightarrow \text{EPID}} = c^{\text{patient} \rightarrow \text{EPID}} \quad (5.18A)$$

Therefore, with equation 5.17A:

$$Sc_{ij}^{\text{patient} \rightarrow \text{EPID}} = \left(\sum_{i,j} PD_{ij}^{\text{EPID, with patient}} \right) \cdot c^{\text{patient} \rightarrow \text{EPID}} \quad (5.19A)$$

The summation runs over all pixels of the imager (except for the parts without the patient in the beam). Thus, in our model the scatter component $Sc^{\text{patient} \rightarrow \text{EPID}}$ is a *constant* offset over the whole EPID image. This homogenous scatter component is proportional to the portal dose $PD^{\text{EPID, with patient}}$ integrated over the whole EPID image, and therefore approximately proportional to both the portal dose on the central axis and the field area. There is no dependence of the scatter on the thickness of the patient in our model.

In the analytical scatter model of Swindell and Evans,¹¹⁹ the scatter-to-primary ratio is for vanishingly small scattering volumes proportional to the irradiated volume, i.e. to the field area and the thickness of the patient or phantom. In our model, the dependence on field area is described correctly, but this is not the case for the dependence on thickness.

In order to obtain the parameter $c^{\text{patient} \rightarrow \text{EPID}}$ for the scatter kernel $K^{\text{patient} \rightarrow \text{EPID}}$, the required data (T^{total} for several field sizes) are measured at the so-called *reference* thickness, for which a representative thickness of a clinical situation for the considered beam energy is chosen. This is certainly an approximation.

However, under our conditions with small scatter contribution [due to relatively large air gaps and a copper plate filtering (scattered) low-energy photons], we found that the errors made here do not hamper an accurate back-projection into the mid-plane (see also §5.6e).

Other models for the kernel, such as a Gaussian or a Lorentzian, have also been tested and can improve the fit slightly. More rigorous treatments of scatter from a patient or a phantom to the EPID, especially for smaller air gaps, are described in the literature.^{46,74,75,112-114,119}

5.5d Scatter within the patient

The total (reconstructed) dose D^{mid} in the patient consists of two parts: the primary dose Pr^{mid} and the scattered dose Sc^{mid} within the patient:

$$D_{ij}^{\text{mid}} = Pr_{ij}^{\text{mid}} + Sc_{ij}^{\text{mid}} \quad (5.20A)$$

We choose to reconstruct the dose in the radiological *mid*-surface, which is defined as the surface connecting those points in the patient, where the transmission of the patient above and below that surface is equal for rays emerging from the radiation source in the direction of the portal imager. To calculate the primary dose in the radiological mid-surface of the patient, $Pr^{\text{mid, radiol}}$, the inverse square law *ISQL* and an attenuation correction *AC* are used. For the attenuation we assume an exponential function $\exp(-\mu_{\text{AC}} \cdot t^{\text{radiol}})$ for the primary transmission T^{primary} [see equations 5.14A and 5.15A), where μ_{AC} represents the linear attenuation coefficient of water for a specific beam energy and t^{radiol} the radiological path length of a ray through the patient. In principle, a model of the beam's energy spectrum should be used for μ_{AC} . However, with the above assumption, an effective attenuation correction can directly be calculated from the experimental primary transmission T^{primary} . The following equation is valid for the reconstruction of the primary dose in the radiological mid-surface:

$$\begin{aligned}
Pr_{ij}^{\text{mid, radiol}} &= Pr_{ij}^{\text{EPID}} \cdot ISQL \cdot AC = Pr_{ij}^{\text{EPID}} \cdot \left(\frac{d_{\text{reconst}}}{d_{\text{EPID}}} \right)^{-2} \cdot \frac{1}{e^{-\mu_{AC} \cdot t_{ij}^{\text{radiol}} / 2}} \\
&= Pr_{ij}^{\text{EPID}} \cdot \left(\frac{d_{\text{reconst}}}{d_{\text{EPID}}} \right)^{-2} \cdot \frac{1}{\sqrt{T_{ij}^{\text{primary}}}}
\end{aligned} \tag{5.21A}$$

where d_{EPID} is the distance of the EPID (“imaging” layer) from the accelerator target and equals 160 cm for our EPID. d_{reconst} is the distance of the reconstruction surface from the accelerator target. In our study, with a homogeneous slab geometry phantom aligned symmetrically around the isocentre plane, the surface of reconstruction is always the isocentre plane, hence the term “mid-plane,” at 100 cm from the target, i.e. $d_{\text{reconst}} = 100$ cm. t_{ij}^{radiol} is the radiological thickness of the patient determined at pixel ij .

For dose reconstruction in an arbitrary *geometrical* plane parallel to the EPID, the attenuation has to be corrected for the radiological path length $l_{ij}^{\text{reconst} \rightarrow \text{exit, radiol}}$ along a ray through the patient from the reconstruction plane down to the exit surface, determined at pixel ij . The primary transmission for this path is then given by $(T_{ij}^{\text{primary}})^{l_{ij}^{\text{reconst} \rightarrow \text{exit, radiol}} / t_{ij}^{\text{radiol}}}$. The ratio of the radiological pathlengths in the exponent is approximated by the ratio of the geometrical pathlengths $l_{ij}^{\text{reconst} \rightarrow \text{exit, geom}} / l_{ij}^{\text{reconst} \rightarrow \text{exit, geom}}$, by using three-dimensional contour information from the patient, e.g. from the CT scan;⁶⁵ note that for a homogeneous phantom, those ratios are equal. Therefore, for dose reconstruction in an arbitrary geometrical plane:

$$Pr_{ij}^{\text{mid, geom}} = Pr_{ij}^{\text{EPID}} \cdot \left(\frac{d_{\text{reconst}}}{d_{\text{EPID}}} \right)^{-2} \cdot \frac{1}{(T_{ij}^{\text{primary}})^{l_{ij}^{\text{reconst} \rightarrow \text{exit, geom}} / t_{ij}^{\text{reconst} \rightarrow \text{exit, geom}}}} \tag{5.22A}$$

The calculation of the scatter component Sc^{mid} within the reconstruction plane is in our model separated into a thickness and a field size dependence. First, the primary mid-plane dose is weighted with the SPR^{ref} , the scatter-to-primary ratio determined under reference conditions (see below).

[Note that in a previous paper⁶⁵, the term normalized scatter-to-primary ratio, $NSPR$, was used.] The SPR^{ref} is a function of the primary transmission T^{primary} , and accounts for the amount of scatter which depends on the (radiological) thickness of the patient. Then, the result is convolved with the scatter kernel K^{mid} , accounting for the field-size dependence of the scattered dose distribution in the reconstruction plane:

$$Sc_{ij}^{\text{mid}} = [Pr_{ij}^{\text{mid}} \cdot SPR^{\text{ref}}(T_{ij}^{\text{primary}})] \otimes K_{ij}^{\text{mid}} \quad (5.23A)$$

In order to parameterize SPR^{ref} , it is first obtained experimentally and then fit as a function of T^{primary} . The dose is measured with an ionisation chamber at the isocentre in isocentrically aligned slab phantoms of several thicknesses at the reference field size (typically 10x10 cm²); the ionisation chamber measurements are used as the reference values for the total dose D on the central axis. EPID measurements are performed with and without the phantom and are used to calculate the primary transmission, $\langle T_{ij}^{\text{primary}} \rangle_{\text{cROI}}$ (see equation 5.15A) and the primary mid-surface/mid-plane dose, (see equations 5.21A and 5.22A), in the central region of interest. The experimental scatter-to-primary ratio $SPR_{\text{exp}}^{\text{ref}}$ is then calculated for every phantom thickness as:

$$SPR_{\text{exp}}^{\text{ref}} = \frac{D_{\text{CAX}}^{\text{ref}} - \langle Pr_{ij}^{\text{mid}} \rangle_{\text{cROI}}}{\langle Pr_{ij}^{\text{mid}} \rangle_{\text{cROI}}} \quad (5.24A)$$

and then fit to a polynomial function, SPR^{ref} , of the primary transmission $\langle T_{ij}^{\text{primary}} \rangle_{\text{cROI}}$:

$$SPR^{\text{ref}}(\langle T_{ij}^{\text{primary}} \rangle_{\text{cROI}}) \approx SPR_{\text{exp}}^{\text{ref}}(\langle T_{ij}^{\text{primary}} \rangle_{\text{cROI}}) \quad (5.25A)$$

For our data a third order polynomial was used. Thus, from the primary transmission at every pixel ij , the scatter-to-primary ratio can be calculated for every pixel ij by using the “ SPR^{ref} polynomial.” In principle, the scatter-to-primary ratio depends on depth. In our current model, however, SPR^{ref} only depends on the primary transmission T^{primary} and is therefore independent of depth (see §5.6e).

As a model for the scatter kernel K^{mid} (see equation 5.23A) we use:

$$K_{ij}^{\text{mid}} = c_{\text{mid}} \cdot \frac{e^{-\mu_{\text{mid}} r_{ij}}}{r_{ij}^2 + \Delta^2} \quad (5.26A)$$

c_{mid} , μ_{mid} and Δ are the parameters of kernel K^{mid} . The parameter Δ was introduced to prevent division by zero for $r_{ij} = 0$; this a slight modification from our previous work.⁶⁵ c_{mid} is a scaling factor. μ_{mid} is the linear attenuation coefficient for water, which depends on energy (and therefore indirectly on patient thickness and off-axis distance).

Because there is a whole distribution of photon energies within the patient, both from the primary and the scattered radiation, μ_{mid} will be the effective attenuation coefficient for the photon energy spectrum in the mid-surface or mid-plane of the patient. Instead of using a model for the beam's energy spectrum, we decided to treat μ_{mid} as a free parameter in our fit procedure. Beam hardening is not directly taken into account.

The mid-plane scatter kernel K^{mid} is obtained by measuring the dose with an ionisation chamber in a phantom and changing the field size fs for the reference phantom thickness (typically 20 cm). EPID measurements are performed for the same field sizes with and without the phantom in the beam. By adjusting the kernel parameters c_{mid} , μ_{mid} and Δ for kernel K^{mid} , the EPID mid-plane dose $\langle D_{ij}^{\text{mid}} \rangle_{\text{cROI}}$ is fit to the ionisation chamber measurements $D_{\text{CAX}}^{\text{ref}}$ on the central axis in the phantom:

$$\langle D_{ij}^{\text{mid}}(fs) \rangle_{\text{cROI}} \approx D_{\text{CAX}}^{\text{ref}}(fs) \quad (5.27A)$$

Summary

The cross-calibration of the EPID is performed (i) against an ionisation chamber in a mini-phantom at the level of the EPID for several field sizes and (ii) against an ionisation chamber in a slab phantom for several field sizes at the reference thickness and for several thicknesses at the reference field size. The (reference) field sizes and phantom thicknesses were chosen to be representative of clinical situations. The effects of field size and patient/phantom transmission are separated in the model. Errors/shortcomings in the determination of the parameters in an earlier step can be compensated later in the procedure. For example, errors in the field size dependence of the scatter from the phantom to the EPID, might be compensated during the cross-calibration of the field size dependence of the total mid-plane dose.

The model is “as physical as possible.” However, it is primarily designed to describe the measured data for the clinically relevant range of field sizes and thicknesses and to accurately predict them. In the end, the accuracy in the phantom after the dose reconstruction is most relevant. For this study, the agreement on the central axis in the phantom between EPID dose reconstruction and reference measurements was better than 1% for all data used to estimate the parameters.

The dose reconstruction for one segment of a treatment field can be summarized as follows:

- take an EPID image with and without a patient and convert the pixel values to relative dose values with the inverse relative dose-response function,
- calculate the portal dose PD_{ij}^{EPID} (equation 5.10A) for both images,
- calculate the primary portal dose (equations 5.13A and 5.19A),
- calculate the primary transmission (equation 5.15A),
- calculate the primary dose in the radiological mid-surface, (equation 5.21A) or in the geometrical mid-plane (equation 5.22A),

- calculate the scatter-to-primary ratio for the scatter within the patient from the primary transmission and the SPRref polynomial,
- calculate the scattered mid-plane dose (equation 5.23)
- calculate the total mid-plane dose (equation 5.20A).

By reconstructing the dose in different planes from the target, i.e. by changing d_{reconst} and f^{reconst} (see equation 5.22A), for each gantry angle and finally adding them up, a three-dimensional dose distribution can be obtained for simple fields.⁶⁵ It should further be noted, that currently no inhomogeneity correction is implemented in our back-projection algorithm. These issues are part of future investigations.

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6

Clinical experience with EPID dosimetry for prostate IMRT pre-treatment verification

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Abstract

The aim of this study was to demonstrate how dosimetry with an amorphous silicon electronic portal imaging device (*a*-Si EPID) replaced film and ionisation chamber measurements for routine pre-treatment dosimetry in our clinic. Furthermore, we described how EPID dosimetry was used to solve a clinical problem.

IMRT prostate plans were delivered to a homogeneous slab phantom. EPID transit images were acquired for each segment. A previously developed in-house back-projection algorithm was used to reconstruct the dose distribution in the phantom mid-plane (intersecting the isocentre). Segment dose images were summed to obtain an EPID mid-plane dose image for each field. Fields were compared using profiles and in 2D with the γ evaluation (criteria: 3%/3 mm). To quantify results, the average γ (γ_{avg}), maximum γ (γ_{max}) and the percentage of points with $\gamma < 1$ ($P_{\gamma<1}$) were calculated within the 20% isodose line of each field.

For 10 patient plans, all fields were measured with EPID and film at gantry set to 0°. The film was located in the phantom coronal mid-plane (10 cm depth) and compared with the backprojected EPID mid-plane absolute dose. EPID and film measurements agreed well for all 50 fields, with $\langle \gamma_{avg} \rangle = 0.16$, $\langle \gamma_{max} \rangle = 1.00$ and $\langle P_{\gamma<1} \rangle = 100\%$. Based on these results, film measurements were discontinued for verification of prostate IMRT plans.

For 20 patient plans, the dose distribution was re-calculated with the phantom CT scan and delivered to the phantom with the original gantry angles. The planned isocentre dose ($plan_{iso}$) was verified with the EPID ($EPID_{iso}$) and an ionisation chamber (IC_{iso}). The average ratio, $\langle EPID_{iso}/IC_{iso} \rangle$, was 1.00 ± 0.01 (1 SD). Both measurements were systematically lower than planned, with $\langle EPID_{iso}/plan_{iso} \rangle$ and $\langle IC_{iso}/plan_{iso} \rangle = 0.99 \pm 0.01$ (1 SD).

EPID mid-plane dose images for each field were also compared with the corresponding plane derived from the 3D dose grid calculated with the phantom CT scan. Comparisons of 100 fields yielded $\langle\gamma_{\text{avg}}\rangle = 0.39$, $\gamma_{\text{max}} = 2.52$ and $\langle P_{\gamma < 1} \rangle = 98.7\%$. Seven plans revealed under-dosage in individual fields ranging from 5% to 16%, occurring at small regions of over-lapping segments or along the junction of abutting segments (tongue-and-groove side). Test fields were designed to simulate errors and gave similar results. The agreement was improved after adjusting an incorrectly set tongue-and-groove width parameter in the treatment planning system (TPS), reducing $\langle\gamma_{\text{max}}\rangle$ from 2.19 to 0.80 for the test field.

Mid-plane dose distributions determined with the EPID were consistent with film measurements in a slab phantom for all IMRT fields. Isocentre doses of the total plan measured with an EPID and an ionisation chamber also agreed. The EPID can therefore replace these dosimetry devices for field-by-field and isocentre IMRT pre-treatment verification. Systematic errors were detected using EPID dosimetry, resulting in the adjustment of a TPS parameter and alteration of 2 clinical patient plans. One set of EPID measurements (i.e. one open and transit image acquired for each segment of the plan) is sufficient to check each IMRT plan field-by-field and at the isocentre, making it a useful, efficient and accurate dosimetric tool.

6.1 Introduction

The introduction of advanced irradiation techniques into a radiotherapy clinic requires extensive dose verification measures that go beyond current routine clinical practice. Amorphous silicon electronic portal imaging devices (a-Si EPIDs) were originally designed for patient set-up verification, however their use has been extended to dose verification over the past few years, since portal images also contain dosimetric information.

Several studies of dose-response characteristics have shown that a-Si EPIDs are suitable for dose verification.^{33,42,43,73,77,131} These studies have shown that the pixel signal is approximately linear with dose and can be converted to absolute dose by measuring the response over a wide range of parameters. In addition, the response of the a-Si EPID is stable within $\pm 0.5\%$ (1 SD) over long periods, up to at least 2 years, provided there are no electronic failures.⁶⁶

Verification of intensity modulated radiotherapy (IMRT) dose distributions requires dosimetry tools in at least 2D (in the absence of readily available 3D dosimetry), and has traditionally relied on the use of radiographic film.^{22,23,26,39,56,72,141} The advantages of using an EPID over film for IMRT dose verification are well known. EPID measurements are simple to perform with minimum set-up requirements, they can be repeated easily and digital data is obtained immediately, unlike films, which require additional time for developing and digitising. Once an EPID is calibrated for a certain linac and energy, EPID images can be immediately converted to absolute dose images, whereas each film batch requires a new calibration, involving additional measurements.⁴⁰ Also recording, storage and archiving of QA measurements becomes more efficient when images are acquired digitally. As more medical departments strive to digitise medical data,¹⁰³ film and associated equipment are becoming more scarce and alternative devices will be required for radiotherapy dosimetry. Alternative 2D detector dosimetry devices have also been proposed based on ionisation chamber or diode arrays.^{57,63,134} While good agreement has been reported at specific points or along profiles, they have limited resolution (0.7 to 1.4 cm grid spacing) and require additional set-up time. The EPID has the advantage of higher resolution and is already fixed to the linac without the need for additional hardware.

As many radiotherapy departments have invested in portal imagers for set-up verification in recent years (and will continue to do so in the coming years), it is attractive if the same device can be used for accurate, absolute dose verification as well.

There are a number of ways to use EPIDs to verify a plan prior to treatment. Some studies have used the detector placed inside a phantom.^{33,84} Other studies converted EPID images to dose images at the detector plane, in some cases behind a phantom to measure the transmission image.^{24,42,48,60,73,87,95,129} Alternatively, EPID images were used to reconstruct the dose in a plane within the patient or phantom^{11,45,65,94,115,131,132}. Of these studies, some have explored the possibility of using an *a*-Si EPID for verification of IMRT fields.^{24,42,94,115,131,132}

The back-projection method (as described in previous studies^{11,132}) forms the basis of the EPID dosimetry program in our department. Dose distributions measured at the level of the EPID are reconstructed in a plane intersecting the isocentre, i.e. perpendicular to the beam axis and parallel with the EPID detector plane. The phantom is positioned isocentrically so this plane intersects the middle of the phantom for all gantry angles. The reason for choosing this method is that the reconstructed dose distribution is in the patient treatment dose range, allowing direct comparison with either the corresponding planned dose distribution or that measured with other dosimetry devices. The quality assurance (QA) system, therefore, is completely independent of the treatment planning system (TPS). Additional motivation for back-projecting to a plane is that it allows for verification of the dose *in vivo*, i.e. determining the dose inside the patient during treatment, and in 3D by back-projecting the dose to multiple planes. *In vivo* and/or 3D dose verification are not possible by directly comparing dose measurements at the level of the EPID. The algorithm was first developed for the liquid-filled ionisation chamber EPID and applied to mid-plane verification of dose to a phantom in 2D¹¹ and 3D⁶⁵, and to patient plans post-treatment.¹⁴ More recently it has been improved and adapted for use with the *a*-Si EPID. Wendling *et al.* demonstrated that this method can be used to verify IMRT plans pre-treatment.¹³² This was a proof of principle study and showed very good agreement for test fields between EPID and film 2D dose distributions, within 2%/2 mm, measured in the mid-plane of a slab phantom.

In February 2005, both a new TPS and linac were commissioned for clinical use, and a new inverse planning technique for prostate cancer treatment was clinically implemented in our department. This increased the clinic's demand for a functional, accurate and efficient means to verify the dose delivered. Following the results of previous studies proving the efficacy of our method, the aim of this study was to demonstrate how EPID dosimetry replaced film and ionisation chamber measurements for routine pre-treatment dosimetry in the clinic, and how the EPID was used to solve a clinical problem.

6.2 Methods & Materials

6.2a Patient plans

IMRT plans were analysed for the first 20 patients calculated with a newly commissioned TPS in our clinic (Pinnacle 7.4f, Philips Medical Systems, Eindhoven, The Netherlands). All patients were treated for prostate cancer, planned with a five field step-and-shoot IMRT technique, with 20 to 40 segments per plan. The 5 beam angles were 0°, 40°, 100°, 260° and 320°. For one plan, a gantry angle of 105° was used instead of 100°, to optimise the PTV dose and better spare the rectum. The dose grid was calculated with a resolution of 0.2x0.2x0.2 cm³. The dose prescribed to the isocentre was 78 Gy, given in 39 fractions. Treatments were delivered with 18 MV photon beams with an Elekta SLi-20 accelerator (Elekta, Crawley, UK).

6.2b EPID dosimetry

All EPID images were acquired with an *a*-Si flat panel imager (iViewGT, Elekta, Crawley, UK). It has a 41 × 41 cm² detection area (1024 × 1024 pixels), a touch guard, a 1 mm Cu build-up layer, a phosphor screen and a hydrogenated *a*-Si:H photodiode array. Images were processed at a lower resolution of 256 × 256 pixels. A 2.5 mm Cu plate was added to provide additional build-up material.⁷⁷ Image acquisition and processing procedures have been reported in previous publications.^{66,77,132}

EPID transit images were converted to a reconstructed 2D dose distribution via an in-house back-projection algorithm developed previously.^{11,132} These publications extensively describe the calibration procedure that converts EPID pixel values to absolute dose (in Gy) at the reconstruction plane for each beam. In summary, the dose distribution is reconstructed in the mid-plane of the attenuating medium (i.e. the patient or the phantom, only the phantom is used in this study).

The mid-plane is defined as the plane intersecting the isocentre, perpendicular to the beam axis and rotates with the gantry angle. Pixel values are converted to a mid-plane absolute dose image using a sensitivity matrix, scatter correction kernels (determined from ionisation chamber measurements), an inverse square law factor and the transmission of the phantom. The sensitivity matrix accounts for the relative variation in response between pixels over the entire panel. The scatter correction kernels are designed to account for 3 types of scatter conditions: the scatter within the EPID, scatter from a phantom (homogeneous, slab geometry, 30x30x20 cm³) to the EPID and scatter within the phantom. Contour information from the phantom CT scan is also used to correct for attenuation by the phantom between the mid-plane and the exit-plane. For IMRT fields, the reconstructed dose image is calculated separately for each segment and then summed to give the reconstructed 2D dose distribution for each field, otherwise referred to as the EPID mid-plane dose image.

6.2c Dose comparison methods

Dose distributions were evaluated using software developed in-house. This software enables the user to compare dose values obtained with EPID, film and the plan. Dose differences can be evaluated for points and profiles, as well as 2D distributions, using difference images and the γ evaluation method.⁶⁹ For 2D evaluations, γ criteria of 3% global dose difference, relative to the maximum field dose, and 3 mm distance-to-agreement were chosen. These criteria were based on results of test cases performed in pre-clinical studies, which used 2%/2 mm¹³², and expanded to 3%/3 mm for clinical use. More relaxed criteria were chosen for the clinic at the request of medical physicists and radiation oncologists in our department, and to include uncertainties encountered in the chain of radiotherapy dose verification.

These uncertainties include TPS calculation accuracy, reproducibility of measurements and resolution of dosimetry devices used for both measurement and calibration of the EPID and TPS.

A region of interest was defined for the evaluation of each field, bounded by the 20% isodose line of the planned dose distribution (or in the case of film vs. EPID, of the EPID dose image). The 20% isodose limit was chosen as it defines the lower edge of the penumbra. Differences in lower dose regions outside the field tend to be very small relative to the maximum dose, which would lower the average γ value and may conceal important errors within the field.

A combination of three scalar parameters was introduced to quantify and summarise γ results within the region of interest; namely the average γ value of the image (γ_{avg}),^{25,117} maximum γ (γ_{max}) and percentage of points with $\gamma < 1$ ($P_{\gamma < 1}$). Plans were considered acceptable if, for each field, $\gamma_{\text{avg}} < 0.67$, $\gamma_{\text{max}} < 2.0$ and $P_{\gamma < 1} > 95\%$. These criteria were arrived at following discussions with clinical physicists having experience with 2D evaluations and the gamma index. They wanted to allow individual fields to have average errors of the order of 2%/2 mm, maximum errors of 6%/6 mm and to permit 5% of the field to exceed 3%/3 mm before an alert was raised.

If different γ criteria were chosen, these values would be also be re-scaled accordingly. If at least one field from a plan exceeded one of these conditions, the plan was investigated further. The combination of these three parameters also provides an informative and detailed summary of the overall agreement between measured and calculated 2D dose distributions for a large number of fields. The value of these parameters may be illustrated by the following example. If 99% of points of a field are within 3% and 3 mm, i.e. $P_{\gamma < 1} = 99\%$, and the γ_{max} value is 1.1, then a γ_{avg} value of 0.33 (corresponding to average error of the order $\pm 1\%/1$ mm) would indicate a much better overall agreement than if the γ_{avg} value was 0.83 (average error of the order $\pm 2.5\%/2.5$ mm). Even if the maximum and percentage of points are considered acceptable, we would not want to accept fields with average dose and distance-to-agreement differences greater than $\pm 2\%/2$ mm ($\gamma > 0.67$).

6.2d Verification of EPID dose images with film

For 10 patient plans, 2D dose distributions were compared field-by-field with EPID and EDR2 film (Eastman Kodak Company, Rochester, NY, USA). Films were placed in a 20 cm thick phantom and positioned isocentrically, with a source-surface distance (SSD) of 90 cm. The gantry angle was set to 0°. The measurement plane corresponded to the EPID dose reconstruction plane. The number of monitor units (MU) was multiplied by 4 to bring the dose of separate fields into the measurable range of the film. EPID images and film measurements were acquired simultaneously for each field.

Films were developed using a Kodak X-OMAT 3000 RA film processor and scanned with a Lumiscan 75 film scanner (Lumisys, Sunnyvale, CA, USA). Films were scanned with a resolution of $0.01 \times 0.01 \text{ cm}^2$. The digitised film images were smoothed using a running average filter with a size of $0.5 \times 0.5 \text{ cm}^2$. This was done to both reduce noise and yield an effective film image resolution approximately equal to the size of the ionisation chamber. EPID images were analysed at a 256×256 pixel resolution, yielding a resolution of $0.1 \times 0.1 \text{ cm}^2$ (at the isocentre plane). Further details regarding the film calibration procedure have been described in a previous article.¹³² EPID and film measurements were compared using clinical γ criteria of 3%/3 mm, as well as using the more stringent criteria of 2%/2 mm.

In some cases, where large discrepancies were found, the total plan was also measured with film. A single film was placed in the phantom, positioned as for the individual field measurements and irradiated with the patient plan using the original beam parameters (i.e. same gantry angles and number of monitor units as for the patient treatment). The film was scanned and calibrated as described above and compared with the corresponding coronal slice (intersecting the isocentre) from the planned dose distribution, calculated by the TPS using the phantom CT scan.

6.2e *Verification of the planned dose: isocentre*

Plans for 20 prostate cancer patients were verified at the isocentre (plan_{iso}) with ionisation chamber (IC_{iso}) and EPID measurements (EPID_{iso}). The ionisation chamber (Semiflex 0.125 cm³, PTW-Freiburg, Freiburg, Germany) was used in combination with an electrometer (Keithley Instruments Inc, Ohio, USA). The calibration factor was determined by comparing readings with a calibrated Farmer ionisation chamber (NE 2571 0.6 cm³, NE Technology Ltd, Reading, UK) irradiated under the same conditions. EPID_{iso} values were obtained by summing the isocentre values of the reconstructed EPID dose images of all fields for each plan.

6.2f *Verification of the planned dose: field-by-field*

Plans for 20 prostate cancer patients were verified in 2D with the EPID field-by-field. This was done by acquiring an EPID image for each IMRT segment, with and without the phantom, at the original gantry angles. The same phantom set-up was used as for film measurements. The phantom remained on the treatment couch in the same position for all fields, so the transmission of the phantom varied with gantry angle.

A mid-plane dose image was reconstructed for each segment in the plane intersecting the isocentre using the software described in §6.2b. The EPID mid-plane dose image of each field was then the sum of all corresponding segment dose images. All fields were compared with the planned 2D dose distribution, a corresponding plane from the 3D dose grid intersecting the isocentre, perpendicular to the beam axis.

6.2g *Test fields*

Two types of discrepancies were found which required further investigation. The first type was located in small regions of over-lapping segments, the second involved errors along the junction of abutting segments. These segment configurations were mimicked in the test fields, as shown in Figure 6.1. The X- and Y-directions and the definition of sides '1' and '2' are arbitrary (specified by the manufacturer). The multileaf collimator (MLC) leaves are indicated by thin lines and the X- and Y-jaw edges are indicated by thick lines.

The collimator for tests C and D was rotated 90° relative to that of tests A and B. All four test fields were 10x10 cm², using 18 MV photon beams, delivered in 2 segments each as follows:

- over-lapping segments: 1 cm², located on-axis
- over-lapping segments: two 1 cm² regions located 2.5 cm off-axis, 5 cm apart
- abutting segments: two segments side-by-side, the abutting region is parallel with the direction of the leaf motion. On the abutting side, segment 1 is blocked by the jaw (X2 side) and segment 2 is blocked by the MLC (X1 side). The minimum leaf gap under the jaw is located in the middle of the field.
- abutting segments: as for C) but with the minimum leaf gap under the jaw shifted 2 cm in the Y1-direction.

Segments were delivered sequentially in step-and-shoot mode. Fields were planned, calculated and measured in the same phantom and set-up as for pre-treatment verification, with the gantry angle set to 0°. EPID dose images were compared with film (measured simultaneously) and with the TPS in 2D at the plane intersecting the isocentre, perpendicular to the beam. Comparisons were made by examining γ images with 3%/3 mm criteria and absolute dose profiles. The time required for film and EPID measurements was also compared.

Test fields C and D, and an IMRT field from a patient plan, all had a region of abutting segments. These fields were re-planned after adjusting a parameter in the TPS, designed to model the width of the tongue-and-groove overlap between leaves. This parameter is denoted in this study as T&Gwidth. The value of this parameter was initially 0.06 cm (as provided by the vendor) and was increased to 0.20 cm for re-planning of selected fields.

6.3 Results

6.3a Verification of EPID dose images with film

EPID and film 2D dose distributions for 10 plans (50 fields) agreed within the set criteria for all points, with $\langle \gamma_{\text{avg}} \rangle = 0.16 \pm 0.07$ (1 SD), $\gamma_{\text{max}} = 1.0$ and $\langle P_{\gamma < 1} \rangle = 100\%$.

The measurements were also re-analysed with more stringent γ criteria of 2% and 2 mm, yielding $\langle \gamma_{\text{avg}} \rangle = 0.25 \pm 0.10$ (1 SD), $\gamma_{\text{max}} = 1.5$ and $\langle P_{\gamma < 1} \rangle = 99.1\%$.

Figure 6.1 Leaf settings and corresponding EPID images for the four test fields ($10 \times 10 \text{ cm}^2$), each with 2 segments. The collimator jaw edges are shown (thick grey lines) for the X1, X2, Y1 and Y2 sides (indicated for segment 1, tests A and C). MLC banks are located on the Y1 and Y2 sides, leaves are shown as thin lines. Test fields A and B produce on- and off-axis 1 cm^2 cold spots, where segments overlap in 1 cm^2 regions. Test fields C and D result in abutting segments, the abutment region is parallel to the leaf motion. In both C and D, the abutment side is blocked by the jaw (X2) in segment 1, and by the MLC (X1) in segment 2. The minimum leaf gap (0.56 cm) under the jaw is located centrally in test C, and shifted 2 cm in the Y1 direction in test D.

6.3b Verification of the planned dose: isocentre

The IC_{iso} and EPID_{iso} results agreed with an average ratio of 1.00 ± 0.01 (1 SD). Figure 6.2 shows absolute and relative isocentre dose values for 20 patient plans. Both EPID and IC measurements fell below the planned dose, revealing a slight systematic under-dosage.

The average ratio of both $\langle \text{EPID}_{\text{iso}}/\text{plan}_{\text{iso}} \rangle$ and $\langle \text{IC}_{\text{iso}}/\text{plan}_{\text{iso}} \rangle$ was 0.99 ± 0.01 (1 SD). All values of EPID_{iso} and IC_{iso} were within 3% of the planned dose value.

Figure 6.2 Isocentre dose values for pre-treatment verification of 20 IMRT prostate plans. Dose values (a) and ratios (b) are given for the plan, EPID and ionisation chamber. Both sets of measured dose values agree, with an average ratio of 1.00 ± 0.01 (1 SD) (b, diamonds), and both fall below the planned dose, with an average ratio of 0.99 ± 0.01 (1 SD) (b, squares and crosses).

6.3c Verification of the planned dose: field-by-field

EPID and planned 2D mid-plane distributions agreed well overall, with $\langle \gamma_{\text{avg}} \rangle = 0.39 \pm 0.10$ (1 SD), $\gamma_{\text{max}} = 2.52$ and $\langle P_{\gamma < 1} \rangle = 98.7\%$. Errors were found in at least 1 field for 7 of the 20 plans. Of these 7 plans, 2 plans had fields with errors that exceeded the acceptance criteria. One of the 2 plans had 2 fields with $\gamma_{\text{avg}} > 0.67$ (0.68 and 0.71), 3 fields with $\gamma_{\text{max}} > 2.0$ (2.42, 2.16 and 2.27) and 4 fields with $P_{\gamma < 1} < 95\%$ (88%, 86%, 91% and 85%). The second plan had no fields with $\gamma_{\text{avg}} > 0.67$, 1 field with $\gamma_{\text{max}} > 2.0$ (2.52) and 2 fields with $P_{\gamma < 1} < 95\%$ (93% and 91%). Histograms of the average and maximum γ values for all 100 fields are shown in Figure 6.3. The 2 fields failing the γ_{avg} criterion and 4 fields failing the γ_{max} criterion can be seen to the right of the vertical lines (indicating the acceptance limits). For five cases with small errors (that passed the acceptance criteria), discrepancies only occurred in one of the 5 fields of each plan. After examining absolute dose line profiles, the 7 plans with errors revealed small regions of measured dose data that were 6% to 20% lower than the planned dose values in the phantom (local dose difference).

Two distinct segment configurations were found in the regions with discrepancies: cold spots, small (intended) low dose regions produced by over-lapping segments ($\sim 1 \text{ cm}^2$ at the isocentre) and abutting segments, along the junction of leaves parallel with the leaf motion.

Figure 6.3 Histogram of γ_{avg} and γ_{max} , derived from γ evaluations, of 100 IMRT prostate fields (20 plans). Each planned field was compared with a 2D EPID dose image, reconstructed in the phantom at the plane perpendicular to the beam, intersecting the isocentre. Acceptance criteria for two γ parameters are also indicated. Two fields (from 1 plan) had $\gamma_{avg} > 0.67$ and 4 fields (from 2 plans) had $\gamma_{max} > 2.0$.

An example of a discrepancy from the planned dose value is given in Figure 6.4, for one field that failed the acceptance criteria. The γ evaluation for EPID vs. plan (gantry angle = 320°) and EPID vs. film (gantry angle = 0°) of this field are given in Figure 6.4a. At the low dose point in the region of disagreement, the plan was 16 cGy (16% local dose difference) higher than both EPID and film results, as shown in the vertical line profile (Figure 6.4b). In addition, a γ evaluation is shown for film vs. the total plan, for all fields combined with the original gantry angles, using γ criteria of 3%/3 mm (Figure 6.4c). The effect of the 16 cGy discrepancy in one modulated field led to a 9 cGy (8% local dose difference) under-dosage in the total plan for this 'cold spot' (1 cm^2), located at the isocentre plane. The under-dosage is compensated in part by a small over-dosage (within tolerance) from the other 4 fields. This over-dosage was determined from dose line profiles of these fields. The total dose from all fields averaged over a 1 cm^2 area of the cold spot was calculated with the TPS to be 129 cGy, and measured with film in the phantom to be 120 cGy.

Figure 6.4 (a) γ evaluation for one IMRT field comparing EPID dose distributions with the plan and (b) γ evaluation for EPID vs film (same field), both with criteria 3%/3 mm. The scale represents gamma values. A discrepancy ('cold spot') in the EPID vs plan image was not found when comparing EPID vs film. (c) Profiles for three dose distributions. In the region with the largest discrepancy, the EPID and film dose values agree (103.5 cGy), and are 16% lower than the planned dose values (120 cGy). (d) γ evaluation of the total plan, comparing the film and planned dose distributions (isocentric coronal plane, all fields, original gantry angles). The dose discrepancy in one field resulted in an 8% local dose discrepancy in the total plan (c, arrow).

Figure 6.5 Transversal slice of the CT scan and planned dose distribution of the same field as shown in Figure 6.4. The intended low dose region along the length of the beam ray shows the location in the patient that would be affected by the discrepancy.

The location of this discrepancy relative to the patient planning CT is indicated in Figure 6.5. While the current back-projection method only verifies the dose at a single plane, it is assumed that the error in dose will extend along the entire ray of the beam. In this case, the under-dosage passes through the prostate and the rectum, assuming that there are no changes in anatomy in the beam path during the actual treatment compared with the planning phase (e.g. no set-up errors or gas pockets).

It should be noted that the absolute dose distribution calculated or measured in the phantom cannot normally be directly translated to the patient. For this patient however, the absolute isocentre dose measured for the combined fields with an ionisation chamber, 198 cGy, is reasonably close to the prescribed patient dose of 200 cGy/fraction.

The results for the other 4 fields for this patient plan indicated discrepancies well below 3%/3 mm in 2D. For these 4 fields, $\langle\gamma_{\text{avg}}\rangle = 0.40$, $\gamma_{\text{max}} = 0.49$ and $\langle P_{\gamma < 1} \rangle = 100\%$. Furthermore, presuming there are no set-up errors or gas pockets, the region of the field in question mostly passes through soft tissue and ~1.5 cm of pelvic bone, and may be considered mostly homogeneous. Therefore the magnitude of the under-dosage within the homogeneous phantom (9 cGy) can be considered an approximation of the effect on the total dose that would be delivered to the patient in the region of the under-dosage.

6.3d Test fields

The results for EPID and planned dose distributions from test fields A and B are shown in Figure 6.6. The γ evaluation results for tests A and B were $\gamma_{\text{avg}} = 0.25$ and 0.35 , $\gamma_{\text{max}} = 1.4$ and 2.2 , and $P_{\gamma < 1} = 99.3\%$ and 95.7% , respectively (within the 20% planned isodose boundary). The over-lapping region is bounded on 2 sides by leaf ends, which are subject to leaf positioning errors, and on 2 sides by the tongue and groove edges, which are subject to penumbra modelling errors. Locally, planned dose values were up to 9% higher than measured dose values for the small over-lapping region on the central beam axis (test A), and up to 12% higher in the two off-axis regions (test B). Such a segment configuration combines both types of errors (leaf sides and leaf ends) in tests A and B, giving rise to under-dosages.

For the test cases, these regions of discrepancy were considered minor since they covered very small areas, approximately 2-3 mm wide. They would not be considered clinically relevant since they are in a high dose-gradient region and therefore would pass the 3 mm distance-to-agreement criterion. Outside this cold spot region however, additional discrepancies were found. These were located at the meeting point of opposing leaves between the cold spots in test B, yielding $\gamma_{\max}$ values of 2.0 and up to 16% local dose difference. The MLC log of leaf positions was checked against the prescribed MLC positions, and these deviations were ± 0.1 cm. EPID and film measurements agreed for tests A and B, with $\gamma_{\text{avg}} = 0.19$ and 0.21 and $\gamma_{\max} = 0.71$ and 0.74 , respectively. Both tests had $P_{\gamma < 1} = 100.0\%$ for the EPID and film comparison.

EPID images and γ evaluations are given for tests C and D, as well as an example of an IMRT field in Figure 6.7. For tests C and D, EPID dose values were both 9% (local difference) below planned doses in the abutment region, resulting in a $\gamma_{\max}$ value of 2.5. For both the test and the clinical IMRT fields, film and EPID agreed well, $P_{\gamma < 1} = 100.0\%$ with more stringent criteria of 2%/2 mm (images not shown).

Increasing the T&Gwidth in the TPS from 0.06 cm to 0.20 cm improved the agreement between measured and calculated dose distributions for all three fields, as shown in the lower three γ images of Figure 6.7. The value of 0.06 is the physical width of the leaf overlap distance. The value of 0.20 cm was chosen because this parameter is designed to model the leaf overlap width at the isocentre (not the physical width), as well as account for systematic uncertainties in calculating dose at field edges defined by the MLC leaf. $\gamma_{\max}$ was reduced from 2.8 to 0.80 for test C, from 2.4 to 0.70 for test D and from 2.32 to 1.39 for the IMRT field.

For all three γ evaluations in Figure 6.7 (2 test fields and 1 IMRT field), there is a small region of agreement in the middle of the line of discrepancy (along the abutting region). It is located in the centre of test C and the IMRT field, and 2 cm off centre (Y1-direction) in test D. This small region of agreement is due to two compensating effects. The leaf gap, although under the collimator jaw, contributes an additional dose to this region at the edge of the collimator (defining the field edge), which increases the measured dose.

Since it is along the abutment region, the measured dose is lower than the planned dose, and so the two errors cancel each other out in this small area. The difference between test C and test D provides support for this explanation. The location of the 'agreement region' along the abutting segment line corresponds exactly to the position of the leaf gap under the collimator in all three cases.

Central profiles (perpendicular to leaf travel) of the mid-plane dose determined with the plan and EPID are given in Figure 6.8 for test D. By comparing dose differences, the EPID measurements are up to 10% lower (local dose difference) than the plan calculated with T&Gwidth of 0.06 cm. Recalculating the plan with a T&Gwidth of 0.20 cm results in a more accurate dose calculation, however the optimisation criteria for this plan were no longer met. On the basis of the test fields, the 2 patient treatment plans with errors exceeding our acceptance criteria were re-optimised. These new plans were also verified prior to treatment and no errors were found.

Figure 6.6 γ evaluation for test fields A and B, EPID vs. plan, with γ criteria 3%/3 mm. A is the combination of 2 rectangular segments with a leaf over-travel of 1 cm, designed to produce a 'cold spot' at the isocentre. A similar design was applied to B, with the intended cold spot regions located either side of centre, 2.5 cm off-axis. In both cases, dose discrepancies were 9% (of D_{max}) and 12% in A and B, respectively, however the distance-to-agreement was within 2-3 mm. Therefore the discrepancy was considered minor. The under-dosage at the junction of opposing leaves, however, lead to discrepancies up to 16% along the thin region where the segments meet.

Figure 6.7 Segment shapes and γ evaluations for test fields C and D, and a clinical pre-treatment IMRT field, using γ criteria of 3%/3 mm. The segments are outlined with the 50% field-edge detection line to indicate the respective segment shapes. The 2 segments in the IMRT field were delivered as separate beams with 12 MUs (upper) and 20 MUs (lower). The calculated dose in the abutting region decreased in all 3 cases after the tongue-and-groove width parameter (T&Gwidth) in the TPS was increased from 0.06 to 0.20 cm. In addition, there is a region of 'agreement' in the middle of the red discrepancy line (along the abutment region), of test C and the IMRT field, and shifted 2 cm to the Y1 direction (right) in test D. This is due to the leaf gap scatter from under the collimator, increasing the measured dose and cancelling out the under-dosage.

For the new plans, the abutting leaf configuration was avoided because the T&Gwidth had not been fully optimised for clinical use at the time. Further tests were undertaken to optimise the value of the T&Gwidth for calculation of all clinical IMRT plans (beyond the scope of this study). It should be noted the value of 0.20 cm was only used for this study, using 18 MV photon beams. The actual value must be optimised for the dose calculation of all beam energies, linacs and on/off-axis locations used for calculation of IMRT plans.

Given the close agreement between EPID and film results, the advantages of using an EPID for these measurements were considerable. After irradiation, film development and processing took approximately 30 min, and additional films were irradiated to calibrate the batch of films used on the day. EPID images, on other hand, were converted to dose images within the software, and ready to compare with the planned dose distribution within seconds of irradiation. In addition, films required extra set-up time for each measurement. For EPID measurements, once the phantom is set up, there is no need to re-enter the treatment room and measurements can be more easily repeated.

Figure 6.8 EPID image and dose line profile for test D. The dose distributions agree within 3%/3 mm at either side of the abutment region. The EPID (black line) gave an 18 cGy (9%) lower dose at the junction of the segments than the plan with T&Gwidth = 0.06 cm (grey solid line). By effectively widening the ‘groove’ width in the dose calculation model to 0.20 cm (grey dotted line), greater attenuation leads to a reduction in the calculated dose, better the matching measured dose distribution.

6.4 Discussion

6.4a Clinical application

The demand for QA in the clinic has increased with the introduction of IMRT. So far the majority of studies reporting EPID dosimetry have focussed on the dose-response characteristics and various methods and algorithms in use. Few have demonstrated the usefulness of EPID dosimetry in the clinic. By 'clinical application' we refer to the use of EPID dose images to directly influence (with the intention to improve) patient treatment.

Chang *et al.*²⁴ compared relative profiles and central axis dose for 25 IMRT prostate fields using an α -Si EPID and planned dose distributions. Besides errors relating to image acquisition, agreement was within 2%, and therefore they concluded the system was an effective verification tool. Dupuyt *et al.*³⁰ introduced errors in pre-treatment verification to demonstrate the usefulness of the γ evaluation method, which was able to detect all deliberate errors. The efficacy of EPID dosimetry via the 'SIFT' method was also tested by deliberately introducing errors in a study by Vieira *et al.*¹²⁹ They found that changes in radiological path length up to 10 cm could be detected to an accuracy of 1%, and subsequently implemented their technique in the clinic. The aim of each of these studies was to show the accuracy of their dosimetry system as a QA tool, not to report clinical errors. No reports were found which demonstrate the usefulness of EPID dosimetry for routine IMRT verification in clinical practice. While other dosimetry devices could have been used to detect the errors, we found EPID dosimetry to be more efficient, providing at least the same amount of information and level of accuracy as film dosimetry. As a result, we improved two erroneous patient plans by identifying and correcting a wrongly set parameter in the TPS (used for all IMRT dose calculations), directly affecting our clinical operation.

6.4b Replacing EDR2 film with EPID dose verification

The time taken to obtain a digital image of a film measurement varies extensively for different departments, depending on the equipment and software available. However, regardless of how long it takes, obtaining a digital EPID image will always be quicker than setting-up, developing and digitising a film.

As a typical example, we estimated the time required to perform a field-by-field dose verification of a prostate treatment using EPID and film, as reported in our previous study.¹³² For the verification of 5 fields (37 segments), delivery, development and scanning of the films take at least 20 min. For EPID dosimetry, delivery takes approximately 6 min (both open and phantom fields) with the original beam parameters. Furthermore, the resulting 2D dose distribution is available almost immediately, since the time to read the image into the EPID dosimetry program, and conversion from raw EPID image to reconstructed dose image, takes a few seconds.

6.4c *Finding the source of the problem*

To explain the under-dosage at 'cold spots' and 'abutment regions' detected in this study, there were initially a large number of possible sources of error considered. These included both random and systematic errors, such as those due to over-travel of a leaf, film measurements, the EPID back-projection algorithm, TPS commissioning, dose calculation by the TPS, the MLC sequencer or data transfer. Both pre-treatment plans calculated on the phantom (with original and 0° gantry angles) were sent to the linac independently so it was unlikely to be a random problem with the re-planning process or data transfer. Problems with either the EPID algorithm or film measurements were ruled out since the field was checked with EPID and film measured simultaneously, as well as at different gantry angles. All measurements yielded exactly the same discrepancies when compared with the plan.

In addition, MLC prescription and log files from the TPS and at the linac for both plans were compared. Here random differences of 0.1 cm in leaf position were found, sufficient to contribute to the error but not large enough to be the only source of the problem. Tests A and B show that the TPS can calculate the dose to small regions of 1 cm² reasonably accurately, within 3%/3 mm, so this was also unlikely to be the source of the error. These investigations lead to the conclusion that there were systematic calculation problems in the TPS, specifically related to particular segment configurations (along abutting segments defined by the tongue and groove side of the leaf edge).

6.4d The TPS tongue-and-groove width parameter

At the time of commissioning the TPS, we were not aware that the parameters defining the MLC were incorrect or needed validation. The problem was not discovered in standard commissioning test fields, which were measured with diode arrays and ionisation chambers. It was not until the 11th IMRT plan that the error occurred (after 5 test and 5 clinical IMRT plans), as it is only relevant to particular segment configurations. The benefits of using an EPID for the tests are that images representing the 2D absolute dose distribution in the mid-plane of the phantom are available instantly and may easily be repeated, unlike film. Discrepancies can also be evaluated to high accuracy over a whole plane, a limitation of (arrays of) point detectors.

Increasing the T&Gwidth improved all dose calculations, making it a reasonable choice as the source of error. It should be noted that this version of Pinnacle (7.4f) has not yet been widely used, and that it is the responsibility of the user to validate the parameter to the required value for a specific type of linac. The width parameter models the overlap width of adjacent leaves at the isocentre. The original default value, 0.06 cm, represented the physical width of the overlap in the MLC bank, corresponding to a projected width of 0.10 cm at the isocentre. In addition to the isocentre width, a margin may also be added to this parameter to account for uncertainties in modelling the penumbra at the leaf edge, such as focal spot motion.¹¹¹ Discrepancies have been reported up to 0.11 cm in the gun-target direction for beams of 2 MUs, and up to 0.03 cm for 20 MUs, with results varying between dose-rates and linac designs. This uncertainty is more relevant for IMRT patient fields than the test fields reported here, since irradiation times are significantly shorter (~2 to 5 s vs. 30 s), for beams with a low number of MUs (< 20 MUs). The value of 0.20 cm was chosen for this study to represent the width at the isocentre (0.10 cm), as well as a reasonably large margin (+0.10 cm), based on associated uncertainties.

It would have been possible to simply re-calculate the clinical patient treatment field with the adjusted parameter, as shown in Figure 6.7, however this is not advisable. A simple recalculation of the patient plan with the same segment configuration would alter the dose distribution, and so the total plan may no longer satisfy the plan optimisation criteria. It should be noted that one T&Gwidth value must be chosen for all IMRT plans calculated with the TPS. The T&Gwidth will depend on the beam energy, since higher energies have a broader penumbra and the uncertainty component will vary. The end value will therefore depend (in part) on the combination of beam energies for which the TPS is commissioned. Further investigations in our department (beyond the scope of this study) have led to an optimised clinical value of 0.15 cm for the T&Gwidth. This is based on a comprise of the optimal value for different beam energies, uncertainties (such as focal spot motion) and off-axis effects.

6.4e *Future directions*

In principle our back-projection method can be used to verify the patient dose *in vivo*, to complement pre-treatment information and possibly replace it in the future. The only difference would be to compare actual patient plans (without re-calculating them on a phantom CT scan) with dose images based on treatment EPID transit images. Any additional discrepancies found with *in vivo* dosimetry may be associated with random events.

For the prostate cancer treatment site, random events would include anatomical changes (gas pockets), table attenuation (due to patient set-up) and image acquisition errors. To extend verification the process further, the EPID dose distribution may be back-projected to multiple planes within phantom or patient, as suggested by previous authors.^{65,80,91} This method would render an EPID-based dose distribution in 3D within the phantom or patient.

6.5 Conclusions

We have demonstrated how EPID back-projection dosimetry can be used to check clinical IMRT plans for prostate cancer patients prior to treatment. The results for the first 10 patients have shown that the EPID can replace film dosimetry for field-by-field verification. Moreover, close agreement for isocentre dose values has shown EPID dosimetry can be used to replace ionisation chamber measurements in a phantom for this treatment group. EPID results for 20 patients have been used to accurately verify the planned dose distribution in 2D for separate fields. Discrepancies between dose distributions of EPID and planned fields for 7 out of 20 patients revealed under-dosage (up to 16% local dose difference) along the abutting region of certain segment configurations. EPID dosimetry used to measure test fields confirmed the source of the problem, which led to the alteration of two patient plans with large discrepancies and the discovery of a systematic error in an MLC parameter of the TPS. The EPID has proven to be an efficient and accurate dosimetry tool and is the basis of our pre-treatment quality assurance protocol for IMRT plans.

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7

Anatomy changes in radiotherapy detected using portal imaging

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Abstract

Background and Purpose: Localisation images normally acquired to verify patient positioning also contain information about the patient's internal anatomy. The aim of this study was to investigate the anatomical changes observed in localisation images and examples of dosimetric consequences.

Materials and Methods: Localisation images were obtained weekly prior to radiotherapy with an electronic portal imaging device (EPID). A series of 'difference images' was created by subtracting the first localisation image from that of subsequent fractions. Images from 81 lung, 40 head and neck and 34 prostate cancer patients were classified according to the changes observed. Changes were considered relevant if the average pixel value over an area of at least 1 cm² differed by more than 5%, to allow for variations in linac output and EPID signal. Two patients were selected to illustrate the dosimetric effects of relevant changes. Their plans were re-calculated with repeat CT scans acquired after 4 weeks of treatment and compared with the difference images of the corresponding days.

Results: Progressive changes were detected for 57% of lung and 37% of head and neck cancer patients studied. Random changes were observed in 37% of lung, 28% of head and neck and 82% of prostate cancer patients. For a lung case, an increase of 10.0% in EPID dose due to tumour shrinkage corresponded to an increase of 9.8% in mean lung dose. Gas pockets in the rectum region of the prostate case increased the EPID dose by 6.3%, and resulted in a decrease of the minimum dose to the planning target volume of 26.4%.

Conclusions: Difference images are an efficient means of qualitatively detecting anatomical changes for various treatment sites in clinical practice. They can be used to identify changes for a particular patient, to indicate if the dose delivered to the patient would differ from planning and to detect if there is a need for re-planning.

7.1 Introduction

Anatomical changes in the path of treatment beams have been shown to alter the dose distribution throughout radiotherapy^{47,71,83,107,118}. Various studies have reported methods for developing planning margins to account for random and systematic changes over weeks of treatment^{50,102,125}. More specifically, Stroom *et al.*¹¹⁸ used portal images to examine the treatment of 15 prostate cancer patients, and gas pockets were detected in 23% of cases. The size of the gas pockets was used to predict changes in dose in the prostate and rectal wall, which are particularly sensitive to larger displacements. Erridge *et al.*³⁵ studied differences between portal images and digitally-reconstructed radiographs (DRRs). They observed that for 40% of the patients studied, the projected area of the tumour regressed by more than 20%. Barker *et al.*⁷ evaluated the systematic volumetric and geometric changes in head and neck cancer patients over the course of treatment using repeat CT scans. They reported tumour shrinkage (GTV) rates of 1.8%/day (median rate), that this volume loss tended to be asymmetric and that decreases in the parotid gland volume was highly correlated with weight loss. While previous studies have tended to focus on quantitative changes observed at specific sites, none have reported on statistics covering the range, frequency and extent of anatomical changes that occur in clinical practice.

Portal images are normally used to check patient position, however their use has been extended to treatment verification based on *in vivo* dosimetry^{14,45,61,91,97}. When the measured dose distributions are compared with planned dose calculations, anatomical changes can disguise delivery or calculation errors. The aim of this study was to investigate the type, frequency, and magnitude of anatomy changes as seen in anterior-posterior (AP) and lateral localisation images. This information can be used in two ways. First, to qualitatively identify possible sources of dose discrepancies due to anatomy changes which will be detected while performing dosimetry *in vivo*. Secondly, the information can be used to detect progressive anatomical changes which will influence the total dose delivered to the patient.

7.2 Methods & Materials

7.2a Classification of anatomical changes

For this study we used an existing database of orthogonal localisation images that were acquired during routine set-up verification in our institution. Normally these images are made at the first 2 or 3 fractions and weekly thereafter (depending on the treatment site and correction protocol). Overall, 81 lung, 40 head and neck and 34 prostate cancer patients were included in the study, each having 4 to 14 pairs of orthogonal localisation images (AP and lateral). This is a random selection of patients with sufficient localisation images for these treatment sites in a 19-month period (April 2002–November 2003). All localisation images were acquired at three of our treatment machines with an amorphous silicon (a-Si) flat panel imager (Elekta iView-GT, Elekta, Crawley, UK). The images were acquired for patient localisation prior to treatment, with a low dose (3–5 monitor units, MUs). The field size ranged from 15x15 cm² to 18x18 cm² at the isocentre and was chosen by the treatment planner to include sufficient bony anatomy in order to match the images. For the dose range used, integrated pixel values for the a-Si EPID were assumed to be linear with dose.⁷⁷

Changes in anatomy throughout treatment were studied using a set of 'difference images', i.e. the portal image of the first fraction (the reference image) was subtracted from that of subsequent fractions for both AP and lateral beams. Each image was first matched (according to our department's automatic matching protocol) on the bony anatomy of the DRR derived from the planning CT scan, to minimise any differences due to set-up error. Difference images were windowed such that black corresponded to local differences of more than +10% (positive $\Rightarrow$ more dose to the imager than day 1 $\Rightarrow$ shorter radiological path length $\Rightarrow$ density decreases or patient has become thinner), and white corresponded to differences less than -10% (negative $\Rightarrow$ less dose to the imager than day 1 $\Rightarrow$ longer radiological path length $\Rightarrow$ density increases or patient has become thicker). No change (0%) was grey. To quantify specific *regions of interest* (ROI), pixel values within difference images were expressed as:

$$ROI_{\%diff} = \left\langle \frac{ROI_{day_n} - ROI_{day_1}}{ROI_{day_1}} \right\rangle \times 100 \quad (7.1)$$

Where ROI_{day_n} is the set of pixel values in a selected region of interest of the localisation image acquired on day n . In the difference images, a change was considered significant when $|ROI_{\%Diff}| > 5\%$ extended over an area of at least 1 cm^2 . Variation in both the linac output in our department and the stability of the EPID signal is within $\pm 2\%$.⁶⁵ Relative changes less than 5% were not considered significant, given these as well as other uncertainties such as small errors in the matching procedure. The observed EPID-dose changes due to changes in anatomy were grouped within each treatment site, type of anatomy change(s) that could be determined, and referenced according to whether any changes were progressive or random (according to the type of change). A radiation oncologists' advice was sought to interpret the changes observed, based on clinical experience with respective patients.

7.2b Case studies

Two patients with notable changes in difference images were selected to illustrate the dosimetric consequences of relevant changes. One had a significant progressive change (a lung case), and the other had a random change (a prostate case). For both patients the treatment plan was first calculated with the planning CT scan and then the same plan, i.e. applying the same beam parameters (field shape and orientation) and number of monitor units, was re-calculated based on a repeat CT scan. The repeat scans were made just prior to treatment several weeks after day 1, on the same day that localisation images were acquired for the patient. The two patient plans were obtained using the Pinnacle treatment planning system (Philips Medical Systems, Eindhoven, The Netherlands, v7.5). The collapsed-cone dose calculation algorithm was used and inhomogeneity corrections were applied. In both cases the repeat CT scan was matched on the bony anatomy of the original planning CT scan to ensure the treatment was calculated at the same relative position of the patient. A 3D automatic chamfer matching algorithm was used to match specific bony regions for each site, the spine for the lung cancer case and the pelvic bone for the prostate cancer case.¹²⁷ In both cases the volume contours from the planning CT scan were copied to the repeat CT scan, and then re-defined (or re-drawn) to reflect the change in anatomy of the repeat CT scan.

The first case was a lung patient who had a significant tumour reduction in the right lung after 4 weeks of radiotherapy. The plan consisted of four conformal, 8 MV photon beams, with beam angles of 30°, 205°, 280° and 345°. The prescription dose was 67.5 Gy in the planning target volume (PTV), delivered as 2.25 Gy per fraction over 6 weeks. The planning CT scan was made two weeks prior to treatment and a repeat CT scan was taken at the beginning of week 5.

The second case was a prostate cancer patient with gas pockets and different levels of rectum filling on different days of treatment. The plan consisted of one AP 8 MV photon beam and two lateral 18 MV photon beams. In this case the prescription dose was 68 Gy in the PTV, delivered as 2 Gy per fraction over 7 weeks. The planning CT scan was made 1 week prior to treatment and a repeat CT scan was made during the fifth week of radiotherapy.

7.3 Results

7.3a *Classification of anatomical changes*

Examples of the changes seen in difference images and histograms representing the relative frequency of various changes are given for each treatment site (Figures 7.1, 7.2 and 7.3). For each site, sets of 3 difference images were selected per patient and beam direction, from a series over the entire treatment course. The 3 fractions were selected from week 1, either week 2 or 3 and week 5 of radiotherapy. Markers defining the beam's central axis are placed at the head of the accelerator only during the first fraction, and so their 'absence' is seen as two dark spots when the images are subtracted to give the subsequent difference images (occasionally the spots are obscured by anatomical features).

The histograms are divided into changes seen in AP and lateral difference images. Since EPID images represent transmission of the radiation beam, 2 orthogonal projections will not contain the same information. Data included in the histograms, unless classified as 'nothing significant', satisfy the '5% change over 1 cm²' criterion. In many cases, more than one type of change can be seen in a set of images for one patient, so the sum of the number of patients exhibiting each change can exceed the total number of patients studied for each treatment site.

7.3b Lung difference images

Four lung cases are shown in Figure 7.1. Figure 7.1a shows a decrease in upper-lobe lung density at day 23, increasing the EPID signal by +8%. This was due to lung re-ventilation, following complete atelectasis of the right lung at the beginning of treatment. The AP difference images in Figure 7.1b and 7.1c, show a darkening halo around the tumour indicating tumour regression. This was confirmed for Figure 7.1c via inspection of repeat CT scans (see case study below). Below the tumour a dark band varying in thickness indicates diaphragm displacement. Figure 7.1d shows an example of the lung density progressively increasing throughout treatment. This was interpreted by the radiation oncologist as increasing amounts of fluid filling the lung.

Significant changes seen in difference images for lung cancer patients were classified as follows (Figure 7.1, histogram):

- lung re-ventilation due to re-opening of air-ways following lung atelectasis (progressive)
- lung density increase, fluid accumulation due to radiation damage, inflammation or internal disease (infection or heart disease) (progressive)
- reduction in tumour size, signified by darkening halo around the tumour (progressive)
- patient displacement, due to shifting of a structure relative to the bony anatomy on which the image was matched (random)
- artefacts due to respiratory motion (random)

Figure 7.1 Examples of difference images for four lung cancer patients. Images were obtained by subtracting localisation images, acquired during the first, second (or third) and fifth week of treatment, from that of the first day. Regions of notable change are indicated (white box). (a) lung re-ventilation following atelectasis, (b) reduction in tumour size (indicated by decrease in density surrounding the tumour), (c) reduction in tumour size (and change in diaphragm position due to breathing) and (d) density increases due to fluid accumulation in the lung. (a) and (d) are lateral images, while (b) and (c) are anterior-posterior fields (AP). The histogram indicates the distribution of anatomical changes observed in the lung cancer patient group, according the type of change and whether it was detected in the AP or lateral localisation image. In many cases several changes were observed for the same patient.(next page)

7.3c Head and neck difference images

Two head and neck cases are shown in Figure 7.2. In Figure 7.2a, the darkening at both sides and the central region of the neck was due to a reduction in neck swelling and tumour size, according to information from the patient's radiation oncologist.

Figure 7.2b shows a gradually increasing EPID dose above the pharynx (upper boxed dark region), which was interpreted by the oncologist as tumour shrinkage resulting in opening of the previously restricted air-way. Displacement due to respiration and/or patient displacement is also apparent below the throat on days 2 and 15 (lower boxed dark region), and back of the neck on day 29. For head and neck cases difference images exhibited the following changes (Figure 7.2, histogram):

- neck thickness, usually due to weight loss, reduction in swelling (oedema following surgery) and/or tumour shrinkage (progressive)
- density, e.g. air pockets due to different positioning of the tongue (random) or tumour shrinkage (progressive)
- patient displacement, especially changing position of the neck or shoulders (due to set-up errors or breathing) on different treatment days (random)

7.3d Prostate difference images

Two prostate cases are shown in Figure 7.3. In both cases, dark regions (boxed) above the prostate indicate the patients had gas pockets at the time of imaging, but not on day 1. Lighter regions indicate gas pockets that were present on day 1 but not at the time of imaging.

Finally, difference images from prostate cases were examined (Figure 7.3, histogram) including:

- patient displacement (random)
- variation in gas pockets (random)

Figure 7.2 Examples of difference images for two head and neck cancer patients. Regions of notable change are indicated (white box). (a) decrease in neck thickness, (b) air pockets due to opening of the epipharynx (dark region, upper box, days 15 and 29) and chest positioning, due to breathing (dark region, lower box. (a) is an anterior-posterior (AP) field, (b) is a lateral field. The histogram indicates the distribution of anatomical changes observed in the head and neck cancer patient group. The most common change observed was patient displacement, usually the flex of the neck, most often viewable in images taken from the lateral direction.

Figure 7.3 Examples of difference images for two prostate cancer patients. Both (a) and (b) show changes due to variation in the presence and location of gas pockets. (a) is an anterior-posterior field (AP) and (b) is a lateral field. The histogram indicates the distribution of anatomical changes observed in the prostate cancer patient group. Position displacement of the femur in the AP direction was only visible in lateral fields, whereas gas pockets were the most common change observed, in up to 80% of patients.

7.3e Progressive and Random Changes

As indicated above, changes in anatomy were either progressive or random. Progressive changes included increase or decrease in lung density, tumour shrinkage, lung re-ventilation, enlargement of air-cavities due to tumour shrinkage and change in neck thickness. Random changes included gas pockets, air-cavities (due to swallowing), patient displacement (due to rotations and translations) and respiratory motion. Evidence of tumour regression could directly be seen in 20/81 lung patients, whereas in many cases only the consequences of tumour regression were apparent; e.g. lung re-ventilation in 30/81 lung cases and unblocking of air-ways in the head and neck region in 8/40 cases. For the 81 lung cases, 5 had no significant change, 30 had only random changes and 46 patients had progressive changes, respectively. For the 40 head and neck cases, 15, 11 and 14 patients had nothing significant, only random and progressive changes, respectively. As expected, the 34 prostate case revealed no progressive changes. Six patients showed nothing significant and 28 patients had random changes (mainly gas pockets in the rectum).

Figure 7.4 CT slices through the isocentre from the original planning CT scan and a repeat CT scan for two patients. The treatment plan was calculated for each CT set, selected isodose lines are given relative to the maximum dose. For the lung case, planning CT scan (a) and repeat CT scan (b) show the calculated dose increases for the reduced GTV. For the prostate case, dose distributions for both CT scans (c and d) are very similar, however gas pockets in the rectum have shifted the rectal wall into the higher dose region.

7.3f Case studies: Example of a progressive anatomy change

Difference portal image images of the lung case study showed a progressive halo-shaped darkening around the tumour, which was located in the lung (boxed area, Figure 7.1c). This tumour shrinkage resulted in $ROI_{\%Diff}$ values of +3.6%, +8.4% and at least +10% for the PTV region in weeks one, two and five, respectively. The gross tumour volume (GTV) decreased by 42% after 4 weeks of treatment (Figure 7.4a and 7.4b), the corresponding PTV (obtained by expanding the GTV by adding ~1 cm margin) reduced by 30.6%. The lung volume (left and right lung volumes excluding the GTV), increased by 7.5%. Results from the calculated dose distribution on both planning and repeat CT scans for the PTV and lung given in Table 7-1, including the mean dose $\langle D \rangle$, minimum dose, D_{min} , and the volume receiving x Gy, $V_x Gy$. Isodose lines, relative to the maximum planned dose value, are also shown in Figure 7.4. The increase in $\langle D \rangle$ to the PTV (3.1%) and the lung (9.8%) is consistent with the change in EPID dose during localisation imaging, which increased +10% after 4 weeks of treatment in the GTV region.

Table 7-1 Clinically relevant dose information for volumes of interest of the lung case for one fraction. The dose distributions were calculated with the same treatment plan using the original planning CT and a repeat CT scan. The original volumes were defined based on the anatomy of the planning CT scan and the re-defined contours were based on the altered anatomy of the repeat CT scan. The dose prescription for the lung case was 67.5 Gy (given in 30 fractions) in the PTV. Changes in dose in each volume are due to both changes in CT scan and re-definition of the volume within each dose distribution. Details include the mean dose $\langle D \rangle$, the minimum dose, D_{min} , and the volume receiving x Gy, $V_x Gy$.

Volume :	Planning CT scan		Repeat CT scan	
	Original	Re-defined	Original	Re-defined
<i>PTV</i>				
$\langle D \rangle$	225 cGy	227 cGy	229 cGy	232 cGy
D_{min}	200 cGy	211 cGy	203 cGy	212 cGy
$V_{64.1 Gy}$	92.1%	97.9%	95.3%	98.8%
<i>Lung</i>				
$\langle D \rangle$	102 cGy	110 cGy	103 cGy	112 cGy
V_{20Gy}	59.0%	63.0%	59. %	63.4%

7.3g Case studies: Example of a random anatomy change

For the prostate case, difference images are given in Figure 7.3a. For this patient, there were no visible gas pockets in either the planning CT or in the localisation images of the first treatment day. However gas pockets were found in the rectum on day 29, effectively increasing the dose to the imager by +6.3% ($ROI_{\%Diff}$). A repeat CT scan was acquired on day 29, prior to treatment, and also revealed gas in the rectum. While this resulted in an increase in dose to the imager, it caused only a slight change in the dose distribution calculated with the repeat CT scan (Figure 7.4c and 7.4d). Isodose lines are given relative to the maximum planned dose value. Dose calculation details are given in Table 7-II for the PTV (prostate + 10 mm margin) and the rectal wall. For each volume, however, a larger difference was found between the original and re-defined volume than between the planning and repeat CT scans. The shift of the rectum (due to gas pockets) increased the rectal wall volume receiving 60 Gy for that fraction from $V_{60Gy} = 3.1\%$ (original volume, planning CT scan) to $V_{60Gy} = 14.5\%$ (re-defined volume, repeat CT scan). Moreover, the change in rectal volume shifted the PTV out of the high dose region. This change reduced the minimum dose to the PTV (D_{min}) by 26.4% for that fraction (155 cGy instead of 196 cGy).

Table 7-II Clinically relevant dose information for volumes of interest of the prostate case for one fraction. The original PTV and rectal wall volumes were defined based on the anatomy of the planning CT and the re-defined contours were based on the altered anatomy of the repeat CT scan. Dose information is given as for the lung case (Table 7-I). The dose prescription for the prostate case was 78 Gy (34 fractions) to the PTV (prostate + 10 mm margin). For each volume, a larger difference is seen between the original and re-defined volume than between the planning and repeat CT scans.

Volume:	Planning CT scan		Repeat CT scan	
	Original	Re-defined	Original	Re-defined
<i>PTV</i>				
<D>	201 cGy	196 cGy	201 cGy	196 cGy
D_{min}	196 cGy	156 cGy	196 cGy	155 cGy
<i>Rectal wall</i>				
<D>	91 cGy	104 cGy	90 cGy	103 cGy
V_{60Gy}	3.1%	13.5%	3.8%	14.5%

7.4 Discussion

In this study we have shown that portal imaging may be easily extended to derive useful information about variation in dose delivered to the patient due to anatomy changes during radiotherapy. If set-up verification protocols are already in place, the acquisition of difference images adds no additional time to patient treatments and the analysis is relatively simple.

7.4a *Progressive and random changes*

It is important to distinguish progressive from random changes because progressive changes are more likely to influence the final treatment. This depends on both the type of change and the timing of its onset. For instance, the opening of an airway and re-ventilation of the lung at week 2 of treatment will influence the overall treatment much more than if it occurs at week 6. The lung case study showed a gradual reduction in tumour volume will both alter the dose distribution and the location of volumes of interest within that dose distribution. From the difference images, it can be seen that the change was less significant in the weeks prior to the repeat CT scan (from week 5), but in the remaining 2 weeks of treatment, the tumour shrank further.

Random changes may be distinguished from progressive changes by their source, such as those related to normal breathing and patient set-up positioning. Such changes are not usually thought to have large dosimetric consequences, since random motion tends to lead to dose blurring, and the effect on the integral dose is less significant than systematic or progressive changes.^{16,34,44,128}

7.4b *Limitations*

Ideally a DRR could be used as the reference image instead of the EPID image of the first day, however our method is simpler and still yields the required information. Using the first portal image as a reference was considered the most logical choice since the purpose of the study was to examine anatomy changes due to radiotherapy. Localisation images were used to qualitatively distinguish random and progressive changes, and cannot be used to accurately determine their effect on the intended dose.

As demonstrated in this study, quantitative information can be obtained by re-calculating the plan using a CT scan acquired at or close to the time of treatment.

7.4c Applications of difference images

A useful application of difference images is a qualitative check for major anatomical changes which may cause the daily dose distribution to deviate significantly from the planned dose distribution. The qualitative information obtained from difference images may also be used to better assess dose discrepancies which are expected to arise while performing *in vivo* dosimetry. Non-patient related discrepancies have been reported for delivered dose distributions due to leaf position errors, unplanned leaf motion, undelivered segments (< 1 MU) and redistribution of MUs among the segments of a segmented field.¹³⁹ Such errors have resulted in dose discrepancies up to 30% in low dose regions, and within $\pm 5\%$ for higher dose regions. Localisation images (EPID images acquired *prior* to treatment) can be used to explain dose discrepancies between planning and treatment specifically relating to anatomical differences when performing 2D (or 3D) *in vivo* dosimetry.

7.5 Conclusions

The use of difference images is an efficient means of detecting anatomical changes during the course of radiation therapy. They serve as an indicator of changes in dose due to changes in patient anatomy, facilitating decisions regarding re-scanning and re-planning. They can also be used to identify the nature of the discrepancies we can expect comparing portal dosimetry to planned dose distributions. Progressive changes were detected in 57% of lung cancer patients and 37% of head and neck cancer patients, while random changes were most predominant, 82%, in prostate cancer patients.

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8

Replacing pre-treatment verification with *in vivo* EPID dosimetry for prostate IMRT

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Abstract

Purpose: To investigate the feasibility of replacing pre-treatment verification with *in vivo* EPID dosimetry for IMRT prostate radiotherapy.

Methods and Materials: Dose distributions were reconstructed from EPID images, inside a phantom (pre-treatment) or the patient (five fractions *in vivo*) for 75 IMRT prostate plans. Planned and EPID dose values were compared at the isocentre and in 2D using the γ index (3%/3 mm). The number of measured *in vivo* fractions required to achieve similar levels of agreement with the plan as pre-treatment verification was determined. The time required to perform both methods was compared.

Results: Planned and EPID isocentre dose values agreed, on average, within $\pm 1\%$ (1 SD) of the total plan for both pre-treatment and *in vivo* verification. For 2D field-by-field verification, an alert was raised for ten pre-treatment checks with clear but clinically irrelevant discrepancies. Multiple *in vivo* fractions were combined by assessing γ images consisting of median, minimum and low (intermediate) pixel values of one to five fractions. The 'low' γ values of three fractions rendered similar results as pre-treatment verification. Additional time for verification was ~ 2.5 h per plan for pre-treatment verification, and 15 min + 10 min/fraction using *in vivo* dosimetry.

Conclusions: *In vivo* EPID dosimetry is a viable alternative to pre-treatment verification for prostate IMRT. For our patients, combining information from three fractions *in vivo* is the best way to distinguish systematic errors from non-clinically relevant discrepancies, save hours of QA time per patient plan and enable verification of the actual patient treatment.

8.1 Introduction

As dose prescriptions and the complexity of radiotherapy plans increase, so too do the demands for accurate and efficient means of verifying the dose delivered to patients. An ideal verification system would enable a check of the patient's absolute dose distribution at the time and place of treatment in two, or preferably three, dimensions. The results would be in a digital format and require no additional time for set-up of additional equipment prior to or during treatment time. The electronic portal imaging device (EPID) is a feasible candidate for such a system.

Pre-treatment dosimetry is a commonly used surrogate verification method whereby the planned dose is verified prior to treatment. EPIDs have been shown to be useful for intensity modulated radiotherapy (IMRT) pre-treatment dosimetry.^{24,78,94,95,131,132,139} Converting an EPID image to a dose distribution pre-treatment (with or without a phantom) allows for verification of the dose calculation and plan deliverability. The drawback is, however, that errors occurring at the time of treatment would be missed and it is not clear *a priori* how errors detected pre-treatment would translate to errors within a patient. Furthermore, the workload becomes insurmountable for most clinics to do this for every patient plan. An alternative is *in vivo* EPID dosimetry, which we define as determination of the dose distribution inside the patient based on EPID images acquired at the time of treatment. *In vivo* EPID dosimetry has several advantages: the panel is already fixed to the linac, high resolution 2D digital images are available immediately after irradiation and the images contain both dose and anatomical information, providing a check and documentation of the actual patient treatment. In addition, *in vivo* EPID dosimetry takes very little additional clinical time, since measurements are acquired during treatment time. These advantages are only relevant, however, if an acceptable error detection accuracy can be achieved with *in vivo* EPID dosimetry.

In vivo dosimetry in radiotherapy has traditionally relied on the use of point detectors, such as thermoluminescent dosimeters and diodes.¹ MOSFETS (metal oxide semi-conductor field effect transmitters) have also been used^{55,101}, with reports of measured dose differences within $\pm 5\%$ of reference measurements. Advantages of MOSFETS over traditional point detectors are their small size, remote read-out and dose-rate independence. Even with multiple point-dose detectors (i.e. 2D matrix devices), spatial limitations make them insufficient for IMRT verification.

Furthermore, measurements tend to be time consuming and changing anatomy makes it difficult to distinguish relevant from irrelevant errors, systematic plan errors can be masked by transient anatomical changes. Possible errors that could be easily missed include wrong leaf positions of the multileaf collimator (MLC), incorrect treatment data transfer and wrong plan delivery. Such errors are less likely to be missed if treatment is verified in at least 2D, at a resolution comparable with the planned dose distribution. In 2D, transmission EPID images acquired during treatment have already been used for *in vivo* dosimetry of conformal fields^{11,45,60,97}, however reports detailing clinical use for IMRT verification are lacking in the literature.

Our department has extensive experience with the use of EPID dosimetry for clinical pre-treatment verification of IMRT prostate plans, whereby the dose is verified inside a homogeneous phantom.⁷⁸ Replacing pre-treatment with *in vivo* dosimetry is not straightforward, however. When acceptance criteria are used to raise an alert for potentially erroneous plans, checking one fraction is not usually sufficient, since random events during treatment (such as changes in patient anatomy and linac output) can obscure systematic errors. Random events that are not clinically relevant raise too many false positives and increase the workload unnecessarily. Waiting for too many fractions before verifying a plan, on the other hand, is potentially dangerous. One would like to combine the results from a few fractions - to distinguish irrelevant, ignorable discrepancies from clinically relevant errors. Our aims, therefore, were to evaluate the verification results for a large patient group, test different protocols combining multiple fractions, find the optimal number of fractions that would render an acceptable detection rate and investigate the potential cost/benefit of replacing pre-treatment with *in vivo* dose verification in the clinic.

8.2 Methods and Materials

8.2a Patient treatment plans

Seventy-five prostate cancer patients were included in this study. Plans comprised a five field step-and-shoot IMRT technique, using 18 MV photon beams, with 15 to 40 segments per plan (average = 25) and beam angles of 0, 40, 100, 260 and 320°. Dose distributions were optimised and calculated with the treatment planning system (TPS) Pinnacle 7.4f (Philips Medical Systems, Eindhoven, The Netherlands).

The prescribed dose was 78 Gy to the prostate, delivered as 2 Gy per fraction.¹⁷ Except for low-risk cases, the prostate contour also included the seminal vesicles. The dose was calculated using the adaptive convolve algorithm with a grid size of $0.4 \times 0.4 \times 0.4 \text{ cm}^3$.

8.2b EPID dosimetry

EPID images were acquired with an amorphous silicon flat panel imager (iViewGT, Elekta, Crawley, UK). Details regarding the imager design, image acquisition, stability and dosimetric characteristics have been reported extensively in previous work.^{66,77} The algorithm used to determine dose images within a patient (or phantom) for the present study has also been described previously^{11,132}, and will be briefly outlined here. Since the same algorithm is used for pre-treatment or *in vivo* dosimetry, 'patient' is used to refer to either the patient or the phantom. The algorithm converts segment images to an absolute 2D dose distribution in the reconstruction plane of the patient, defined as the plane perpendicular to the beam axis, intersecting the isocentre.^{14,65,132} Therefore this plane will rotate with the gantry. Pixel values of the transit dose image are processed using scatter kernels (for scatter within the EPID and scatter from the patient to the EPID), the scatter-to-primary ratio (for scattered radiation within the patient), the inverse square law and the measured transmission, to obtain the absolute dose distribution in the isocentric plane of the patient. The measured transmission of the beam through the patient is determined from images acquired for each field (or segment) both with and without the patient.

The location of the reconstruction plane is arbitrary, so a correction is required to account for attenuation of the beam from the isocentric plane to the exit surface. The external contour of the patient CT scan is used to obtain the ratio of geometrical path lengths, which is used to calculate the attenuation per pixel. The density of the transmission medium is assumed to be homogeneous, therefore the dose may be incorrect for areas on the plane where the beam passed through media of non-tissue equivalent density. Reconstructed 2D dose distributions for each field are then the sum of the reconstructed dose distributions of all segments belonging to that field. We should note that the accuracy of our EPID dosimetry method ($\pm 2\%$ or 2 mm) has been published for 18 MV¹³², and equivalent levels of accuracy have been achieved for verification of 6, 8 and 10 MV photon beams both at research level and in clinical practise.

8.2c *Dose verification in the phantom and the patient*

Dose distributions of each plan were verified in 2D with EPID images pre-treatment (in a phantom), and *in vivo* (in a patient) during five treatment fractions.

For phantom verification, plans were re-calculated with the TPS, replacing the patient planning CT scan with a phantom CT scan. The phantom was a polystyrene slab phantom of base $30 \times 30 \text{ cm}^2$ (parallel with the table surface) and height 20 cm. The source-surface distance (SSD) was 90 cm at a gantry angle of 0° . No plan parameters were changed, so the same MLC settings, collimator and gantry angles, energy and numbers of monitor units were used as for the patient treatment. The dose distribution was re-calculated at a higher resolution for higher accuracy using a grid size of $0.2 \times 0.2 \times 0.2 \text{ cm}^3$.

For prostate IMRT patients treated in our department (including all patients for this study) patient set-up is verified at the first two fractions and once per week thereafter. Additional fractions are included if set-up corrections are required, according to shrinking action level decision rules.⁸ *In vivo* EPID dose verification was performed for the same fractions as set-up verification. Additional EPID dosimetry images were always acquired at the 3rd fraction to ensure five *in vivo* measurements were made at most within the first two weeks plus one day of treatment.

Therefore EPID treatment images were acquired at the 1st three fractions and then once/week, as well as for any fractions requiring additional set-up verification. The first five measured fractions for each patient were included in this study, yielding data for 375 fractions measured *in vivo*, with all 75 plans verified in a phantom pre-treatment.

Plans were first compared at the isocentre, by summing the planned and EPID isocentre doses for each field, respectively. Each field was then compared in 2D at the plane corresponding to the location of the reconstructed dose distribution determined with the EPID. The resolution of the EPID dose distribution was $0.1 \times 0.1 \text{ cm}^2$. Evaluations were performed using the γ index⁶⁹, with a dose difference tolerance of 3% of the maximum planned dose per field and a distance-to-agreement tolerance of 3 mm. Plans were assessed based on a combination of three γ parameters, namely the average (γ_{avg}), maximum γ (γ_{max}) and the percentage of points in agreement ($P_{\gamma < 1}$). These parameters were calculated from the γ evaluation of each field within the 20% isodose line of the planned dose distribution. Discrepancies were counted according to their source for both pre-treatment and *in vivo* dosimetry.

8.2d Assessing multiple fractions

Once 2D acceptance criteria are defined, it is straightforward to apply them to EPID *in vivo* measurements of a single fraction. Due to random events, however, it is better to combine multiple fractions. The objective is to automatically accept/reject dosimetry images, avoid detecting irrelevant discrepancies, and more importantly, avoid missing real errors. Taking one field at a time, corresponding γ pixel values from one to n fractions were sorted in ascending order. Composite γ images were created based on three different methods combining multiple fractions for assessment (per field). The methods included the median γ value per pixel (median- γ -image), the minimum γ value per pixel (min- γ -image), and the 'low' γ value per pixel (low- γ -image), half-way between the minimum and the median. For example, if nine fractions were assessed, the γ values would be arranged in ascending order per pixel and numbered one to nine.

The median- γ -image would be a composite γ image comprising all the pixel values at the 5th (middle) position, the min- γ -image would comprise all the 1st (lowest) values and the low- γ -image would comprise all the pixel values in the 3rd position.

8.2e Alert criteria

Four criteria levels were applied to each median-, min- and low- γ -image to raise an 'alert' to potentially problematic plans, based on γ_{avg} , γ_{max} and $P_{\gamma < 1}$. The four levels tested were labelled 'strict', 'medium', 'easy' and 'very easy' (Table 8-1). The medium level corresponded to the clinical criteria used in our department for both pre-treatment and *in vivo* dosimetry. Additional levels were designed to compare the sensitivity of the results. The number of plans for which an alert was raised was counted for pre-treatment (i_{pt}) and for each of n fractions *in vivo* ($i_{iv}(n)$). A flow chart describing the process is given in Figure 8.1.

Furthermore, the correlations between pre-treatment and *in vivo* results of the three γ parameters (γ_{avg} , γ_{max} and $P_{\gamma < 1}$) were compared pairwise for each field, for one to n fractions, using the three combination methods.

Table 8-1 Criteria levels for comparing measured (EPID) and planned (TPS) dose distributions field-by-field. Corresponding percentage dose difference, ΔD (%) or distance-to-agreement, DTA (mm) values are also shown, given that $\gamma = 1$ if $\Delta D = 3\%$ or DTA = 3 mm. The medium level is used clinically in our department for *in vivo* dosimetry of IMRT prostate treatments.

Level	γ_{avg}	γ_{max}	Corresponding ΔD (%) and DTA (mm)		$P_{\gamma < 1}$
			avg	max	
Strict	0.50	1.33	$\pm 1.5 \%$, 1.5 mm	$\pm 4.0 \%$, 4.0 mm	99%
Medium	0.67	2.00	$\pm 2.0 \%$, 2.0 mm	$\pm 6.0 \%$, 6.0 mm	95%
Easy	0.83	2.67	$\pm 2.5 \%$, 2.5 mm	$\pm 8.0 \%$, 8.0 mm	90%
Very easy	1.00	3.33	$\pm 3.0 \%$, 3.0 mm	$\pm 10.0 \%$, 10.0 mm	80%

8.2f *Developing a clinical protocol*

Once the optimal number of treatment fractions required to replace pre-treatment dosimetry was found, a plan of action was devised for the clinic based on *in vivo* dosimetry alone. To this end, discrepancies encountered from verification of 75 patient plans were divided into three groups. If the influence of a discrepancy was isolated to a single field, if it were due to an easily identifiable random cause, and if it would not be considered clinically relevant, the discrepancy was classified as group A. If the influence of a discrepancy was isolated to individual fractions (all fields), but not more than two of the five fractions investigated, and could not be easily identified from *in vivo* dosimetry, the discrepancy was classified as group B. Otherwise the discrepancy was considered plan dependent, systematic and would affect one or several fields in every treatment fraction. This type of error was classified as group C.

8.2g *Time*

For both pre-treatment checks and *in vivo* dosimetry, the additional time outside routine patient planning and treatment time was assessed and compared. This included additional time to plan, measure and analyse the dose distributions in 2D for each field.

8.3 Results

8.3a *Verification at the isocentre*

Comparison of point dose values at the isocentre showed that EPID and planned values agreed well. For pre-treatment verification of 75 plans, the average ratio of the EPID and planned isocentre dose values in the phantom was 0.99 ± 0.01 (1 SD), ranging from 0.96 to 1.01. For the fields measured *in vivo*, the ratio of EPID and planned values over 1860 fractions was 0.99 ± 0.01 (1 SD), ranging from 0.96 to 1.02. Outliers due to image acquisition errors were excluded (15 fields). The correlation between *in vivo* and pre-treatment isocentre values for the total plan was low, with a correlation coefficient $R = 0.023$, i.e. the magnitude of the discrepancies detected was much smaller than the measurement uncertainty.

Figure 8.1 Flow chart to compare the number of plans alerted with pre-treatment and in vivo dosimetry. The composite in vivo γ image of n fractions was made using the median-, min- and low- γ -image methods. The values i_{pt} and $i_{iv}(n)$ are the number of plans for which an alert was raised for pre-treatment and in vivo verification, respectively. These were counted for all four criteria levels (Table8-I).

8.3b Verification in 2D

Individual measured fields compared very well with planned dose distributions. An example of dose profiles for one IMRT field measured in a phantom pre-treatment and for five fractions *in vivo* is shown in Figure 8.2. This was a patient with gas pockets in the rectum on two of the five fractions measured *in vivo*. Since our EPID dosimetry algorithm does not account for inhomogeneities, an accurate determination of dose in the ray-path intersecting the gas pocket is not possible. It does, however, indicate where potential dose discrepancies would occur due to different patient anatomy between treatment and planning.

Figure 8.2 Planned and measured absolute dose profiles for one field of an IMRT plan. The location of the profile is indicated in the EPID image. (a) calculated and measured in a phantom, (b) calculated in a patient and measured *in vivo* over five treatment fractions. Random discrepancies occurred at two fractions due to gas pockets in the rectum.

Figure 8.3 shows an example of γ evaluations for one patient plan: (a) pre-treatment, (b) γ images and (c) low- γ -images for five *in vivo* fractions. For this patient, both a systematic dose calculation error and random discrepancies can be seen by comparing pre-treatment verification in a phantom with *in vivo* measurements. By considering more fractions, the low- γ -images ‘improve’ as large random errors are suppressed, allowing optimal detection of systematic errors after three fractions. The systematic error for this plan (12% local under-dosage) was not considered clinically relevant since the error was in one field, covered a small area ($< 4 \text{ mm}^2$), and did not pass through the prostate volume.

Figure 8.3 Examples of (a) pre-treatment γ images, (b) in vivo γ images and (c) in vivo low- γ -images for verification of a patient treatment (five fields). The low- γ -image is calculated half-way between the minimum and the median of one to n fractions ($n = 1$ to 5). The percentage of points with $\gamma < 1$ ($P_{\gamma < 1}$) is given below each image. For the 100° field, the random error (gas pockets, 4th fraction) is suppressed in the low- γ -image. For the 320° field, a systematic error is visible in the pre-treatment check and the low- γ -image for up to five fractions. This error was not clinically relevant.

8.3c Comparing pre-treatment and *in vivo* dosimetry

The results for the combination of multiple fractions using three methods (median-, min- and low- γ -image) are shown in Figure 8.4 (process outlined in Figure 8.1), along side the number of plans alerted after a pre-treatment check. Each histogram illustrates i_{pt} and $i_{iv}(n)$, the number of plans for which an alert would have been raised for the four levels of alert criteria. To ensure a similar error-detection rate for *in vivo* dosimetry as pre-treatment, a similar group of plans should be alerted. Therefore i_{iv} should be similar to i_{pt} for a given number of fractions, method and criteria level. Overall, the median- γ -image renders much higher values of $i_{iv}(n)$ than i_{pt} , indicating unnecessary workload required to check error free plans with a phantom (Figure 8.4a). With the min- and low- γ -image methods (Figure 8.4b and 8.4c), checking one or two fractions would render high $i_{iv}(n)$ values, however three or more would provide an appropriate rate of detection, for all levels of criteria. For the min- γ -image method, however, the number of alerts raised continues to fall after 3 fractions, as random events and/or measurement uncertainty compensate potentially erroneous plans. Considering more fractions, zero errors would be detected much sooner with the min- γ -image than the low- γ -image method, increasing the chance of false negatives. Therefore the low- γ -image with the medium level criteria was considered the best option.

Figure 8.4 The number of plans for which an alert was raised after a pre-treatment phantom check (i_{pt}) for 75 IMRT prostate plans is given in (a-c). Due to small dose calculation errors, more plans were alerted with strict criteria, decreasing as the criteria were relaxed. Corresponding data is also shown considering one to five in vivo fractions (i_{iv}). For in vivo measurements, the criteria were applied to the (a) median- (b) min- and (c) low- γ -images. Ideally, i_{pt} and i_{iv} should alert and pass the same plans at each level. Compared to pre-treatment, too many plans are alerted using the median- γ -image due to ignorable outliers (e.g. gas pockets). The number of plans alerted converges to zero using the min- γ -image. Three fractions is sufficient using the low- γ -image and the medium criteria to achieve a similar accuracy as a check of every plan in a phantom.

Assuming that pre-treatment dosimetry gives an ‘actual’ measure of agreement between planned and measured dose, the decision to replace pre-treatment with *in vivo* dosimetry was justified by assessing the relative correlation between both methods for the range of evaluation parameters. Figure 8.5 shows an example of the correlation between pre-treatment and *in vivo* dosimetry for γ_{max} , with multiple fractions combined using low- γ -images. The medium criterion for γ_{max} ($\gamma = 2.0$) is also plotted, defining the following quadrants:

- lower-left = both pre-treatment and *in vivo* pass,
- upper-right = both pre-treatment and *in vivo* raise an alert,
- upper-left = false positives (work load too high) and
- lower-right = false negatives (detection accuracy too low).

Assessing the *in vivo* results over increasing number of fractions improves the correlation, rendering fewer false positives. As random outliers are suppressed, the low- γ -image approaches a measure of the ‘actual’ agreement between the plan and the delivered dose distribution.

Figure 8.5 An example of the correlation (R) between pre-treatment and *in vivo* dosimetry. Each dot represents the γ_{max} value of one field. The γ_{max} values for all pre-treatment fields are compared with the γ_{max} of the low- γ -image calculated for $n = 1$ to 5 fractions. The limits of the medium-level alert criteria are also shown. Assessing the *in vivo* results over increasing number of fractions improves the correlation with the pre-treatment results. As random outliers are suppressed, the low- γ -image approaches a better measure of the agreement between the plan and the delivered dose distribution.

Figure 8.6 summarises the correlation for all three methods used to combine *in vivo* fraction measurements (median-, min- and low- γ -image), for each of the three γ parameters (γ_{avg} , γ_{max} and $P_{\gamma<1}$). The correlation improves from one to three fractions in all cases, with little improvement after four or five fractions. The min- and low- γ -images render better correlation than median- γ -images. For the min- γ -image, however, the γ_{avg} and $P_{\gamma<1}$ correlations decrease at five fractions. This decrease indicates ‘false good days’ whereby random events reduce the measured discrepancy, giving a deceptively better result for *in vivo* than pre-treatment verification. All correlations were significant ($p < 0.05$) after two fractions. These results strengthened the argument for using the low- γ -image and three fractions.

Figure 8.6 The correlation and p-value ($R \neq 0$) of the comparison between pre-treatment (pt) and *in vivo* (iv) dosimetry. *In vivo* measurements from fractions one to five were combined based on the median-, min- and low- γ -image. For each γ parameter (γ_{avg} , γ_{max} and $P_{\gamma<1}$), the correlation improves from one to three fractions, with little improvement after four or five fractions. The p-value shows the correlation is significant ($p < 0.05$) after two fractions in all cases.

The plans that were alerted either pre-treatment or *in vivo* (low- γ -images, three fractions) contained discrepancies due to dose calculation errors. The errors occurred at the region of abutting segments, and were due to a wrongly set parameter in the TPS, as described in a previous publication.⁷⁸

For these plans, while the dose discrepancies relatively large for the field in which they occurred, only one field of the five was alerted and the absolute discrepancy was considered to be a small proportion of the total planned dose at this location ($< 5\%$).

Therefore re-planning was not considered necessary for these patient plans. For this patient group, no clinically relevant false negatives would have been missed by checking three fractions with the low- γ -image method and using the medium criteria level.

8.3d Types of errors detected

A summary of the type of errors, as alerted with the medium criteria, can be found in Table 8-II for pre-treatment and *in vivo* measurements. The errors are grouped according to A, B and C. *In vivo* fractions were assessed separately.

Group A errors were easily determined by checking raw EPID treatment images. Gas pockets were detected in 7% of fields. An obstructing table arm (behind the patient, 4%) was detected if the patient was not positioned centrally on the treatment couch, and was therefore a random error. Image acquisition errors (1%) occurred when the operator was too late to start image acquisition. Additional checks are in place at the linac to ensure all segments were delivered to the patient. Additional fractions should be checked to verify these fields.

Group B errors could not be identified with certainty by checking treatment fields, e.g. variation in linac output (outside tolerance) or dose differences due to errors in patient set-up. These plans would require a phantom check to verify any systematic errors. The number of fractions affected by a gas pocket was also included (17% of fractions). For pre-treatment verification, EPID measurements were corrected for linac output variation.

The number of group C errors was higher for *in vivo* dosimetry (23%) than for pre-treatment checks (13%). This is because there are five *in vivo* measurements for each plan, compared to one pre-treatment. Random events and measurement uncertainty will result in variation in the measured dose, and the same plan will have a different dose distribution when calculated on a phantom.

So errors will be a different proportion of the maximum dose (per field). Many will fall on the border of the alert criteria, so more *in vivo* fields are likely to raise an alert. Typical action for a group C error in a clinical protocol would require fixing the error (such as a systematic MLC leaf position or linac output calibration error), or re-planning the intended treatment. Data transfer errors and systematic linac output errors would also be included in this group, however no instances were found in this study.

8.3e Designing a clinical protocol

The chart in Figure 8.7 shows the proposed clinical protocol based on different types of errors encountered for this patient group. Results from the 75 patient plans of this study are also included. An initial check for large errors is first made for each field individually, using the 'very easy' criteria. After applying the medium criteria to low- γ -images of initially three fractions, 64 plans passed. Four plans were alerted due to gas pockets or the table arm in two or three fractions. By checking an additional fraction, each of these passed. It should be noted that in clinical practice the additional measurement should be made at the next treatment fraction. Three plans had group B errors whereby both the pre-treatment check and subsequent fractions revealed no systematic errors.

Table 8-II Discrepancies for 75 IMRT prostate plans, based on the medium alert criteria. Plans were verified both pre-treatment and in vivo for five treatment fractions with EPID dosimetry.

Group	Source	Pre-treatment	<i>In vivo</i>
A # fields		375	1875
	gas pocket	N/A	128 (7%)
	table arm	2 (1%)	77 (4%)
	image acquisition	0 (0%)	21 (1%)
B # fractions		75	375
	gas pocket	N/A	63 (17%)
	patient setup or linac output	corrected	42 (11%)
C # plans		75	75
	dose calculation	10 (13%)	17 (23%)
-	no discrepancy	64 (85%)	9 (12%)

The remaining four plans with systematic dose calculation errors were assessed individually and the errors were not considered clinically relevant. These four plans were also alerted pre-treatment, and the errors were found to be not clinically relevant. Ten plans were alerted pre-treatment (Figure 8.4) six of these passed the *in vivo* check. These discrepancies were close to the criteria, and after three fractions, the *in vivo* dose passed. Therefore only seven plans of this patient group (three from group B, four from group C) would have needed to be checked with a phantom, with such an *in vivo* dosimetry protocol in place.

Over 1.5 years, 75 IMRT prostate patient plans from this study were clinically verified both pre-treatment and *in vivo*, as well as an additional 85 patient plans with *in vivo* dosimetry alone. These 85 patients were not included in the study because routine pre-treatment dosimetry was discontinued. For 83 cases there were no phantom measurements to compare with *in vivo* data for these patients. Two cases, however, did require an additional phantom check and were found to have dose calculation errors. These were corrected (by changing a parameter in the TPS) and the plans were re-optimised.

Figure 8.7 Clinical protocol for EPID in vivo dosimetry. The chart indicates action to be taken in the event of different types of potential discrepancies that persist through at least three treatment fractions. If a plan is alerted due to reasons A or passes the phantom check after reason B, additional fractions should be measured ($n = 4, 5$ etc). The white numbers in grey boxes indicate the number of plans that made it through each stage from the 75 plans tested in this study. Seven plans would have needed a phantom check with such an in vivo dosimetry protocol, instead of all 75 with pre-treatment dosimetry.

8.3f Time

The time required to re-calculate a five-field patient plan with the phantom CT scan, and then send the separate plan to the linac, was approximately 60 min. To set-up the phantom, acquire transit and open EPID images prior to patient treatment (usually performed outside daily linac treatment times) and measure the linac output required an additional 60 min. Analysis involved reading in plan data and EPID images for each segment, calculating the 2D dose distribution and performing the γ evaluation; on average, this required 15 min. Additional time to re-plan, measure and analyse for pre-treatment verification was 2 h 15 min per plan.

To perform *in vivo* dosimetry, no additional time is required at the planning stage. An additional 10 min is required per plan, to acquire one open image (no attenuating medium) per segment. Analysis of each fraction typically takes 10 min, to read in EPID images and run the γ evaluation. An additional 5 min is required at the 1st fraction, to read in plan information, and link measured and calculated fields. For *in vivo* dosimetry, only an additional 15 min + 10 min per fraction was required for analysis of each plan.

8.4 Discussion

The advantages of *in vivo* dosimetry are that a check and record of the actual treatment is gained without additional cost in measurement time. This is only an advantage if the method can be shown to be as accurate, and provide as much information as necessary, as pre-treatment dosimetry. The number of measured *in vivo* fractions required to replace pre-treatment verification is a balance between early detection and workload. There are no precedents or recommendations to follow regarding 2D *in vivo* dosimetry, so our protocols have arisen from clinical experience. Checking three fractions with *in vivo* EPID dosimetry is sufficient to replace pre-treatment verification of every plan for this patient group, allowing average discrepancies up to $\gamma = 0.67$ (corresponding to $\pm 2.0\%/2.0$ mm with γ criteria 3.0%/3.0 mm), maximum discrepancies up to $\gamma = 2.00$ (corresponding to $\pm 6.0\%/6.0$ mm) and permitting 5% of the field within the 20% isodose line to have $\gamma > 1$. When one or more of these criteria fail, the plan is verified in a phantom.

It should be noted that both the acceptance levels applied and the probability that a phantom check is required depend on a number of factors. These include the treatment site, complexity of the treatment delivery, patient positioning, dose delivery and accuracy of the TPS. We would also like to stress that for this study and in our department, *in vivo* dosimetry has only replaced patient-specific phantom checks. It should not be used to replace routine MLC, linac or administration (data transfer) QA, nor provide the only dosimetric verification for the introduction of new techniques or equipment.

Statistics on a small number of fractions is complicated by the probability of large, ignorable errors (group A). An obvious choice would be to take the median. However ignorable outliers (gas pockets, obstructing table arm etc) can be large, give too many false positives and potentially obscure systematic errors. For example, considering three fractions for which discrepancies due to gas pockets occurred during two of the fractions, one would want to weight the assessment on the 'good fraction'.

For the same reason, we did not want to average the reconstructed dose images before comparing them with the plan. Given the γ value is one-sided, the γ values of combined fractions *after* comparison with the plan can be weighted towards the values of better agreement, this is not possible if dose values are first averaged over multiple fractions.

With the aim to suppress clinically irrelevant random errors, and still detect any systematic errors occurring at every fraction, a solution would be to take the minimum γ value per pixel over multiple fractions. A problem with this method is that measurement uncertainty and compensating random events, after enough fractions, will result in a high probability of all γ values converging to zero. Therefore we have chosen to use the low- γ -image, a compromise between the minimum and the median. In principle the precise level of compromise between the minimum and median could be optimised, incorporating measurement uncertainty and probability of outliers. This would be overkill, however, since we are dealing with so few fractions. A half-way approximation was, therefore, considered appropriate.

The strategies proposed in this paper are specifically suited to prostate treatments, since the main changes in homogeneity are due to randomly occurring gas pockets, and these are easy to detect in EPID images. Future investigations will involve incorporating inhomogeneity corrections in our algorithm, as well as addressing other treatment sites. In the end, *in vivo* dosimetry is intended as a safety net, to be the last check in a series of routine QA procedures. It is intended to catch large, clinically relevant errors, so calculation accuracy does not need to match that of the TPS. Currently our tolerance levels are based on 3%/3 mm for prostate treatments, therefore we consider the $\pm 2\%/2$ mm accuracy of our model more than sufficient for routine use of *in vivo* dosimetry.

8.5 Conclusions

A technique has been presented for replacing pre-treatment verification with EPID *in vivo* dosimetry. The number of measured *in vivo* fractions required to replace pre-treatment verification is a balance between early detection and workload. Allowing 5% of the field outside 3.0%/3.0 mm, average discrepancies of $\sim 2.0\%/2.0$ mm and maximum discrepancies of $\sim 6.0\%/6.0$ mm, checking three fractions is optimal to detect similar number of systematic errors with *in vivo* dosimetry as pre-treatment verification. The advantage of EPID *in vivo* dosimetry is that data is acquired during treatment, with little additional time required for measurement and analysis.

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9

General Discussion

9.1 Introduction

The paradigm of radiotherapy dose verification is currently undergoing a shift. It is no longer sufficient to check the planned dose distribution at only one or a few points. Especially with the advent of IMRT, it is considered necessary to check the dose in at least two dimensions.²³ As radiotherapy departments move to become film-less, multi-dimensional digital solutions are being sought. Imaging modalities combining 3D or 4D information from CT, MRI and PET are improving the ability with which we can visualise and delineate target volumes. Image guidance tools such as CT scanners located in the treatment room, mean that 3D or 4D images can be acquired directly prior to treatment and enable target positioning accuracy in the order of millimetres. IMRT, tomotherapy and robotic radio-surgery enable well localised, high-dose target areas. The advantages of high geometric accuracy are, however, severely compromised if the intended radiation dose is not delivered as planned.

9.2 What we can verify with an EPID today

Recent advances in dose verification have focussed on efficiency and accuracy. Therefore radiotherapy departments and vendors world-wide are interested in dosimetry with an EPID. Reports in the literature to date, however, have barely made it beyond the research stage, and very little clinical data has been published. Still, a range of possibilities has been proposed. The particular errors one can detect are heavily dependent on how EPID images are used.

There are two main approaches to 2D EPID dosimetry. In the “forward-approach”, the measured portal image is compared to a predicted dose or photon fluence at the plane of the EPID, whereby the radiation beam is transmitted through air or patient/phantom.^{28,48,60,73,87,97} It is necessary to use either the TPS or an independent dose calculation algorithm (e.g. a Monte Carlo-based system) to estimate the ‘planned dose’ at the EPID level, in order to compare the measured and calculated dose distributions.

In the “back-projection approach”, portal images are used to reconstruct the dose within the patient/phantom.^{2,11,131,132} Back-projection methods are more complicated than those using the forward approach, especially when an independent dose calculation algorithm is used to determine the ‘measured dose’ inside the patient/phantom from EPID measurements.

The main benefit is that the measured dose can then be directly compared with the TPS calculation. Back-projection methods also make it possible to compare EPID results with those of other dosimetry devices in phantoms. Since an image measured behind a patient can be used to determine the dose inside a patient, *in vivo* dosimetry is also feasible with back-projection methods.

Descriptions of the various ways an EPID may be used to verify dose distributions in 2D/3D are summarised in Table 9-I. The methods are divided into two categories: pre-treatment verification (image measured with open beams or behind a phantom) and treatment verification (*in vivo*, image measured behind a patient). Under ‘potential errors’, various possible sources of error in radiotherapy are listed, followed by the type of error that can be verified by each method.

Several types of errors are described as follows:

Machine errors are related to hardware faults, either random or systematic (occurring at every treatment fraction). During pre-treatment measurements, if a random error occurs, it can either be corrected or the measurement can be repeated. Pre-treatment measurements can indicate the type of random errors that might occur, however they cannot be used to predict or detect random errors occurring during actual treatment.

Plan errors relate to problems with the TPS dose calculation algorithm. If the particular error is related to the heterogeneity of the patient anatomy, the error will not be detected by re-calculating the dose in a homogeneous phantom. Errors due to poor modelling of the MLC, however, are likely to be detected. By back-projecting the EPID image and converting pixel values to dose values inside the phantom, an absolute dose comparison can be made between the TPS dose calculation and dose determined with the EPID. Nevertheless, this will only be an approximation of the actual error in the patient at the time of treatment.

Patient errors are specifically related to errors due to changes in the patient's positioning or anatomy from the situation at planning. Verification of the dose based on measurements prior to treatment cannot detect any of these types of errors. For treatment sites where anatomy changes are common, only if the dose is determined in 3D, and is based on a CT scan acquired close to the time of treatment, can one say anything meaningful about the dose delivered to the ROI (i.e. target volumes or organs at risk) or the total dose distribution.

In the past, treatments were fairly standardized, so radiographers, physicists and radiation oncologists knew what to expect in terms of sizes and shapes of treatment fields, and number of monitor units delivered, for a given type of treatment. With the introduction of advanced radiotherapy techniques and higher dose prescriptions, a wide range of parameters is possible, so deviations are less obvious and it is much more difficult to know when something is wrong. The biggest advantage of *in vivo* dosimetry is that it provides a safety net; a last check in a series of routine QA procedures. In the end, the main objective of *in vivo* dosimetry is to detect large errors before they can do serious harm to patients. This holds regardless of whether the event is due to a machine-, plan- or patient related-error.

Even with simple techniques and 'normal' dose prescriptions, things can go wrong. The replacement of pre-treatment verification with *in vivo* dosimetry (in combination with other linac, MLC and data transfer QA measures) could have prevented serious errors in various centres around the world that have occurred in recent years. The International Commission on Radiological Protection (ICRP) recommends that "adequate *in vivo* dosimetry would prevent most accidental exposures."⁸⁸ Cases of mis-administration have been reported recently⁵³ where patients have been treated with unacceptably higher doses over all fractions. Such accidents are usually due to new systems and lack of updated training.

In vivo dosimetry would raise an alarm from the first fraction (after other procedures and checks fail), alerting clinical staff to what often turn out to be a simple errors with drastic consequences. Ideally, when EPID treatment images can be acquired for every fraction and analysed automatically, a check and record of the entire treatment will be guaranteed without any cost to patient treatment time or clinical workflow.

Table 9-1 The different ways an EPID can be used to verify the planned dose distribution. The list outlines various aspects of radiotherapy that can or cannot be checked by each method, and whether the errors that could be detected are systematic or random.

	Pre-treatment verification				Treatment verification		
Potential errors	no phantom	2D behind phantom	2D inside phantom	3D inside phantom	2D behind patient	2D inside patient	3D inside patient
Machine							
Wedge presence & direction	systematic errors	systematic errors			systematic & random errors		
Presence of segment							
MLC leaf position /speed							
Leaf sequencing							
Collimator angle							
Beam flatness & symmetry							
Linac output during treatment	no	no			yes		
Gantry angle	no	yes (for asymmetric phantom)			yes		
Plan							
Steep dose gradients	no	yes			yes		
Dose calculation							
Transmission through leaves & hot spots							
TPS modelling parameters for MLC (e.g. T&G width)							
Patient							
Table arm obstruction	no	no			yes		
Obstructions from immobilisation devices							
Anatomical changes in patient since planning CT							
Anatomical movements during treatment							
Wrong patient during treatment							
Under/over-dose to volumes of interest					no	single plane	yes
Dose distribution in patient					no	single plane	yes

9.3 What we will be able to verify with an EPID in the future

With the well paraded advantages of EPID dosimetry, there are still some limitations in current models. Since images are processed to represent a dose distribution, the measurement is indirect. While most measuring devices require processing to convert a raw reading to the desired form, the potential for error increases as the complexity of the calibration and reconstruction procedure increases. The accuracy of the dose determined from EPID measurements will depend on the accuracy of the dose reconstruction method, in particular on calibration, accuracy of parameters, and the validity of the CT scan used. Our current method may be included in different categories; 2D or 3D inside a phantom or patient, for both pre-treatment or *in vivo* dosimetry (Table 9-I).

Pre-treatment dosimetry will not be able to verify any patient-related errors, since the measurement is performed prior to treatment. Also, the same plan calculated in a patient and a phantom will be different, due to differences in shape and density of the irradiated volumes. Therefore any errors detected in the plan cannot be directly translated as errors received by the patient. They may however serve as an indication that an error exists, as well as give a rough estimate of its magnitude and location. The ‘closeness’ of the measured error pre-treatment to the actual patient situation will depend on how closely the phantom resembles the patient in terms of shape and density.

The most conspicuous limitation of our *in vivo* dosimetry method is that for the sake of simplicity, we do not yet account for inhomogeneities in our model. This is not a significant problem for prostate cases, where the only relevant anatomical inhomogeneities are gas pockets and bone. Variation in the position of bony anatomy within the treatment field region (during and between fractions) is negligible for prostate treatments. A strategy to verify a treatment field and suppress the influence of gas pockets was described in chapter 8. This strategy, however, heavily relies on the fact that their occurrence is random. Other treatment sites, such as head and neck and lung, have inhomogeneous regions that do not change. For this we will need to introduce a correction method, such as one based on an effective path length.

Before an inhomogeneity correction is developed, it is highly likely that the attenuation correction through heterogeneous media will be wrong. Therefore the dose determined in regions of higher or lower density (than soft tissue) will be wrong. An exception is if the radiological path length above and below the reconstruction plane is the same. This is one of the main limitations of the back-projection method in its current form. An alert is still raised for potential errors, however, even if it is not accurately quantified. While these discrepancies can be dismissed if they correspond to high/low density regions visible in the raw EPID treatment images, they will potentially obscure real errors, such as dose calculation or delivery errors. When an inhomogeneity correction is incorporated, the difference between the planned and the measured dose can be more accurately quantified.

Regarding dosimetry of changes in anatomy, it is interesting to consider the case where patients lose weight, i.e. the thickness of the irradiated volume is reduced. The transmission measurement will be accurate, since it is based on a measurement of the patient at the time of treatment. The attenuation factor (determined from CT data), however, will only be correct if the ratio of the isocentre - patient surface distance and the total thickness is the same as that of the CT scan used in the dose calculation model. This is only true if the CT scan that is used is acquired just prior to treatment (e.g. using CBCT) instead of the original planning CT scan (for which the patient thickness was greater). Since the error depends on this ratio, it is less sensitive than if it depended on the absolute change in thickness. Even though the dose is determined incorrectly, because the wrong attenuation factor is used, an alert will be raised and warn of a potential error.

9.4 Acceptance criteria for IMRT in 2D

Decision rules for pre-treatment and *in vivo* dosimetry become increasingly complicated when assessing more dimensions, yet at the same time they become increasingly more intuitive. In the past rules have been simplified by the fact that they have been based on measurements at a point. It is easy to assign pass/fail criteria, to only check discrepancies if the measurement is different from the planned dose by, for example, more than $\pm 5\%$.¹ It is difficult to tell, however, if the entire dose distribution is acceptable and if errors occur, what the clinical consequences will be.

Determining acceptance criteria for measurements in multiple dimensions is more complicated than at a point (or a number of points), not only because more information is available to quantify and compare, but also because information from multiple fractions should be combined when measuring the dose *in vivo* (chapter 8). On the other hand, the task is more intuitive since one can first determine the location of the error in the patient, find out which volumes of interest (organs at risk or target volumes) are involved and then apply meaningful constraints for individual volumes of interest.

To quantify the agreement between a calculated 2D dose distribution and that measured using the EPID, we have used the gamma index, as presented by Low *et al.*⁶⁹ This method combines dose difference (ΔD) and distance-to-agreement (DTA) criteria for comparing two dose distributions. When defining tolerance limits, they can be expressed as ΔD_{tol} and DTA_{tol} , respectively. The dose difference can be expressed in several ways, such as relative to the local dose or the maximum dose of either the distribution being evaluated or the reference distribution. The DTA is the distance between a measured dose point and the nearest point of the same dose value in the calculated dose distribution. Combining these two metrics allows for a fair comparison between dose distributions containing low- and high-dose gradient regions. In low dose gradient regions, the agreement can be more easily quantified by considering ΔD . In high-dose gradient regions, large dose differences can exist with very low DTA values, so one would not want to fail the measurement based on ΔD values alone. The gamma index combines both ΔD and DTA into one quadratic form.

There is no consensus, however, regarding acceptance criteria in clinical practice. The protocols resulting from this thesis have therefore evolved from clinical use. In our department, we use ΔD_{tol} relative to the maximum dose per field, instead of the local dose difference. This is because we wanted to focus on verification of the high dose region. The disadvantages of using the local dose difference criterion over an entire field are that a uniform increase or decrease in dose (to a change in delivered number of MUs or linac output) would appear as a large relative error in low dose regions, and a small relative error in high dose regions. Both situations could potentially lead to false positives or false negatives, respectively. Of course if one wants to verify the dose in a particular region of the field, then the local dose difference is more useful and meaningful.

By using a global ΔD_{tol} , and the same numerical value for ΔD_{tol} and DTA_{tol} , γ values correspond linearly to absolute ΔD and DTA values over the entire dose distribution. For example, if $\Delta D_{\text{tol}} = 3\%$ and $DTA_{\text{tol}} = 3 \text{ mm}$, and the maximum dose in the distribution being evaluated is 80 cGy, then a γ value of 0.83 corresponds to DTA of 2.5 mm or ΔD of $2.5\% = 2 \text{ cGy}$, regardless of whether the dose is high or low. This makes it straightforward to perform statistics over the entire evaluated area (or volume), rather than using a local ΔD_{tol} .

To evaluate the gamma image of each field, it was not considered sufficient to only check the percentage of points that failed the 3% (of maximum field dose) and 3 mm DTA gamma limits ($P_{\gamma < 1}$). This is because $P_{\gamma < 1}$ says nothing about the magnitude of the errors outside 3%/3 mm tolerance. Childress *et al.*²⁵ evaluated 16 plans with deliberate errors, testing seven different scalar metrics designed to measure the agreement between two 2D dose distributions. These included average γ , percentage of points with $\gamma < 1$ and parameters based on similar comparison methods. They found no single metric had sufficient detection accuracy to be used as the sole clinical analysis technique, but suggested that a combination of 2 or 3 different parameters would suffice. An additional issue to consider when verifying treatments field-by-field is the contribution of the single field to the total dose distribution. If a relatively large error is detected in a beam contributing less than 10% of the total dose, the clinical relevance of the error is usually low.

Development of our clinical protocol originated in the assessment of test cases (where no deliberate errors were introduced). For each field, three parameters were calculated within an area the γ image bound by the 20% isodose line of the planned field dose. These parameters were the average and the maximum gamma values (γ_{avg} and γ_{max}), and $P_{\gamma < 1}$. Stock *et al.*¹¹⁷ reported use of a similar combination of γ parameters, supporting the case that ΔD and DTA are not sufficient to adequately verify plans in at least two dimensions. Calculating these three parameters was useful for a number of reasons. The average (γ_{avg}) and maximum (γ_{max}) parameters serve to limit the proportion and magnitude of the discrepancy allowed for the points with $\gamma > 1$. Even if all points compared are within 3%/3 mm, it is useful to know if the average difference is closer to 0.5%/0.5 mm or 2.5%/2.5 mm (for example).

When a small percentage of points exceeds 3%/3 mm, one would want to know by how much, and over how large an area they extend. If γ_{avg} , γ_{max} or $P_{\gamma<1}$ exceeds the pre-set criteria, then an alert is raised and one can check the magnitude and form of the discrepancy, and elucidate its source. More importantly, anatomical features are visible within the field, and it is possible to locate the discrepancy with respect to target volumes and organs at risk. The radiation oncologist responsible for the patient in question can then determine if the discrepancy is clinically relevant, taking into account the location, size and source of the discrepancy.

Additional benefits of the parameters (γ_{avg} , γ_{max} and $P_{\gamma<1}$) were that comparison with film became relatively easy and it was more straightforward to assess the results of a large patient group. Since our method has been introduced into the clinic, it has become a simple and effective means of identifying potentially problematic plans; alerting physicists, radiographers and radiation oncologists (where appropriate) when errors exceeded pre-set criteria. Therefore for verification of all IMRT prostate plans since February 2005 in our department, it was decided that for each field the following three criteria should be met: the average difference between the TPS and EPID dose distributions should be less than 2% or within 2 mm, maximum differences should not exceed 6% or 6 mm and 95% of points should be within 3% or 3 mm. The tolerance limits for each parameter were largely based on measurement uncertainties and approved by clinical staff. Once a technique was developed to quantify the 2D verification for a single treatment fraction, the next step was to combine data from multiple fractions, which was extensively described in Chapter 8.

9.5 Beyond 2D EPID dosimetry

There are three elements that ensure good radiotherapy: accurate tumour identification, conformal planning and precise treatment delivery. With the advent of biological imaging, the radiotherapy community is beginning to get a grasp of the first step.

IMRT has ensured that the middle step is well on the way. As for the third step, we are only just beginning to get somewhere. Since radiotherapy is treating something one cannot directly see, image-guided radiotherapy and dose verification are essential tools that must progress hand in hand. The opportunities for dose verification based on EPID images are abundant, however reports of clinical use are limited to a few radiotherapy centres world-wide.

3D dose reconstruction based on EPID images has been shown to be feasible.^{2,45,58,65,79,81,91,104,115,121,133} The hardware (EPID) is currently available in most clinics, only additional software is necessary. A limitation, however, is the additional time required to reconstruct the dose in 3D, an issue rarely addressed in reported studies since all methods are still at the research level and not used clinically.

Regardless of the method chosen, more work is necessary to find a solution that is fast, accurate, independent of the treatment planning system and able to detect a wide variety of potential errors that would affect patient treatments. The advantages of 3D over 2D dose reconstruction include being able to determine the dose to volumes of interest, compare dose-volume histograms (DVHs) and examine dose distributions at arbitrary planes. Common dose comparison methods include dose profiles, isodose lines at arbitrary planes and the gamma evaluation method. While determining pass/fail criteria for volumes may be more intuitive than for points, lines or planes, it is not trivial.

Biological models and extensive randomised trials provide probability distributions for tumour control in target volumes and risk of complication for sensitive organs, based on dose levels and fractionation. With more experience at measuring the dose in 3D over multiple fractions, in the future these models can be used to assign tolerance limits for measurement of particular volumes. Scalar verification parameters and DVHs combining information from the first few fractions can be used to verify that the treatment is being delivered as planned.

As mentioned earlier, the next stage in the development of our work is to account for inhomogeneities in the dose reconstruction model. Not only would this improve the accuracy of our dose verification method, but the protocol could then incorporate changes in anatomy (between treatment time and planning), and also determine any changes in dose over many fractions. To this end, a CT scan acquired within minutes prior to treatment, e.g. using CBCT, could provide up-to-date anatomical information and replace the planning CT scan ('planCT') in the EPID dosimetry algorithm. This would be relevant for large changes in tumour size, weight loss, presence of gas pockets (though this can change within minutes¹⁰⁹) and patient positioning errors. CBCT images are not currently used to calculate dose, since voxel values are not linearly related to electron density, necessary for dose calculation. One solution would be to modify the planCT data to match the CBCT data^{64,98}, so that the 'new' planCT would resemble the patient just before treatment. This could be done by warping soft-tissue structures of the planCT and replacing correspondingly located electron density values, such as that of tissue with that of air, in the case of air cavities in the CBCT that were not present in the planCT.

When the planned treatment can be calculated on a CBCT, four different comparisons can be made combining dose data and CT data. Both the planned dose and the *in vivo* dose can be calculated based on either the planCT or the CBCT. First, the plan and the planCT will (obviously) give the planned dose. Secondly, the plan and the CBCT will isolate the influence of inter-fractional anatomy changes on the planned dose distribution. Thirdly, the *in vivo* dose and the planCT will combine discrepancies due to anatomical changes and delivery errors. This latter scenario was described in chapter 8 of this thesis, along with strategies to deal with combination of multiple sources of information. Finally, the *in vivo* dose and the CBCT will raise the flag to any delivery errors. A potential 'gap' in information occurs when the patient experiences intra-fraction anatomy variation. In this case the patient's anatomy at the time of treatment (and *in vivo* measurement) will differ from the time of CBCT acquisition. Examples include respiratory motion, rapidly changing gas pockets or patient shifting on the couch between or during scanning and treatment. Since treatment EPID images also contain anatomy information, only the more subtle occurrences of this kind would not be detectable.

In the future, the dose reconstruction and γ evaluation could be extended to 4D, to incorporate intra-fractional differences. Frames acquired during treatment could be individually converted to a measured dose volume rendering a 4D dose distribution of the fraction treatment. This would be especially useful to assess changes in dose to treatment sites where respiratory motion plays a role. Another issue to consider is inter-fractional differences. A strategy to assess this is warping of dose distributions from multiple fractions to account for translations, rotations and deformations of relevant structures. This strategy involves mapping dose pixels/voxels of the original dose distribution to corresponding location of the structure at the time of treatment. In this way, a cumulative dose distribution can be obtained over the entire treatment providing more detailed picture of the resulting dose delivered.

9.6 and one more thing ... Ghosting and IMRT

Image lag and ghosting effects result in an under-dosage of the EPID at shorter irradiation times for single fields, relative to that of calibration fields (typically 30s). Despite our conclusive results confirming the dependence of the EPID signal on irradiation time for non-segmented fields, an anomaly arose. The 'pragmatic correction factor', as discussed in Chapter 2, was not found to be useful for IMRT measurements. Our proposed theory is that for segmented IMRT, since images of each segment are acquired in quick succession, the dose that is 'missed' due to lag of one segment image is 'collected' in successive segment images. Image lag typically lasts for 10-20 s, and there are often 4-6 segments for each field lasting 2 to 10 s each. The total integrated dose over one field would therefore include the dose from the irradiation time of each segment, as well as dose from the lag of the first few segments. Therefore segmented IMRT fields 'correct themselves', without the need of an additional ghosting correction. For prostate treatments, the first 2 or 3 segments are typically longer than the later segments, so the dose of lag that is still missed from the later segments is negligible.

We do not yet, however, have a full grasp of the consequences for other situations. This includes fields whose segments do not follow the same pattern (i.e. long segments followed by a few short segments), or dynamic IMRT. Further investigation is necessary to solve this problem for IMRT in general. Such investigations would need to consider the irradiation time and sequence over the entire panel and, for example, develop a pixel-based correction strategy.

9.7 Conclusions of the thesis

EPIDs have enormous potential to solve the myriad of radiotherapy QA problems that exist today. From this thesis, it can be concluded that with proper calibration, the *a*-Si EPID is suitable for reliable and accurate absolute dose verification. In addition, the EPID can replace traditional dosimetry devices to verify patient plans pre-treatment, because it is more efficient and at least as (in some cases more) accurate than film and ionisation chamber measurements. Using the back-projection method, the EPID can be used to verify the actual dose delivered to the patient during treatment in 2D. For prostate treatments in our department, by applying decision rules over three fractions measured *in vivo*, an alert is raised for potentially problematic plans, minimising the risk of false negatives and false positives. Therefore time is saved by obviating the need for routine pre-treatment verification. More importantly, the delivered dose can be checked at the time of treatment. Currently the algorithm is being developed to extend the method to verification of other treatment sites and include information from CT scans acquired just prior to treatment. These advances will result in a large volume of verification data and providing an effective, efficient and accurate radiotherapy ‘safety net’. This net provides radiation oncologists and physicists with the confidence to raise dose prescriptions, introduce new techniques and advance radiotherapy to achieve better cure rates for cancer patients.

10

Summary / Samenvatting

Summary

The development of new treatment techniques such as intensity-modulated radiotherapy (IMRT) has enabled radiation oncologists to deliver higher dose levels to tumour cells, while sparing surrounding healthy tissue. These sophisticated advances in radiotherapy, as well as the occasional use of unusual treatment strategies, run a large risk that the dose is not delivered to the patient as planned. Therefore effective dose verification is necessary up until the time of treatment.

The purpose of this thesis was first to investigate the dosimetric characteristics of a new detector, the amorphous silicon electronic portal imaging device (*a*-Si EPID). Secondly, to further develop an algorithm that determines the 2D dose distribution within a patient or phantom based on EPID images of treatment fields. Thirdly, to design a verification method that saves time without sacrificing accuracy, by developing clinical protocols for the verification of IMRT with an EPID, both prior to and during radiotherapy. The final objective was to introduce *in vivo* dosimetry into the clinic, obtain an overview of the nature and extent of discrepancies found, and develop strategies to detect clinically relevant errors.

Dosimetric characteristics of the EPID are presented in chapter 2. EPID measurements were performed using three *a*-Si detectors equipped on two linear accelerators with a wide range of photon energies. There was an over-response of the EPID signal of up to 18%, with no additional build-up layer over a phantom-EPID air gap range of 10 to 60 cm. The addition of a 2.5 mm thick copper plate sufficiently reduced this over-response to within 1% at clinically relevant patient-detector air gaps (>40 cm). The EPID had an under-response at short beam times due to ghosting effects, which depended on the irradiation time. With an appropriate build-up layer and corrections for dose per pulse, PRF and ghosting, we found that the variation in the *a*-Si EPID sensitivity can be reduced to well within $\pm 1\%$.

While many other studies have reported dosimetric characteristics of *a*-Si EPIDs, they are not all consistent where ghosting and image lag are involved. Some studies ascribed a non-linear signal to gain ghosting and image lag. Other reports, however, state the effect is negligible. Chapter 3 extends the study of ghosting effects to compare the signal-to-monitor unit (MU) ratio for three different brands of EPID systems. All EPIDs exhibited a relative under-response for beams of few MUs; giving 4 to 10% lower signal-to-MU ratio relative to that of 1000 MUs. This under-response is consistent with ghosting effects due to charge trapping.

A reproducible response is essential for any dosimeter, and so the long term stability of the *a*-Si detector is investigated in chapter 4. As direct parties to stability issues, temperature dependence and the use of a dynamic dark field (for back-ground signal correction) were investigated. Temperature fluctuations were corrected for by introducing a continually updated dark-field correction. Following this correction, excellent stability of the response over the entire panel of all imagers was found to be 0.5% (1 SD), up to 23 months. The *a*-Si EPIDs tested therefore have a very stable response and this compelled us to conclude that EPIDs are well suited for dosimetry.

Then came the time to approach our existing EPID dosimetry algorithm, which was designed for non-segmented fields and a liquid-filled EPID, and modify it. The algorithm was re-vamped for *a*-Si EPIDs and IMRT, as described in chapter 5. In accordance with the back-projection method, pixel values of the transit dose image were processed using scatter kernels (to account for scatter within the EPID and patient), the scatter-to-primary ratio (to account for scattered radiation from the patient to the EPID), the inverse square law and the measured transmission, yielding the 2D absolute dose distribution in the reconstruction plane of the patient. The accuracy of the approach was tested by comparing the dose distribution of a prostate IMRT plan measured in a phantom with EPID and film. For this purpose, the γ evaluation method was used with a dose-difference criterion of 2% of dose maximum and a distance-to-agreement criterion of 2 mm. Excellent agreement was found between EPID and film measurements over all fields.

With verification results of these plans and those of other beam energies and treatment sites, we then concluded that our modified algorithm was able to accurately predict the dose in the mid-plane of a homogeneous slab phantom. EPID dosimetry is, therefore, a reliable and potentially fast tool to check the absolute dose in two dimensions inside a phantom for IMRT fields.

Spurred on by such positive results, our new verification tool was soon introduced into the clinic. Further motivation for such swift progress was the addition of a new treatment planning system and two newly commissioned linacs. The results of verification for the first 20 IMRT prostate plans are presented in chapter 6. Dose distributions compared in 2D were evaluated using the γ index, with dose difference and distance-to-agreement tolerance limits of 3%/3 mm. The average gamma (γ_{avg}), maximum gamma (γ_{max}) and percentage of points in agreement ($P_{\gamma<1}$) were calculated for each field within an area bound by the planned 20% isodose line. Fields of the first 10 patient plans were measured with EPID and film in a phantom, at gantry set to 0°. All 50 fields agreed well for EPID vs. film, with $\langle\gamma_{avg}\rangle = 0.16$, $\langle\gamma_{max}\rangle = 1.00$ and $\langle P_{\gamma<1}\rangle = 100\%$. For all 20 patient plans, EPID and ionisation chamber measurements were acquired using the original gantry angles. The average ratio of measured dose values was 1.00 ± 0.01 (1 SD), and both were systematically 1% lower than planned. We could not then but conclude that the EPID was a suitable replacement of these dosimetry devices for IMRT pre-treatment verification. Furthermore, seven plans revealed under-dosage (5% to 16%), occurring at the junction of abutting segments. Systematic errors were detected using EPID dosimetry, resulting in the adjustment of a TPS parameter and alteration of two clinical patient plans. One set of EPID measurements (i.e. one open and transit image acquired for each segment of the plan) was deemed sufficient to check each IMRT plan in 2D field-by-field and at the isocentre for the total plan, rendering a useful, efficient and accurate dosimetric tool.

Taking a small side-step to dosimetry, chapter 7 demonstrates how EPID localisation images can be used to look at patient anatomy changes throughout the course of treatment. The purpose of this study was to make an inventory of anatomical changes observed for three treatment sites and show examples of dosimetric consequences, which was not considered un-useful for interpreting *in vivo* dosimetry data too. Localisation images were acquired weekly prior to radiotherapy with an EPID. A series of 'difference images' was created for each patient by subtracting the first localisation image from that of subsequent fractions. Images from 81 lung, 40 head and neck and 34 prostate cancer patients were classified according to the changes observed.

Progressive changes were detected for 57% of lung and 37% of head and neck cancer patients studied. Random changes were observed in 37% of lung, 28% of head and neck and 82% of prostate cancer patients. Two plans were re-calculated with repeat CT scans acquired after 4 weeks of treatment and compared with the difference images of the corresponding days. For the lung case, an increase of 10.0% in EPID dose due to tumour shrinkage corresponded to an increase of 9.8% in mean lung dose. Gas pockets in the rectum region of the prostate case increased the EPID dose by 6.3%, and resulted in a decrease of the minimum dose to the planning target volume of 26.4%. From this study we learnt the value of difference images as an efficient means of detecting anatomical changes for various treatment sites. They also serve to indicate the discrepancies that an *in vivo* dosimetry algorithm that does not account for inhomogeneities might expect to find.

Back to dosimetry and along-side clinical pre-treatment verification of the first IMRT prostate patients in the clinic, images of treatment fields for the same patients were also being acquired during treatment. Comparing these *in vivo* dose measurements with the patient plan provided a rich source of data with which to compare two dosimetry methods. Chapter 8 describes the comparison between pre-treatment and *in vivo* dosimetry, and how the latter replaced the former in the clinic for IMRT prostate cancer patients. We had 75 treatment plans to investigate, after which routine pre-treatment dosimetry was dropped from our clinical protocol. Planned and EPID dose values were compared at the isocentre and in 2D using the γ index with tolerance values of 3%/3 mm.

Planned and EPID isocentre dose values were, on average, within 1% (1 SD) of the total plan for both pre-treatment and *in vivo* verification. An alert was raised for 10 pre-treatment checks with clear but clinically irrelevant errors. Multiple *in vivo* fractions were combined by assessing gamma images comprising median, minimum and low (intermediate) pixel values of 1 to 5 fractions. The low gamma values of 3 fractions gave similar results as pre-treatment verification (11 plans with discrepancies detected). Additional time for verification was ~2.5 h per plan for pre-treatment checks and 15 min + 10 min/fraction for *in vivo* dosimetry. This study showed that *in vivo* EPID dosimetry is an efficient alternative to pre-treatment verification for prostate IMRT treatments. The number of *in vivo* fractions used is a balance between accurate detection and workload. It was decided that checking three fractions *in vivo* is appropriate for this patient group, fulfilling the clinic's wish for an efficient and accurate dosimetry system for all of our IMRT prostate cases.

To end, a general discussion is presented in chapter 9, delving into the subject of errors that can be detected in radiotherapy; namely various methods of employing EPID dosimetry. *In vivo* dosimetry of an optimal number of treatment fractions, in 2D or preferably 3D, is a good way to ensure the patient really received the treatment as planned.

Samenvatting

De ontwikkeling van nieuwe bestralingsmethoden voor kanker zoals intensity-modulated radiotherapy (IMRT) stelt oncologen in staat om een hogere dosis straling toe te dienen aan tumoren zonder omringend gezond weefsel extra te beschadigen. Deze vooruitgang, in combinatie met het in bepaalde gevallen toepassen van ongebruikelijke bestralingsplannen, kunnen er toe leiden dat de van tevoren berekende dosis voor een patiënt niet juist wordt toegediend. Daarom is verificatie van de toegediende dosis nodig tijdens de gehele behandeling.

Het eerste doel van dit proefschrift was om de dosimetrische eigenschappen te onderzoeken van een nieuw type detector: de “amorphous silicon electronic portal imaging device” (a-Si EPID), een elektronische camera waarmee twee-dimensionale (2D) doorlichtingsbeelden gemaakt kunnen worden. Daarnaast is gewerkt aan het verder ontwikkelen van een algoritme om de 2D dosisverdeling in een patiënt of fantoom te bepalen en een verificatiemethode te ontwikkelen die tijd bespaart zonder aan nauwkeurigheid in te boeten. Hiervoor zijn klinische protocollen ontwikkeld ten behoeve van de verificatie van een IMRT bestralingsplan met een EPID, zowel vóór als tijdens de bestraling. Het laatste was bedoeld om met behulp van *in vivo* dosimetrie de aard en omvang van de dosimetrische afwijkingen in kaart te brengen en om op basis daarvan strategieën te ontwikkelen waarmee klinisch relevante fouten gedetecteerd kunnen worden.

In hoofdstuk 2 worden de dosimetrische kenmerken van de EPID gepresenteerd. EPID metingen werden uitgevoerd met drie verschillende a-Si detectoren op twee lineaire versnellers met een breed bereik van fotonenergieën. Zonder extra opbouw op de EPID was er een te hoge respons van het EPID signaal tot 18% over een fantoom-EPID afstand van 10 tot 60 cm. De toevoeging van een 2.5 mm dikke koperplaat bracht de respons voor klinisch relevante patiënt-EPID afstanden (>40 cm) terug tot minder dan 1%. Ten gevolge van zogenaamde “ghosting effecten” had de EPID een te lage respons bij korte bestralingstijden, waarbij de mate afhing van de bestralingstijd. Met de juiste opbouwlaag en correcties voor de dosis per puls, puls frequentie en ghosting effecten, bleek dat de variatie in de gevoeligheid van de EPID gereduceerd kon worden tot ruim binnen $\pm 1\%$.

In een aantal andere studies zijn de dosimetrische kenmerken van de a-Si EPID beschreven. Deze gegevens zijn echter niet consistent ten aanzien van “ghosting” and “image lag”. Een aantal studies benoemt een niet-lineair signaal als oorzaak voor de toename van “ghosting” en “image lag”. Andere studies stellen echter dat de effect verwaarloosbaar is. In hoofdstuk 3 wordt het onderzoek naar ghosting effecten uitgebreid ten behoeve van een vergelijking van de signaal/monitor unit (MU) verhouding voor drie verschillende EPID merken. Alle EPIDs lieten een te lage respons bij bestraling met een paar MU's zien: een 4 tot 10% lagere signaal/MU verhouding ten opzichte van 1000 MU's. Deze te lage respons is consistent met ghosting effecten ten gevolge van “charge trapping”.

Een reproduceerbaar signaal is essentieel voor elke vorm van dosimetrie. Derhalve is de stabiliteit op lange termijn van de a-Si detector onderzocht in hoofdstuk 4. De temperatuursafhankelijkheid van het signaal en het gebruik van een dynamisch donkerbeeld (ten behoeve van achtergrondsignaal correctie) zijn onderzocht. Fluctuaties in temperatuur zijn gecorrigeerd door de introductie van een voortdurend aangepast donkerbeeld. Na toepassing van deze correctie werd een uitstekende stabiliteit van het signaal gevonden over het gehele oppervlak van de detectoren: 0.5% (1 SD) tot 23 maanden. De geteste a-Si EPIDs zijn dus zeer stabiel en op basis hiervan hebben wij geconcludeerd dat EPIDs zeer geschikt zijn voor dosimetrie doeleinden.

Vervolgens is het bestaande EPID dosisberekeningsalgoritme, dat oorspronkelijk was ontwikkeld voor niet-IMRT behandelingen en voor een ander type EPID, bekeken en gemodificeerd. Het algoritme is aangepast voor een a-Si EPID en IMRT volgens een methode die in hoofdstuk 5 is beschreven. Volgens de “terugprojectie” methode worden de doorlichtingsbeelden gecorrigeerd met zogenaamde “scatter kernels” (correctie voor verstrooiing (a) in de EPID, (b) van de patiënt naar de EPID en (c) in de patiënt). Verder wordt er rekening gehouden met de verzwakking door de patiënt en de afstand van de patiënt tot de EPID. Dit levert uiteindelijk de absolute dosisverdeling in de patiënt in het reconstructievlak op. De nauwkeurigheid van deze methode werd getest door de dosisverdeling van een IMRT plan voor prostaatbestraling in een fantoom zowel met EPID als met film te bepalen en te vergelijken met het plan.

Hiervoor hebben we gebruik gemaakt van de γ evaluatiemethode met een dosisverschilcriterium van 2% van de maximale dosis en een afstandscriterium van 2 mm. Uitstekende overeenstemming werd gevonden tussen EPID- en filmmetingen voor alle velden. Op basis van de verificatieresultaten van deze plannen en die van andere bundelenergieën en tumorgroepen hebben wij geconcludeerd dat ons gewijzigd algoritme in staat was om de dosis in het middenvlak van een homogeen fantoom accuraat te voorspellen. EPID dosimetrie is derhalve een betrouwbaar en efficiënt hulpmiddel om de absolute dosis in een fantoom voor IMRT velden te controleren.

Vanwege de positieve resultaten is ons nieuwe verificatiehulpmiddel snel geïntroduceerd in de kliniek. Extra motivatie voor een snelle implementatie was de ingebruikname van een nieuw planningssysteem en twee nieuwe lineaire versnellers. De resultaten van de verificatie van de eerste twintig IMRTprostaatplannen worden gepresenteerd in hoofdstuk 6. 2D dosisverdelingen van EPID en plan zijn geëvalueerd met de γ evaluatie methode, waarbij dosis- en afstandscriteria van 3% en 3 mm werden gehanteerd. De gemiddelde gamma (γ_{avg}), maximale gamma (γ_{max}) en percentage van overeenstemmende punten ($P_{\gamma<1}$) zijn berekend voor elk veld binnen een gebied dat begrensd werd door de geplande 20% isodosislijn. Velden van de eerste 10 patiëntenplannen werden gemeten met EPID en film in een fantoom. Voor alle 50 velden was de EPID dosis in overeenstemming met film, met $\langle \gamma_{avg} \rangle = 0.16$, $\langle \gamma_{max} \rangle = 1.00$ and $\langle P_{\gamma<1} \rangle = 100\%$. De gemiddelde verhouding van de gemeten dosiswaarden in het isocentrum was 1.00 ± 0.01 (1 SD), waarbij beide stelselmatig 1% lager waren dan voorzien. De conclusie was derhalve onontkoombaar dat de EPID een geschikte vervanging vormt van de dosimetrie apparaten voor IMRT pre-treatment verificatie. Ook lieten zeven plannen een onderdosering zien (van 5 tot 16%) bij de aansluiting van segmenten zien. Vanwege deze detectie van systematische fouten door de EPID dosimetrie procedure is een parameter in het treatment-planning systeem aangepast en zijn twee klinische patiëntenplannen gewijzigd.

Het werd als voldoende beschouwd om één set van EPID metingen (dwz. één beeld met, en één beeld zonder patiënt of fantoom, verkregen voor ieder segment van het plan) te gebruiken voor controle van een IMRTplan in 2D. Voor elk plan werden de afzonderlijke velden en de dosis in het isocentrum vergeleken. Het resultaat is een bruikbaar, efficiënt en accuraat dosimetrisch systeem.

In hoofdstuk 7 wordt een uitstapje gemaakt van de dosimetrie. In dit hoofdstuk wordt aangetoond hoe EPID localisatiebeelden gebruikt kunnen worden om te kijken naar anatomische veranderingen bij patiënten gedurende de behandeling. Het eerste doel van deze studie was om een inventarisatie te maken van anatomische veranderingen die zijn waargenomen bij drie tumorlocaties. Een tweede doel was om voorbeelden van dosimetrische gevolgen te tonen, zeker omdat dit nut zou kunnen hebben bij de interpretatie van *in vivo* dosimetriegegevens. Localisatiebeelden werden wekelijks voor de radiotherapie met een EPID verzameld. Een serie 'verschilbeelden' werd gemaakt voor elke patiënt door het eerste localisatiebeeld af te trekken van die van opvolgende fracties. Beelden van 81 long-, 40 hoofd-hals- en 34 prostaatkankerpatiënten zijn geclassificeerd naar de waargenomen veranderingen.

Progressieve veranderingen werden gevonden bij 57% van de bestudeerde long- en 37% van de bestudeerde hoofd-halskankerpatiënten. Willekeurige veranderingen werden gevonden bij 37% van de long-, 28% van de hoofd-hals- en 82% van de prostaatkankerpatiënten. Twee plannen zijn opnieuw berekend op basis van nieuwe CT scans die 4 weken na behandeling plaatsvonden en werden vergeleken met verschilbeelden van de corresponderende dagen. In het geval van de longkankerpatiënten correspondeerde een toename van 10.0% in EPID-dosis t.g.v tumorreductie met een toename van 9.8% in de gemiddelde longdosis. Gasbellen in het rectum van een prostaatkankerpatiënt zorgden voor een toename van de EPID dosis met 6.3% en resulteerde in een afname van de minimale dosis voor het geplande doelvolume van 26.4%. Uit deze studie hebben we geleerd dat het gebruik van verschilbeelden een efficiënte manier is om anatomische veranderingen voor verschillende tumorlocaties waar te nemen. Het stelt ons ook in staat om de verschillen te bepalen die gevonden zouden kunnen worden met een *in vivo* dosimetriealgoritme dat geen rekening houdt met inhomogeniteiten.

Terug naar dosimetrie en specifiek naar de klinische pre-treatment verificatie van de eerste IMRT prostaatpatiënten. Beelden voor dezelfde patiënt werden zowel pre-treatment als tijdens de behandeling opgenomen. Het vergelijken van deze *in vivo* dosismetingen met het patiëntenplan was een rijke bron van gegevens voor de vergelijking van deze twee dosimetriemethoden. Hoofdstuk 8 beschrijft de vergelijking van pre-treatment en *in vivo* dosimetrie. Ook wordt beschreven hoe de laatste methode de eerste verving in de kliniek voor verificatie van de behandeling IMRT prostaatkankerpatiënten. Nadat 75 behandelplannen pre-treatment én *in vivo* onderzocht waren, werd pre-treatment dosimetrie weggelaten uit het klinische protocol.

Geplande en EPID dosiswaarden werden vergeleken in het isocentrum en in 2D met behulp van de γ -index met tolerantiewaarden van 3%/3 mm. Geplande en EPID dosiswaarden in het isocentrum waren gemiddeld overeenstemmend binnen 1% (1 SD) van het totaalplan voor zowel pre-treatment als *in vivo* verificatie. Een waarschuwing werd gegeven bij 10 pre-treatment controles met duidelijke, maar klinisch irrelevante fouten. Meerdere *in vivo* fracties zijn gecombineerd door het analyseren van gammabeelden die mediane, minimum en “lage” (tussen mediaan en minimum) pixelwaarden van 1 tot 5 fracties bevatten. De lage gamma waarden van 3 fracties lieten vergelijkbare resultaten zien als pre-treatment verificatie (11 plannen met gedetecteerde verschillen). De extra tijd voor pre-treatment verificatie was ~2.5 uur per plan en 15 min + 10 min/fractie voor *in vivo* verificatie. Deze studie liet zien dat *in vivo* EPID dosimetrie een efficiënt alternatief voor pre-treatment verificatie van prostaat IMRT behandelingen is. Het aantal *in vivo* fracties dat geanalyseerd wordt, is een compromis tussen precieze detectie en werklust. Besloten werd dat het controleren van drie fracties *in vivo* geschikt is voor deze patiëntengroep, tegemoetkomend aan de wens van het ziekenhuis voor een efficiënt en accuraat dosimetrie systeem voor al onze IMRT prostaat patiënten.

Aan het einde van dit proefschrift wordt in hoofdstuk 9 een algemene discussie gepresenteerd, over welke soort fouten in de radiotherapie gedetecteerd kunnen worden met verschillende methoden van EPID dosimetrie. *In vivo* dosimetrie met een optimaal aantal fracties, in 2D of bij voorkeur in 3D, is een goede manier om te garanderen dat patiënten de geplande behandeling ook daadwerkelijk krijgen.

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Abbreviations

3D-CRT	three-dimensional conformal radiotherapy
AP	anterior-posterior (direction)
a-Si	amorphous silicon
CAX	central axis
CBCT	cone-beam computed tomography (scan)
CT	computed tomography
ΔD	dose difference
DRR	digitally reconstructed radiograph
DTA	distance-to-agreement
DVH	dose-volume histogram
EPID	electronic portal imaging device
fps	frames per second
GTV	gross tumour volume
IGRT	image-guided radiotherapy
IMRT	intensity-modulated radiotherapy
kV	kilo-volt
Li-Fi	liquid-filled ionisation chamber
MLC	multileaf collimator
MRI	magnetic resonance imaging
MU	monitor units
MV	mega-volt
NTCP	normal tissue control probability
OAR	organ at risk
PDI	portal dose image
PET	positron emission tomography
planCT	planning CT scan
PMMA	polymethylmetacrylate
PRF	pulse-repetition frequency
PS	polystyrene
PTV	planning target volume
QA	quality assurance
ROI	region of interest
SD	standard deviation
SDD	source-detector distance
SSD	source-surface distance
TCP	tumour control probability
TLD	thermoluminescent dosimeter
TPS	treatment planning system

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	2	4	6	8	10	12	14	16	18	20										
	M	N	A	T	H	A	L	I	E	K	D	O	U	G	L	A	S	N	F	F
2	A	A	O	K	W	E	V	S	A	E	M	E	L	I	E	J	E	A	S	I
	N	X	D	E	D	O	J	T	L	N	K	S	S	D	R	B	C	C	A	Y
4	N	A	Q	D	L	I	R	U	Y	N	M	A	Y	R	R	E	K	L	I	O
	A	V	Y	X	A	X	V	A	P	E	A	E	I	E	P	B	E	H	R	M
6	N	E	I	R	O	L	F	R	C	T	R	O	G	E	J	X	E	O	F	R
	T	U	Z	I	M	N	E	T	A	H	C	K	T	L	A	G	B	N	G	E
8	G	V	K	D	B	N	F	N	I	Z	O	E	A	N	C	R	N	H	M	L
	N	I	T	S	U	J	D	G	A	N	R	A	D	N	I	X	N	L	S	L
10	P	E	E	R	S	R	M	E	I	K	E	R	S	T	N	O	Y	S	T	Y
	M	A	R	I	E	P	A	U	L	E	A	J	V	L	T	E	R	O	E	G
12	H	D	W	W	Q	R	D	L	A	D	I	E	E	N	A	T	I	P	P	H
	G	E	I	A	E	V	E	F	I	H	O	I	A	J	O	O	S	S	H	Å
14	P	J	I	E	K	A	Q	P	T	X	H	R	T	E	N	N	A	S	A	K
	E	E	D	D	T	R	I	T	S	C	F	S	O	A	X	P	K	E	N	A
16	P	M	J	Z	I	M	A	C	I	A	M	I	L	T	E	S	N	E	I	N
	L	C	A	V	Z	M	A	M	I	A	J	R	K	O	H	N	M	C	E	Y
18	L	I	N	H	L	B	L	R	R	R	O	H	J	V	A	Y	E	A	Y	M
	Z	A	E	L	A	A	R	C	I	Q	T	C	S	S	M	H	H	H	R	X
20	S	K	O	K	M	R	E	A	B	O	K	A	J	N	A	J	C	S	R	E
	F	Y	P	B	E	L	G	N	M	L	Y	Z	P	A	G	U	O	A	A	K
22	D	F	E	S	U	K	R	A	M	Y	V	E	T	T	E	D	J	T	H	I
	W	R	A	N	U	L	V	E	G	Q	F	E	W	O	U	D	E	A	D	M
24	T	T	X	E	D	D	Z	O	K	H	S	A	D	W	W	X	T	N	Q	F

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Publications

- (i) L.N. McDermott, R.J.W. Louwe, J.-J. Sonke, M. van Herk and B.J. Mijnheer "Dose-response and ghosting effects of an amorphous silicon electronic portal imaging device"
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- (ii) R.J.W. Louwe, L.N. McDermott, J.-J. Sonke, R. Tielenburg, M. Wendling, M. van Herk et al. "The long-term stability of amorphous silicon flat panel imaging devices for dosimetry purposes"
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- (iii) M. Wendling, R.J.W. Louwe, L.N. McDermott, J.-J. Sonke, M. van Herk and B.J. Mijnheer "Accurate two-dimensional IMRT verification using a back-projection EPID dosimetry method"
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- (iv) L.N. McDermott, M. Wendling, J.J. Sonke, M. van Herk and B.J. Mijnheer "Anatomy changes in radiotherapy detected using portal imaging"
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- (v) L.N. McDermott, S.M.J.J.G. Nijsten, J.-J. Sonke, M. Partridge, M. van Herk and B.J. Mijnheer "A comparison of ghosting effects for three commercial a-Si EPIDs"
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- (vi) L.N. McDermott, M. Wendling, B. van Asselen, J.C. Stroom, J.-J. Sonke, M. van Herk et al. "Clinical experience with EPID dosimetry for prostate IMRT pre-treatment dose verification"
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- (vii) L.N. McDermott, M. Wendling, J.-J. Sonke, M. van Herk and B.J. Mijnheer "Replacing pre-treatment verification with *in vivo* EPID dosimetry for prostate IMRT"
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Curriculum Vitae

Born on the 20th of September, 1975 in Melbourne, Australia, after her last 5 years of no formal study, she attended St Agatha's Primary School, Cranbourne for 7 years and Sacred Heart Girls' College, Oakleigh for 6 years. This was followed by another 6 years at Monash University, Clayton for which she was awarded a Bachelor of Arts with a major in Philosophy and Bachelor of Science (Honours), with a major in Experimental Physics. Just prior to her final year at University, she came across the field of Radiotherapy. Subsequently she undertook two successive Summer Scholarships (3 month student projects) at the William Buckland Radiotherapy Centre, The Alfred, Prahan. These projects focussed on dose calculation accuracy in inhomogeneous media. With undergraduate studies completed at the end of 1999, she left Melbourne, bound for the northern hemisphere in search a Radiotherapy PhD project. Along the way, 6 months were spent in Baden, Switzerland in 2000 working as a computational fluid dynamics 'Praktikant' for Alstom Power Generation. She soon returned to Radiotherapy by way of a 1 year research project at Linköpings Universitätsjukhuset, Sweden in 2000-2001. As a 'radiofysikmedarbetare', this role entailed the development of dose verification methods for intensity-modulated radiotherapy. In the meantime, she heard about dose verification with EPIDs, as well as a PhD project in the Netherlands on this very topic. Another year and another European country later, she finally began her PhD at the Netherlands Cancer Insititute in Amsterdam, the subject of this thesis. Just under 5 years later, this marks the end of her 24 years of formal study (hopefully).

Brief Summary

Radiotherapy is the use of ionising radiation beams to treat cancer. Advanced treatment techniques today are focused on increasing the dose to the tumour and avoiding healthy tissue. More complicated radiotherapy methods require a way to check the treatment as accurately and efficiently as possible. To this end, we have used a new type of electronic portal imaging device (EPID). The EPID is a flat-panel imager, similar to a large digital camera, and is positioned behind the patient, in the path of the radiation beam. Normally the EPID is used to acquire x-ray images just before treatment to check the patient's position. The objective of this thesis was to use EPID images acquired during treatment to check the patient's dose.

First a series of studies were performed to determine how the new EPID signal varies when the dose varies. After correction, the stability of the EPID signal over time was very stable over 2 years. A method was developed to determine the dose inside the patient based on images acquired behind the patient. The method was based on earlier work for an earlier type of EPID. Tests revealed the dose could be measured very accurately, and so the method was introduced into the clinic. Small but clinically relevant errors in the computer system used to calculate treatment plans were detected (and later corrected). Daily EPID images acquired prior to treatment were also studied to determine the influence of anatomy changes. This was measured over the course of treatment (5-7 weeks), for lung, head-and-neck and prostate cases. It was found that respiratory motion, variation in gas pockets in the rectum and patient positioning were the main anatomy changes that would affect the dose delivered to patients. The conclusion is then that the a-Si EPID is suitable for reliable and accurate absolute dose verification during radiotherapy. In addition, the EPID can replace traditional dosimetry devices, being more efficient and just as accurate. The method developed for this thesis is a safety net, making it easier to raise dose levels and introduce sophisticated treatment techniques which will eventually lead to higher cure rates for patients.

Korte Samenvatting

In de radiotherapie worden bundels ioniserende straling gebruikt om kanker te behandelen. Vandaag de dag worden gecompliceerde behandeltechnieken geïntroduceerd om de tumordosis te verhogen zonder de gezonde weefsels extra te belasten te verhogen. Deze technieken vragen echter om methoden om de behandeling zo accuraat en efficiënt mogelijk te controleren. In dit proefschrift wordt hiertoe een nieuw soort “electronic portal imaging device” (EPID) gebruikt. Een EPID is een soort platte röntgencamera, vergelijkbaar met een grote digitale camera, die achter de patiënt in de bundel wordt geplaatst. Met de röntgenfoto's van deze camera wordt normaal de plaats van de patiënt ten opzichte van de bestralingsbundel geverifieerd. Het doel van deze studie was om ook de dosis in de patiënt te verifiëren met deze foto's.

Eerst zijn er studies gedaan naar de nauwkeurigheid van de nieuwe EPID's om dosis te meten. Na enkele correcties bleek de EPID stabiel te zijn over een termijn van twee jaar. Daarna is een methode ontwikkeld om de patiëntdosis te bepalen uit de EPID beelden, gebaseerd op eerder werk voor een ander soort EPID. Nadat de nauwkeurigheid was vastgesteld, werd de methode geïntroduceerd in de kliniek, en werden kleine maar klinisch relevante fouten gevonden (en later gecorrigeerd) in het computersysteem dat de behandeling voorbereid. Ook werden anatomische veranderingen bestudeerd die optreden tijdens de bestraling van long, hoofd-hals en prostaat kanker patiënten. Het bleek dat ademhaling, variatie in darmgassen en patiëntpositionering de belangrijkste factoren zijn die veranderingen in de behandel dosis veroorzaken. Geconcludeerd kan worden dat de nieuwe methode geschikt is voor zeer nauwkeurige dosisverificatie in de radiotherapie. Daarnaast blijkt het systeem veel efficiënter te zijn dan andere methoden om het behandelplan te controleren. De in deze dissertatie beschreven methode dient daarom als een goed “vangnet” om fouten te voorkomen. Daardoor wordt de introductie van nieuwe technieken veiliger, en wordt het makkelijker de bestralingsdosis te verhogen om daarmee de genezingskansen van de patiënt te vergroten.