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Treatment plan robustness in pancreatic patients treated with scanned ion-beam therapy: Inter- and intra-fractional aspects

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Pancreatic cancer is still an unsolved oncological challenge, however radiotherapy with charged particles has been considered a promising approach to improve the patients overall survival. These patients might benefit from dose escalation, although uncertainties during the beam delivery (intra-fractional) or along the treatment course (inter-fractional) can compromise the accuracy of the treatment.
In this thesis, inter- and intra-fractional anatomy changes are explored in order to define the potential source of uncertainties, quantify their effect, and to define strategies towards their reduction.
Anatomical changes along the course of the treatment showed to lead target under-dosages up to 20% and an increase in the dose to the normal tissues. However, this can be lowered through the selection of beam arrangements from the patient's posterior side and beam-specific margins. From the results of this work, it was concluded that a combination of an Internal Target Volume (ITV), obtained by a geometric expansion of 3 mm from the Clinical Target Volume (CTV), and two oblique posterior beams can reduce the mean V_{95CTV} variations to less than 1%. For other beam directions, the calculation of ITVs including the water-equivalent path length (WEPL), suggested the need of a CTV asymmetric expansion in depth, and minimal in lateral beam direction.
Additionally, weekly monitoring of the patient anatomy using computed tomography (CT) might easily be included in the clinical workflow and will assist in the decision of treatment re-planning, when substantial anatomical changes occur. The suggested prediction model was based on the variations of the accumulated WEPL (ΔaccWEPL) relative to the planning CT, and showed a strong correlation between the ΔaccWEPL and the gamma index of the dose distributions. The gamma criterion was selected as dose distribution quality metric, since it includes dosimetric changes in the target and normal tissues.
Regarding intra-fractional variations, the induced breathing motion together with a dynamic beam delivery, affect the dose distribution in terms of homogeneity and target coverage. This effect is stronger (ΔV_{95CTV} > 10\%) for patients with a tumour motion amplitude superior to 5 mm and a highly modulated dose distribution intra- and inter-fields. The concept of modulation index was employed, it showed that different optimisers produce plans with contrasting distribution of the number of particles, resulting in unlike robustness against range and positioning uncertainties. It was concluded that under internal motion, the use of homogeneous plans, multiple beams, and geometric ITVs, originated dose distributions exhibiting a slight mean decrease of the dose homogeneity (H_{CTV}) and V_{95CTV} of 4% and 1%, respectively.
Finally, a first approach to the use of 4D-Magnetic Resonance Imaging (MRI) for motion detection was performed. The results revealed cases of non-linear correlation between the breathing signal (diaphragm position) and the pancreas motion, and variability of the motion amplitude along the acquisition time and between sessions. This reinforces the need of an alternative method, comparative to the use of external surrogates, for simulation of a 4D dose distribution. Therefore, MRI will allow to include baseline drifts, amplitude variations and anatomical alterations in the 4D dose distribution assessment.

In summary, the key for a precise delivery of the treatment is the monitoring of anatomical changes, and a prompt reaction in order to minimise or eliminate potential uncertainties. In future, it is expected that the methods suggested in this thesis, the experience gained at HIT on treating moving organs and, the developments in treatment planning and treatment delivery will allow us to move towards the robust plan optimisation, prediction of changes in the dose distribution, and enable treatment without a constant and complex monitoring of the patient's movement.