Reducing uncertainties in image-guided radiotherapy of rectal cancer

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Chapter 8

Summary

SUMMARY

Improvements in the treatment of rectal cancer patients have led to increased survival. As a result, long-term outcome has become an increasingly important factor. In addition, the introduction of population screening will lead to earlier detection of the disease with probably improved survival as a result. Both preoperative (chemo)radiotherapy and TME surgery are associated with toxicity and complications. As a result, research for rectal cancer treatment has focused on the reduction of radiation dose to (healthy) tissue and less extensive surgery or omission of surgery in selected patients. The work described in this thesis can be used to decrease the uncertainties related to image-guided external beam radiotherapy and high-dose-rate endorectal brachytherapy (HDREBT) of rectal cancer.

HDREBT can be used to deliver high doses to the tumor while sparing surrounding organs at risk due to a steep dose gradient. Most publications on the use of HDREBT focus on oncological outcomes, but do not report on the technical aspects of the procedure. **Chapter 2, 3 and 4** of this thesis focus on improvements of the HDREBT treatment planning procedure in terms of required imaging and the transition to MRI-only treatment planning.

Chapter 2 compares the use of a single planning CT for all subsequent fractions and the use of a planning CT at each fraction (repeat CT) in terms of target volume coverage and dose to organs risk. In 8/22 fractions, a CTV D98 of at least 85% could not be achieved due to incorrect applicator balloon setup or remaining air and/or feces between the CTV and the applicator and an intervention would be necessary. Therefore, repeat CT imaging should be the minimal standard practice to check for a correct applicator setup. In addition, replanning based on repeat CT imaging resulted in more conformal treatment plans and is therefore recommended.

To be able to use MRI for treatment planning for HDREBT, MRI-compatible fiducial markers were needed as an alternative to endoluminal clips. In **Chapter 3**, the MRI visibility of four different gold fiducial markers is evaluated. Four observers identified fiducial locations on two MRI exams per patient in two scenarios: without and with corresponding (CB)CT available to provide an estimate of fiducial location on MRI. Fiducial identification was poor without a corresponding (CB)CT. With corresponding (CB)CT, the Visicoil 0.75 and the Gold Anchor were the most consistently identified fiducials and were best visible on T1 3D GRE images.

To enable MRI-only planning for HDREBT, the applicator and the individual channels need to be visible on MRI. However, the applicator creates a signal void on currently used anatomical MRI images. **Chapter 4** shows that an ultrashort-echo time (UTE) MRI sequence can be used to visualize the applicator and the individual channels for HDREBT treatment planning. On the UTE images, there was sufficient contrast to discern the individual channels within the applicator, both in a phantom and in patients. After rigid registration to a 3D T_1-weighted sequence, the residual 95th percentile of the geometric distortion

inside a 550 mm diameter sphere was 0.8 mm (LR), 1.0 mm (AP) and 0.9 mm (CC) mm, which is within acceptable range.

Complete response rates might be increased by delivering a higher dose to the tumor, which is beneficial in organ preservation strategies. Although extensive research has been performed on the inter- and intrafraction displacement of the CTV relative to the bony anatomy, limited research was performed on the inter- and intrafraction displacement of the GTV relative to bony anatomy to determine margins for an external beam radiotherapy GTV boost. As a result, a wide range of clinically used PTV margins of 7-30 mm is described in literature. Setup correction could potentially be performed based on the fiducials instead of bony anatomy. To do so, the fiducials need to be representative of the GTV and the fiducials should be visible on MRI to accurately determine the fiducial-GTV spatial relationship. In **Chapter 5**, the stability of fiducials relative to the GTV and the inter- and intrafraction displacement of fiducials relative to bony anatomy is determined. A fiducial displacement of around 3 mm (LR and AP) and 4 mm (CC) relative to the GTV was observed. In addition, large interfraction displacements of the GTV and the fiducials relative to bony anatomy were found. Therefore, despite the observed fiducial displacement relative to the GTV, the use of fiducials as a surrogate for GTV position reduces the required margins from 20 mm to 8 mm in the AP direction and from 20 mm to 13 mm in the CC direction. A sub analysis shows that this reduction in margin may be larger in patients with tumors located in the mid- and upper rectum compared to the lower rectum.

In order to facilitate organ preservation in early stage rectal cancer patients, (chemo)radiotherapy has to be given in order to control the tumor. It is doubtful whether the typically used large target volume is required for these patients and reduction of the target volume to only include the peritumoral region of the primary tumor and mesorectum seems reasonable. The significant volume reduction might lead to decreased treatment-related toxicity without compromising oncological outcome. This is currently being investigated in the STAR-TReC trial, which assesses the feasibility of short-course radiotherapy or long-course chemoradiotherapy with subsequent two-stage response assessment as an alternative to TME surgery. The radiotherapy target volume only includes the mesorectum. **Chapter 6** determines the treatment plan variability in terms of dose to OAR and assesses the effect of a national study group meeting on the quality and variability of treatment plans for mesorectum-only treatment planning. Eight centers produced treatment plans for five cases and a study group meeting for the participating centers was organized to discuss the planning results. At the meeting, the values of the treatment plan DVH parameters were distributed among centers so that results could be compared. Subsequently, the centers were invited to perform replanning if they considered this to be necessary. Dose to OAR varied considerably between centers, especially for dose levels below 20 Gy. The study group meeting and the distribution of the initial planning results among centers resulted in lower dose to the defined OAR and reduced variability between centers after replanning.