First clinical experiences with a high field 1.5 T MR linac.

Abstract:

Purpose: A 1.5 T MR Linac (MRL) has recently become available. MRL treatment workflows (WF) include online plan adaptation based on daily MR images (MRI). This study reports initial clinical experiences after five months of use in terms of patient compliance, cases, WF timings, and dosimetric accuracy.

Method and materials: Two different WF were used dependent on the clinical situation of the day; Adapt To Position WF (ATP) where the reference plan position is adjusted rigidly to match the position of the targets and the OARs, and Adapt To Shape WF (ATS), where a new plan is created to match the anatomy of the day, using deformable image registration. Both WFs included three 3D MRI scans for plan adaptation, verification before beam on, and validation during IMRT delivery. Patient compliance and WF timings were recorded. Accuracy in dose delivery was assessed using a cylindrical diode phantom.
Results: 19 patients have completed their treatment receiving a total of 176 fractions. Cases vary from prostate treatments (60 Gy/20F) to SBRT treatments of lymph nodes (45 Gy/3F) and castration by ovarian irradiation (15 Gy/3F).

The median session time (patient in to patient out) for 127 ATPs was 26[21-78] min, four fractions lasted more than 45 minutes due to additional plan adaptation. For the 49 ATSs a median time of 12[1–24] min was used for contouring resulting in a total median session time of 42[29-91] min. Three SBRT fractions lasted more than an hour.

The time on the MRL couch was well tolerated by the patients. The median gamma pass rate (2mm,2% global max) for the adapted plans was 99.2[93.4-100]%, showing good agreement between planned and delivered dose.

Conclusion: MRL treatments, including daily MRIs, plan adaptation and accurate dose delivery is possible within a clinically acceptable timeframe and is well tolerated by the patients.
Introduction

The latest promising new technology within radiotherapy (RT) of cancer is the MR linac (MRL), an integration between a linear accelerator and an MR scanner [1]. The MRL enables real time MR imaging (MRI), providing supreme soft tissue contrast, while delivering conformal treatments adapted to the visualized normal tissue and tumour [2,3]. This can potentially reduce the treated volumes, which could decrease the risk of adverse effects, facilitate RT dose escalation, or enable delivery of the RT dose in fewer fractions, and treat sites situated close to critical structures, which currently cannot be treated [4,5]. Beside the geometrical and anatomical advantages, the daily MRI performed during treatment also supports more accurate dose accumulation, which could improve current dose response models. Furthermore, by assessing biological information with MRI, e.g. diffusion weighted images, the treatments could be adjusted to the biological response of the individual patient [5-7].

The 1.5 T MRL (Unity, Elekta AB, Stockholm, Sweden) has been developed in close collaboration between the vendors and seven leading radiotherapy departments [8,9] and have been commercially available since the autumn 2018. The centres involved in the development have so far published a few feasibility studies [2,10]. This study reports the initial experience after 5 months use of a commercial 1.5 T MRL system and assesses feasibility in terms of variation in patient cases, patient compliance, treatment session timings and dose delivery accuracy.

Method and Materials
The Unity 1.5 T MRL was installed at our institution during 2018. Concurrent with the installation dedicated RT staff were trained in aspects of MRI, the design and operation of the ring based accelerator, the associated treatment planning system (TPS) (Monaco 5.4, Elekta AB, Stockholm, Sweden) as well as the treatment delivery workflow (WF). Furthermore, a range of QA procedures had to be implemented taking into account the new linac design and the use of MRI for image guidance [11].

**Patient cohort and clinical data**

At this initial phase of clinical implementation only patients with targets in pelvic and lower abdomen region were referred for treatment on the MRL. All treated patients were included in feasibility protocols [12] [13] prior to treatment to be able to record information about delivery time, patient compliance, and treatment outcome and to be able to access the acquired image information.

The patient experience of MR-guided radiotherapy was evaluated with interviews based on a semi-structured interview guide with the topics physical discomfort, psychological coping, environment, communication with the staff and informational needs. Due to the short follow up time, outcome data is not included in this study.

**Patient pre-treatment workflow and QA**

The pre-treatment WF is depicted in the upper part of figure 1. A reference RT plan was created for all patients based on a reference MRI acquired in treatment position at a 1.5 T Ingenia Philips MR Scanner or using the corresponding MR part of the MRL. One of two types of reference scans were used; 3D T2W (TR 1300 ms TE 87 ms) for soft
tissue tumours or 3D T1W (TR 8 ms TE 4.6 ms) for bone stereotactic treatments, both with a slice thickness of 2 mm and pixel size of 1.5x1.5 mm$^2$. A CT scan was acquired immediately after the reference MRI to obtain information about the electron densities needed for dose planning (see supplemental materials Appendix A).

Target delineation was performed on the reference MRI by a radiologist and an oncologist in cooperation, while organs at risk (OAR) were delineated by radiographers trained in MRI delineation. Margin expansions from the GTV to CTV and PTV were performed following department guidelines. In Monaco, a diagnose specific locally developed plan template was loaded and adjusted to match the specific patient case thereby forming a patient specific template to be used for the online plan adaptation.

The plans were optimized using 7-11 beam step-and-shoot IMRT with a maximum of 60 segments, a minimum segment area of 4 cm$^2$ and a minimum number of 5 Monitor Units (MU) per segment. To include the effects of the 1.5 T magnetic field, a Monte Carlo (MC) dose engine was used for dose calculation with a statistical uncertainty of 1% and a dose grid size of 3 mm. Also a detailed structure model of the MRL couch and the anterior coil was included in the dose calculation.

The reference plan was approved by an experienced oncologist and exported to the standard Record and Verify (R&V) system (MOSAIQ, Elekta AB, Stockholm, Sweden). RadCalc (ver 6.2 LifeLine Software Inc.) was used for a secondary dose check, and a cylindrical diode phantom ArcCheck MR (SunNuclear)[14] was used for a pre-treatment quality assurance of the dose delivery. All reference plans were measured using ArcCheck before the first fraction to make a patient specific assessment of the dose delivery accuracy and to validate the initial data transfer between the TPS and the MRL. The first adapted fraction was measured after the first treatment fraction.
Furthermore, each of the first 100 delivered fractions were measured using ArcCheck. Gamma criteria of 2 mm, 2% global max, 10% threshold, and absolute doses were used for evaluation of the Arccheck measurements [15,16].

**Online Treatment workflow**

The online treatment WF at each fraction is depicted in the lower part of figure 1. The patient was positioned in the immobilisation equipment on the couch together with an anterior RF receiver coil. The patient and the coil were aligned with index numbers on the couch as specified by the R&V system. The couch was moved to a prefixed longitudinal position in the bore of the MRL and the staff left the treatment room by performing a ring out (turning the last man out key).

For the daily plan adaptation, an MR scan was acquired with the same contrast type as the reference MRI, either a 3D T2W or a 3D T1 MR scan (see supplemental materials Appendix B). The consistency in image type between MR reference scan and MR session scan increases the accuracy of the deformable registration between the image sets and eases the subsequent manual correction and validation of the deformed structures [17]. The session MR of the day was automatically sent for import into the online MONACO TPS and an automatic rigid registration was performed between the reference MRI and the session MRI of the day followed by a manually adjustment if required.

Two different plan adaption WF were applied depending on the clinical situation of the day: The first option was Adapt To Position (ATP), where the shape and weight of beam segments in the reference plan were adjusted to match the current position of targets
and OARs based on the rigid registration. Thus, ATP is an alternative to move the treatment table, which is fixed during a treatment session, and was used if there were relatively modest changes to the anatomy compared with the reference plan. The second option was Adapt To Shape (ATS), where a new plan was created to match the anatomy of the day using deformable image registration for contour propagation from the reference plan to the session MRI, followed by manual adjustment of the contours if necessary [18]. For ATP the dose calculation of the day was performed on the reference scan while the session MRI scan of the day was used for dose calculation for ATS. No corrections in beam angles were made between the reference plan and the adapted plan. No correction in optimization parameters were done for ATP while IMRT objectives were adjusted for ATS to match the anatomy of the day.

A second MR scan was acquired during plan adaptation, automatically imported into online MONACO, and used to make a visual exhaustive survey of the adapted plan. The plan evaluation was performed by an experienced oncologist. RadCalc was used for the secondary check of the dose calculation and changes in number of MU and segments relative to the reference plan were evaluated to be able to catch severe changes in the adapted plan.

After approval, the adapted plan was automatically exported to the R&V system and sent to the MRL. Immediately before beam on 2D MR motion monitoring (see supplemental materials Appendix B) in one or two orthogonal planes (coronal and/or sagittal) was enabled to validate that the target was still in the desired position. If movements were observed during motion monitoring the beam was terminated and a corrected treatment plan was created. Motion monitoring was switched off after the
first two beams were delivered and a third MR scan identical to the first two was initiated.

Timings of all main steps in the online WF were recorded together with information about any deviations in the planned WF due to technical or clinical reasons.

**Results**

During the first 5 months 19 patients, one with two targets, have been treated at the MRL receiving a total of 176 fractions of which 49 fractions (28%) were ATS. For one patient two fractions could not be delivered due to initial technical problems, and the patient was treated on a conventional linac using a backup plan. The patient cases are listed in table 1 and vary from prostate treatments to SBRT treatments of lymph nodes as well as bone metastases and castration by irradiation of the ovaries.
### Treatments

<table>
<thead>
<tr>
<th># Patient treatments</th>
<th>Prescribed dose [Gy]</th>
<th>Planned MR seq</th>
<th>Fx</th>
<th>Adaptation</th>
<th>Number of ATS delivered</th>
<th>Number of ATS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prostate</strong></td>
<td></td>
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<td></td>
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<tr>
<td>PRISM protocol</td>
<td>4</td>
<td>60</td>
<td>20</td>
<td>ATP</td>
<td>T2</td>
<td>7B</td>
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<tr>
<td>Prostate only</td>
<td>1*</td>
<td>60</td>
<td>20</td>
<td>ATP</td>
<td>T2</td>
<td>20</td>
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<td></td>
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<tr>
<td>Recurrence</td>
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<td>42.7</td>
<td>7</td>
<td>ATP</td>
<td>T2</td>
<td>20</td>
</tr>
<tr>
<td><strong>Ovaria irradiation</strong></td>
<td></td>
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<tr>
<td></td>
<td>3</td>
<td>15</td>
<td>3</td>
<td>ATS</td>
<td>T2</td>
<td>9</td>
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<tr>
<td><strong>SBRT treatments</strong></td>
<td></td>
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<td></td>
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<tr>
<td>Bone</td>
<td></td>
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<tr>
<td>Ilium</td>
<td>2</td>
<td>30</td>
<td>3</td>
<td>ATP</td>
<td>T1</td>
<td>6</td>
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<tr>
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<td>5</td>
<td>ATP</td>
<td>T1</td>
<td>5</td>
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<td>ATP</td>
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<tr>
<td></td>
<td>**</td>
<td>1</td>
<td>30</td>
<td>ATP</td>
<td>T2</td>
<td>5</td>
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<tr>
<td>Soft tissue</td>
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<td>27</td>
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<td>ATP</td>
<td>T2</td>
<td>3</td>
</tr>
<tr>
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<td>45</td>
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<td>ATS</td>
<td>T2</td>
<td>3</td>
</tr>
<tr>
<td>Abdomen</td>
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<td>60</td>
<td>8</td>
<td>ATP</td>
<td>T2</td>
<td>8</td>
</tr>
<tr>
<td>Uterus boost</td>
<td>1</td>
<td>30</td>
<td>6</td>
<td>ATS</td>
<td>T2</td>
<td>6</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>20</td>
<td>176</td>
<td>49</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**Table 1: List of delivered treatments.** * One prostate cancer patient also had lymph node SBRT. ** For one bone treatment at T2 sequence was used because it was needed to be able to see the spinal cord for plan adaptation. The last column shows the number of ATS used; at some sessions it was decided to use ATS, based on clinical observations, even though it was planned for ATP.
The patients had a median age of 62 (range 43-80) and generally was in good shape with a performance status (PS) of 0 except for one patient with PS = 2. All patients found the treatment couch and position comfortable, and the noise in the room was easily tolerated. No discomfort, dizziness, or metallic taste was experienced, and no anxiety was reported. One patient felt a tingling sensation in his feet, and two patients felt warm during treatment; however the heat was not related to the treatment. The treatment time was acceptable to all patients. No patient-related issues caused repeated scans or interrupted treatments.

Figures showing data on timing are provided in the supplemental material Appendix C. The median session time for ATP was 26 min (ranging 21 to 78 min). At several occasions it was possible to treat two patients within 55 min. Four ATP fractions lasted more than 45 min due to additional plan adaptation: During two fractions the accelerator needed restart during delivery, at one fraction there was a failure in the connection to the accelerator before beam on, and at one fraction there were problems with the image transfer from the MR scanner.

The median total session time was 42 min (ranging 29 to 91 min) for the 49 ATS fractions. Three ATS sessions lasted longer than 60 min: One SBRT fraction lasted 91 min due to accelerator related problems after 2/3 of the treatment delivery. For this case the patient was off couch while a plan was created for the residual fraction. One lasted 70 min due to incorrect sequence setup for a session scan and due to Monaco related problems. Another one lasted 65 min due to a large change in target positon during the online planning, observed using motion monitoring, which required a restart of the WF.
The time from start of session scan (ring out) to beam off is crucial for fast plan adaptation of changing anatomy. For sessions without any deviations the median time (ring out to beam off) for ATP was 19 min (ranging 15 to 34 min) and 34 min (ranging 23 to 59 min) for ATS.

The difference in session time between ATS and ATP is mainly caused by the additional time for contouring using ATS. For ATP a median time of 2 min is spent on manual fusion and evaluating the anatomy of the day while a median time of 11.5 min (ranging 1 to 24 min) was spent for ATS on the manual work which also included additional contouring if needed. Another difference between ATP and ATS WFs is the time spent on plan optimization and dose calculation; ATP median time of 2 min (ranging 1 to 7 min) and ATS median time of 6 min (ranging 3 to 12 min).

The IMRT beam delivery time was below 10 minutes for fraction doses less than 8 Gy, while fraction doses of 15 Gy were delivered in 14 minutes.

A median time of 6 min (ranging 4 to 13) was used for patient setup in the MR environment (MR safety screening, handling of coil, hearing aids).

Gamma pass rates, with the criteria of 2% and 2mm of the measured fractions shows excellent agreement between calculated and measured dose distributions with a median pass rate of 99.2 % (ranging 93.4% to 100 %) (See supplemental materials Appendix C).

Discussion

This is to our knowledge the first study reporting on the feasibility of the 1.5 T MRL for multiple patient cases and the first feasibility study published from a clinic not directly involved in the development of the commercial MRL system.
Despite being the first commercial version of the system, it was possible to obtain median session times of less than 30 min for ATP and 45 min for ATS, which is in agreement with recently published results by Werensteij-Honingh et al. [2].

Initially, the MRL had to be restarted due to a faulty computer component on the accelerator at some treatment fractions. The remaining deviations caused by technical problems were mainly related to small software issues in the online Monaco. This was experienced as a temporary frozen user interface or software crashes. In the event of a software termination, Monaco restarts from the point in the WF where the crash occurred. User related deviations during WF were; time spent on contouring of a structure not used for plan adaptation, choice of incorrect MRI sequence for the session scan, ring out not properly completed.

The overall impression of the dosimetric stability and accuracy of the accelerator is good, also verified by the Arccheck gamma pass rates which is superior to our standard clinical use [15].

The patients tolerated the treatment and treatment time, which may be due to thorough patient information before and during treatment combined with the good performance status of the patients. This was well in agreement with findings from centres using a 0.35 T MR accelerator [3].

For some of the patients treated higher does to larger OAR volumes would have been the case, if the same dose to the target should have been delivered on a standard linac. For example, it would have been challenging without superior soft tissue contrast compared to CBCT based treatments to treat oligo metastases in soft tissue regions, prostate without seeds, as well as partial prostate RT where urethra sparring was crucial. In terms of normal tissue sparring, it was possible for the castration treatments
of the ovaries to reduce the treated volume (receiving 15 Gy) from 1000 cm$^3$ to 50 cm$^3$ using the MRL, because it is now possible to see the ovaries. Without daily adaptation it would have been impossible to deliver the same dose in the uterus boost treatment while achieving strict dose constraints to the surrounding critical OAR with large inter fractional changes in shape and position. Based the 3D MRIs acquired during beam on it seems likely that the PTV margin could be reduced when daily plan adaptation and MR image guidance is used. But more experience with the system and daily plan adaptation are needed before such changes can be applied.

So far, mainly targets in the pelvic region and lower abdomen region have been treated at our institution using the MRL. The next indications will probably be treatments of bladder, rectum, cervix as well as prostate including lymph node irradiation. However, to be able to treat e.g. bladder there is a need to improve the speed of the adaptive WF as well as treatment delivery due to the ever ongoing change in anatomy (e.g. bladder filling). This requires continuous session WF training and software optimization to minimize the time used for decision making and manual work.

Another limitation currently is the intersegment time during beam delivery, which could be reduced by enabling sliding window IMRT or VMAT. Treating targets in the upper abdominal and lung region requires handling of respiratory motion to avoid artefacts in the MR images and to obtain precise and accurate treatment delivery. A simple approach would be to introduce breath hold MRI together with gated treatments, while more advanced solutions would be to generate 4D MRI [19-21] for mid ventilation based treatments or use of tracking.

The short session times for CBCT based treatments (typically 10 min in our department) will never be possible with MRL due to the nature of MRI acquisition, handling of
patients in the MRI environment and time for online planning. Instead, the potential of the MR-linac will be the high precision of the dose delivery using online adaptation guided by the superior soft tissue contrast. For many patients this may facilitate reduction of the treated volume and hypofractionation regimes, and, hence, reduce the side effects and the total treatment duration. In addition, the MRL offers the possibility to evaluate the response observed on MRI of the individual patient could change the future of RT [22]. This of course requires evidence built on randomized trials and cooperation between centres with MRLs [1,23,24]. Due to the limited capacity on the MRL there is also a need for an assessment of which patients will benefit the most from MR image guided treatments [25].

**Conclusion**

Introducing MRL treatments requires additional resources for quality assurance, online adaptive planning, WF optimization and handling of technical problems. MRL treatment, including daily MRIs, plan adaptation and accurate dose delivery is possible within a clinically acceptable timeframe, which is well tolerated by the patients. This feasibility patient cohort establishes the basis for clinical studies that will explore the next era of high precision RT in terms of individualized treatments based on MR guided adaptive RT.

**Conflicts of interests**

None

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References


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Figure 1: Flowchart for pre-treatment and online MRL workflow.

Pre-treatment workflow

Online Workflow

Figure 1: Flowchart for pre-treatment and online MRL workflow.
Supplemental materials

Appendix A:
If needed, the contouring was supported by image information from the CT scan and diagnostic image sets (PET/CT or other MRI sequences) rigidly fused to the reference MRI. Delineations were performed using (Pinnacle 16.0, Philips) which is our standard TPS to reduce the initial number of staff members trained in Unity TPS MONACO. Density structures were generated in Pinnacle using the CT scan to create a pseudo CT scan with three density layers (spongious bone, cortical bone, soft tissue). The reference MRI, the CT scan, and assigned structures were exported to MONACO. In Monaco the CT scan density structures and their relative electronic densities were transferred from the CT scan to the MRI using deformable image registration.

Appendix B:
During the online treatment sessions the following MRI sequences were used:

3D T2W( 3:41 min, TR = 1300 ms, TE = 87 ms, scan voxel size 1,5x1,5x2 mm^3,reconstruction voxel size 0.83x0.83x2 mm^3 , FOV 400x448x250 mm^3)

3D T1W( scan time 3:57 min, TR = 8 ms, TE = 4,6 ms, scan voxel size 1,5x1,5x1,5 mm^3 , reconstruction voxel size 0.5x0.5x 1,5 mm^3 , FOV 400x400x250 mm^3)

2D MR motion monitoring, bFFE scan with realtime reconstruction. TR: 3.8 ms, TE: 1.92 ms, framerate: 5 Hz Hz) in one or two orthogonal planes (coronal and/or sagittal)

Appendix C:
Histograms showing a) total session time and b) time from Ring out to beam off for MRL fractions. The black fraction of the bar indicates sessions without any technical or clinical deviations.
Histograms and scatter plots showing a) time used for manual image registration and contouring, b) beam delivery time as function of fraction dose, and c) time used to handle the patient in the MRI environment for all MRL sessions.
2% (global max) and 2mm gamma pass rates for the MRL treatments measured using ArcCheck.