Comparison of Correction Protocols for Image-Guided Radiation Therapy

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In radiation therapy, patient positioning uncertainty and organ motion require that a volume larger than the actual tumour (named the planning target volume [PTV]) be irradiated to ensure that the tumour receives the prescribed dose. Image-guided patient positioning can correct targeting errors, thus reducing the uncertainty in the position of the tumour, and therefore, the size of the PTV. Positioning uncertainties are reduced with frequent imaging, but require increasing the overall time of a treatment session. We compare conventional 'off-line' error correction protocols to our 'on-line' correction protocol for prostate cancer patients. Simulations indicate that our on-line protocol leads to much smaller residual uncertainty than off-line protocols, leading to much smaller PTV margins. Our on-line protocol allows the irradiation of substantially smaller volumes than conventional off-line protocols, leading to reduced normal tissue complications. Introducing an "intervention threshold" has retained some of the efficiency of the off-line strategy.

1 Introduction

The goal of radiation therapy is to deliver a high dose to the tumour while maintaining a low dose to the surrounding healthy organs. When planning a course of radiation therapy, diseased areas are contoured on computed tomography (and potentially other) images to define a clinical target volume (CTV), which comprises both gross tumour and areas of potential microscopic disease. However, the CTV is not fixed in space. This is because radiation treatment spans several daily treatment 'fractions', and daily patient repositioning uncertainties and internal organ motion may result in the displacement of the CTV within the treatment beam. One usually accounts for the random position of the CTV by defining a fixed planning target volume (PTV) by adding an anisotropic safety margin to the CTV [1]. The treatment is then designed to create a high dose volume that surrounds the PTV while avoiding healthy tissue. The size of the PTV is very important. An excessively large PTV ensures that the CTV always receives the prescription dose, but results in the irradiation of large volumes of healthy tissue, thus increasing complications. Conversely, if the PTV is too small, the CTV may move outside of the high dose volume, reducing the probability of controlling the tumour.

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Reducing or eliminating the uncertainties in the CTV position can reduce the size of the PTV, thus sparing healthy tissues with no reduction in tumour control. This can be achieved by using immobilization devices and by verification of the patient position with portal imaging. Portal imaging uses the radiation exiting the patient from a treatment beam to produce a radiograph of the patient while positioned for treatment. An image is produced that indicates the alignment of the patient relative to the treatment beam. Since the high energy x-rays produced by the medical linear accelerator are not optimal for imaging, only bony anatomy and air pockets are visible [2]. Therefore, a surrogate for the actual CTV position is necessary. We currently have a protocol that permanently implants three gold 'seeds' into the prostate of prostate cancer patients prior to treatment [3]. These seeds are cylindrical pins that are 1 mm in diameter and 5 mm long. Prior to treatment, these three seeds are implanted into the apex, middle, and base of the prostate gland under ultrasound guidance. While the soft tissue of the prostate is not visible on portal images, the gold seeds implanted within the prostate are visible and can be used to assess the targeting of the prostate. A linear accelerator with an electronic portal imaging device is shown in Figure 1a. Figure 1b illustrates a typical lateral portal image through the pelvis of a prostate patient positioned for treatment. The implanted gold seeds are visible as three high density points.

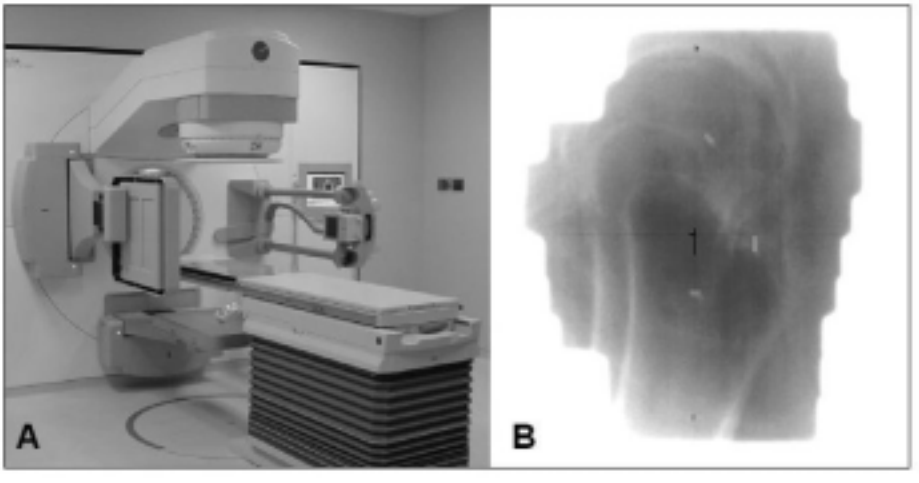

Fig. 1. (a) A medical linear accelerator with an electronic portal imaging device and an experimental kilovoltage imaging device mounted orthogonally, and (b) a portal image for a lateral radiation beam. The implanted seeds appear as three small high density objects. The irregular outline of the radiograph demonstrates the extent of the radiation field.

Portal images can be used for either 'off-line' or 'on-line' corrections. Both methods compare radiographic images of the patient in the treatment position with digitally reconstructed radiographs of the patient that were generated at the time of treatment planning. Off-line correction strategies acquire images that are retrospectively assessed for systematic errors that should be corrected in subsequent treatment fractions. Protocols have been suggested to maximize the benefit from off-line corrections, while minimizing the workload [4,5]. On-line imaging involves daily imaging

to determine if a correction is required before treatment, using only a small part of the radiation dose. This allows more accurate positioning, however, it requires more time and intervention. In addition, the acquisition of many images may increase the dose to healthy tissues, although this may be accounted for in treatment planning. Off-line portal imaging allows the reduction of systematic positioning uncertainty, while on-line imaging has the potential to reduce both systematic and random uncertainty.

In this work, we perform simulations to compare our current on-line protocol to conventional off-line correction protocols. We determine the size of the PTV required to properly account for the residual uncertainties for each protocol.

2 Methods

2.1 Correction Protocols

The three correction protocols compared in this work are briefly summarized below. First, the shrinking action level (SAL) protocol is an off-line protocol that is intended to reduce systematic geometric uncertainty [4]. An average of the systematic uncertainty is measured. If this average exceeds a threshold, a correction is performed on subsequent treatments. This threshold decreases by the inverse square root of the number of images and is given by

$$\frac{\alpha}{\sqrt{N}} \tag{1}$$

where α is a pre-defined tolerance level, and N is the number of fractions since the last correction (or the beginning of treatment, if no corrections have been performed). If a set number of images, defined by a parameter named N_{max}, are acquired without requiring a correction, the systematic error is deemed to be within tolerance and no further images are acquired [4]. This shrinking action level is intended to reflect the fact that the estimate of the systematic error improves with an increasing number of samples.

Second, the no action level (NAL) protocol is another off-line protocol that images every patient a set number of treatment fractions (N_{max}), and uses the mean measured displacement to define a correction that is applied to all subsequent fractions, with no further image acquisition [5]. The basis for the NAL protocol is that the mean displacement is the best estimate of the systematic error after any given number of treatment fractions.

Finally, our on-line correction protocol images the patient prior to every treatment. Before treatment, the images are acquired using a small fraction of the therapy dose. These images are subsequently analyzed using a workstation at the treatment unit to determine if the positioning error exceeds a defined threshold. If so, the patient's position is adjusted by the calculated displacement and treatment proceeds [3]. No veri-

fication of the accuracy of the correction is performed. The use of a threshold improves the efficiency of the on-line process by eliminating the need to correct very small displacements that may be clinically irrelevant.

2.2 Correction Protocol Simulation

We compared these three methods using a Monte Carlo simulation based on published data for the magnitude and direction of prostate patient positioning uncertainty and internal prostate motion [6,7]. The uncertainties were decomposed into anterior-posterior (AP), lateral (LAT), and superior-inferior (SI) translations, although the model may be extended to include rotations. All probability distributions were assumed to be Gaussian. The distributions reflect the composite uncertainty in the position of the centre of mass of the prostate. Simulations are performed to determine the distributions of residual uncertainties for four protocols: no correction, SAL, NAL, and our on-line correction protocol. Since some uncertainty may exist in the corrections, we approximate this effect by applying an addition random uncertainty to each correction that is equal to the random patient repositioning uncertainty. We use α=6.0 mm and N_{max}=6 for SAL, N_{max}=5 for NAL, and a fixed threshold of 3.0 mm for the on-line correction protocol. The off-line correction parameters were allowed to result in more image acquisitions than usually suggested since they were compared with an on-line protocol.

The simulated treatment histories of 10 000 patients were modeled for each protocol. The distributions of residual random and systematic error are generated from this simulation. Each distribution was fit to a Gaussian and the standard deviations were quantified. In addition, the number of treatment fractions that had image acquisitions, and the number of fractions where a new correction was applied are determined from the simulations.

2.3 PTV Margin Simulation

The residual distribution data is used as the input to a simulation to determine the required PTV margin. This simulation follows the method of van Herk et al [8]. A dose distribution that perfectly conforms to the PTV is modeled. A treatment goal is set such that the PTV must account for residual uncertainties so there is a 95% probability (or for 95% of the patient population) that the minimum CTV dose will be 95% of the prescription dose.

The CTV in this simulation is modeled as a sphere with a radius of 2.0 cm. This is a reasonable approximation to the size and shape of a prostate gland. The dose distribution is modeled as the convolution of a bitmapped sphere with a Gaussian distribution (3.2 mm standard deviation). This generates a spherical dose distribution surrounding a spherical PTV and CTV. The dose distribution is defined such that the minimum PTV dose is 95%.

The random and systematic uncertainties tend to have different effects, and are therefore simulated separately. Random uncertainties tend to 'blur' the dose distribution relative to the patient anatomy, while systematic uncertainties tend to 'shift' the dose distribution. Random uncertainties are assessed by convolution of the planned dose distribution with the distribution of random residual uncertainties. This results in a blurred version of the intended dose distribution. This blurred dose distribution is then displaced relative to the CTV, and it is determined if the minimum CTV dose is greater than 95%. The distribution of residual systematic uncertainty is used to determine the probability of this displacement. This is performed for all displacements defined by the systematic uncertainty distribution. The sum of the probabilities at all displacements that meet the treatment goal is the probability of a minimum CTV dose of 95%. If the value is larger or smaller, the PTV is appropriately increased or decreased, a new dose distribution is defined, and the simulation is performed again. This is performed iteratively to find the smallest margin that meets the treatment goal. This is used to determine 'optimal' margins for treatment with no correction protocol, SAL, NAL, and our on-line correction.

3 Results

The standard deviations of the distributions of residual geometric uncertainty are listed in Table 1. All of the correction protocols were able to reduce the systematic uncertainty. However, only the on-line correction protocol reduced random uncertainties. In fact, the random uncertainties were slightly larger for both off-line protocols than when no correction protocol was used.

Table 1. Standard deviations of residual geometric uncertainties for each correction protocol.

Protocol	Systematic (mm)			Random (mm)		
	AP	LAT	SI	AP	LAT	SI
No correction	4.4	2.8	3.0	3.9	2.2	2.4
SAL	1.4	1.3	1.3	4.7	2.6	2.9
NAL	1.6	1.1	1.1	4.7	3.1	3.2
On-line	0.5	0.7	0.6	1.8	1.8	1.7

As shown in Table 2, the number of images acquired varied for each protocol. Interestingly, NAL produced very similar results to the SAL protocol, but requires (on average) less than half the number of image acquisitions. The on-line correction protocol images on every one of the 20 treatment days, requiring more images than the off-line protocols. Table 2 also indicates that for the uncertainties and threshold used in this simulation, the on-line correction requires a correction on almost every fraction. The off-line corrections do not change on a daily basis; therefore the required correction needs to be recalculated much less often.

Table 2. The number of imaged fractions and calculated corrections for each protocol.

Protocol	Imaged Fractions	Corrections Calculated
No correction	0	0
SAL	12.9	3.7
NAL	5	1
On-line	20	17.3

We determined a set of required margins, shown in Table 3, by directly modeling the geometric uncertainties. The off-line protocols reduce the required margin to two-thirds of that required with no correction protocol. The on-line correction reduces this much further, to approximately one-quarter of that required by the off-line correction protocols.

Table 3. PTV margins for 95% probability of 95% mimimum dose for each correction protocol

Protocol	PTV Margin (mm)
No correction	12
SAL	8
NAL	8
On-line	2

4 Discussion

Geometric uncertainties are a significant problem in radiation therapy. The use of imaging to ensure accurate target localization may allow for substantial gains in tumour control and healthy tissue complications. These results indicate that off-line correction protocols can decrease the required PTV size, and that our current on-line correction protocol may allow the use of very small margins.

The relative value of a particular correction protocol will depend on the specific interests of each centre. If the goal is to maximize patient throughput, the NAL protocol is the most desirable protocol to reduce uncertainties. However, if the time required for the improved accuracy is deemed acceptable, then the on-line method is more valuable. At our institution, the total time required for on-line imaging and correction is approximately three minutes. We consider this time to be acceptable for the substantial decrease in uncertainty this method allows. In addition, the frequency of on-line corrections is higher in this simulation than in our clinical experience. This implies that our patient population may have smaller uncertainties prior to corrections than the population in published uncertainty data used for our simulation. This may be due to our careful attention to minimize organ motion due to rectal and bladder filling [3]. Uncertainty data from our centre should be used to validate these results before we consider clinical applications.

For simplicity, we have examined PTVs obtained from uniform, isotropic margins. There is often a clinical benefit to the use of non-uniform PTVs, such as a smaller

posterior margin to reduce the dose to the rectum in prostate patients. Although the results may change, the methods described in this work may be applied equally well to non-uniform margins.

Future work can extend these investigations to determine optimal correction protocols for novel technologies that we are evaluating, such as on-line cone-beam computed tomography imaging. We can also apply this method to determine the appropriate margins for sites other than our prostate patients.

In conclusion, although our on-line correction protocol requires many image acquisitions, it provides a considerably greater benefit than conventional off-line correction protocols.

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