Patient-specific in-vivo QA in MRGRT: 3D EPID dosimetry for the Unity MR-linac

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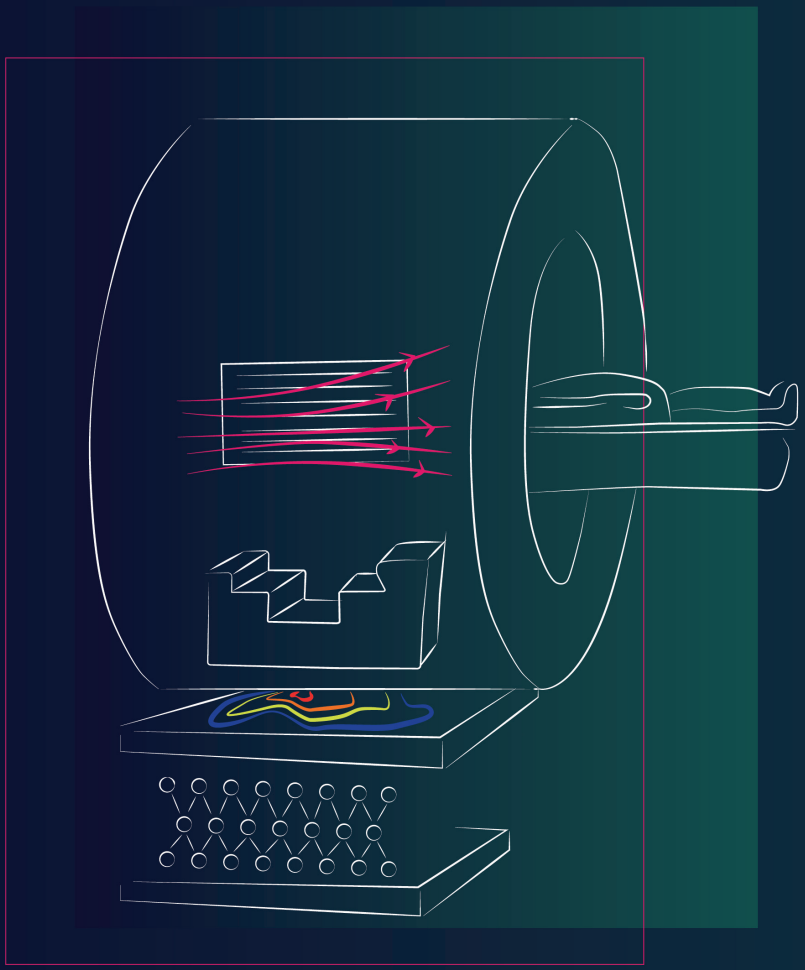

7.

GENERAL DISCUSSION

7.1. General discussion and thesis achievements

In-vivo EPID dosimetry is a quality control method to improve patient safety in radiotherapy[51,193]. In this thesis we aimed to develop and validate a method for pre-treatment and *in-vivo* 3D dosimetric verification of Unity MR-linac treatments using EPID dosimetry. This aim was met by adapting the physics models and software used for EPID dosimetry on conventional linacs. We provided clinical evidence that 3D portal dosimetry is feasible and can be a valuable tool for QA in the workflow of the Unity MR-linac. To this end, in Chapter 3 we characterized the dosimetric properties of the a-Si EPID panel in the Unity MR-linac and its behavior in close proximity to the MRI scanner. We further adapted an existing back-projection algorithm used with conventional linacs to the geometry of the Unity MR-linac. Based on the results presented in Chapter 2 and Chapter 4, the EPID dosimetry software was adapted to provide a comparison between EPID reconstructed dose distributions and the TPS. The first 3D in-vivo verification results were reported in Chapter 5.

The position of the panel with respect to the patient and the beam represented the main challenges when using the EPID for back-projection portal dosimetry. To avoid the presence of the Lorentz force in the accelerator gun, it is mounted on a rotating ring gantry in a low magnetic field area. The EPID is located in the same low B-field donut, opposite to the linac head. Furthermore, due to the MRI design, only the central part of the beam arrives to the panel with homogeneous attenuation. Outside this window, the beam is considerably more attenuated before reaching the panel. As a result, using the method described in Chapter 5, EPID dose distributions are accurately reconstructed only for radiation detected through the window free of gradient coils and shimming hardware. In Chapter 6 we developed a method that uses deep learning to correct the extra attenuation outside

the aforementioned window, making in vivo dosimetric validation feasible for the entire EPID image.

While automation is not the focus of the presented work, the development of an automated QA EPID-based solution is being implemented clinically now, which is essential to create a smooth system capable to generate verification reports. With such a system available, physicists can focus on the clinical relevance of dosimetric deviations instead of performing tedious manual labor for plan QA.

7.2. The use of EPID Dosimetry in MR-guided Radiotherapy

Currently, the first centers are gaining experience in the use of MR-guided radiotherapy with the Unity system and the methods for QC and QA that need to be applied. The needs for in-vivo dosimetry in MR-guided radiotherapy clearly differ from the needs in conventional External Beam Radiation Therapy (EBRT) QA.

In conventional EBRT, dosimetric verification is first of all performed to verify the accuracy of TPS dose calculation, but, depending on the workflow, also for data transfer verification. Given the fact that a plan is created off-line, prior to the treatment, pre-treatment verification is applied. However, with in-vivo EPID dosimetry, a complete end-to-end dosimetric verification of the treatment chain became feasible. It was shown that errors related to data transfer, dose delivery, patient set-up, MLC calibration and dose calculation could be detected [105]. Furthermore, clinical workload of in vivo EPID dose verification was limited with respect to pre-treatment verification.

With the rise of newly developed systems for MR-guided radiotherapy [93,106,108,109], workflow concepts have evolved and QA needs have changed. For instance, in the Unity system, for every fraction a different plan

is created online while the patient is on the couch [96,194,195]. In some institutions, an independent TPS is employed to perform online verification of the dose calculation. Even when such a TPS does not consider the magnetic field, it should detect gross deviations. At NKI we use an in-house developed program that conducts a simple check of plan characteristics, such as number and area of segments, number of MU's etc.

It is obvious that conventional pre-treatment dosimetry methods are of limited use for such a workflow. Therefore, it is necessary to establish a routine tool for the dosimetric verification of the TPS dose calculation that also serves as an end-to-end check of the entire chain. In MRgRT, the end-to-end check is actually more important due to the unprecedented complexity of the workflow. The sensitivity of EPID in-vivo for dosimetric verification is still to be further investigated, but what we can claim is that, as it is a measurement-based method, it is a perfect candidate for such an end-to-end check.

Most of the existing measurement devices, such as 2D arrays, film or IC's in rotating phantoms can only perform pre-treatment verification of the reference plan, which serves to validate issues such as MLC calibration, dose calculation, linac delivery errors and data transfer. However daily adapted plans can't be dosimetrically verified prior to irradiation with these techniques as the new plan is only generated once the patient is in position.

At this moment, the use of a pseudo CT is not yet clinical for the Unity system. Instead, an attenuation map is used for dose calculations that can either be a pre-treatment planning CT that doesn't represent the anatomy of the time of treatment, or an MRI with density overrides. In the future this may be replaced by a pseudo CT, with a representative attenuation map derived from MRI.

Dosimetric verification of Unity treatments can also be achieved by using the linac log files in combination with an (independent) dose engine and an accurate patient model. Potentially, when the actual anatomy of the patient is used, patient related errors (patient set-up, intra-fraction motion, tumor shrinkage, etc.) can be detected without additional measurement time. A drawback of this method is that it is not based on an independent transmission measurement and its reliability depends on the assumption of a correct determination of both the output of the linear accelerator and the anatomy (pre-treatment planning CT, MRI with density overrides or pseudo CT), which can only be verified with measurements. In this sense, EPID in vivo dosimetry is a more comprehensive check as it verifies the entire adapted chain.

For the MR-linac, recent studies [166,196] show that pre-treatment QA performed using 2D IC arrays in phantoms in different institutes have detected minimum differences when comparing measured and planned dose distributions. This suggests that the reproducibility and accuracy of the Unity systems is high and that errors in dose calculation and delivery are rare. While this may reduce the need for on-line verification of the dose calculation, errors related to data transfer, patient setup, and pseudo-CT determination are still feasible. A measurement-based system that efficiently and independently checks the entire workflow from end-to-end with almost no added time will help understand the weak points of the new workflow and its most relevant error sources and types.

7.3. Challenges and future work

7.3.1. Implementation challenges

The presented results show very good agreement between EPID and TPS dose distributions, but several issues still need to be addressed to create a tool for the clinic that can be used for all fractions automatically, reducing workload and adding value to existing methods. This is both the research and implementation work that needs to be done to have a full-working in-vivo EPID dosimetry solution for the Unity MR-linac.

Verification of every treatment by means of in-vivo EPID dosimetry to date requires manual work, which should be automated to make it a practical tool for all deliveries. This requires acquired data to be automatically transferred and linked to the correct daily CT and plan data. It further requires software to operate in batch mode and store results in a proper inspection software for quick analysis.

If the software is implemented to run in real-time during delivery[89,133] gross error detection could potentially be used to halt the machine. This would result in a solution that would not only catch but also prevent major dose deviations. This requires automation, but also a reduction of computational time of the dose calculations to allow synchronization with the delivery. It further needs integration with the Unity software. Additionally, thresholds for errors that should stop the linac would need to be established based on a retrospective analysis of the deviations detected. This would probably be necessary for each treatment site.

One of the main drawbacks of the design of the machine for the presented algorithm is the position of the EPID with respect to the beam and the patient. Some parts of the beams arriving to the panel are either not uniformly attenuated because they traverse a thicker in-

homogeneous region of the MRI scanner, or are directly not captured by the panel because they fall outside the detection area.

EPID-based dosimetric verification for fields falling outside the central region is not accurate, as is the case, for instance, in current clinical IMRT rectum plans. However, in Chapter 6 we explore an approach that uses used Deep Learning to correct the limitations of the EPID dose back-projection algorithm in the outer attenuated region of the 2D EPID frames making *in vivo* dosimetric validation feasible for the entire EPID frame. However, the clinical development of such solution represents a major challenge in terms of platform implementation. Moreover, the extension of 2D to 3D deep learning-based correction is also not straightforward and would require further research. Another option would be to improve the physical model at the EPID level to account and correct for the in-homogeneous attenuation of the primary beam and the MRI to EPID scatter arriving to the panel.

Beams, falling outside the panel (parts exceeding 8.1 cm in the caudal direction at isocenter plane) cannot be reconstructed with any possible method, as that information is not captured at all. The only alternative would be the engineering of new larger panels integrated in the machine, or the combination of two panels covering the entire field area.

7.3.2. Clinical considerations of in-vivo EPID dosimetry for the MR-Linac

Once the issues described in the previous section are resolved, the focus needs to shift to the decision making that is done based on observed EPID dose deviations

In our clinical practice for conventional linacs only 3 fractions are inspected per treatment. However, in the daily adapted workflow, all fractions could potentially be verified by means of in-vivo EPID

dosimetry, at no additional cost in terms of measurement time. Nevertheless, this would require more work from the medical physicists to inspect QA reports of all fractions or it would need further automation. It is an open issue to set a good balance between the number of fractions to verify and the amount of inspection work that it would arise.

Although in Chapter 6 we introduce errors (±5% MU, ±1.5 mm shifts) in the delivery of rectum plans to assess the degree of confidence of our deep-learning based correction, the exact magnitude of the errors that can be detected with EPID in-vivo dosimetry is still not determined. Its main use in the Unity system is aimed to catch gross errors, but finding out its limitations will ultimately determine the use of this tool in the clinic. In order to have an estimate of such, a specificity and sensitivity study should be performed. It would help to set optimal thresholds for the chosen evaluation criteria (γ, DVH), leading to a good balance between false positives and false negatives, and reasonable inspection workload in the clinic. For the completeness of this study, it would be interesting to carry out a study about the magnitude of errors per site, to establish site-specific thresholds, allowing more or less restrictive criteria for sites that usually show larger deviations than others. For instance, lung and head-and-neck are traditionally more difficult to verify given their inhomogeneities.

As for now, all results shown in this thesis compare TPS doses that include the presence of the magnetic field to back-projected dose distributions that do not account for it. It has been shown that for large inhomogeneities in the irradiated volume, the dose re-distributions due to the electron return effect caused by the magnetic field are significant [91,100,136,197]. However, as γ-results of the examples of this work are comparable to values of previous studies performed with conventional linacs [198], it suggests that the impact of the ERE is limited in the

high dose volume in quite homogeneous regions. However, for other treatment sites (lung, head-and-neck) this might give more problems. It can be argued, that in-vivo EPID dosimetry in its current form is more suitable to detect large deviations rather than small discrepancies. A dedicated study would be required to assess its importance (by introduction of errors related to the absence of the magnetic, as stated in previous paragraph), which ultimately will determine the scope of its use: gross error detection or accurately reconstruction of the delivered dose. In any case, as discussed throughout this thesis, two alternatives are on the table to cope with this issue: first, a comparison of the EPID back-projected doses to a version of the TPS that switches off the magnetic field; second, to back-project the EPID dose to a plane above the patient, to be used to feed an independent forward dose-engine [170] that accounts for the magnetic field, and then compare it to the TPS.

We might be able to shed light on some of the discussed open issues and limitations by means of introducing different magnitudes of errors to EPID in-vivo dose reconstructions. By doing so, we will be able to establish the extent of our solution and determine proper alert criteria. Within the scope of these studies, it is of particular interest to observe the response of our solution to the introduction of the following errors:

- errors in the patient anatomy (MRI with wrong density overrides -for now-) and in the set-up, to have a clear idea of the magnitude of errors that we are capable to detect related to this new step of the adapted workflow.

- a study on the response of our method to introduced errors in the outer region of the panel -where reconstruction is poor- would also shed light on the accuracy and sensitivity of the deep learning method proposed in Chapter 6.

- Errors related to the absence of the magnetic field in the EPID reconstructed dose distributions. If studies show large deviations due to ERE effects, this issue needs to be addressed with high priority.

7.4. Conclusion

We have developed the first system to verify MR-guided RT treatments using transit EPID images acquired during irradiation.

The work presented in this thesis represents a step forward in MR-guided radiotherapy patient safety to verify both pre-treatment and in-vivo fractions and provide a strong reduction in clinical workload.

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