

PhD Thesis Title: Optimisation of the treatment quality in head-and-neck radiation oncology

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ABSTRACT:

Emerging literature has reported reduced treatment toxicity in the head-and-neck radiotherapy (HNRT) with 3 instead of 5 mm planning target volume (PTV) margins. However, the loco-regional (LR) control rate was not preserved in all studies. It was considered whether it was possible to implement reduced treatment margins at the Wellington Blood & Cancer Centre (WBCC) with the aim to improve patients' treatment-related toxicity. It was recognised that many department-specific aspects of HNRT can influence the treatment outcomes and all should be considered when the treatment margins are amended. PTV margins are applied to target volumes during the treatment planning to account for uncertainties, such as patient positioning, geometrical accuracy of the treatment machine and geometrical accuracy of the target volume definition. However, these margins do not standardly account for non-rigid anatomy changes (e.g., changes in patient pose, weight loss, tumour response), which are commonly observed during HNRT and can undermine the planned dose objectives. Under the assumption is that a loss in target coverage during treatment may occur more often and may become more relevant with reduced mm PTV margins. It was proposed that a safe PTV margin reduction could be achieved by accounting for systematic changes in patient anatomy using timely and appropriate treatment adaption. This approach required the quantification and separation of the different modes of anatomical changes during treatment, and subsequent investigation of their dosimetric impact. Therefore, the retrospective studies included in this dissertation first investigated the application of deformable image registration (DIR) in combination with Exponentially Weighted Moving Average (EWMA) Statistical Process Control (SPC) charts, and DIR-facilitated dose accumulation.

In the first study, the DIR between the computed tomography for treatment planning (pCT) images of twelve patients and their daily on-treatment cone beam computed tomography (CBCT) images quantified anatomical changes during treatment to investigate corresponding trends using EWMA charts. The application of EWMA SPC charts showed that trends in patient positioning of bony anatomy with respect to the first five treatment fractions could only be confirmed at a 90% confidence level in a small number of cases when EWMA process limits were used. Whereas, the absolute patient position deviations could be confirmed in the vast majority of cases when an *a priori* 2 mm clinical limit was used. The EWMA process

limits were however effective when detecting trends of soft tissue structures. Structure-specific action thresholds for trend detection using SPC charts, enabled the detection of systematic anatomical changes.

The second study defined the intended clinical workflow based on DIR-facilitated dose accumulation to assess the actually delivered dose and the uncertainty in the delivered dose was determined using *in silico* deformations based on clinically observed anatomical changes as ground truth. The uncertainty in DIR-facilitated dose accumulation was accurately quantified and the methodology on how to incorporate these prospectively in dose-volume histograms (DVHs) was described. These results demonstrated that the intended clinical workflow is sufficiently accurate to assess the adequacy of target coverage during HNRT.

In the third study, the estimated uncertainty derived in the second study was included in the dose reconstruction and accumulation over all fractions for the twelve patients to investigate the robustness of volumetric modulated arc therapy (VMAT) plans that were optimised using either 3 or 5 mm PTV and planning risk volume (PRV) margins. It was shown that loss in the target coverage was independent of the margin expansion and very patient specific. In addition, it was found that the tightness of the target volume coverage at planning was a common factor leading to underdosage.

The developed clinical workflow to reconstruct the delivered dose using DIR-facilitated dose accumulation, found that PTV/PRV margin reduction did not significantly reduce the robustness of the treatment plans to attain the adequate target coverage during treatment. This indicates that a safe PTV margin reduction from 5 to 3 mm in HNRT can be achieved. Patient specific verification of the delivered dose using the developed methodology is recommended irrespective of the applied margin expansions considering the patient specific nature of the potential loss in the target coverage.

References to author publications that relate specifically to the dissertation:

1. **Lowther, N.J.**, Hamilton, D.A., Kim, H., Evans, J.M., Marsh, S.H. and Louwe, R.J., 2019. Monitoring anatomical changes of individual patients using statistical process control during head-and-neck radiotherapy. *Physics and Imaging in Radiation Oncology*, 9, pp.21-27.
2. **Lowther, N.J.**, Marsh, S.H. and Louwe, R.J., 2020. Quantifying the dose accumulation uncertainty after deformable image registration in head-and-neck radiotherapy. *Radiotherapy and Oncology*, 143, pp.117-125.
3. **Lowther, N.J.**, Marsh, S.H. and Louwe, R.J., 2020. Dose accumulation to assess the validity of treatment plans with reduced margins in radiotherapy of head and neck cancer. *Physics and Imaging in Radiation Oncology*, 14, pp.53-60.