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### Improving radiation dose delivery for moving targets using image guidance

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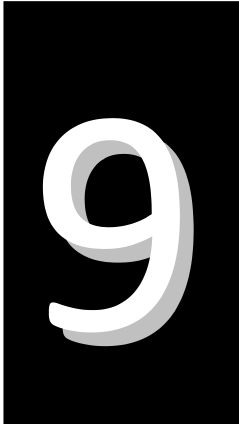
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**English summary**

Since the introduction of the linear accelerator in the clinic, there have been many developments in the field of radiotherapy. The introduction of CT provided us with a three-dimensional view of the patient, both of the tumor and the surrounding healthy tissue. The development of the high precision technique intensity modulated radiotherapy (IMRT) enabled more precise shaping of the dose distribution and a steeper dose gradient. Because of this, more healthy tissue can be spared while the same dose is delivered to the tumor as before. Alternatively the dose in the tumor can be increased while the same dose is given to the organs at risk. Since the rise of image-guided radiotherapy (IGRT) set-up errors can be reduced and interfraction variation can be corrected. In this thesis the recent developments of IMRT and IGRT are applied to improve the treatment of two targets: bladder carcinoma and non-small cell lung carcinoma.

The variation of the volume of the bladder results in a large day-to-day variation for the position of the tumor, because it is located on the bladder wall. Because of the uncertainty of the position of the tumor, bladder tumors were irradiated with a large margin, which resulted in a large volume of healthy tissue receiving a high dose. The introduction of the cone-beam CT (CBCT) and the injection of the contrast fluid lipiodol around the tumor led to accurate determination and, if necessary, correction of the position of the tumor at the start of the irradiation. By combining this with IMRT, the healthy tissue will profit even more.

For the bladder cancer patients we chose to create two IMRT plans for each patient: one plan for the boost on the tumor and one plan for the elective field on the whole bladder with pelvic lymph nodes (chapter 2). This solution was chosen because the tumor and the lymph nodes move independently of each other and with two separate plans position correction can be applied independently as well. The IMRT plans were compared with plans that were created using the field-in-field (FiF) technique, which was the planning technique in our department up till then. The benefit of IMRT with respect to the FiF technique is largest for the small bowel. The volume of the small bowel that receives more than 40 Gy reduces with almost 50%. Of the organs in proximity of the bladder, the small bowel is the one that is most sensitive for irradiation and therefore it got priority during treatment planning. The volume of rectum that receives more than 45 Gy also reduces with almost 50%. Another remarkable difference between IMRT and the FiF technique was that a part of the lymph nodes was missed with the FiF technique, which did not occur in the IMRT plans. This is most likely caused by the fact that the lymph nodes were not yet delineated during the period that the FiF plans were made. The elective field in the FiF plan was based on the bony anatomy.

If during treatment the position of the bladder tumor has moved compared to the moment that the treatment plan was made, position correction should be applied to correct for this. When the displacement is large it may occur that beams pass through more or less tissue than planned, or through a different tissue type. This causes a changed attenuation of the beam compared to the moment that the treatment plan was made. In this thesis a simulation was done to study the effects of the changed path lengths on the dose distribution (chapter 3). After position correction the dose in the target varied from 91.9% to 100.4% of the prescribed dose, while the goal was 95%. The probability that a systematic underdosage occurs is small. Besides, the amount of underdosage was small, and therefore the tumor control probability will not decrease. A margin component of 2 mm is sufficient to completely rule out underdosage due to this effect.

As described before, two treatment plans were made for each bladder cancer patient: one for the boost field and one for the elective field. The tumor moved with respect to the pelvic lymph nodes and therefore we wanted to apply position correction for both targets separately. To prevent overdosage, the dose that the lymph nodes receive from the boost plan is taken into account. In this thesis, the effect of four different scenarios on the dose distribution is investigated: 1: No position correction is applied. 2: The correction of both plans is based on the bone match. 3: The correction of both plans is based on the tumor match. 4: The correction of the elective plan is based on the bone match and the correction of the boost plan is based on the tumor match (chapter 4). Options 1 and 2 resulted in a reduced tumor coverage as compared to the treatment plan, with option 3 there was no difference and with option 4 the difference was small. For the pelvic lymph nodes the difference was largest for option 3. No additional hot spots occurred in the organs at risk. Therefore we conclude that irradiation and position correction with two separate plans is safe and on average gives the best coverage for both targets.

Lung tumors are very well visible on CBCT. This enables stereotactic treatment for early-stage lung tumors. A stereotactic treatment is a treatment with a small number of fractions, with a very high dose per fraction. Because of this high fraction dose it is important that the tolerance dose of the organs at risk is not exceeded. The good visibility of lung tumors on CBCT enables accurate positioning of the patient and therefore the margin around the tumor to compensate for uncertainties can be small. Sometimes however, the tumor moves with respect to an organ at risk and in such cases it is hard to estimate whether the tolerance dose of an organ will be exceeded.

In order to make a right decision when the tumor moves towards an organ at risk in case of a stereotactic treatment of a lung tumor, it would be convenient to know the actual

dose distribution. The CBCT that was made for position verification purposes provides the geometry of the patient at the moment of treatment. We investigated whether this data set is also suitable for calculation of the actual dose distribution (chapter 5). For this study the grey values of the CBCT data were rescaled (rescaling the DICOM export parameter RescaleIntercept ) to resemble CT Hounsfield units. We found that after this rescaling, the dose distribution on the CBCT was acceptable for calculation of a dose distribution.

For dose calculation on CBCT it is necessary to have the body contour available. Manual delineation of the body contour is too time-consuming and the conventional methods for automatic segmentation of the body contour on CT fail on CBCT. The combination of applying a threshold for segmentation and applying several edge detectors in a novel way, results in a body contour that is very suitable for dose calculation (chapter 6).

In order to study whether dose-guided radiotherapy (DGRT) can improve decision making for lung cancer patients treated with SBRT, we evaluated the CBCTs of ten patients (chapter 7). In total, 54 position corrections were executed for these ten patients. The dose was calculated on both the CBCT that was made before correction and the CBCT scan that was made after the correction and both dose distributions were compared with the original treatment plan. In the majority of the cases the coverage of the target was already sufficient before position correction was applied. An important predictor for target coverage was the magnitude of the set-up error. When the set-up error was smaller than the margin, the target coverage was likely to be adequate. After position correction the difference of the maximum dose in the OARs was within 5% compared to the treatment plan, in the majority of the cases. Before correction the range of differences was larger. When the dose was not recalculated, but estimated based on assuming an invariant dose distribution, clinically relevant errors occurred both in the ITV and the OARs.

The developments in the field of radiotherapy of the last years have decreased the set-up errors and uncertainties due to interfraction motion significantly. The irradiation technique volumetric modulated arc therapy (VMAT), which was developed recently, yields a dose distribution that is comparable to IMRT. However, the treatment time for a treatment with VMAT is shorter. This reduces the uncertainties due to intrafraction motion. By using the options that are provided by the fields of radiology and nuclear medicine, we can determine our target area with increasing accuracy. Developments in those fields can provide us with an even more accurate tumor definition, with which we can further improve radiotherapy.