Abstract

Radiation therapy is a widely used modality for treating malignancies in e.g. brain, breast, lung, prostate and the head and neck (H&N) region. The search for the optimal radiation treatment approach for a specific patient is a complex task, ultimately seeking to maximize the tumour control probability (TCP) while minimizing the normal tissue complication probabilities (NTCP). Conventionally, the radiation quality used to achieve this has been photons of various energies. In the modern treatment era, photon energy spectrums in the megavoltage region delivering 2 Gy per fraction in approximately 20 to 40 daily fractions has been the standard curative treatment regime. However, during the last decades, the interest in hypofractionated treatments and proton therapy has rapidly increased. This adds complexity to the plan selection process, as decision criteria are needed to determine which patients that are eligible for hypofractionated treatment and/or proton therapy. For the latter, the focus has been on the possibility of lowering the normal tissue toxicity compared with conventional photon therapy. Given the same TCP for a photon and a proton plan, the plan selection could then be made purely based on the reduction in NTCP. Since photon therapy is substantially cheaper than proton therapy and far more treatment units are being available, the proton plan must demonstrate a substantial NTCP reduction in order to be selected for treatment. Such a plan selection system between photon and proton plans is clean and elegant, but is not flawless. The nominal plans are typically optimized on a single CT scan of the patient and do not account for all the uncertainties during treatment delivery related to patient setup, breathing motion, proton range etc. It also relies on some modelling of the relative biological effectiveness (RBE) between photons and protons as their energy deposition characteristics differ. The clinical standard of using a constant proton RBE of 1.1 does not reflect the complex nature of the RBE, which varies with parameters such as fractionation dose, linear energy transfer, tissue type and biological endpoint.

These aspects of proton plan evaluation and selection have been investigated in this thesis through three individual studies, papers I, II and III. Paper I investigates the impact of including variable RBE models in the plan comparison between proton and photon prostate plans for various fractionation schedules. It also presents a pragmatic re-optimization method of proton plans, which accounts for the variability in the RBE. In paper II, a method of incorporating RBE model uncertainties into the plan robustness evaluation is proposed and subsequently applied on three
treatment sites using two RBE models. Paper III evaluates the impact of variable RBE models and breathing motion for breast cancer treatments when comparing photon and proton plans.

The results from papers I, II and III indicate that the inclusion of variable RBE models and their uncertainties into the proton plan evaluation could lead to differences from the nominal plans made under the assumption of a constant RBE of 1.1 for both target and normal tissue doses. The dose for high $\alpha/\beta$ targets (e.g. H&N tumours) was predicted to be slightly lower, whereas the opposite was predicted for low $\alpha/\beta$ targets (e.g. breast and prostate) in comparison to the nominal dose. For most normal tissues, the predicted doses were often substantially higher, resulting in higher NTCP estimates. By combining uncertainties in patient setup, range and breathing motion with RBE uncertainties, comprehensive robustness evaluations could be performed and possibly be included in the plan selection process in the search for the optimal treatment approach.