

**PhD Thesis Title:** 'Stepping source prostate brachytherapy: From target definition to dose delivery'

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### **Abstract**

Temporary implant brachytherapy is an effective way to treat tumors locally and conformably, and is widely used in the treatment of prostate cancer. The planned dose is delivered using a single (<sup>192</sup>Ir) stepping source, remotely controlled by an after loading machine. Safe and accurate treatment depends on accurate tumor definition, stability of the implant and patient anatomy, and high quality treatment planning.

Prior to the treatment, a CT or MRI scan is acquired for tumor delineation and treatment planning. The use of MRI led to a mean increase of 3% in dose coverage of the planning target volume. Despite this limited mean difference, in some cases the use of MRI resulted in an increase in target coverage of 5%-10%. Using a radiobiological model to predict tumor control based on the dose to the prostate, it was estimated that the use of MRI results in a 6%-10% higher tumor control probability.

During the brachytherapy treatment, deviations from the planned dose can occur. A minor decrease in target coverage was measured using self-anchoring catheters. Two repeat CTs were obtained 24 and 48 hours after the implantation procedure, to study the effect of anatomy changes and/or catheter displacements during the treatment. At the AMC (Amsterdam, the Netherlands), a pulsed dose rate (PDR) treatment was applied of 24 pulses of 1.2 Gy given every 2 hours. Rectum dose increased by 17.3% on average, during the treatment. For the bladder, a mean increase of 24.8% was observed. This observation led to the conclusion that a possible significant increase in dose to the surrounding organs should be taken into account during treatment planning.

Changes in prostate volume during treatment may lead to a decrease in target dose coverage. The change in prostate volume could not accurately be established from the CT data due to the delineation uncertainty. Therefore, we used the catheter positions to derive volume changes, assuming that if the prostate expands, the distance between the catheters will increase. This resulted in a mean increase of 4% in prostate volume, ranging from -10% to +16%. The differences found were not considered clinically relevant. These measurements reaffirm the stability of the prostate implants with self-anchoring catheters used for the PDR treatments, which guarantees safe and reliable delivery of the planned dose.

Two novel tools for treatment plan optimization of temporary implant brachytherapy were developed. These tools were developed to offer a user-friendly alternative to graphical optimization,

while maintaining the speed in treatment planning from more recently developed inverse optimization algorithms. The first, enhanced geometrical optimization, EGO, creates a dose distribution that is as homogeneous as possible across the implant. With the second tool, interactive inverse planning (IIP), the user subsequently shapes the dose distribution according to the patient's anatomy by (local) adaptations of the dose in specific regions of interest. All interactions with the dose distribution are in real-time. In a proof of principle study two users, one inexperienced and one experienced treatment planner, each optimized the dose distribution for 24 prostate cases using our software. This resulted in treatment plans with comparable quality to the clinically used treatment plans, and comparable compliance to the clinical dose objectives.

Like graphical optimization, but unlike automated inverse methods, IIP offers the possibility of local adjustments to the dose distribution. In addition, interacting in real-time with the dose distribution allows the user and physician to explore the possibilities and trade-offs for each individual patient.

Four treatment planning methods were compared using 26 prostate implants. A single experienced treatment planner optimized the dose distributions using graphical optimization, two automated inverse methods (IPSA and HIPO) and the combined use of EGO-IIP. Planning time was shortest with the automated methods. Between the resulting dose distributions no apparent difference in quality was observed. Differences in DVH parameters were small, but the inverse methods, including EGO-IIP, showed a slight advantage as compared to graphical optimization.

EGO and IIP will be further developed to improve and simplify the treatment planning process of prostate brachytherapy, but also for other tumor sites, such as gynecological cancers. In addition to standard dose optimization, IIP allows the direct optimization of radiobiological dose.

#### **References to author publications that relate specifically to the dissertation:**

A.M. Dinkla, B.R. Pieters, K. Koedooder, N. van Wieringen, R. van der Laarse, J.N. van der Grient, C.R. Rasch, C.C. Koning, and A. Bel, "Improved tumour control probability with MRI-based prostate brachytherapy treatment planning," *Acta Oncologica* 52(3): 658-665, 2013

A.M. Dinkla, B.R. Pieters, K. Koedooder, P. Meijnen, N. van Wieringen, R. van der Laarse, J.N. van der Grient, C.R.N. Rasch, and A. Bel, "Deviations from the planned dose during 48 hours of stepping source prostate brachytherapy caused by anatomical variations," *Radiotherapy and Oncology* 107(1): 106-111, 2013

A.M. Dinkla, B.R. Pieters, K. Koedooder, N. van Wieringen, R. van der Laarse, and A. Bel, "Prostate volume and implant configuration during 48 hours of temporary prostate brachytherapy: limited effect of edema," *Radiation Oncology* 9: 272, 2014.

A.M. Dinkla, R. van der Laarse, K. Koedooder, H.P. Kok, N. van Wieringen, B.R. Pieters, and A. Bel, "Novel tools for stepping source brachytherapy treatment planning: enhanced geometrical optimization and interactive inverse planning," *Medical Physics* 42(1), 348-352, 2015

A. M. Dinkla, R. Van der Laarse, E. Kaljouw, B. R. Pieters, C. Koedooder, N. van Wieringen, and A. Bel, "A comparison of inverse optimization algorithms for HDR/PDR prostate brachytherapy treatment planning," *Brachytherapy* 14(2): 279-288, 2015