The first clinical implementation of real-time image-guided adaptive radiotherapy using a standard linear accelerator

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Purpose: Until now, real-time image guided adaptive radiation therapy (IGART) has been the domain of dedicated cancer radiotherapy systems. The purpose of this study was to clinically implement and investigate real-time IGART using a standard linear accelerator.

Materials/methods: We developed and implemented two real-time technologies for standard linear accelerators: (1) Kilovoltage Intrafraction Monitoring (KIM) that finds the target and (2) multileaf collimator (MLC) tracking that aligns the radiation beam to the target. Eight prostate SABR patients were treated with this real-time IGART technology. The feasibility, geometric accuracy and the dosimetric fidelity were measured.

Results: Thirty-nine out of forty fractions with real-time IGART were successful (95% confidence interval 87–100%). The geometric accuracy of the KIM system was −0.1 ± 0.4, 0.2 ± 0.2 and −0.1 ± 0.6 mm in the LR, SI and AP directions, respectively. The dose reconstruction showed that real-time IGART more closely reproduced the planned dose than that without IGART. For the largest motion fraction, with real-time IGART 100% of the CTV received the prescribed dose; without real-time IGART only 95% of the CTV would have received the prescribed dose.

Conclusion: The clinical implementation of real-time image-guided adaptive radiotherapy on a standard linear accelerator using KIM and MLC tracking is feasible. This achievement paves the way for real-time IGART to be a mainstream treatment option.

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Until now, real-time image-guided adaptive radiation therapy (IGART) has been the domain of dedicated and often expensive cancer radiotherapy systems such as the CyberKnife Synchrony [1] and Mitsubishi/BrainLab Vero [2]. The purpose of this study was to clinically implement and investigate real-time IGART using a standard linear accelerator.

We developed two real-time image guidance technologies for standard linear accelerators: (1) Kilovoltage Intrafraction Monitoring (KIM) that finds the target position in real-time during radiotherapy and (2) multileaf collimator (MLC) tracking that aligns the radiation beam to the moving target.

KIM is an image-based real-time localization method first clinically implemented in 2014 [3] that has been used in over 1200 treatment fractions for prostate cancer in five different cancer centers. Prior to the current study, all treatments with KIM have been gated. When the observed target motion exceeded a threshold the treatment was interrupted and a manual couch shift was performed to realign the target with the radiation beam. The motion threshold is typically ≥3 mm displacement for 5 s for conventional fractionation, and >2 mm of motion for 5 s for stereotactic ablative body radiotherapy (SABR).

MLC tracking is a real-time adaptive radiotherapy method first clinically implemented in 2013 [4] that has been used in over 800 treatment fractions for prostate and lung cancer. Prior to the current study, the clinical implementation of MLC tracking had been restricted to a research version of the Calypso [5] electromagnetic transponder-guided localization method. Calypso is an add-on to the standard equipped linear accelerator, and requires additional hardware. KIM is a software-based real-time system that uses the hardware of a standard equipped linear accelerator.

When put together, KIM and MLC tracking enable real-time IGART using a standard linear accelerator without any additional hardware. The purpose of this study was to clinically implement and investigate real-time IGART using KIM and MLC tracking.

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Methods

Clinical details

Eight prostate SABR patients enrolled on the TROG 15.01 SPARK (NCT02397317) clinical trial were treated. SPARK = Stereotactic Prostate Adaptive Radiotherapy Utilising Kilovoltage Intrafraction Monitoring. The CTV margins were 5 mm isotropically except 3 mm posteriorly. The prescribed dose was 36.25 Gy to 95% of the PTV in five 7.25 Gy fractions. Study protocol details are given in Ref. [6] and https://clinicaltrials.gov/ct2/show/NCT02397317.

Clinical process

Patients were implanted with three gold fiducial markers and hydrogel one week prior to simulation. Simulation images were acquired on a Philips BigBore CT scanner with 1.5 mm slices. Fiducial markers were defined as high definition structures and the centroid position of the three fiducials was defined to be the treatment isocenter. Eligibility criteria included a patient lateral dimension of <40 cm at level of isocenter and correct positioning of fiducials (three markers intact and no markers at the same superior–inferior level). A dual arc volumetric modulated arc treatment was planned using Eclipse v13.6 (Varian Medical Systems, Palo Alto) to satisfy the SPARK trial dose–volume constraints. After the treatment plan optimization was complete, the field size was manually enlarged by 1.6 cm (0.8 cm on each side) without changing the MLC to allow MLC tracking without causing a beam hold if the target moves below the jaw. The change in jaw position required the dose to be recalculated and the plan was renormalized, and the dose–volume constraints were reconfirmed against SPARK trial requirements.

Patients were treated on a Varian Trilogy linac with Millennium MLC. Positioning was verified with CBCT to align fiducials and cross-checked with CTV and PTV structure overlay. Framegrabber hardware cables and acquisition software (Varian iTools) were used to acquire kV and MV images during treatment. The images were streamed to a research computer on which the KIM and MLC tracking programs were installed. The research computer was integrated into the linac intranet to enable MLC positions and beam holds to be sent from the MLC tracking software to the linac. The KIM software was activated following patient alignment and preceding treatment delivery, requiring the patient’s implanted marker positions determined from the treatment plan to be loaded and acquisition of kV fluoroscopy during a 120° imaging only arc to populate the KIM probability density function [3]. The MLC tracking software was activated with the MLC positions as a function of gantry angle and monitor unit obtained by reading the DICOM RT plan. Treatment was delivered with kV fluoroscopy (125 kVp, 80 mA, 13 ms, 6 × 6 cm², 10 Hz). The estimated additional kV dose from the KIM procedure is 0.4 Gy [7]. A gating threshold of 1 cm was applied. Following treatment a second CBCT was acquired according to the SPARK protocol.

Quality assurance

For the TROG 15.01 SPARK trial, in addition to routine departmental procedures, the contours and dose distributions for each patient’s plan were independently reviewed. The KIM and MLC tracking quality assurance processes were based on previous publications [8,9]. System tests (repeated monthly) included coordinate system check, dynamic tracking accuracy, treatment interruption, latency measurement, dosimetric accuracy for standard delivery and kV panel offset correction with gantry angle. We also deployed software-based, patient-specific geometric and patient-specific dosimetric controls as a comprehensive quality assurance program applied pre-treatment, during treatment and post-treatment. The pre-treatment quality assurance included:

- Planning task checklist.
- Monitor Unit check with IMSURE (Standard Imaging) with a tolerance of ±3%.
- Delivery of the plan using KIM and MLC tracking to a motion phantom programmed with typical prostate motions to determine deliverability (i.e. no beam holds) and geometric accuracy (tolerance as mean value and root mean square error <1 mm).
- Measurement of delivered dose with MLC tracking applied to a programmable motion phantom containing GAF film in the coronal plane attached to HexaMotion (ScandiDos, Uppsala, Sweden). Applied tolerance of 98% of points within 2%/2 mm gamma comparing measurement with motion and tracking against measurement without motion. A further comparison was made between measured and planned dose distribution.

The post-treatment quality assurance included:

- Visual inspection of segmentation and that the reported motion corresponded to segmented positions relative to planned positions.
- Software controlled measures (inside KIM software) leading to beam hold interlocks on the linear accelerator, including: loss of communication between KIM, MLC tracking or MLC controller; detection of motion outside tracking zone; reduction of correlation below a threshold (to detect migration, or segmentation error); change in inter-marker distances (to detect deformation, segmentation error, or 2D → 3D conversion error); acceleration of centroid over a threshold value (to detect 2D → 3D conversion error).

The post-treatment quality assurance included:

- kV/MV triangulation as ground truth and comparison with KIM real-time trajectory to assure accuracy of prostate motion trajectory feeding MLC tracking.
- reconstruction of delivered dose utilizing prostate motion trajectory, MLC logfiles and original treatment plan as described elsewhere [10,11].

Measurements

Three factors affecting the patient’s treatment were analyzed: feasibility, geometric accuracy of the KIM system, and dosimetric fidelity of the integrated KIM–MLC real-time IGART system.

1. Feasibility was measured using maximum likelihood estimates (Matlab’s binofit function) assuming a binomial distribution of a successful or unsuccessful treatment. A successful treatment was defined as the entire treatment fraction was delivered with KIM-guided MLC tracking.
2. The geometric accuracy of the KIM system was measured by comparing the KIM-measured motion to the motion measured using post-treatment kV/MV triangulation.
3. The dosimetric fidelity of the integrated KIM–MLC IGART system was measured using a previously published dose reconstruction technique [10]. The dose reconstruction method combines the original treatment plan, the KIM-measured motion files and the treatment log files that have the MLC leaf positions, gantry angles, couch shifts and monitor units delivered, to estimate the dose delivered in the presence of motion, both with and without IGART. A limitation of the dose reconstruction method is that the dose reconstruction is performed on the initial plan.
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