

# Biologically conformal radiation therapy and Monte Carlo dose calculations in the clinic

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## Abstract

The development of radiation therapy treatment planning has always relied strongly on the available imaging technologies. Anatomical imaging techniques like computed tomography (CT) can visualize spatial changes in physical properties within patients. Additionally, tumor biology plays an important role in the diagnosis, treatment decision-making and the assessment of therapeutic response. Recent advances in biological imaging techniques, mainly based on positron emission tomography (PET), offer the opportunity to further individualize radiotherapy.

Highly structured dose distributions can be delivered using intensity- modulated radiation therapy (IMRT). IMRT can thus reduce toxicity by allowing a selective reduction of the dose to organs at risk, or allow dose escalation with the aim to improve local control. In current clinical practice, IMRT optimization is based on the assumption of a uniform biology distribution within each target volume and aims at achieving geometrically conformal dose distributions. By using the spatially heterogeneous biology distribution provided by one or several biological imaging modalities to guide the IMRT dose prescription, biologically conformal radiation therapy (BCRT) can be delivered.

In this thesis, BCRT is implemented into the IMRT treatment planning process at Ghent University Hospital by developing a biology-based segmentation tool and extending the objective function. A bound-constrained linear relationship between the image signal and the desired radiation dose is put forward. Additional tools are developed to assess the obtained biological conformity of the final treatment plan.

The feasibility of [18F]fluoro-deoxy-glucose (FDG)-PET guided BCRT for head and neck cancer is demonstrated in a planning study. It is shown that BCRT does not compromise the planning constraints for the organs at risk. The obtained biological conformity is the best for the lowest level of dose escalation. Compared to uniform dose escalation within a contoured FDG-PET lesion, improved target dose coverage is achieved using BCRT.

Monte Carlo (MC) can be used to calculate radiation therapy dose distributions with great accuracy. The use of MC is especially advantageous in case of small, irregular treatment fields delivering dose to regions of great tissue inhomogeneity, for example in IMRT treatment of head and neck or lung tumors. In this thesis, the added value of MC compared to pencil beam and convolution/superposition algorithms is demonstrated for IMRT lung cancer patients.

Monte Carlo Dose Engine (MCDE) was developed at Ghent University as a highly accurate MC dose engine for IMRT patient dose calculations. In this thesis, the conversion of CT numbers into material composition data for MC dose calculations is studied in detail. Stoichiometric CT scanner calibration and the creation of dosimetrically equivalent tissue subsets result in a 14 bin CT conversion scheme. MCDE is further improved by the introduction of uncertainty-based stopping criteria, enabling accurate clinical treatment plan evaluation in the shortest possible time. Finally, the feasibility of integrating MCDE into the IMRT optimization process at Ghent University Hospital is demonstrated for an ethmoid sinus cancer patient case.

Optimal use of the new tools for incorporating biological imaging information into the treatment planning process will require an improved understanding of the radiobiology of tumors. Patients may benefit from the improvements in dose calculation accuracy using full MC. While faster but less accurate MC dose engines are currently being implemented into commercial treatment planning systems, highly accurate dose engines like MCDE remain indispensable benchmarking tools.