This work investigates the hypothesis that evaluating geometric uncertainties will allow the development of image guidance strategies to reduce uncertainties during treatment and will aid in the optimization of predicted treatment outcome, in terms of tumour control (TCP) and normal tissue complication (NTCP) probabilities.

To investigate this hypothesis, various modeling techniques have been utilized to simulate geometric uncertainties during laser-guided and image-guided radiation therapy treatment courses including: convolution, Monte Carlo simulation, and deformable image registration techniques. The studies were focused towards prostate cancer treatments.

First, limitations of the convolution technique for modeling random geometric uncertainties were quantified using the Monte Carlo numerical simulation technique as the gold standard, in terms of TCP and NTCP. For both indices, the errors became negligible beyond about 20 fractions.

Then, a thin-plate-spline-based deformable dose-tracking technique, in addition to the convolution technique, was utilized to evaluate the effectiveness of different laser-guided and image-guided patient set-up techniques (currently in clinical use) to mitigate geometric uncertainties and facilitate treatment outcome optimization. Five-patient CT data sets were used. The results suggest that CT-based image guidance strategies best mitigate geometric uncertainties, in various fractionation schemes, and allow the best optimization of simulated treatment courses for prostate cancer radiotherapy.

Finally, an issue that is of significant clinical importance in the implementation of CT-based image guidance strategies is the inter- and intra-observer prostate contouring uncertainties. Therefore, five CT studies, acquired using a mega-voltage computed tomography (MVCT) system on board a helical tomotherapy unit, were analyzed. Direct comparison was made with the same analysis using kilo-voltage computed tomography (KVCT) studies of the same patients. The results suggest that the application of MVCT for use in image guidance strategies for prostate cancer treatments may not be as effective as the use of KVCT for the same role.

In conclusion, based on the findings reported in this thesis, the hypothesis is proven. Specifically, the use of image guidance enhanced the precision in prostate cancer radiotherapy and consequently improved the predicted treatment outcome (i.e., TCP and NTCP) compared to more conventional clinical strategies.

Key words: prostate cancer, geometric uncertainties, image-guided radiation therapy, adaptive radiation therapy, convolution, Monte Carlo simulation, deformable dose warping, dose escalation, hypofractionation, $\alpha/\beta$ ratio, on-line image guidance, off-line image guidance, contouring uncertainties, helical tomotherapy, mega-voltage computed tomography, kilo-voltage computed tomography