Academic title and name: M.Sc., Andreas Hagner

Project title: Real-time reconstruction of the dose delivered to moving anatomy during radiotherapy with an MR-linac

Background

Tumour motion and motion monitoring on a conventional accelerator

During radiotherapy delivery, tumours and organs can move due to bodily processes, such as breathing. This motion can compromise the tumour dose (Fig. 1) and give unacceptably high doses to organs at risk [1-2]. Motion is usually accounted for by treating an increased volume around the tumour site [3]. This comes at the expense of more normal tissue irradiation [4][5], potentially enhancing side effects [6]. Yet, parts of the tumour may still move outside the pre-defined high-dose volume, reducing treatment efficiency. Therefore, intra-treatment motion monitoring is highly desirable, especially for treatments with high doses and steep dose gradients delivered in few fractions, such as stereotactic body radiotherapy (SBRT).

To date, four research groups worldwide have implemented real-time tumour motion monitoring during clinical radiotherapy treatments with conventional accelerators [7]. The most established method is kilovoltage intrafraction monitoring (KIM), which was invented by the main supervisor Per Poulsen [8] and clinically implemented for prostate radiotherapy by co-supervisor Paul Keall in Sydney [9]. The only method that has been used clinically for real-time monitoring of respiratory tumour motion is COSMIK, which was also invented by the group of the main supervisor [10].

MR-linac

Real-time motion monitoring with conventional accelerators is limited as it relies on x-ray imaging and invasive implanted fiducial markers near or in the tumour. Unfortunately, the positions of the organs at risk (OAR) remains unknown. However, the new technology of combining an MRI scanner with a linear accelerator, making an MR-linac, has the potential to solve these problems [11][12]. It can monitor both tumour and OAR motion during treatment [13] with excellent soft tissue contrast and no need for implanted markers and no additional dose from imaging.

There are four different MR-linac systems in the world; two commercial systems (Elekta and ViewRay) and two prototype systems (Australian MR-linac and MagnetTX).

At Odense University Hospital (OUH) the Elekta MR-linac has been clinically operational since October 2018, while the ViewRay MR-linac has been used at Rigshospitalet (RH) since early 2019. The Australian MR-linac was recently used for its first live treatment of a rat brain tumour [14]. The systems have different capabilities: the commercial systems both have a perpendicular field direction (Fig. 2b) with different field strengths (0.35 T for ViewRay[15] and 1.5 T for Elekta[16]) while the Australian MR-linac has the capabilities of both perpendicular and in-line beam-field direction (Fig. 2a) and an intermediate field strength of 1 T [17]. These configurations have different advantages and disadvantages.

Real-time dose reconstruction

While the MR-linac provides real-time motion monitoring, the clinically most relevant quantity for radiotherapy is the radiation dose delivered to the tumour and OARs. Research into the reconstruction of delivered dose has been pioneered by the research group of the main supervisor and collaborator Thomas Ravkilde at Aarhus University Hospital (AUH) [18-21] by construction of the software program DoseTracker. DoseTracker performs real-time dose reconstruction and continuous dosimetric evaluation of radiotherapy treatments. It was recently used for the world's first tumour dose reconstruction performed on-the-fly as the treatment was delivered [21]. The applicant's master's thesis work involved improvements of the dose calculation algorithm of DoseTracker and integration of DoseTracker with radiotherapy treatment simulations.

Real-time adaption during radiotherapy

The optimal way to adapt to tumour motion during radiotherapy delivery is tracking, where a real-time motion signal is used for continuous re-alignment of the treatment beam to the moving tumour.

On a conventional therapeutic linear accelerator, tracking has been realized clinically as multi-leaf collimator (MLC) tracking (Fig. 3) by the group of co-supervisor Paul Keall in Sydney [22]. Poulsen's research group also has extensive experience with the technology being a central part of

its development for more than a decade [22-27]. The applicant also has experience with the technology from his master's thesis work on MLC tracking simulations and experimental validation thereof [28].

Currently, Keall's group is working on bringing MLC tracking to the Australian MR-linac, but quality assurance (QA) of tracking treatment plans is a major concern as the plan is adapted in real time and therefore not known in beforehand. Therefore, combining the two state-of-the-art techniques of the intra-treatment motion monitoring capabilities of the MR-linac with on-the-fly dose reconstruction in DoseTracker will pave the way for clinical real-time treatment evaluation and adaptation with the MR-linac. The combination will allow exploiting these two novel systems to their fullest potential.

Overall Aim

The overall aim of this PhD project is to develop and investigate real-time motion monitoring and real-time dose reconstruction during radiotherapy on MR-linacs

Part 1: MRI motion monitoring in phantoms with the Elektra Unity MR-linac

Aim: To establish synchronization between MR-segmented tumour and the beam of the Elekta Unity MR-linac at OUH.

Hypothesis: It is possible to perform real time motion monitoring on the Elekta Unity MR-linac.

Material and Methods / Research Plan

The first step is to develop real-time MR localization at OUH during radiotherapy by use of a fast 2D MR imaging sequences (single-slice balanced fast field echo, bFFE). The localization will be developed using a 4D-MRI phantom with an MR and MV visible tumour insert containing a radio-chromic film. Next up is to perform real-time motion monitoring of the tumour insert using MRI during treatment delivery and using cine MV-images to synchronize the imaging with the phantom motion. The final step is to quantify the latency and localization accuracy of the MRI tumour localization by cine-MV imaging by use of ground truth knowledge of the phantom motion.

Part 2: Adaption of real-time dose reconstruction to the Elekta Unity MR-linac at OUH and to the ViewRay MRIdian MR-linac at RH

Aim

To adapt the motion-including dose reconstruction algorithm of DoseTracker to the MR-linacs at OUH and RH and quantify the accuracy of real-time reconstructed dose errors in phantoms.

Hypothesis

Real-time dose reconstruction is possible for the Unity and MRIdian MR-linacs and accurate dose error calculations can help increase the dosimetric accuracy of both MR-linac systems.

Material and Methods / Research Plan

The software program, DoseTracker, developed at AUH by Thomas Ravkilde et al., can currently model doses of a conventional accelerator with an MLC and a simplified beam model. DoseTracker will be extended to model the specifications of the two available commercial MR-linac systems. The two systems have very different magnetic field strengths and their impact on the delivered dose will be modelled by replacing the current cylindrically symmetric dose kernels with suitable skewed dose kernels. DoseTracker's input and output (DICOM-RT plans, doses, linac parameters, etc.) will be modified to fit the MR-Linac systems.

The accuracy of DoseTracker's real-time dose reconstruction will then be investigated by performance of a large range of experiments with dose measurements in 4D MRI phantoms. The motion monitoring with the Elekta Unity MR-linac will be based on part 1 while motion monitoring with the ViewRay MRIdian will be developed as part of another PhD at RH concurrently with part 1. DoseTracker's algorithm will be improved upon until satisfactory accuracy is obtained.

Part 3: Real-time dose reconstruction during MR-guided MLC tracking of motion phantoms

Aim

To implement DoseTracker at the Australian MR-linac at Sydney University and perform real-time dose reconstruction during MR-guided MLC tracking treatments.

Hypothesis

Real-time dose reconstruction is possible for the Australian MR-linac and accurate dose error calculations during MLC tracking can help increase the dosimetric treatment accuracy.

Material and Methods / Research plan

This part of the project will be executed as an extended stay (~10 months) at the University of Sydney with co-supervisor Paul Keall. Sydney University has built their own research MR-linac [29-30], allowing one to change many of the specifications of the machine (e.g. different imaging sequences), as well as using the equipped MLC for real-time motion adaption during treatment.

During the stay, DoseTracker will be integrated with the Australian MR-linac. Different beam-field directions will be accounted for by implementing different types of skewed dose kernels. Real-time motion including dose reconstruction will be performed for a large range of experiments including MLC tracking deliveries while dose is measured in 4D MRI phantoms. The accuracy of the dose error reconstruction will be quantified by comparison with the measurements.

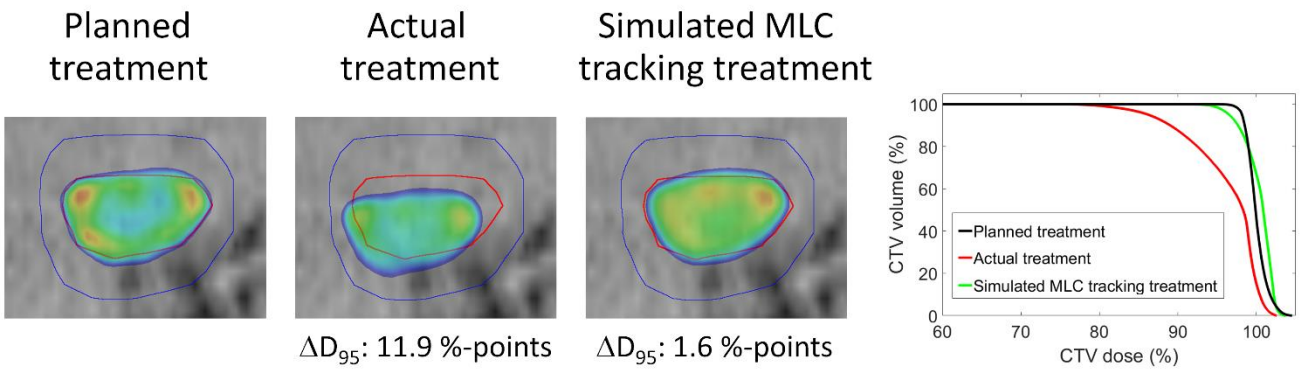

Figure 1 – From left to right: Planned dose distribution, the actual reconstructed dose distribution from the treatment, the treatment simulated with MLC tracking and the CTV DVHs of the three previous pictures. [Per Rugaard Poulsen, unpublished]

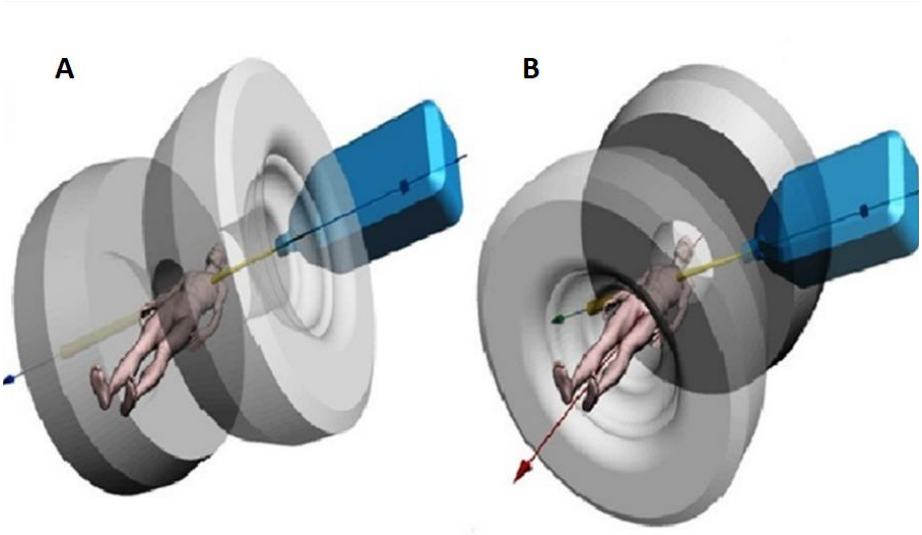

Figure 2 - Illustration of different beam-field orientation of MR-linac system. (A) In-line orientation. (B) perpendicular orientation [31].

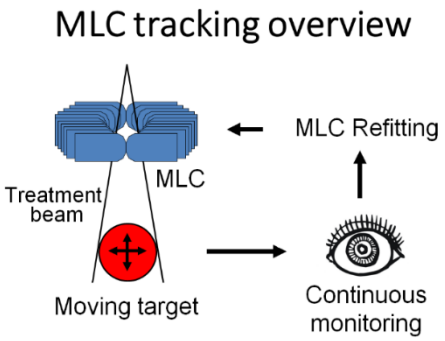

Figure 3 – *Principle of multi-leaf collimator (MLC) tracking. In MLC tracking, continuous monitoring of the target position is used to reshape the MLC to follow the target motion.* [Received from Per Rugaard Poulsen, unpublished].

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