PhD Thesis Title: Introduction of Monte Carlo Dosimetry and Edema in Inverse Treatment Planning of Prostate Brachytherapy

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ABSTRACT:

Prostate cancer is the second most common cancer in men. Two-thirds of the cases are diagnosed in developed countries and France is ranked third in incidence rate. Low-doserate (LDR) brachytherapy is a widely used treatment option. During LDR brachytherapy, radioactive seeds are permanently implanted in the prostate gland to deliver a therapeutic dose locally in the cancerous region, while sparing the tissues and organs at risk (OARs). Despite its high success rate (75% to 91%), the side-effects (sexual and urinary problems) remain high.

The dose delivered to the tumor depends on the implantation positions of the seeds, which implies that treatment planning is essential. Clinical inverse planning systems automatically provide optimal implantation positions. However, this prediction is based on a simplified dosimetric model where the human body is considered an infinite volume of water. When tissue heterogeneity is not considered, the expected dose differs from the actual administered dose. The dose received by 90% of the prostate volume (D_{90}) may be overestimated up to 7%, and may be associated with malignant recurrence.

Another important factor that induces treatment errors is the occurrence of prostate edema during brachytherapy that involves a volumetric change of the organ. Edema can lead to a significant underestimation of the D_{90}, for example, by 13.6% for a volumetric change of 20%. Moreover, the magnitude of edema varies considerably (10% to 96%) between patients. Today the exact mechanism of edema formation remains unknown. Changes in edema lead to significant uncontrolled degradation of treatment planning and therefore to the actual dose that the patient receives, resulting in overdose of the OARs and increased chance of side-effects. To solve the first major limit of the treatment planning presented here, namely the calculation of dose, we propose an inverse planning system based on Monte Carlo (MC) dosimetry. GPU-accelerated dosimetry is combined with a fast-simulated annealing method. The cost function of the optimization directly uses the dose volume histograms so that they reached solution perfectly matches the dosimetric criteria, which is not the case for current systems used in clinical routine. Our method provides precise and automatic prediction of optimal implantation positions according to a personalized dosimetry in clinically compatible time. The treatment plans obtained from the proposed method were evaluated with a database of clinical

treatment plans of 18 patients. The method proposed in this thesis makes it possible to obtain a treatment plan in barely a minute, with results that satisfy all the dosimetric criteria of the treatment.

In order to answer the second limit of a precise planning, that related to prostate edema, we propose a biomechanical model based on the finite element method (FEM) in order to estimate the effect of the tissue elastic parameters on the characteristics of the edema. We show that the large variation in edema as well as the varying half-life are correlated with changes in the elastic properties of the prostate. Variations in the characteristics of edema are studied with a database of 15 patients. To account for the impact of edema in dosimetry, we propose a dynamic dosimetry scheme. A prostate volume resampling algorithm allows to consider the volumetric changes associated with edema during the MC dosimetry. Dynamic dosimetry with edema shows consistent results with previous studies in the literature. That is, the underestimation of the dose due to edema. For example, for a magnitude of edema of 20%, the prostate dose D_{90} and the urethra D_{10} are 13.6% and 10.6%, respectively.

To conclude, we propose a system of inverse treatment for prostate brachytherapy which takes into account a precise personalization of the dosimetry but also of the edema of the prostate. This work can also be used in other clinical contexts, such as high-dose-rate brachytherapy, but also be adapted to treat other organs. In the future, our work will focus on the study and the ability to adapt the proposed prostate biomechanical model to each patient using elastic measurements via prostate elastography. Due to the inherent limitations of FEM, the incorporation of the biomechanical model of edema into the treatment planning system is costly in computation time. An alternative method would be to propose a new meshless model to improve the simulation of edema during intraoperative planning.

Keywords: prostate, brachytherapy, inverse planning, edema, biomechanics

References to author publications that relate specifically to the dissertation:

1. **Mountris, Konstantinos A**., et al. "Modeling the impact of prostate edema on LDR brachytherapy: a Monte Carlo dosimetry study based on a 3D biphasic finite element biomechanical model." *Physics in Medicine and Biology* 62.6 (2017): 2087.

2. **Mountris, Konstantinos A**., et al. "ORACLE: A DVH-based inverse planning system for LDR prostate brachytherapy using MC dosimetry." *International Conference on Monte Carlo Techniques for Medical Applications*. 2017.

3. **Mountris, Konstantinos A.**, Julien Bert, and Dimitris Visvikis. "Prostate brachytherapy optimization using GPU accelerated simulated annealing and Monte Carlo dose simulation." *Nuclear Science Symposium, Medical Imaging Conference and Room-Temperature Semiconductor Detector Workshop (NSS/MIC/RTSD), 2016*. IEEE, 2016.