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Short Communication

Feasibility of stereotactic radiotherapy using a 1.5 T MR-linac: Multi-fraction treatment of pelvic lymph node oligometastases

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ABSTRACT

Online adaptive radiotherapy using the 1.5 Tesla MR-linac is feasible for SBRT (5 × 7 Gy) of pelvic lymph node oligometastases. The workflow allows full online planning based on daily anatomy. Session duration is less than 60 min. Quality assurance tests, including independent 3D dose calculations and film measurements were passed.

Daily magnetic resonance imaging (MRI) directly before each treatment session enables online adaptive external beam radiotherapy based on excellent soft tissue contrast [1]. This may allow for planning target volume (PTV) margin reduction, improved sparing of organs at risk (OAR), dose escalation and hypofractionation [2–4]. Recently, the 1.5 Tesla (T) MR-linac system has become clinically available [5–8]. This system is composed of a 1.5 T MRI scanner and a ring-based gantry that contains a 7 MV standing wave linear accelerator.

In August 2018, routine clinical use of the MR-linac was started at our department with treatment of patients with pelvic lymph node oligometastases. Treatment aim for these patients is local control of the affected nodes and delay of potentially more toxic systemic therapy [9]. Based on institutional experience, we hypothesized that online MRI will yield improved lymph node visibility compared with cone beam computed tomography (CBCT). With treatment for pelvic lymph node oligometastases on the MR-linac, clinical experience is gained of multi-fraction, stereotactic radiotherapy (SBRT) treatment of soft tissue lesions, thereby expanding the knowledge from the 'first in mankind' trial [7].

Clinical treatment with the 1.5 T MR-linac using the vendor-provided commercially-available clinical workflow software has not been described before. Our aim was to report on the feasibility of SBRT on the 1.5 T MR-linac for lymph node oligometastases, based on our first clinical experiences.

Materials and methods

Patients

Five patients have undergone clinical treatment on the 1.5 T MR-linac (Unity, Elekta AB, Stockholm, Sweden) at our institute between August and October 2018. They have provided written informed consent for use of their data as part of an ethics review board approved observational study. All patients had single pelvic lymph node metastases originating from prostate cancer, median 64 months (range 19–129) after initial diagnosis of the primary tumor. Diagnosis of the metastatic lymph nodes was based on Gallium-68 prostate-specific membrane antigen positron emission tomography (PSMA PET) scans. The metastatic lymph nodes were situated in obturator or external iliac regions and had a median diameter of 7 mm (range 5–8).

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Feasibility criteria

Criteria for feasibility evaluation in this report were:

- treatment delivery using the MR-linac, with full online planning based on daily anatomy;
- maximum session time of 60 min;
- passed all quality assurance (QA) tests, including independent 3D dose calculations and film measurements.

Clinical workflow

The clinical workflow is illustrated in Fig. 1.

Pre-treatment imaging, planning and QA

Pre-treatment imaging included CT and MRI. The radiation oncologist contoured the gross tumor volume (GTV) on a multi-sequence MRI scan acquired on a 1.5 T Philips Ingenia MRI scanner (Philips Medical Systems, Best, NL), which was registered to the PSMA-PET and CT scans (Brilliance CT big bore, Philips Medical Systems, Best, NL). Nearby OAR (rectum, sigmoid, bladder, bowel bag, ureter, sacral plexus) were contoured on the CT scan. A special table overlay was used for CT scan acquisition, to enable patient set-up using specific couch index points. A vacuum mattress (BlueBAG, Elekta AB, Stockholm, Sweden) was used for immobilization.

A 3 mm PTV margin was applied [7,8,10]. For each patient, a pre-treatment step-and-shoot intensity-modulated radiotherapy (IMRT) plan was created in Monaco, to serve as a patient-specific template for online treatment planning. Calculation grid size was 2 mm. Monaco takes into account the 1.5 T magnetic field along the direction of the scanner bore ($-Y_{IEC1217}$). Seven non-uniformly spaced beam angles were used, avoiding the couch at beam angles of 115–135° and 225–245° and the cryostat connection pipe at 8–18°. Similar to our current clinical practice, 35 Gy in five fractions (2–3 fractions per week) was prescribed to 95% of the PTV. OAR dose constraints (Supplementary material: Table 1) were prioritized above PTV coverage.

Offline QA for the pre-treatment plan included an independent 3D dose check with 50% dose threshold in Oncentra version 4.5.2 (Elekta AB, Stockholm, Sweden) which was compared to the Monaco plan via Gamma analysis [11]. The dose recalculation in Oncentra is intended as a fast check of the dose calculation from Monaco, using an independent beam model and algorithm. Oncentra is based on a collapsed cone algorithm that does not account for effects of the magnetic field, but was shown to be feasible for voxel-to-voxel comparisons in the target volume for different target sites [11]. Further, GafChromic absolute dose EBT3 film measurement was performed with a 10% low dose threshold, which took into account doses ranging from 10% of D_{max} up until D_{max} (Ashland ISP Advanced Materials, NJ, USA) [7,11]. Pass criterion was 90% with a Gamma index of $\leq$1, with 3%/3 mm for independent dose check pass criterion and with 5%/2 mm for film measurement. In case of a 90–95% Gamma pass rate a visual inspection would be performed by the attending physicist.

Online patient set-up

Patients were positioned on the MR-linac couch using specific couch index points, which were intended to ensure that the position of the patient along the length of the couch is known and reproducible between the CT scan and each treatment session. Lasers were also used for patient positioning, these were institutionally added to the MR-linac. An MRI scan for online treatment planning was acquired: a transverse 3D T1-weighted FFE scan, for patients 1–2 the acquisition time was 5 min (TR 11 ms, TE 4.6 ms, acquired voxel size $1.2 \times 1.2 \times 2.0\ mm^3$, FOV

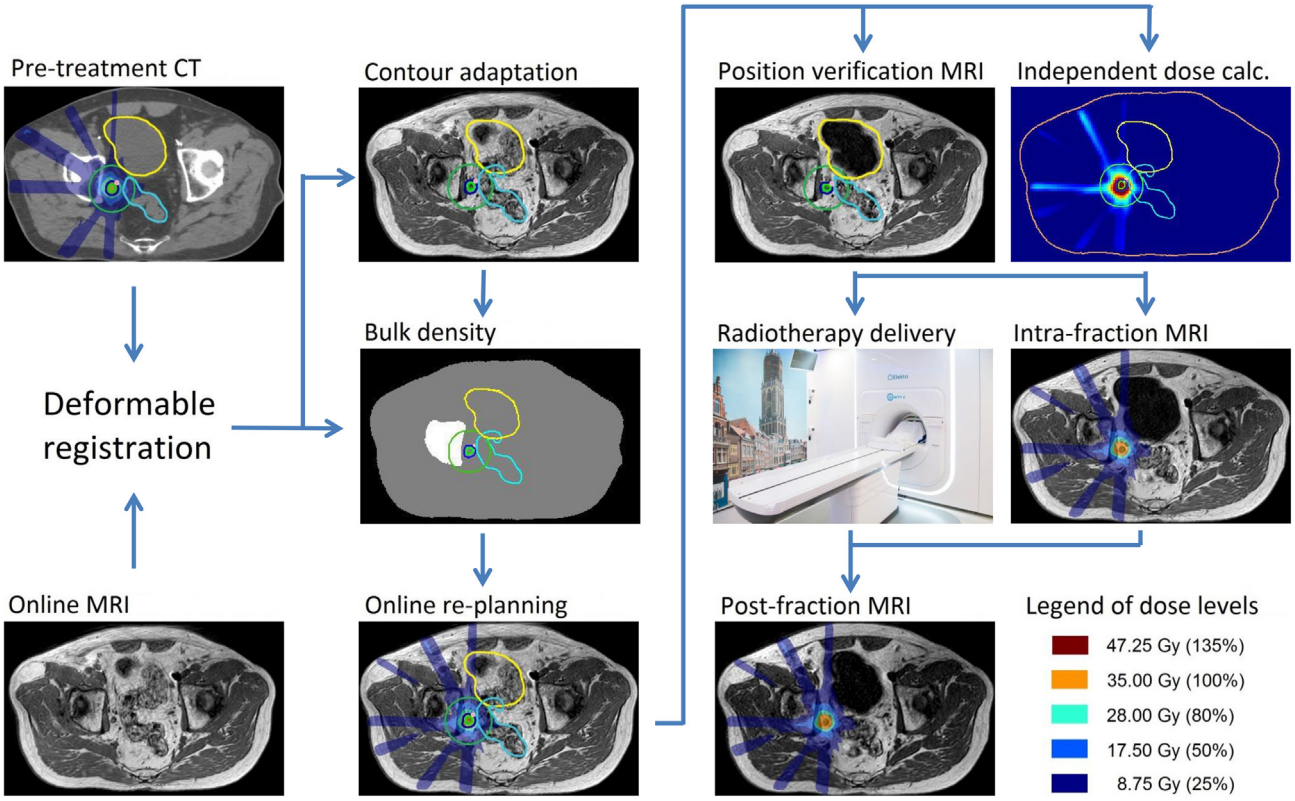

Fig. 1. Flow chart of online MR-linac workflow. Anatomical contours: yellow: bladder; light blue: sigmoid; pink: ureter; light green: GTV; dark blue: PTV; green oval: PTV + 2 cm. Images are shown for the first fraction of the second patient. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

400 × 447 × 300 mm^3), for patients 3–5 the acquisition time was reduced to 2 min (TR 11 ms, TE 4.6 ms, acquired voxel size 1.5 × 1.5 × 2.0 mm^3, FOV 400 × 400 × 300 mm^3). Contours were propagated from pre-treatment CT using a rigid and deformable registration in Monaco, version 5.4 build 19 (Elekta AB, Stockholm, Sweden). Electron density was based on assignment to structures: bones were assigned the average bone density from pre-treatment CT, all other tissues were assigned a relative electron density of 1. If necessary, contours of GTV and OAR within 20 mm of the (propagated) pre-treatment PTV were manually adapted by the radiation oncologist, to limit contouring time.

Online planning

Multiple online planning options are available in Monaco for the 1.5 T MR-linac. We used the 'adapt to shape' workflow to perform full online planning with the 'optimize weights and shapes from fluence' option [12]. As for the pre-treatment plan, calculation grid size was 2 mm and OAR dose constraints (Supplementary material: Table 1) were prioritized above PTV coverage. Beam angles were identical to the pre-treatment plan.

Online position verification and QA

During plan optimization, a position verification MRI scan was acquired, with the same parameters as the online planning MRI scan (5-min sequence for patients 1–2, 2-min sequence for patients 3–5). An overlay of anatomical contours from the online MRI scan was used to exclude significant motion of the target before radiotherapy delivery.

Online QA for the optimized plan was performed by comparing the number of monitor units and segments of the optimized treatment plan to the pre-treatment plan and by performing an independent 3D dose calculation in Oncentra, as described for pre-treatment QA.

Radiotherapy delivery

Radiotherapy was delivered using 7 MV FFF IMRT. An intra-fraction MRI scan (5-min sequence) was acquired during dose delivery and a post-fraction MRI scan (2-minute sequence) directly after treatment, with the same parameters as the online planning MRI scans. Both scans were used for offline assessment of intra-fraction motion by recalculating GTV coverage on the actual anatomy.

Post-treatment QA

For all patients, post-treatment film measurement was performed for the online treatment plan of at least the first session, as described for pre-treatment QA.

Results

All five patients completed the full course treatment on the MR-linac. Contour adaptation of the GTV and/or nearby OAR was performed and new online treatment plans were created for each treatment session. Fig. 2 gives two examples of inter-fraction anatomical differences of OAR positions and shapes, with the corresponding dose distributions after online planning.

All treatment plans from online planning were clinically accepted and used for treatment. For patients 1–4, the predefined coverage and OAR constraints were met by the online treatment plans for all treatment sessions. For patient 5, the PTV coverage planning aim was not met for the pre-treatment and two online plans (respectively 90.5, 92.8 and 93.9%, aim >95%), the sacral plexus was situated very close to the target lymph node for this patient.

All treatment sessions were completed within 60 min, shown in Supplementary material: Fig. S1 with time to completion results for each of the workflow items. For patients 1–2, the average online session duration was 44 min (range 39–49), including an average of 36 min on couch time (range 32–39). After the introduction of

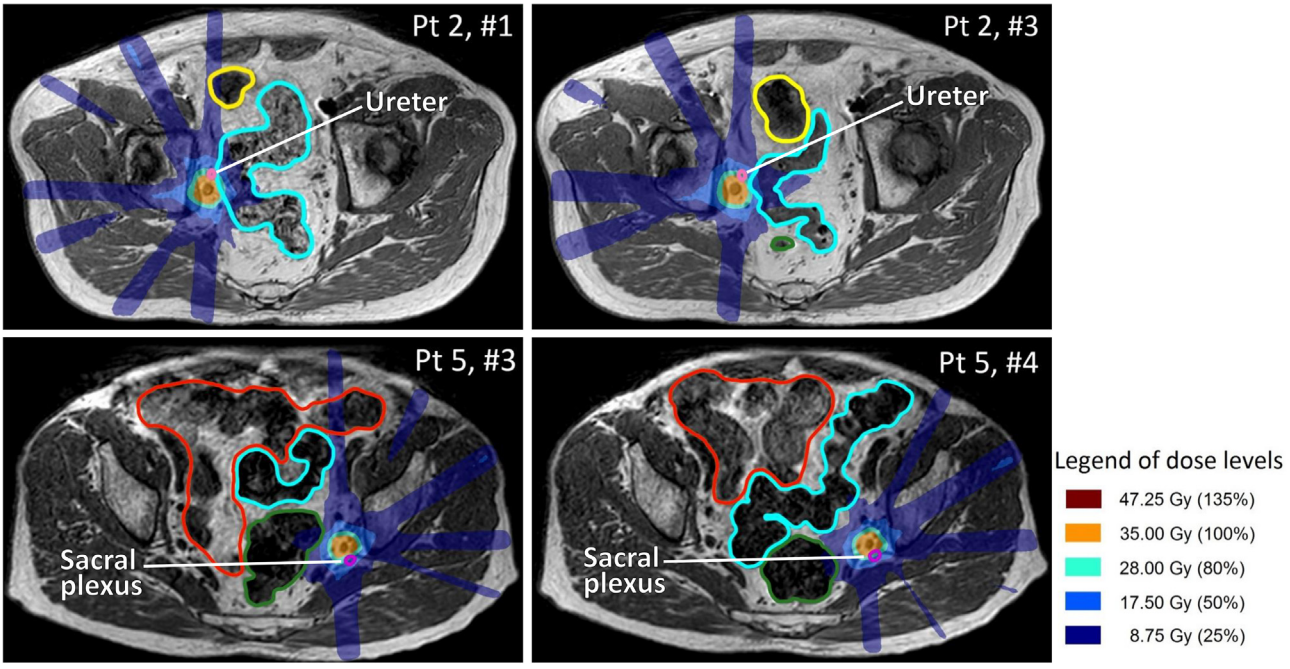

Fig. 2. Illustration of inter-fraction anatomical differences in OAR location with corresponding online treatment plans. Online MRI scans with OAR contours (contoured offline) and corresponding online treatment plans for illustrative treatment sessions (#). Anatomical contours: yellow: bladder; light blue: sigmoid; pink: ureter (denoted); green: rectum; purple: sacral plexus (denoted); red: bowel bag. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

shorter MRI scans for planning and position verification, starting with the third patient, average online session duration was 39 min (range 33–58) for patients 3–5, with 32 min on couch time (range 27–51). For one session, the Monaco software crashed during planning, which prompted a restart of the treatment session (visible in Supplementary material: Fig. S1 with a longer maximum session duration for patient 4).

QA for the pre-treatment plans yielded an average Gamma pass rate of 97.1% (range 94.7–98.8%) for the independent dose check and a Gamma pass rate of 99.9% (range 99.7–100%) for film measurements. The online independent dose calculations in Oncentra resulted in an average Gamma pass rate of 97.8% (range 90.4–99.3%). Post-treatment film measurements of online treatment plans resulted in an average Gamma pass rate of 99.9% (range 99.4–100%). All treatment plans with Gamma pass rates 90–95% were accepted by the attending physicist after visual inspection.

Discussion

To our knowledge, this is the first report on the clinical use of the commercially available 1.5 T MR-linac including the associated clinical workflow. In this report feasibility for SBRT treatment of pelvic lymph node oligometastases was evaluated using three criteria (treatment delivery using the MR-linac, with full online planning; maximum session time of 60 min; passed all QA tests).

All 25 treatment fractions were delivered as scheduled using the 1.5 T MR-linac. For each treatment session, online planning was used to generate new treatment plans based on daily anatomy. All treatment plans were clinically accepted and used for treatment. For patient 5, the pre-treatment and two online plans did not satisfy the PTV planning aim due to the proximity of the sacral plexus to the target lymph node. All patients could also have been treated with SBRT using a CBCT-linac, but for patient 1 a larger PTV margin of 8 mm would have been used because of poor target visibility on CBCT. In a preliminary investigation, the daily target coverage seemed to be slightly improved with MR-linac treatment compared with simulated CBCT-linac treatment [13].

All treatment sessions were completed within 60 min, even with a software problem in Monaco that resulted in a session restart for one session. To reduce the online session time, a shorter MRI scan was used for planning and position verification starting with the third patient (acquisition time 2 min instead of 5). This contributed to a 5-minute decrease in average online session duration (from 44 min for patients 1–2 to 39 min for patients 3–5). Timing results varied between patients, mainly depending on the amount of contour adaptation performed for lymph nodes and OAR. Further reductions of online session duration could be achieved by ongoing optimization of the online planning parameters and by improving the deformable image registration. Other options for reducing session duration include faster data transfer between the different applications using a different treatment session manager [7] or the use of other treatment planning software that is currently being developed [14].

Finally, all QA tests were passed, which encompassed independent 3D dose calculations and film measurements. Therefore, all three feasibility criteria being evaluated in this report have been satisfied.

With clinical feasibility having been established for multi-fraction stereotactic radiotherapy using the MR-linac, we are currently implementing MR-linac treatment for multiple lymph node oligometastases in pelvic or low para-aortic regions. Future treatment of abdominal lymph node metastases will likely require breathing motion management, such as the use of an abdominal compression device [15], an internal target volume (ITV) or future tracking and gating functionality of the treatment machine [16].

Conclusions

Clinical use of the 1.5 T MR-linac (Unity, Elekta AB, Stockholm, Sweden) was feasible for multi-fraction stereotactic radiotherapy, applied for pelvic lymph node oligometastases. All sessions were delivered using the MR-linac, new treatment plans were generated based on daily anatomy, all treatment sessions were completed within 60 min and all quality assurance tests were passed including independent 3D dose calculations and film measurements.

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Conflict of interest

The University Medical Center Utrecht MR-linac scientific project, including employment of multiple authors, has been partly funded by Elekta AB (Stockholm, Sweden) and Philips Medical Systems (Best, The Netherlands). K.J. Brown is an employee of Elekta AB (Stockholm, Sweden). R.H.N. Tijssen receives research support from Philips Medical Systems (Best, The Netherlands). The other authors declared that there is no other conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radonc.2019.01.024.

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