**PhD Thesis Title:** 'Modelling and verification of doses delivered to deformable moving targets in radiotherapy'

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**ABSTRACT:**

This thesis addresses the pressing need to investigate dose distributions in targets that deform during and/or between treatments, to ensure robust calculations for dose accumulation and delivery, thus providing the most positive outcomes for patients. This involves the direct measurement of complex and re-distributed dose in deforming objects (an experimental model), as well as calculations of the deformed dose distribution (a mathematical model). The comparison thereof aims to validate the dose deformation technique, thereby to apply the method to a clinical example such as liver stereotactic body radiotherapy.

To facilitate four-dimensional deformable dosimetry for both external beam radiotherapy and brachytherapy, methodologies for three-dimensional deformed dose measurements were developed and employed using radiosensitive polymer gel combined with a cone-beam optical CT scanner for gel dosimetry. This includes the development of a novel prototype deformable target volume using a tissue-equivalent, deformable gel dosimetric phantom, dubbed "DEFGEL". This can reproducibly simulate targets subject to a range of mass- and density-conserving deformations representative of those observable in anatomical targets. This novel tool was characterized in terms of its suitability for the measurement of dose in deforming geometries. It was demonstrated that planned doses could be delivered to the deformable gel dosimeter in the presence of different deformations and complex spatial re-distributions of dose in all three dimensions could be quantified.

For estimating the cumulative dose in different deformed states, deformable image registration (DIR) algorithms were implemented to 'morph' a dose distribution calculated by a treatment planning system. To investigate the performance of DIR and dose-warping technique, two key studies were undertaken. The first was to systematically assess the accuracy of a range of different DIR algorithms available in the public domain and quantitatively examine, in particular, low-contrast regions, where accuracy had not previously been established. This work investigates DIR algorithms in 3D via a systematic evaluation process using DEFGEL suitable for verification of mass- and density-conserving deformations. The second study was a full three-dimensional experimental validation of the dose-warping technique using the evaluated DIR algorithm and comparing it to directly measured deformed dose distributions from DEFGEL. It was shown that the dose-warping can be accurate, i.e., over 95% passing rate of 3D-gamma analysis with 3%/3mm criteria for given extents of deformation up to 20 mm.

For the application of evaluating patient treatment planning involving tumour motion/deformation, two key studies were undertaken in the context of liver stereotactic body radiotherapy. The first was a 4D evaluation of conventional 3D treatment planning, combined with 4D computed tomography, in order to investigate the extent of dosimetric differences between conventional 3D-static and path-integrated 4D-cumulative dose calculation. This study showed that the 3D planning approach overestimated doses to targets by ≤ 9% and underestimated dose to normal liver by ≤ 8%, compared to the 4D methodology. The second study was to assess a consequent reduction of healthy tissue sparing, which may increase risk for surrounding healthy tissues. Estimates for normal tissue complications probabilities (NTCP) based on the two dose calculation schemes are provided. While all NTCP were low for the employed fractionation scheme, analysis of common alternative schemes suggests potentially larger uncertainties exist in the estimation of NTCP for healthy liver and that substantial differences in these values may exist across the different fractionation schemes.

These bodies of work have shown the potential to quantify such issues of under- and/or over-dosages, which are quite patient dependent in RT. Studies presented in this work consolidate gel dosimetry, image guidance, DIR, dose-warping and consequent dose accumulation calculation to investigate the dosimetric impact and make more accurate evaluation of conventional 3D treatment plans. While liver stereotactic body radiotherapy (SBRT) was primarily concerned for immediate clinical application, the findings of this thesis are also applicable to other organs with various RT techniques. Most importantly, however, it is hoped that the outcomes of this thesis will help to improve treatment plan accuracy. By considering both computation and measurement, it is also hoped that this work will open new windows for future work and hence provide building blocks to further enhance the benefit of radiotherapy treatment.

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


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