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Short Communication

Comparison of beam segment versus full plan re-optimization in daily magnetic resonance imaging-guided online-adaptive radiotherapy

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ABSTRACT

The optimal approach for magnetic resonance imaging-guided online adaptive radiotherapy is currently unknown and needs to consider patient on-couch time constraints. The aim of this study was to compare two different plan optimization approaches. The comparison was performed in 238 clinically applied online-adapted treatment plans from 55 patients, in which the approach of re-optimization was selected based on the physician's choice. For 33 patients where both optimization approaches were used at least once, the median treatment planning dose metrics of both target and organ at risk differed less than 1%. Therefore, we concluded that beam segment weight optimization was chosen adequately for most patients without compromising plan quality.

1. Introduction

Daily radiotherapy plan adaptation using integrated magnetic resonance imaging linear accelerators (MRI-linac) aims to reduce organ at risk (OAR) dose and/or improve target coverage, by using anatomical information of the MRI-of-the-day [1,2]. Several studies have proposed a dosimetric benefit of daily online adaptations [3–6], which is expected to translate into a clinical benefit if the difference in dose distributions reaches beyond established thresholds. To minimize intra-fractional anatomical changes in the time window between acquisition of the MRI and the actual radiation treatment delivery, the treatment re-optimization time should ideally be as short as possible, without compromising treatment plan quality [7,8]. There are several possible strategies for plan adaptation, where different approaches have been shown to result in variable plan quality and plan adaptation time [9,10]. The time window for online plan adaptation could be shortened by, amongst others, reducing the time for optimizing the treatment plan. Therefore, this study aimed to compare two different plan optimization strategies, intensity-modulated radiotherapy (IMRT) segment weight re-optimization versus full re-optimization, in terms of time requirements and treatment plan quality.

2. Materials and methods

2.1. Patients

Fifty-five patients treated with daily online MRI-guided adaptive radiotherapy using the ViewRay MRIdian Linac (Viewray, Inc., Oakwood Village, Ohio, USA) between April 2019 and November 2019, receiving a total of 238 online-adapted treatment plans, were included in this retrospective study. General consent for data use was available for all patients and ethics approval of the study was received (BASEC-2018-01794). Characteristics of these treatment plans are shown in Table 1.

2.2. Planning

All patients were treated with step-and-shoot IMRT and the majority with an SBRT dose prescription. An MRI-of-the-day was acquired prior

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Table 1
Characteristics of the 238 online-adapted treatment plans included in this study. IQR = Interquartile range.

	Weight optimization	Full optimization
Number of treatment plans		
All	85 (36%)	153 (64%)
Lung	13 (32%)	28 (68%)
Liver	7 (18%)	31 (82%)
Pelvic	14 (58%)	10 (42%)
Prostate	22 (41%)	32 (59%)
Pancreatic	2 (13%)	13 (87%)
Adrenal	14 (58%)	10 (42%)
Kidney	4 (44%)	5 (56%)
Other abdominal	11 (31%)	24 (69%)
Optimization time		
Median [IQR]	5 min [2 min]	8 min [4 min]
Number of plans with a certain tumor volume change with respect to plan that was optimized from		
0%	31 (46%)	36 (54%)
(0%–2%)	23 (50%)	23 (50%)
(2%–4%)	12 (32%)	26 (68%)
>4%	19 (22%)	68 (78%)

to each daily treatment, to which the contours were transferred by means of a deformable registration; manual adaptation was then performed to compensate for insufficiencies of the automatic image registration and contour propagation process. The dose was recalculated on the MRI-of-the-day with adapted contours, resulting in a 'predicted' treatment plan. This predicted plan was then optimized with a fast weight optimization (i.e. automatic optimization of the weights of the static multi-leaf collimator (MLC) field segments), as a first step of the adaptive process. In cases where OAR dose constraints or target coverage goals were not met or dose conformity was not acceptable, a full IMRT re-optimization was always performed. Further responsibility on the decision for full re-optimization was at the discretion of the clinician. The goal of the re-optimization process was to achieve a treatment plan quality similar to the original plan or better. Objectives were only adjusted if the full optimization did not result in an acceptable plan. Note that weight optimization thus always preceded a full optimization. For all patients included in this study, OAR dose was prioritized over target coverage. Additional details on the online adaptation process and the OAR constraints have been described previously [7].

2.3. Analysis

Thirty-three patients received at least one weight-optimized and one full-optimized adapted plan during the course of treatment. For these patients, the dose parameters of these plans were compared. In case a patient had more than one plan with weight optimization or more than one plan with full optimization, the average over the dose parameters per optimization technique was calculated first. Eighty-five online-adapted plans, belonging to 37 patients, were clinically optimized with weight optimization only. Therefore, these were subjected to a full optimization for the purpose of this study, to be able to evaluate what would have been the benefit of a full optimization.

The following dose parameters were evaluated for both gross tumor volume (GTV) and planning target volume (PTV): dose to 2%, 95% and 98% of the volume ($D_{2\%}$, $D_{95\%}$ and $D_{98\%}$) and the mean dose to the volume (D_{mean}). For the 2 cm ring around the PTV, D_{mean} and $D_{5\%}$ were evaluated. For the treatment plans of the abdomen patients, dose to 1.0 cc ($D_{1.0cc}$) of the bowel, duodenum or stomach, depending on which organs overlapped with the 2 cm ring around the PTV, was evaluated. For prostate cancer patients, doses to rectum and bladder were evaluated. The percentage differences in dose parameters between both optimization strategies were assessed. Wilcoxon signed-rank test was applied to test for significance, considering p-values below 0.05 significant. All statistical analyses were performed in the software R (version 3.6.2).

3. Results

The optimization time was reported for 129/153 full-optimized plans and this was significantly different ($p < 0.001$) from the time for weight optimization (Table 1), for which the optimization time was reported for 67/85 plans.

The relative difference for all target- and OAR treatment planning dose metrics of the full-optimized plans with respect to the weight-optimized plans were calculated and shown in Fig. 1a. The mean and median differences between the optimization approaches were below ±1% for all dose parameters, except for rectum-$D_{1.0cc}$ (median 3.2%), for which 7 patients could be evaluated, and for abdomen-$D_{1.0cc}$ (median −1.9%) for which 14 patients could be evaluated (Fig. 1a). PTV-D_{mean} and PTV-$D_{95\%}$ were significantly lower in the full-optimized plans ($p = 0.046$ and $p < 0.01$, respectively).

Eighty-five plans were fully optimized for the purpose of comparing both optimization strategies applied to the same plan. The median change of all dose parameters remained within ±1% (Fig. 1b), whereas some large relative differences were observed for prostate and pelvis (Supplementary Material Fig. S1). The most changes larger than 3% ($n = 18$) were seen in ring-D_{mean} (Figs. 1b and S1). PTV-D_{mean}, PTV-$D_{2\%}$ and ring-$D_{5\%}$ significantly decreased after full optimization ($p < 0.01$, $p = 0.045$ and $p < 0.001$, respectively), whereas PTV-$D_{98\%}$ significantly increased ($p < 0.01$) (Fig. 1b).

4. Discussion

This study evaluated the plan quality between online-adapted radiotherapy treatment plans using either faster IMRT segment weight re-optimization or more time-consuming full IMRT re-optimization. We observed advantage of full re-optimization for individual patients and treatment fractions (Fig. 1a). These mainly originated from patients for which the OAR was close or within the PTV, such that at certain days a full optimization was required due to large anatomical changes, which additionally resulted in a compromise in PTV coverage or higher OAR dose.

For a few patients a suboptimal procedure during the treatment planning was used that caused larger changes than expected after applying a full optimization. For one adrenal metastasis patient (three treatment plans), the constraint on the 2 cm ring around the PTV was set too strict, which caused reduced target coverage in the full optimization. For two lung patients (four treatment plans), the GTV coverage was low due to high constraints on the structure PTV-GTV, which required a high normalization that caused a 'hot plan' after the full optimization. In general, for lung patients, a slightly incorrect deformation of the CT densities can lead to density changes inside the PTV, which are more challenging to cope with using the full optimization. Nevertheless, for all treatment plans for which large changes were observed after full optimization, the dose constraints were met in both the weight-optimized and the full-optimized plans. So, for the patients for which clinically no full optimization was performed, a full optimization would not have resulted in a clinically relevant improvement of plan quality.

Previous studies have investigated different online plan adaptation strategies using an MR-linac for lumbar spine bone metastases and lymph node oligometastases [9,10]. The calculation time of the plan adaptation methods in these studies was shown to range between 11 and 119 s and between 10 and 223 s. In our study, we found a difference of about three minutes between optimization strategies. Both studies of Winkel et al. showed that the most advanced method – full online replanning – achieved the best dosimetric results and can be performed within an acceptable time window, but the clinical relevance of these differences was not determined [9,10]. Another study investigated optimization strategies and the number of optimization iterations for pancreatic cancer, and showed that the number of optimizations could

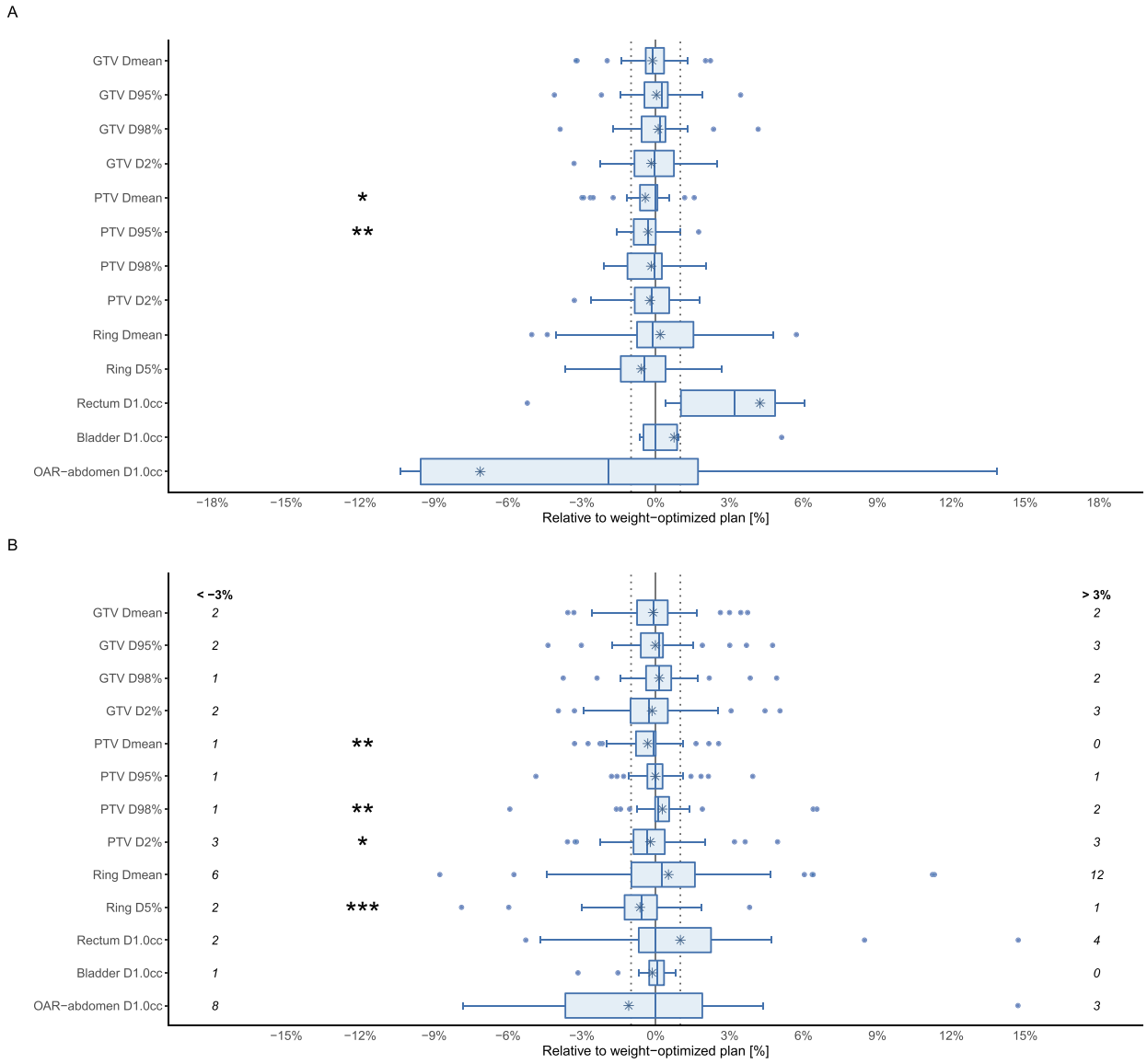

Fig. 1. Boxplots representing full versus weight optimization. A) Relative difference in mean dose parameters of treatment plans clinically optimized with full optimization versus weight optimization of 33 patients. Four outliers, for which the $D_{1.0cc}$ changed from 3.7 Gy to 1.9 Gy (−49%), 4.6 Gy to 3.3 Gy (−28%), 1.5 Gy to 1.8 Gy (+20%) and 4.6 Gy to 3.3 Gy (−28%) for bowel, duodenum, rectum and bowel, respectively, were not displayed for visualization purposes. B) Relative change of the dose parameters of all 85 treatment plans that were full-optimized for the purpose of this study, with respect to their corresponding weight-optimized plans. One outlier, for which the bowel-$D_{1.0cc}$ decreased by 22% from 2.85 Gy to 2.23 Gy, was not displayed for visualization purposes. Numbers of the left and right represent the number of treatment plans that decreased or increased more than 3% after full optimization, respectively. Dotted lines indicate ±1%. The stars in each boxplot represent the mean. Asterisks indicate significance levels: *: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$.

be reduced when using patient-specific geometric parameters to automatically define optimization objectives [5]. To the best of our knowledge, no study has yet compared beam segment weight optimization and full plan re-optimization.

In the current study, the benefit of the weight optimization versus the predicted treatment plan was not investigated. However, previous studies have shown, for various treatment sites, that for the majority of fractions the optimized plan was improved compared to the predicted plan [4,11–15]. Another study aimed to develop a model for predicting improved target coverage by online adaptations, this showed that the change in GTV and OAR volume were the most important predictors [3]. The OAR volume could not be evaluated in this study since the OAR contours are only adapted in the image slices that contain the 2 cm ring around the PTV to save time, but it was shown that treatment plans with large tumor volume changes were more often optimized with a full optimization.

The main limitation of this study is that at least the evaluation was performed retrospectively. This means that only clinically weight-optimized plans could be directly compared to the full-optimized version, since already full-optimized plans cannot be re-optimized with only weight optimization. Unfortunately, weight-optimized plans are not saved in case a full optimization was performed. Therefore, we do not know the benefit of performing the full optimization for these treatment plans, and the reasoning behind the decision to perform a full optimization were unfortunately not reported. This means that we cannot know in how many cases the full optimization was not beneficial and could have been omitted to save treatment time. Besides that, the weight-optimized plans were clinically acceptable and thus it was expected that the benefit of a full optimization was small for these treatment plans.

To conclude, our results show that full optimization would in none of the weight-optimized treatment plans have resulted in a clinically relevant benefit. Further evaluation is required to evaluate whether the full optimization could be more often omitted to reduce total treatment time, especially for cases with small target volume changes.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.phro.2021.01.001.

References

[1] Corradini S, Alongi F, Andratschke N, Belka C, Boldrini L, Cellini F, et al. MR-guidance in clinical reality: current treatment challenges and future perspectives. Radiat Oncol 2019;14:92. https://doi.org/10.1186/s13014-019-1308-y.

[2] Chin S, Eccles CL, McWilliam A, Chuter R, Walker E, Whitehurst P, et al. Magnetic resonance-guided radiation therapy: a review. J Med Imaging Radiat Oncol 2020; 64:163–77. https://doi.org/10.1111/1754-9485.12968.

[3] Palacios MA, Bohoudi O, Bruynzeel AME, van Sörsen de Koste JR, Cobussen P, Slotman BJ, et al. Role of daily plan adaptation in MR-guided stereotactic ablative radiation therapy for adrenal metastases. Int J Radiat Oncol Biol Phys 2018;102: 426–33. https://doi.org/10.1016/j.ijrobp.2018.06.002.

[4] Bohoudi O, Bruynzeel AME, Meijerink MR, Senan S, Slotman BJ, Palacios MA, et al. Identification of patients with locally advanced pancreatic cancer benefitting from plan adaptation in MR-guided radiation therapy. Radiother Oncol 2019;132:16–22. https://doi.org/10.1016/j.radonc.2018.11.019.

[5] Bohoudi O, Bruynzeel AME, Senan S, Cuijpers JP, Slotman BJ, Lagerwaard FJ, et al. Fast and robust online adaptive planning in stereotactic MR-guided adaptive radiation therapy (SMART) for pancreatic cancer. Radiother Oncol 2017;125: 439–44. https://doi.org/10.1016/j.radonc.2017.07.028.

[6] Finazzi T, van Sörnsen de Koste JR, Palacios MA, Spoelstra FOB, Slotman BJ, Haasbeek CJA, et al. Delivery of magnetic resonance-guided single-fraction stereotactic lung radiotherapy. Phys Imaging Radiat Oncol 2020;14:17–23. https://doi.org/10.1016/j.phro.2020.05.002.

[7] van Timmeren JE, Chamberlain M, Krayenbuehl J, Wilke L, Ehrbar S, Bogowicz M, et al. Treatment plan quality during online adaptive re-planning. Radiat Oncol 2020;15:203. https://doi.org/10.1186/s13014-020-01641-0.

[8] van de Schoot AJAJ, van den Wollenberg W, Carbaat C, de Ruiter P, Nowee ME, Pos F, et al. Evaluation of plan quality in radiotherapy planning with an MR-linac. Phys Imag Radiat Oncol 2019;10:19–24. https://doi.org/10.1016/j.phro.2019.04.004.

[9] Winkel D, Bol GH, Werensteijn-Honingh AM, Kiekebosch IH, van Asselen B, Intven MPW, et al. Evaluation of plan adaptation strategies for stereotactic radiotherapy of lymph node oligometastases using online magnetic resonance image guidance. Phys Imag Radiat Oncol 2019;9:58–64. https://doi.org/10.1016/j.phro.2019.02.003.

[10] Winkel D, Bol GH, Kiekebosch IH, Van Asselen B, Kroon PS, Jürgenliemk-Schulz IM, et al. Evaluation of online plan adaptation strategies for the 1.5T MR-linac based on "First-In-Man" treatments. Cureus 2018;10. https://doi.org/10.7759/cureus.2431. e2431-e.

[11] Tetar SU, Bruynzeel AME, Lagerwaard FJ, Slotman BJ, Bohoudi O, Palacios MA. Clinical implementation of magnetic resonance imaging guided adaptive radiotherapy for localized prostate cancer. Phys Imag Radiat Oncol 2019;9:69–76. https://doi.org/10.1016/j.phro.2019.02.002.

[12] Henke LE, Olsen JR, Contreras JA, Curcuru A, DeWees TA, Green OL, et al. Stereotactic MR-guided online adaptive radiation therapy (SMART) for ultracentral thorax malignancies: results of a phase 1 trial. Adv Radiat Oncol 2019;4:201–9. https://doi.org/10.1016/j.adro.2018.10.003.

[13] Finazzi T, Palacios MA, Haasbeek CJA, Admiraal MA, Spoelstra FOB, Bruynzeel AME, et al. Stereotactic MR-guided adaptive radiation therapy for peripheral lung tumors. Radiother Oncol 2020;144:46–52. https://doi.org/10.1016/j.radonc.2019.10.013.

[14] Finazzi T, Palacios MA, Spoelstra FOB, Haasbeek CJA, Bruynzeel AME, Slotman BJ, et al. Role of on-table plan adaptation in MR-guided ablative radiation therapy for central lung tumors. Int J Radiat Oncol Biol Phys 2019;104:933–41. https://doi.org/10.1016/j.ijrobp.2019.03.035.

[15] Henke L, Kashani R, Robinson C, Curcuru A, DeWees T, Bradley J, et al. Phase I trial of stereotactic MR-guided online adaptive radiation therapy (SMART) for the treatment of oligometastatic or unresectable primary malignancies of the abdomen. Radiother Oncol 2018;126:519–26. https://doi.org/10.1016/j.radonc.2017.11.032.