



Original Article

Target coverage and dose criteria based evaluation of the first clinical 1.5T MR-linac SBRT treatments of lymph node oligometastases compared with conventional CBCT-linac treatment



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ARTICLE INFO

Article history:

Received 14 June 2019

Received in revised form 13 February 2020

Accepted 13 February 2020

Keywords:

Radiotherapy

Lymph node oligometastases

MRI-guided radiotherapy

Online plan adaptation

MR-linac

ABSTRACT

Background and purpose: Patients were treated at our institute for single and multiple lymph node oligometastases on the 1.5T MR-linac since August 2018. The superior soft-tissue contrast and additional software features of the MR-linac compared to CBCT-linacs allow for online adaptive treatment planning. The purpose of this study was to perform a target coverage and dose criteria based evaluation of the clinically delivered online adaptive radiotherapy treatment compared with conventional CBCT-linac treatment.

Materials and methods: Patient data was used from 14 patients with single lymph node oligometastases and 6 patients with multiple (2–3) metastases. All patients were treated on the 1.5T MR-linac with a prescribed dose of 5×7 Gy to 95% of the PTV and a CBCT-linac plan was created for each patient. The difference in target coverage between these plans was compared and plans were evaluated based on dose criteria for each fraction after calculating the CBCT-plan on the daily anatomy. The GTV coverage was evaluated based on the online planning and the post-delivery MRI.

Results: For both single and multiple lymph node oligometastases the GTV V_{35Gy} had a median value of 100% for both the MR-linac plans and CBCT-plans pre- and post-delivery and did not significantly differ. The percentage of plans that met all dose constraints was improved from 19% to 84% and 20% to 67% for single and multiple lymph node cases, respectively.

Conclusion: Target coverage and dose criteria based evaluation of the first clinical 1.5T MR-linac SBRT treatments of lymph node oligometastases compared with conventional CBCT-linac treatment shows a smaller amount of unplanned violations of high dose criteria. The GTV coverage was comparable. Benefit is primarily gained in patients treated for multiple lymph node oligometastases: geometrical deformations are accounted for, dose can be delivered in one plan and margins can be reduced.

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In recent years stereotactic body radiation therapy (SBRT) has become the standard treatment option for the treatment of patients with lymph node oligometastases in many centers [1,2]. SBRT allows for the delivery of a relatively high amount of dose in few fractions with a very steep dose gradient [3] and is often given to postpone the start of systematic therapy and improve progression-free or overall survival without compromising the quality of life [4,5]. In the majority of the patients treated for lymph node oligometastases the affected nodes originate from prostate cancer and have a low α/β ratio [6]. This means that,

through SBRT, a high biologically effective dose (>100 Gy) can be given which is associated with high local control [7].

For accurate dose delivery, image-guided radiotherapy (IGRT) has become increasingly important for target visualization [8]. This reduces the effect of possible setup errors, caused by anatomical changes in the location of the target and organs at risk (OAR). Most modern radiotherapy systems are nowadays equipped with cone-beam computed tomography (CBCT) to visualize the tumor [9]. This has led to increased precision of radiotherapy treatment for tumors which are well visible on CBCT. However, compared to magnetic resonance imaging (MRI), CBCT yields relatively poor soft tissue contrast [10]. This makes it difficult to accurately identify soft tissue targets, based on CBCT imaging alone. For this reason, position verification may be performed on nearby bony anatomy

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Table 1

Patient data characteristics.

Single lymph node oligometastases patients (N = 14)			
	CBCT-linac		MR-linac
GTV [cc]			0.53 [range, 0.15 – 6.83]
ΔGTV Pretreatment – Rx [cc]			0.01 [range –2.25 – 0.82]
PTV margin[mm]	3 (N = 10), 8 (N = 4)		3 (N = 14)
Multiple lymph node oligometastases patients (N = 6)			
	CBCT-linac		MR-linac
GTV per patient [-]			2 (N = 3), 3 (N = 3)
GTV [cc]			0.36 [range, 0.08 – 1.49]
ΔGTV Pretreatment – Rx [cc]			0.01 [range, –1.04 – 0.29]
PTV per patient [-]	1 (N = 1), 2(N = 4), 3 (N = 1)		2 (N = 3), 3 (N = 3)
PTV margin[mm]	3 (N = 8), 5 (N = 2), 8 (N = 3)		3 (N = 6)
Treatment plans per patient [-]	1 (N = 4), 2 (N = 2)		1 (N = 6)

or other surrogate structures. This is generally less accurate and could provide erroneous results for both localization and verification [11]. As an alternative, artificial markers may be implanted in the patient. While this may provide good target visualization, the procedure is invasive for the patient [12,13].

During SBRT of lymph node oligometastases on CBCT-linacs, inter-fraction motion is accounted for by couch translations and sometimes also for rotations. These translations and rotations can compensate for rigid target motion, but not for non-rigid changes of the target such as changes in size or shape or, for multiple lymph nodes, independent motion of the targets [14,15]. Additionally, it is not possible to account for anatomical changes in the location of the target and OARs, as well as path length changes and tissue attenuation. This can cause differences between the planned dose and delivered dose after position correction [16]. Therefore using position verification and correction procedures, but not optimally taking the new patient anatomy into account, may still result in unplanned violations of dose constraints [17,18]. Additionally, it may result in underdosage of the PTV prior to delivery, which in turn can cause underdosage of the GTV due to intra-fraction motion.

Inter-fraction variations of soft tissue targets can be more optimally dealt with using MR-guided radiotherapy systems such as the 1.5T MR-linac (combined 1.5T MR scanner and linear accelerator, Unity, Elekta AB, Stockholm, Sweden) [19,20]. This system provides diagnostic quality imaging of the patient anatomy before and during treatment, which allows for MR-guided online adaptive workflows [21]. In August 2018, SBRT of lymph node oligometastases on the 1.5T MR-linac has commenced within our institute using online MRI-based delineation of the target and OARs, full-online replanning and MRI based position verification [22].

A R-IDEAL [23] stage 0 study simulating the dosimetric impact of online replanning for SBRT of lymph node oligometastases on the 1.5T MR-linac compared to online position correction showed beneficial dosimetric outcomes and a reduction of unplanned violations of dose constraints [18]. The purpose of this study was to perform a target coverage and dose criteria based evaluation of the clinically delivered online adaptive radiotherapy treatment compared with simulated conventional CBCT-linac treatment.

Material and methods

Patient characteristics

Patients were treated at our institute for single and multiple lymph node oligometastases on the 1.5T MR-linac (Unity, Elekta AB, Stockholm, Sweden) since August 2018. For this study, patient data was used from 14 patients with single lymph node

oligometastases and 6 patients with multiple (2–3) metastases located in the pelvic and para-aortic region (Table 1).

Clinical treatment

Pre-treatment CT and MR imaging were acquired for each patient and registered. To provide reproducibility of the patient position along the length of the couch between the pre-treatment CT scan and each MRI based treatment session, the pre-treatment CT was acquired using a special table overlay to enable patient set-up using specific couch index points [22]. To reduce potential intra-fraction motion, patients with lymph node metastases in the pelvic and low para-aortic region were initially immobilized using a vacuum mattress (BlueBAG, Elekta AB, Stockholm, Sweden) with both hands on the chest and the elbows along the body [20]. The patients with affected nodes in the high para-aortic region (above the renal veins) were treated whilst wearing an abdominal corset with the arms along the body [24].

All patients were treated on the 1.5T MR-linac with a prescribed dose of 5×7 Gy to 95% of the PTV. For each patient, a six-, seven- or ten-beam MR-linac IMRT pre-treatment plan was created with a GTV-PTV margin of 3 mm using Monaco TPS (Elekta AB, Stockholm, Sweden), taking into account the presence of the 1.5T magnetic field. One patient was treated with adapted margins for fractions 2–5 (2 mm in inferior, left and anterior direction and 6 mm in superior, right and posterior direction). For patients treated with the arms along the body, beam angles were selected such that

Table 2

Clinical dose criteria.

Structure	Offline constraints (pre-treatment plan)	Online constraints
PTV	$V_{35\text{Gy}} > 95\%$ $D_{0.1\text{ cm}}^3 < 47.25\text{ Gy}$	$V_{35\text{ Gy}} > 95\%$ $D_{0.1\text{ cm}}^3 < 47.25\text{ Gy}$
Aorta	$V_{53\text{Gy}} < 0.5\text{ cm}^3$	$V_{53\text{Gy}} < 0.5\text{ cm}^3$
Bladder	$V_{38\text{Gy}} < 0.5\text{ cm}^3$ $V_{18.3\text{Gy}} < 15\text{ cm}^3$	$V_{38\text{Gy}} < 0.5\text{ cm}^3$
Bowel bag + Colon	$V_{32\text{Gy}} < 0.5\text{ cm}^3$ $V_{25\text{Gy}} < 10\text{ cm}^3$	$V_{32\text{Gy}} < 0.5\text{ cm}^3$
Duodenum + Stomach	$V_{35\text{Gy}} < 0.5\text{ cm}^3$ $V_{25\text{Gy}} < 10\text{ cm}^3$	$V_{35\text{Gy}} < 0.5\text{ cm}^3$
Esophagus	$V_{34\text{Gy}} < 0.5\text{ cm}^3$ $V_{27.5\text{Gy}} < 5\text{ cm}^3$	$V_{34\text{Gy}} < 0.5\text{ cm}^3$
Kidney	$V_{16.8\text{Gy}} < 67\%$	$V_{16.8\text{Gy}} < 67\%$
Nerve root + Sacral plexus	$V_{32\text{Gy}} < 0.1\text{ cm}^3$	$V_{32\text{Gy}} < 0.1\text{ cm}^3$
Rectum + Sigmoid	$D_{\text{max}} < 40\text{ Gy}$ $V_{32\text{Gy}} < 0.5\text{ cm}^3$	$V_{32\text{Gy}} < 0.5\text{ cm}^3$
Spinal cord	$D_{\text{max}} < 28\text{ Gy}$	$D_{\text{max}} < 28\text{ Gy}$
Ureter	$D_{\text{max}} < 40\text{ Gy}$	$D_{\text{max}} < 40\text{ Gy}$

the beams would not traverse the arms. Additionally a CBCT-linac VMAT back-up plan was created for each patient. A radiation oncologist determined whether the lymph node oligometastases were well visible or not on CBCT. A PTV margin of 8 mm was used for poorly visible lymph nodes and 3 mm for visible lymph nodes [18]. For patients with multiple lymph node oligometastases, the plans consisted of one, two or three PTV's. For the CBCT-linac plans, a medical physicist and radiation oncologist decided on one or two separate plans, placement of the isocenter, depending on the specific anatomical situation of the patient and PTV margins (Table 1). OAR dose was lowered as much as possible, while maintaining a sufficient PTV coverage of $V_{35Gy} > 95\%$ and a D_{max} between 120–135%. Clinical dose criteria for the OARs were based on the UK SABR consortium guidelines (2016) (Table 2).

During each online treatment session the adapt to shape (ATS) workflow was followed to allow for adaptive treatment planning [21]. A daily MRI was acquired onto which the pre-treatment contours were automatically deformed. If necessary, the contours of the target lymph node(s) and OARs within 2 cm of the PTV(s) were manually adapted by a radiation oncologist [22]. Based on the daily MRI and adapted contours, a new plan was created [25]. Radiation delivery according to the new plan was performed after MRI based position verification. After each treatment session offline assessment of the intra-fraction motion was performed by recalculating the GTV coverage on the actual anatomy as seen on the post-delivery MRI. Contouring of the GTV on the post-delivery MRI was performed by multiple observers. Inter-observer contouring variation on MRI is considered negligible for these small and well visible lesions.

Retrospective analyses

Dosimetric comparison of MR-linac and CBCT-linac treatment

The differences in target coverage between the clinically delivered MR-linac and the CBCT-linac plans were compared for each treatment session. Additionally, the plans were evaluated based on the clinical dose criteria for the target coverage and OAR dose. The CBCT-linac plan was recalculated on the daily MRI and using the contours from the online treatment. The electron density information was retained by matching and deforming the initial planning CT to the daily MRI data. During treatment on a CBCT-linac online translation correction is performed by matching using a 0.5 cm mask around the GTV or a clipbox with nearby structures for lymph nodes with good or poor visibility, respectively. To simulate a best-case outcome of the online translation correction pro-

tol, as performed in our current clinical practice for CBCT-linac treatment of these targets, we assumed that the correction reference point for single lymph nodes was equal to the isocenter and placed at the center of the daily contoured GTV. Modern CBCT-linac treatment systems could also have the possibility to compensate for rotational errors using six degrees of freedom (6DOF) couches. For this purpose, the lesions were automatically matched to each other making use of a clipbox around the lesions. For lesions adjacent to bony anatomy, this information was minimally included. The result of the match was manually inspected and verified. If the lesions were well visible, the plans were also recalculated after performing 6DOF rotational correction. For multiple PTV's, the isocenter was placed manually at the same location as was done in the pre-treatment planning of the CBCT-linac plans. This choice was made by the physician and was either in the middle of one of the targets or in-between the targets. If CBCT-linac treatment would be performed with two plans, the doses were summed. Additionally, the distances between the center of gravities between the targets was calculated to investigate the relative intra-fraction motion for each fraction compared to the pre-treatment data. The plans were evaluated using the clinical dose constraints and compared based on PTV and GTV coverage.

Intra-fraction GTV coverage analysis

To determine whether dose coverage was sufficient during treatment and if PTV margins were adequate, the GTV coverage for the clinically delivered (ATS) plans and the CBCT-linac plan were evaluated over all five fractions. This was done by evaluating the dose on both the online planning MRI, acquired at the start of the treatment fraction, as well as the post-delivery MRI, acquired after dose delivery.

Results

For single lymph node oligometastases the clinically delivered MR-linac plans had a median GTV V_{35Gy} value of 100% [99.7–100%] compared to 100% [98.7–100%] for the CBCT-linac plans recalculated on the daily anatomy after translation correction. The PTV V_{35Gy} was significantly higher (p -value < 0.01) with a median of 100% [90.7–100%] compared to 94.9% [47.7–100%] for the CBCT-linac plans (Fig. 1). All dose criteria (PTV coverage and OAR constraints) were met for the MR-linac plans in 59/70 (84%) fractions. Violations of OAR criteria occurred with a maximum of 3 Gy above the set threshold. For the CBCT-plans recalculated on the daily anatomy all dose criteria were met in 13/70 (19%)

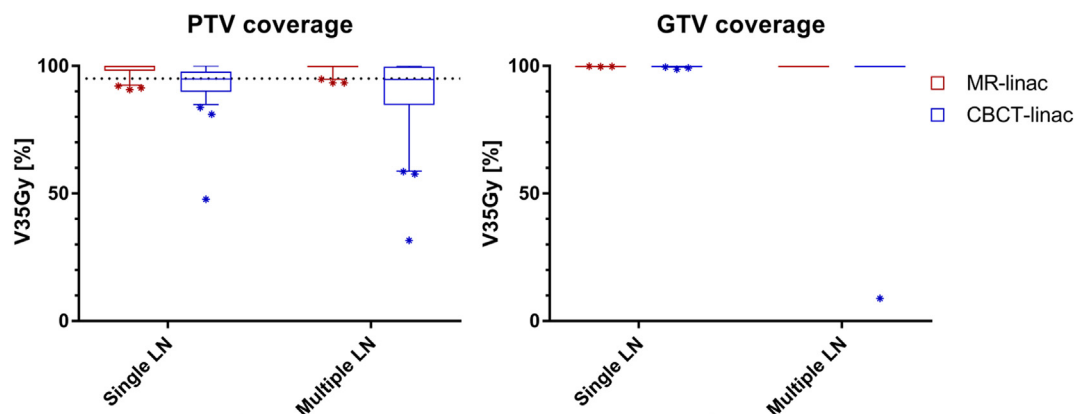


Fig. 1. Boxplot of the target dose coverage described as planning target volume (PTV) and gross target volume (GTV) V_{35Gy} in % for the adapted treatment plans and CBCT-linac plan recalculated on the daily anatomy after translation correction ($N = 14$ single and 6 multiple lymph node patients). The bars show the upper and lower quartiles. The whiskers show the 5–95 percentiles. Outliers are denoted with an asterisk. The dotted line for the PTV graph (left) denotes the minimal required coverage according to the dose constraints.

fractions. Violations of OAR criteria occurred with a maximum of 2.5 Gy or 0.1 cc above the set threshold.

For multiple lymph node oligometastases the clinically delivered MR-linac plans had a median GTV $V_{35\text{Gy}}$ value of 100% [100–100%] compared to 100% [8.9–100%] for the CBCT-linac plans recalculated on the daily anatomy after translation correction. Also here the PTV $V_{35\text{Gy}}$ was significantly higher (p -value <0.01) with a median of 100% [93.4–100%] for the MR-linac compared to 94.7% [31.6–100%] for the CBCT-linac (Fig. 1). All dose criteria were met for the MR-linac plans in 20/30 (67%) fractions. Violations of OAR criteria occurred with a maximum of 0.5 Gy or 0.1 cc above the set threshold. For the CBCT-plans all dose criteria were met in 6/30 (20%) fractions. Violations of OAR criteria occurred with a maximum of 0.5 Gy or 0.7 cc above the set threshold. For the clinically delivered single lymph node oligometastases plans the median GTV $V_{35\text{Gy}}$ was 100% [99.7–100%] and the median GTV D_{mean} was 43.0 Gy [37.6–46.1 Gy] on the online planning MRI. On the post-radiation delivery MRI the median GTV $V_{35\text{Gy}}$ was 100% [98.0–100%] and the median GTV D_{mean} was 42.9 Gy [37.9–45.8 Gy]. For 62 of the 70 fractions (89%) the GTV $V_{35\text{Gy}}$ on the post-delivery MRI remained 100%. For one patient, a slight reduction of the GTV coverage was necessary during online treatment planning for 3 fractions due to the dose constraint for the sacral plexus in the vicinity of the target. For the CBCT-linac plans the median GTV $V_{35\text{Gy}}$ was 100% [98.7–100%] and the median GTV

D_{mean} was 44.5 Gy [41.6–46.8 Gy] on the online planning contours. On the post-radiation delivery contours the median GTV $V_{35\text{Gy}}$ was 100% [72.4–100%] and the median GTV D_{mean} was 44.5 Gy [37.2–46.2 Gy]. For 56 of the 70 fractions (80%) the GTV $V_{35\text{Gy}}$ was 100% on the post-delivery contours (Fig. 2).

The clinically delivered multiple lymph node plans showed a median GTV $V_{35\text{Gy}}$ of 100% [100–100%] and the median GTV D_{mean} was 43.5 Gy [39.8–46.3 Gy] on the online planning MRI. On the post-radiation delivery MRI the median GTV $V_{35\text{Gy}}$ was 100% [57.7–100%] and the median GTV D_{mean} was 43.2 Gy [35.8–46.1 Gy]. For 63 of the 75 targets (84%) the GTV $V_{35\text{Gy}}$ on the post-delivery MRI remained 100%. For the CBCT-linac plans the median GTV $V_{35\text{Gy}}$ was 100% [8.9–100%] and the median GTV D_{mean} was 44.2 Gy [33.4–46.7 Gy] on the online planning contours. On the post-radiation delivery contours the median GTV $V_{35\text{Gy}}$ was 100% [0–100%] and the median GTV D_{mean} was 43.7 Gy [32.4–46.4 Gy]. For 61 of the 75 targets (81%) the GTV $V_{35\text{Gy}}$ was 100% on the post-delivery contours (Fig. 2).

In total 11 of the single and 6 of the multiple lymph node oligometastases cases were eligible for rotational correction using a 6DOF-couch. For single lymph node oligometastases the CBCT-linac plans with 6DOF correction had a median GTV $V_{35\text{Gy}}$ value of 100% [98.9–100%] and a median PTV $V_{35\text{Gy}}$ value of 96.4% [85.6–100%] compared to 100% [98.7–100%] and 95.4% [86.1–100%] for the CBCT-linac plans with only translational correction.

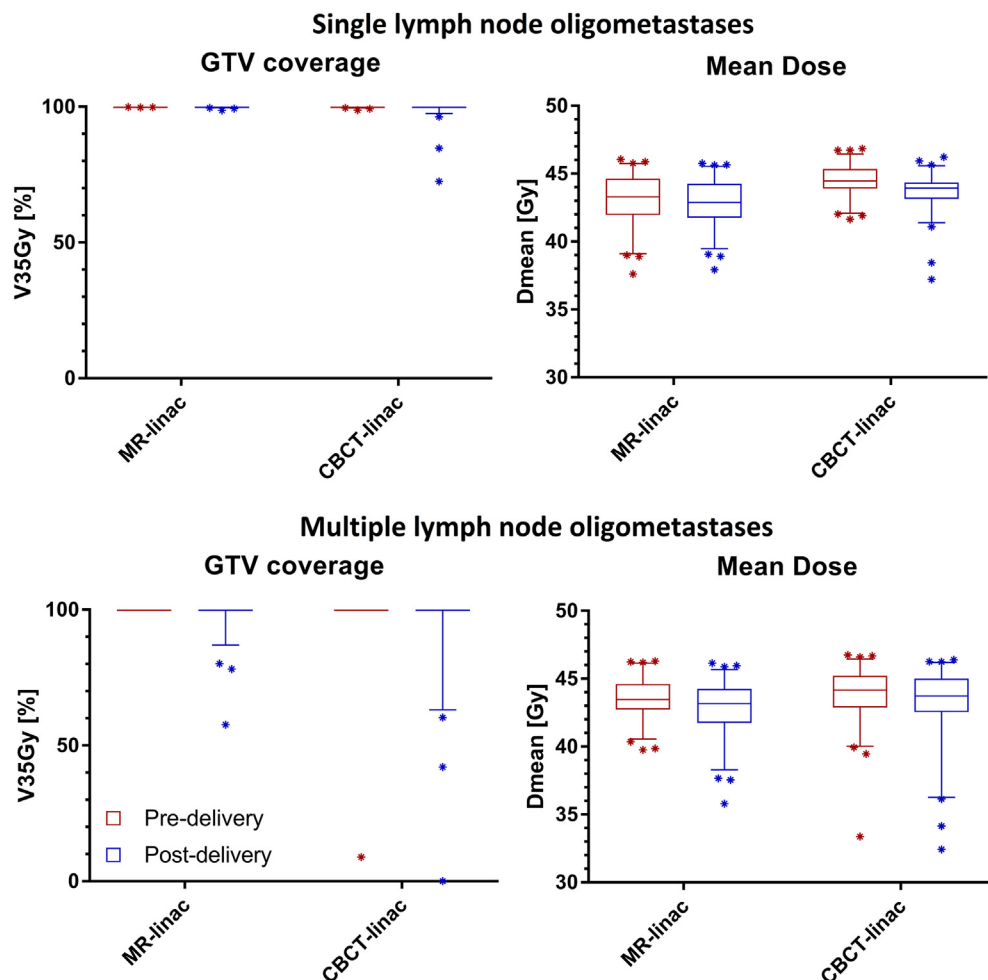


Fig. 2. Boxplot graph of the GTV coverage and mean GTV dose of single ($N = 14$ patients) and multiple ($N = 6$ patients) lymph node oligometastases described as $V_{35\text{Gy}}$ in % and D_{mean} in Gy for the clinically delivered MR-linac plans and the CBCT-linac evaluated on pre- and post-delivery contours after translation correction. The bars show the upper and lower quartiles. The whiskers show the 5–95 percentiles. Outliers are denoted with an asterisk.

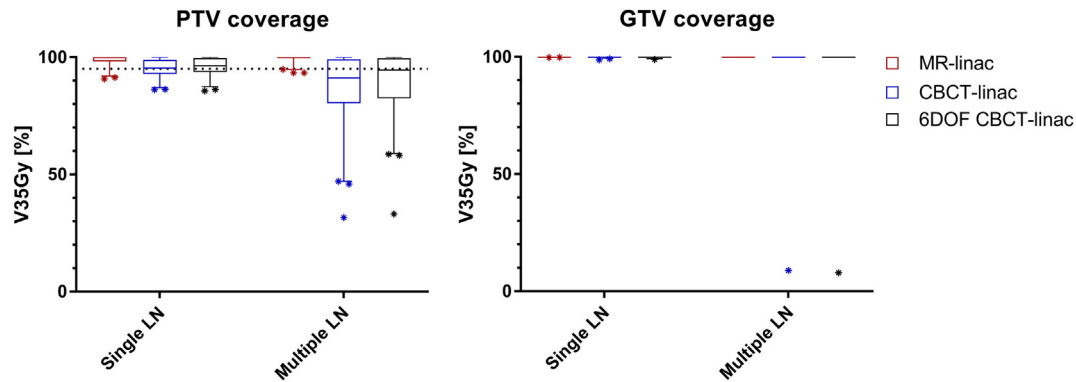


Fig. 3. Boxplot of the target dose coverage described as planning target volume (PTV) and gross target volume (GTV) V_{35Gy} in % for the adapted treatment plans and CBCT-linac plan recalculated on the daily anatomy, which were eligible for rotation correcting through a 6DOF-couch ($N = 11$ single and 6 multiple lymph node patients). The bars show the upper and lower quartiles. The whiskers show the 5–95 percentiles. Outliers are denoted with an asterisk. The dotted line for the PTV graph (left) denotes the minimal required coverage according to the dose constraints.

Independent target inter-fraction motion in a patient with multiple lymph node targets.

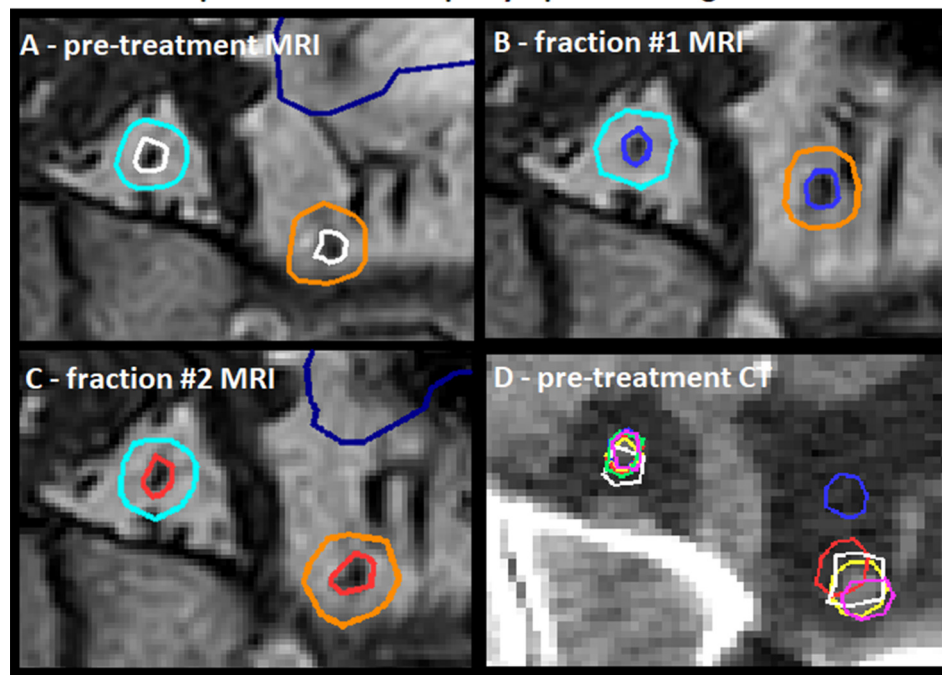


Fig. 4. A depicts the pre-treatment situation on MRI and B and C show the online MRI and GTV and PTV contours of two targets (CBCT backup plan with PTV margins of 8 mm for these two targets, due to distance from isocenter/third target) in a multiple lymph node case for fraction one and two, respectively. In fraction one a large variation can be observed in the Euclidean distance between the center of gravities of both targets which decreased from 34.8 mm to 30.6 mm for this particular case because of bowel (dark-blue) influence. D depicts the pre-treatment CT with the online GTV contours for each fraction. The white contour shows the target in pre-treatment situation and the colored contours each represent the contours used in one of the five online fractions and correspond to those in the MRI images. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

For the multiple lymph node oligometastases the CBCT-plans with 6DOF correction had a median GTV V_{35Gy} value of 100% [7.9–100%] and a median PTV V_{35Gy} value of 94.5% [33.1–100%] compared to 100% [8.9–100%] and 91.1% [31.6–100%] for the CBCT-linac plans with only translational correction. The clinically delivered MR-linac plans for this subset had a median GTV V_{35Gy} value of 100% [99.7–100%] and a median PTV V_{35Gy} value of 100% [90.7–100%] for single lymph nodes and a median GTV V_{35Gy} value of 100% [100–100%] and a median PTV V_{35Gy} value of 100% [93.4–100%] for multiple lymph nodes (Fig. 3). There was a median difference of 0.8 mm [0.1–6.0 mm] in intra-target distance between the

pre-treatment situation and the five treatment fractions. An example of large inter-fraction target motion can be seen in Fig. 4.

Discussion

In this study we have compared the target coverage of the clinically delivered online adaptive radiotherapy treatment with CBCT-linac treatment for patients with both single or multiple lymph node oligometastases and evaluated the plans based on the clinical dose criteria. Our results show no significant difference between the GTV coverage and mean GTV dose between the MR-linac and

the simulated CBCT-linac treatment. Even though the PTV coverage was significantly higher for the MR-linac treatment, which corresponded to earlier findings [18], the GTV remained adequately covered for most fractions with both treatments. Because the post-delivery GTV coverage for the CBCT-linac plans was also evaluated on the post MR-linac delivery MRI, this potentially shows a worst-case scenario. The CBCT-linac plans are VMAT plans which have shorter delivery times and so less intra-fraction motion might be expected. In addition to the longer delivery times, the entire workflow for MR-linac treatment is longer than the clinical used workflow of our CBCT-linac treatment. For targets which are poorly visible on CBCT, margins can be reduced, but this is not always the case. This means that the benefit with regards to improved GTV coverage for the group of single lymph node oligometastases for this particular patient group seems limited as with the necessary experience and expertise, manual positioning on CBCT can be adequately performed. Therefore, from an economic perspective, the justification of online MR-guided radiotherapy for these patients with a five fraction fractionation scheme is questionable at present. However, the performed treatments contributed greatly towards gaining clinical experience with MRI-guided treatment using the MR-linac and can be used as a step towards further hypofractionation and possibly even single fraction treatments. In these cases, target coverage and OAR constraints are more demanding for which benefit could be obtained through MR-guided treatment.

A benefit for treatment of multiple lymph node oligometastases is present in cases with large deformation of the patient anatomy and can additionally be explained by independent inter-fraction motion of the targets, which may occur [26]. Position correction through couch translations may therefore not always be sufficient. This can be seen in particular for one fraction in a patient receiving simultaneous treatment of three lymph node metastases. While GTV coverage was adequate in four fractions with a $V_{35\text{Gy}}$ of 100% for all targets, one target would receive only a GTV $V_{35\text{Gy}}$ of 8.9% and 0% in one fraction in the pre- and post-delivery situation, respectively (Fig. 5). This is caused by independent motion of the targets due to deformation of the patient anatomy. In clinical practice each treatment is manually checked. If thresholds were exceeded, a physician and medical physicist would be called and appropriate action would be determined. Roper et al. [27] have shown that in general, the risk of compromised coverage increased with decreasing target volume, increasing rotational error and increasing distance between targets. This also corresponds with the relatively large distance and distal position of this particular target to the other two targets for this particular case. Although in general excellent plan quality and clinical efficiency can be reached with single-isocenter treatment of multiple targets [28], rotational errors cannot be ignored for high precision treatment, especially when the distance between a target and the isocenter is large [29]. Treating patients with multiple lymph node oligometastases on the 1.5T MR-linac means that the use of

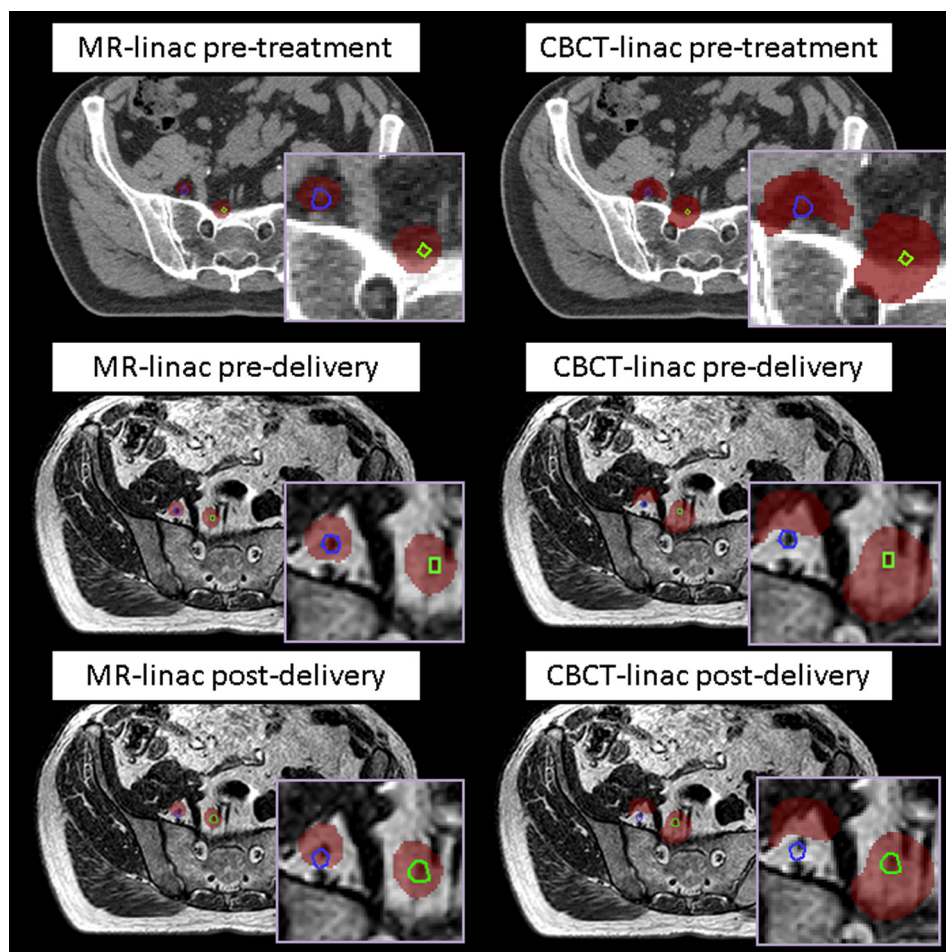


Fig. 5. Pre-treatment, pre-delivery and post-delivery example of a multiple lymph node oligometastases case with three targets. Visible are the two most distal GTVs (blue and green) the 35 Gy dose level (red). Geometrical variations, causing independent motion of the targets, would have led to under-dosage ($V_{35\text{Gy}}$ of 8.9%) of the distal GTV (blue) when using the CBCT-linac plan in the pre-delivery situation and under-dosage ($V_{35\text{Gy}}$ of 0%) in the post-delivery situation, regardless of the use of a 8 mm PTV margin. GTV coverage remained adequate with a $V_{35\text{Gy}}$ of 100% for the MR-linac plans, using 3 mm PTV margins. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

multiple plans and larger margins to account for inter-fraction rotational uncertainties are no longer required.

The 1.5T MR-linac allows for plan adaptation based on the new patient position (Adapt to Position, ATP) or based on the actual patient anatomy (Adapt to Shape, ATS) [21]. The CBCT-linac workflow is essentially comparable to the ATP workflow, as potential changes in target position are accounted for. Using the ATP workflow for poorly visible targets, in which no large deformations are expected, can also give direct benefit by taking advantage of improved target visibility through MR-guidance and could eliminate the need for larger margins. The possibility for accurate dose delivery using the ATS workflow in which the patient anatomy is fully taken into account to mitigate for inter-fraction motion of target and OAR opens up further opportunities. One of such opportunities is improved patient comfort through hypo-fractionation and potentially single fraction treatment of lymph node oligometastases. While at this moment different hypo-fractionated schemes are already being applied [7], this is sometimes done using fiducial marker implantation which is invasive for the patient [30,31]. The superior soft-tissue contrast provided by MR-guidance might eliminate the need for such fiducial markers. Other opportunities for dosimetric improvements are expected in other tumor sites with the potential for large inter-fraction motion and anatomical deformations such as cervix [32], prostate [33] and rectum [34].

With online MR-guided adaptive radiotherapy being a relatively new technique, its distinct features already show to be able to effectively deal with day-to-day geometrical deformations of the target and surrounding OARs. Further research and technical improvements are expected to make this technique even more versatile and allow for various methods of dose delivery, intra-fraction plan adaptation [35] and adequate tissue tracking. Increased delivery speed will reduce the window of intra-fraction motion and may therefore also lead to further margin reduction. While it is currently possible to perform full online replanning in approximately one minute [36], computer power is also expected to grow over the years, decreasing computational time for some of these techniques. Additionally, it is important to have reliable quality assurance and contour propagation [37]. These developments may further contribute towards precise and patient-specific treatments.

Our results also show that with the use of MR-linac online plan adaptation, the amount of unplanned violations of online dose criteria (PTV coverage and OAR constraints) can be reduced, which corresponds to earlier studies [17,18,38]. A limitation of this study is that OARs were only evaluated based on high OAR dose constraints. Further research should be conducted to investigate the impact of daily online adaptive replanning on the OAR dose more thoroughly.

In conclusion, target coverage and OAR constraint based evaluation of the first clinical 1.5T MR-linac SBRT treatments of lymph node oligometastases compared with conventional CBCT-linac treatment shows a smaller amount of unplanned violations of these dose criteria. The GTV coverage was comparable. Benefit is primarily gained in patients treated for multiple lymph node oligometastases: geometrical deformations are then accounted for, dose can be delivered in one plan and margins are reduced.

Acknowledgement

The authors wish to thank the Dutch Cancer Society for their financial support (grant 2015-0848).

Conflict of interest statement

The University Medical Center Utrecht MR-linac scientific project, including employment of multiple authors, has been partly funded by Elekta AB (Stockholm, Sweden).

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