Daily quantitative MRI for radiotherapy response monitoring

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SUMMARY

Hybrid systems that combine an MRI scanner with a linear accelerator for radiation treatment, called MR-linacs, were first introduced in the clinic in 2014. The MRI images provide better soft tissue contrast when compared to CT, enabling excellent depictions of the tumor and surrounding tissue. By integrating this with a linac, scans of the patient can be made during treatment. Besides the potential for reducing treatment margins, the MRI can also be used to acquire images that provide quantitative information about the patient biology (qMRI), such as diffusion weighted imaging (DWI) from which apparent diffusion coefficient (ADC) maps can be derived. Values from these images have the potential to be used as quantitative imaging biomarkers (QIBs) for treatment response monitoring or prediction. The MR-linac provides the benefit of acquiring qMRI with a high frequency, where daily acquisition is possible in most cases without increasing patient burden. The work in this thesis is focused on the acquisition of daily qMRI parameters on the 1.5 T Unity MR-linac system.

The Unity MR-linac was first used clinically in 2018. Because it is a newly introduced machine, it is important to assess its qMRI capabilities in phantoms. In the study described in Chapter 2, we showed that the Unity MR-linac is capable of acquiring T_1, T_2, and ADC maps, with comparable accuracy and repeatability to diagnostic systems, although for the ADC maps some adjustments related to SNR had to be made to produce comparable metrics. A series of phantom tubes with an increasing amount of DCE contrast agent showed that we could accurately determine the concentration up to around 0.5 mM, but underestimated larger concentrations. Finally, we demonstrated feasibility of acquiring these qMRIs on the Unity MR-linac in a prostate cancer patient.

One of the benefits of the Unity MR-linac is that the system is identical in all centers. This reduces challenges with reproducibility which are common when acquiring the same QIBs on different systems. However, it is then also important to unify the way that specific QIBs are acquired on the Unity MR-linac. In Chapter 3, we provide recommendations for the acquisition of the ADC. These recommendations specifically focus on the Unity MR-linac, and how the adjusted design of the system might influence the ADC value. Specific recommendations include limiting the highest b-value to 500 s/mm², scanning in close proximity of the iso-center to reduce the influence of spatial variations. We also showed that scanning while the gantry holding the linac is moving does not significantly increase the accuracy or repeatability, concluding that acquiring the ADC during treatment is possible.

Perfusion imaging is of interest as it has been shown to relate to hypoxia which is a known biomarker for treatment response. One clinically established way to measure quantitative parameters that are related to perfusion on MRI is dynamic contrast-

enhanced (DCE) MRI, which necessitates the use of a contrast agent. Using a contrast agent on a daily basis, is undesirable and therefore investigating alternatives that may provide perfusion information without the use of contrast agent is of interest. In Chapters 4 and 5, IVIM, which is such a technique is investigated in terms of treatment response monitoring (Chapter 4) and correlation to DCE (Chapter 5). In the multi-center study described in Chapter 4, 43 prostate cancer patients who received 20 fractions of 3 Gy were included, and daily IVIM scans were acquired. The change over time of the IVIM parameters D, f, and D* were analyzed using a mixed effects model. The model indicated no change in D in the healthy prostate tissue, while the D increased in the tumor. The perfusion parameters f and D* increased in both the prostate and healthy tissue, showing that IVIM parameters could potentially be used for treatment response monitoring.

Correlations between IVIM- and DCE parameters have been investigated before, but mainly on values acquired at a single time point. For treatment response purposes, it is also valuable to determine if they correlate longitudinally, as that could indicate that IVIM can be used instead of DCE for treatment response monitoring. In Chapter 5, we investigated the longitudinal correlations between IVIM and DCE measurements. In a cohort of 20 prostate cancer patients, weekly DCE scans were acquired in the same session as an IVIM scan. The repeated measures correlation was calculated for different ROIs. On the group level, an increase in IVIM and DCE parameters was found over the course of treatment, except for D in the peripheral- and transition zones. Statistically significant longitudinal correlations, although all below 0.5, were found between IVIM- and DCE parameters in the transition zone and peripheral zone of the prostate, while no statistically significant correlations were found in the tumor. The results suggest that IVIM could potentially be used as an alternative for DCE when measuring longitudinally.

$T_{1\rho}$ is a type of qMRI sequence that is most commonly used in cartilage imaging. Recently, some studies suggested that it might also be useful as a QIB for tumor localization and treatment response monitoring in oncology. In Chapter 6, a study is described where a $T_{1\rho}$ sequence was implemented and tested on the Unity MR-linac. Accuracy and repeatability were tested with a custom-made Agar phantom, and showed values comparable to previously reported values from diagnostic systems. Ten rectal cancer patients were scanned during their treatment of 5 fractions of 5 Gy. Results showed an increase in the GTV $T_{1\rho}$ for most patients, with a statistically significant difference between the first and last fraction for the incomplete responder group ($n = 5$). Evaluation in a larger cohort is needed to determine if there is a clinical benefit for the use of $T_{1\rho}$ as a treatment response QIB.

In conclusion, this thesis describes studies assessing the acquisition of daily qMRI on the Unity MR-linac. Initial feasibility was shown, including accuracy, repeatability and reproducibility in phantoms and patients, and changes in different qMRI parameters over the course of radiation treatment were measured in several patient groups. Daily qMRI has potential in terms of treatment response monitoring, and MR-linacs seem to be an excellent platform to help advance this field.