MLC tracking for lung SABR reduces planning target volumes and dose to organs at risk

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Abstract

Purpose

Assess the dosimetric impact of multi-leaf collimator (MLC) tracking and mid-ventilation (midV) planning compared with the internal target volume (ITV)-based planning approach for lung Stereotactic Ablative Body Radiotherapy (SABR).

Method

Ten lung SABR patients originally treated with an ITV-based plan were re-planned according to MLC tracking and midV planning schemes. All plans were delivered on a linac to a motion phantom in a simulated treatment with real lung motions. Delivered dose was reconstructed in patient planning scans. ITV-based, tracking and midV regimes were compared at the planning and delivered stages based on PTV volume and dose metrics for the GTV and OAR.

Results

MLC tracking and midV schemes yielded favourable outcomes compared with ITV-based plans. Average reduction in PTV volume was (MLC tracking/MidV) 33.9%/22%. GTV dose coverage performed better with MLC tracking than the other regimes. Reduction in dose to OAR were for the lung (mean lung dose, 0.8 Gy/0.2 Gy), oesophagus (D3 cc, 1.9 Gy/1.4 Gy), great vessels (D10 cc, 3.2 Gy/1.3 Gy), trachea (D4 cc, 1.1 Gy/0.9 Gy), heart (D1 cc, 2.0 Gy/0.5 Gy) and spinal cord (D0.03 cc, 0.5 Gy/−0.1 Gy).

Conclusion

MLC tracking showed reduction in PTV volume, superior GTV dose coverage and organ dose sparing than MidV and ITV-based strategies.

Stereotactic Ablative Body Radiotherapy (SABR) delivering hypofractionated doses to the tumour is increasing in use due to the encouraging local control rates with minimal toxicity [1], [2]. Lung SABR treatments require careful treatment planning and extensive pre-treatment image guidance to ensure the high dose is correctly placed in the lung [3]. In the presence of motion, this task becomes challenging. The prevalent approach, recommended by the ICRU 83, is to apply the Internal Treatment Volume (ITV)-based motion-inclusive method that enlarges the treatment fields to account for motion and uncertainty. Since dose to organs-at-risk (OAR) generally shows a relationship with toxicity [4], numerous strategies have been deployed to moderate unnecessary dose spillage such as treatment beam gating [5], adaptive couch tracking [6], adaptive real-time tumour tracking [7-9] and passive strategies such as the mid-ventilation (midV) planning treatment volume (PTV)-based approach [10].

Multi-leaf collimator (MLC) tracking for lung tumours is an active motion management technique that utilizes the MLC leaves within the head of the linac. During tracking, the radiation beam is shifted to correct for tumour motion from respiration. This strategy has the potential to increase the dose distribution conformity despite fast moving tumours or baseline shifts. The midV approach for lung SABR is a planning approach that accounts for the population-based statistical uncertainties to define the set of margins used for the PTV [11,12].

The purpose of this study is to investigate potential clinical benefits of MLC tracking compared against midV and ITV-based planning for lung SABR in end-to-end clinically realistic planning and delivery scenarios. We performed a dosimetric comparison between motion management strategies using real patient motion traces to allow comparison between the three techniques. This study supported the implementation of a current prospective clinical trial (NCT02514512) to evaluate the use of MLC tracking for lung SABR to meet requirements of practicability in a clinical environment and its operability at meeting dosimetric constraints.

Methods and material

Treatment planning

Ten consecutive patients were previously treated with ITV-based SABR-VMAT (Volumetric Modulated Arc Therapy) in the period 2014–2015 at our institution. Patients were diagnosed with non-small cell lung carcinoma (NSCLC) stage I or oligometastatic lung metastases. The original treatments were based on a conventional ITV-based plan. Patients were planned based on the dose constraints from RTOG 0813 and 0915 with 100% of the Gross Tumour Volume (GTV) receiving no less than 100% of the dose and at least 97% of the PTV receiving 100% of the dose [13,14]. Three patients received 48 Gy in 4 fractions and seven patients received 50 Gy in 5 fractions. Planning was performed in the Eclipse treatment planning system (v. 11.3, Varian Medical Systems, Palo Alto) using the analytical anisotropic algorithm (AAA). The ITV was contoured using the maximum intensity projection from a 4D-CT dataset. The planning treatment volume ($PTV_{ITV\text{-}BASED}$) was created as a uniform 5 mm expansion of the ITV. Collimator angles of 40°/50° were used.

The first step was for each patient to be replanned following an adaptive tracking protocol. The GTV was defined on the end-of-exhale phase, namely the GTV_{TRACK}, to assure a proper localization and delineation of the tumour [7, 15-17]. Collimators were angled to have the leaf trajectory parallel to the superior–inferior motion (85/95°) [18]. Around the GTV_{TRACK}, a 5 mm uniform margin was applied to create the PTV_{TRACK}. This PTV_{TRACK} accounts for motion-related errors from a range of sources including motion prediction errors, Calypso positioning system uncertainties, MLC leaf width, and beacon-to-tumour centroid surrogacy errors. The prediction algorithm was tested on 110 lung traces from 22 patients [19] with an accuracy estimated to be ±0.8 mm (95% confidence interval). Calypso tracking system positioning errors were reported to be ±0.56 mm [20]. Motion along the MLC leaves translates with sub-millimetre accuracy but the perpendicular motion can misalign the target, contributing to the maximum possible error of ±2.5 mm (i.e. ± half a leaf width on a Varian

Trilogy linac). The maximum error was implemented into the margins calculation to accommodate for the worst-case scenario. Surrogacy between markers and tumour positions were found to be ±1.0 mm [21], [22]. These uncertainties add in quadrature to 2.9 mm. The decision to keep 5 mm is therefore more conservative than needed but offered reassurance for the start of the clinical trial.

The second step was for the original patients' plans to be adjusted for the mid-ventilation passive strategy. Margins were defined based on the work of Van Herk [11]. Parameters were obtained from Sonke et al. [12] while the method applied for selecting the mid-ventilation phase was done following the work of Peulen et al. [10]. The same collimator angle as the ITV-based plans was used to respect planning consistency. For all patients, the margins calculated for the left–right and anterior–posterior amplitude were 6 mm. In the superior–inferior direction, the margins were also 6 mm when the motion was less than 7 mm, or the margins were extended to 7 mm otherwise. The margin recipe calculates with high accuracy the margin necessary but the TPS discretizes the margins values to the nearest millimetre.

The target structures were all contoured by a single experienced radiation oncologist and optimized by a single senior radiation therapist to ensure that the plans were optimized comparably between each other. Dose to OARs was optimized to be as low as possible following our strict in-house regulation conforming to the RTOG guidelines.

Treatment plan delivery

For each motion management strategy, the treatment plans were delivered to a moving phantom (Fig. 1) to generate MLC tracking logs from which simulated delivered doses can be reconstructed. Respiratory motion for each patient was estimated from the 4D-CT motion extent and matched with the closest trace available in a Synchrony (Accuray Inc., Sunnyvale, CA) motion database [13]. Each patient plan was matched with the first fraction of a Cyberknife patient based on both the 3D Peak to Trough (PTT) distance and the most dominant tumour motion direction. The motion in the next fraction for that same Synchrony patient was used as the clinically realistic target trajectory input for a programmable motion phantom for simulated treatment. Table 1 provides details of the PTT distance of each patient and their respective match in the synchrony database.

The 30 plans were delivered to a programmable motion phantom as shown in Fig. 1. Three electromagnetic beacon transponders were placed onto the HexaMotion 6D platform (Scandidos, Uppsala) programmed with the selected lung motion traces moving in three dimensions. The in-house MLC tracking software is integrated with the Calypso real-time position monitoring system and a Varian linear accelerator. Real-time positions are fed to the MLC tracking software which calculates the new leaf positions and sends them to the MLC controller. MLC log files (Dynalog) and target trajectory files were collected for use in dose reconstruction.

Dose reconstruction

Two strategies were deployed for dose reconstruction to differentiate organs that move with respiration and static organs, with separate reconstructions for each summarized in Fig. 2. The GTV and lung were considered structures moving equivalently with breathing cycle while spinal cord, heart, oesophagus, great vessels and trachea were simulated as static (Fig. 3).

To evaluate the dose that would have been delivered for each motion management strategy, the MLC positions and target trajectory files were inputted into the dose reconstruction software. The software provided the dose distribution post-treatment for moving structures by binning the treatment arc into multiple isocentre shifts according to the detected tumour motions. The target motion was divided into 1 mm bins so that a series of sub-arcs, each corresponding to motion within that 1 mm bin was created with the isocentre at the centre of the bin. The multiple sub-arc plan was then imported into Eclipse for dose calculation. With this method, the sum of the

arcs in the bins equal the angle spanned for the original treatment arcs. Further details on the dose reconstruction framework can be found in Poulsen et al. [23]. For the evaluation of the dose distribution for static organs, tumour motion trajectory files were not used and a single treatment isocentre was used instead (using delivered MLC and no motion).

For dose reconstruction of the ITV-based plan, the GTV dose coverage is simulated by the dose reconstruction method above. However the OARs are considered static, so the dose to static organs during ITV-based treatment therefore equated to the planned dose (MLC and no motion).

Data analysis

The analysis to determine the potential role of each motion management strategy was assessed based on the target dose coverage and the OAR dose reductions comparatively from ITV-based to MLC tracking or midV approaches. The statistical differences between strategies was assessed using a Wilcoxon signed-rank non-parametric statistical test (one-tail).

Assessment of target dose coverage

To validate the delivered target doses for the motion management strategies, the reconstructed GTV_{TRAC}K, GTV_{MidV} and $GTV_{ITV\text{-}BASED}$ D98% (the dose received by 98% of the volume, i.e. near-minimum dose), D95% and D2% (i.e. near-maximum dose) were compared to their planned equivalent dose metric values.

OAR exposure in the presence of motion

For both planned and reconstructed dose, a set of statistical comparisons of dose-metrics was used to report the dose difference for both target and OAR structures from ITV-based plans. This scheme provides the dose difference as positive values to reflect a dose reduction) compared to ITV-based planning. Mean lung dose and V20 are commonly used as a metric for dose reporting and were shown to be correlated with pulmonary toxicities [24 - 27]. We report mean lung dose reduction (bilateral lung volume minus the GTV) and V20 reduction (percentage of the bilateral lung volume minus the GTV receiving 20 Gy). Further, OAR dose–volume metrics, as prescribed by the ICRU 83 [28], were reported for the spinal cord (D0.3 cc), heart (D1 cc), oesophagus (D3 cc), trachea (D4 cc) and great vessels (D10 cc).

Uncertainties of dose reconstruction

The dose reconstruction method utilized in this study relies on assumptions regarding relative motion and dose accumulation across moving/deforming organs that lead to uncertainty in the reported dose metrics. Specifically, the MLC tracking and midV plans were set on one specific reference phase. A sensitivity analysis method was developed to provide the range in dose metric values as an uncertainty estimate across the full 4D-CT phases for each OAR. The first step in this sensitivity analysis was to transfer the reference plan to the other phases of the 4D-CT. The isocentre was shifted according to the GTV position for each phase, and each OAR was re-contoured. The second step was to calculate the dose on each phase and calculate the dose metrics (i.e. mean lung dose, D3 cc etc.) associated with each OAR. The standard deviation of each dose metric across phases then constitutes the sensitivity to motion and the uncertainty in dose reconstruction. The average of standard deviations was calculated for each organ to indicate the magnitude of error and estimate the errors during the dose reconstruction of both static and moving organs.

Results

PTV reduction

The mean PTV of the ITV-based plans (39.6 cm^3), was reduced with MLC tracking (24.8 cm^3) representing a mean percentage reduction of 37.3% (range 9–56%). The mean PTV was also reduced with the midV plans (29.3 cm3) compared to the ITV-based plans with a mean percentage reduction of 26% (range −5–33%).

As expected, the magnitude of the PTV percentage reduction for midV plans was smaller than MLC tracking. The margins for MLC tracking are set to 5 mm for all patients, whereas with midV plans the PTV margins start at ~6 mm for GTV without motion and increase with motion. In one instance, the PTV_{MidV} was larger than its $PTV_{ITV\text{-}BASED}$ comparator due to small motion and artefacts in the mid-ventilation phase planned (See Table 1, patient 6).

Assessment of target dose coverage

For each motion management strategy, the reconstructed dose to the target is consistently higher or closer to planned dose using MLC tracking than the other motion management strategies. The GTV_{TRACK} dose coverage across patients were all superior and statistically different ($p < 0.01$, one sided) than the midV and ITV-based dose coverage.

Comparing MLC tracking planned against delivered, the GTV dose metrics D95%, D98% and D2% obtained during treatment were larger than the equivalent planned dose metrics with the percentage changes of 1.8% (±2.0%, $p < 0.01$), 2.1% (±1.8%, $p < 0.01$) and 2.8% (±2.8%, $p < 0.01$) respectively. The increase in dose metric values is thought to be contributed to by errors in prediction algorithm and MLC tracking errors.

For the midV regime, the delivered GTV D95%, D98% and D2% is different from midV planned by −0.5% (±1.6%, $p > 0.2$), −0.6% (±1.6%, $p > 0.2$), and −0.2% (±3.1%, $p > 0.2$) respectively. The average delivered dose to the target is close to zero, whereas variation between patients (i.e. standard deviation) is larger than without tracking.

For the ITV-based regime, the GTV dose metrics of D95%, D98% and D2% being −0.4% (±2.1%, $p = 0.3$), −0.65% (±1.6%, $p = 0.3$) and −0.4% (±3.2%, $p = 0.3$) compared with their planned values. No significant differences were seen between planned and delivered in these cases.

OAR exposure in the presence of motion

Using MLC tracking and midV, dose reductions to the OAR for both planned and dose reconstruction dose metrics suggest benefit over the ITV-based planning method. Differences in dose metrics are shown in Fig. 4. Every organ shows a positive average dose reduction implying that, for this cohort of patients, midV and MLC tracking regimes both improve the treatment quality over the ITV-based planning method. For the delivered treatment, reduction in dose to OAR were (MLC Tracking/MidV) for the lung (mean lung dose, 0.8 Gy/0.2 Gy and V20 Gy, 1.6/0.3%), oesophagus (D3 cc, 1.9 Gy/1.4 Gy), great vessels (D10 cc, 3.2 Gy/1.3 Gy), trachea (D4 cc, 1.1 Gy/0.9 Gy), heart (D1 cc, 2.0 Gy/0.5 Gy) and spinal cord (D0.03 cc, 0.5 Gy/−0.1 Gy). Using MLC tracking, the dose distribution was shown to be significantly different from the ITV-based plan for the lung, oesophagus, heart and trachea (only the delivered data for trachea). However, no statistical differences were found for the mean lung dose, V20 and spinal cord. Similarly, the mid-ventilation approach demonstrated that on average the dose was reduced using mid-ventilation planning, however the dose distributions were not significantly different than the ITV-based plan.

The accuracy of the dose reconstruction is reported as the range in dose metrics across all phases for each patient. Using the 4D-CT, the mean lung dose exported for each 10 phases of each patient showed a mean lung dose range of ±0.2 Gy across all phases. Similarly, it was calculated a range of ±0.2% for the V20, ±0.3 Gy for the oesophagus, ±0.2 Gy for the great vessels, ±0.6 Gy for the trachea, ±0.4 Gy for the heart and ±0.2 Gy for the spinal cord.

For both MLC tracking and midV strategies, individual large dose reductions were shown. Heart D1 cc shows reduction up to 17.6 Gy for Patient 2 (See Supplementary Fig. 1 for an example of dose distribution) where the original $PTV_{ITV\text{-}BASED}$ overlaps with the heart, while the reduction in target defined by the PTV_{TRACK} avoids this overlap. Similar dose reductions for other OAR (expressed as delivered dose metrics reduction for Tracking/MidV) were observed for oesophagus (Patient 3, 6.5/4.8 Gy for D3 cc), great vessels (Patient 3, 10.8/8.4 Gy for D10 cc), trachea (Patient 1, 6.0/4.0 Gy for D4 cc), heart (Patient 2, 17.6 Gy/5.5 Gy) and spinal cord (Patient 10, 3.2/2.0 Gy for D0.3 cc). These individual cases all had in common the position of the OAR either close to the target or at the same superior–inferior level as the treatment field.

Discussion

MLC tracking dosimetric performance

Potential dosimetric benefits for lung SABR with MLC tracking and midV have been shown by quantifying a reduction in dose delivered to the OAR while maintaining the target dose coverage. For tracking, the 30% reduction in PTV found in this study is consistent in magnitude with the PTV reduction of 30.2% and 36% reported with the Cyberknife experience [29] and the Vero gimbal linac [7], respectively. This study was conducted in a clinically realistic scenario, in that the treatment workflow was followed and real patient motion trajectories applied, supporting clinical translation from benchtop to bedside of a prospective clinical trial for MLC tracking with implanted electromagnetic transponders (NCT02514512).

This study underlines and refocuses on the purposes of MLC tracking for lung. For this cohort of patients, the use of motion management mildly influenced the delivered target dose coverage, showing for all 10 patients acceptable doses even without using MLC tracking or mid-ventilation. The strength of MLC tracking was found in its ability to significantly reduce the dose spillage to the OAR. This study also showed that MLC tracking in this context offers greater benefits not only for tumours with large motion, but also tumours located in close vicinity with OARs.

Mid-ventilation planning was tested along with MLC tracking to investigate any potential differences between passive and active motion management strategies. Although the dose reductions were not statistically different from the ITV-based plan in this study, other studies evaluating mid-ventilation have found significant differences [30] based on film dosimetry.

This study illustrated that MLC tracking reduces doses to surrounding organs in Radiotherapy treatments specifically for stage I or oligometastatic metastases. It is hypothesized that a similar effect will be seen in other lung tumour sites such as node-negative large tumours (>5 cm) or tumours adjacent to critical structures [31]. These sites pose a challenge due to the difficulty of sparing adjacent structures with ablative doses which lead to the formulation of a more conservative dose escalation and lower biological equivalent dose (RTOG 0813). While this prescription spares surrounding structures, it could also reduce local control and overall survival. Motion management techniques, like MLC tracking, can help maximize the clinical outcomes of these patients by reducing the margins and delivering a most accurate treatment. This could allow increased dose escalation to

the tumour while still sparing surrounding structures and thereby improve the clinical outcomes of these patients.

Dose reconstruction limitations

The dose reconstruction method relies on the assumption that the patient is subjected to no OAR motion and deformation, with the exception of the lung assumed to move rigidly with the tumour. The impact of this assumption is estimated with our sensitivity analysis that showed errors in the range of ±0.2 Gy for most organs and up to ±0.6 Gy for small organs. Fig. 4 shows that given the magnitude of some dose reductions during tracking and midV, errors for not accounting for 4D motion is mostly outweighed for the majority of organs. A fully developed dose reconstruction algorithm would account for deformation (organs stretching and/or organ rotation). However, deformation, even at the best of times is not a guaranteed technology, and would also require its own quality assurance which is beyond the scope of this paper, as seen in the AAPM TG132.

Relationship between mean lung dose and pulmonary toxicity

SABR techniques are increasingly used in the oligometastatic setting where local recurrence and retreatment to nearby lesions within the lung is not uncommon. Application of compact dose distributions with accurate targeting will be advantageous in this setting to keep lung dose, and potential toxicity, as low as reasonably achievable. Mean lung dose has been correlated with the risk of radiation induced pneumonitis; a study of 251 patients [32] showed a cut-off point for toxicity with grade 2 to grade 4 toxicities reported in 4.3% of patients with MLD < 4 Gy and 17.6% of patients with MLD > 4 Gy. For our cohort, the average MLD presented was estimated to be above this 4 Gy cut-off value with ITV-based planning, and was lowered below 4 Gy with MLC tracking (3.5 Gy). A recent study simulated the effect of MLC tracking during MR-LINAC treatment and showed a mean lung dose reduction of 0.3 Gy, against our study with 0.8 Gy [33].

Conclusion

MLC tracking and mid-ventilation have the potential to provide dosimetric benefits compared to conventional lung treatments by reducing the PTV and subsequent normal lung dose. Delivered MLC tracking plans showed PTV reduction of more than 30%, full GTV dose coverage and reduction in the OAR dose spillage, supporting full clinical implementation of the technology.

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Table 1. Summary of patient motion evaluated at 4D-CT compared with the motion used during physical experiments. 4D-CT motion was evaluated and matched with the first fraction obtained from a synchrony database. Fraction 2 of that same synchrony patient was used as the tumour motion input into the motion platform.

Patient #	4DCT PTT	PTT Delivered Tumour Motion	PTV ITV-based	PTV Tracking	PTVMidV	Lobe	PTV Characteristics	Baseline shift*	PTV Excursion**
1	0.31 cm	0.24 cm	23 cm^3	14 cm^3	18 cm^3	Right UL	Overlaps with the bronchi; ultra-central tumour	1 mm lateral toward periphery	No
2	0.67 cm	0.68 cm	49 cm^3	32 cm^3	39 cm^3	Right ML	Overlaps with the heart	No	No
3	0.05 cm	0.02 cm	17 cm^3	13 cm^3	11 cm^3	Left UL	Sitting right above the heart in transverse plan – transverse plan of trachea and bronchi	No	No
4	0.18 cm	0.23 cm	15 cm^3	10 cm^3	12 cm^3	Right UL	Overlaps with upper chestwall	No	No
5	0.25 cm	0.23 cm	13 cm^3	7 cm^3	9 cm^3	Right ML	Superior to the heart – dose out of range of the OAR	No	No
6	0.56 cm	0.16 cm	68 cm^3	62 cm^3	71 cm^3	Right ML	Tumour very large – no motion – close proximity to the spinal cord	No	No
7	0.34 cm	0.33 cm	19 cm^3	13 cm^3	16 cm^3	Left UL	Relatively distant from any OAR	No	No
8	0.18 cm	0.81 cm	116 cm^3	51 cm^3	52 cm^3	Right ML	Relatively distant from any OAR	No	No
9	1.10 cm	0.88 cm	41 cm^3	28 cm^3	35 cm^3	Right LL	Overlaps with posterior chestwall	No	No
10	0.42 cm	0.85 cm	36 cm^3	23 cm^3	29 cm^3	Right LL	Overlaps with posterior chestwall	1 mm lateral 2 mm anterior	No

Abv: PTT = Peak-to-trough.
* Baseline shift detected when maximum to minimum position exceeded 0.5 mm. Taken over an averaging window of 10 s.

**PTV excursion occurs during ITV-based treatment when GTV position is outside the PTV. PTV excursion was estimated using the detected tumour motion and calculating the time the GTV within the ITV would have spent outside the $PTV_{ITV\text{-}BASED}$.

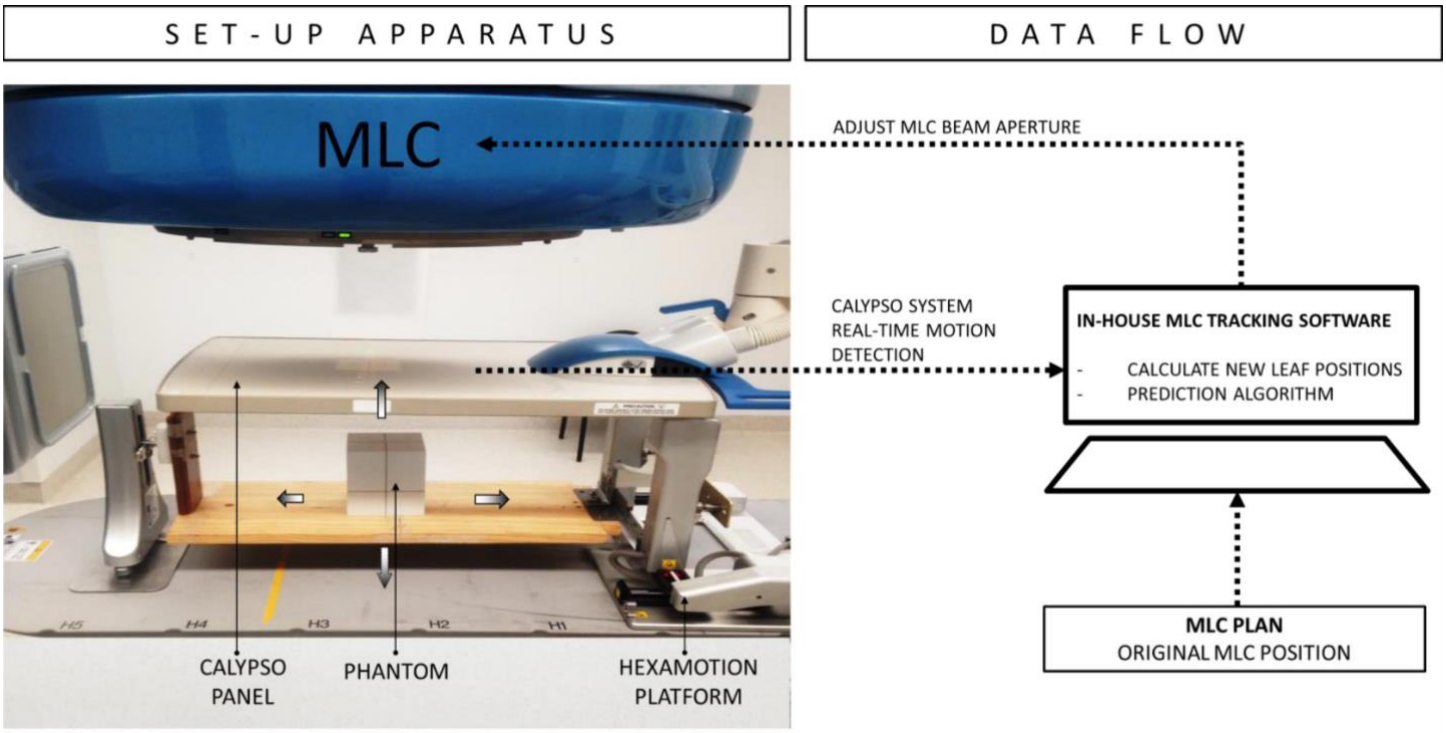


Fig. 1. Experimental set-up and data flow of the MLC tracking system. Motion of the phantom containing electromagnetic transponders on the HexaMotion platform was detected by the Calypso tracking system and sent to an in-house tracking software to calculate and reshape the MLC leaves in real-time.

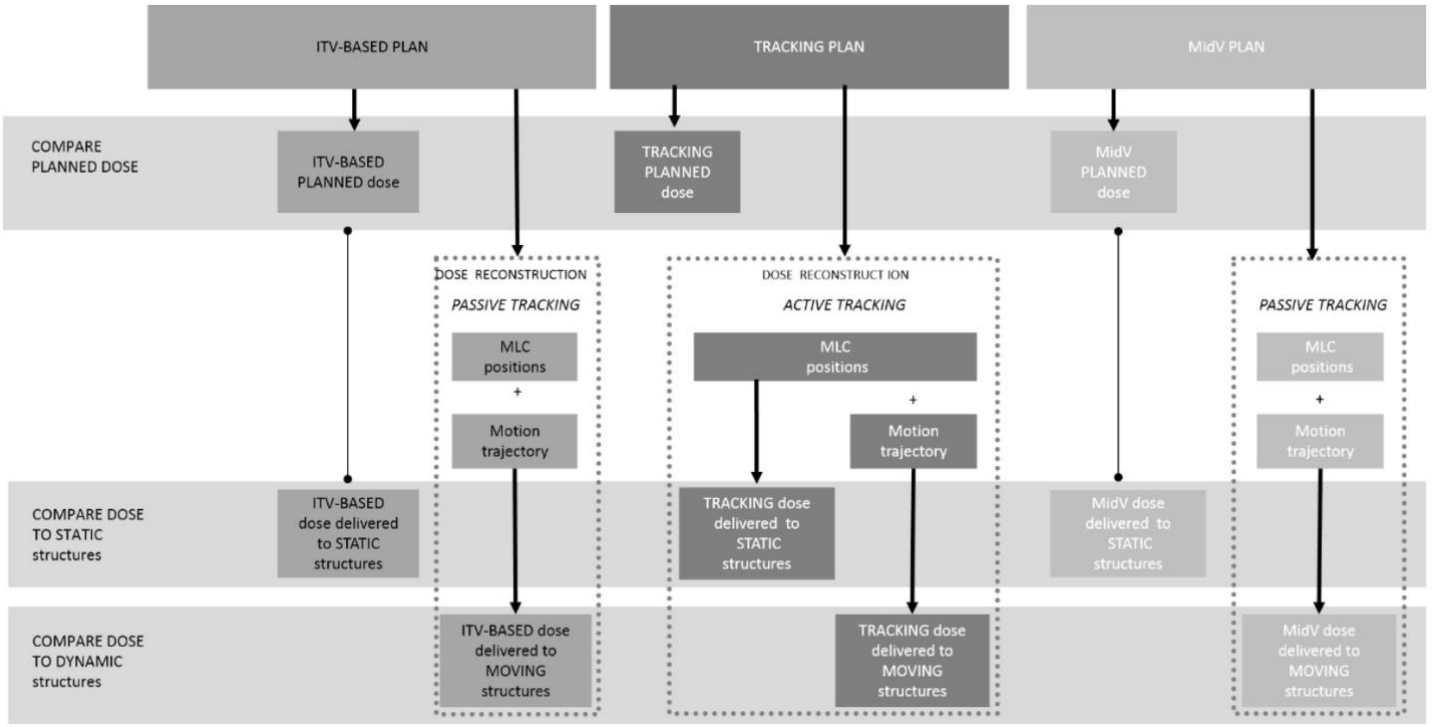


Fig. 2. Overview of the planned and reconstructed dose comparisons for ITV-based, MLC tracking and mid-ventilation. The estimation of the delivered doses during ITV-based, MLC tracking, and midV treatments to static (spinal cord, heart, oesophagus, trachea and great vessels) and moving targets (lung and target) required different inputs acquired through delivery of the two treatment plans: the MLC positions for static organs and both the MLC positions and the trajectory positions for the moving structures. Dose–Volume Histogram metrics of the motion management strategies were then compared.

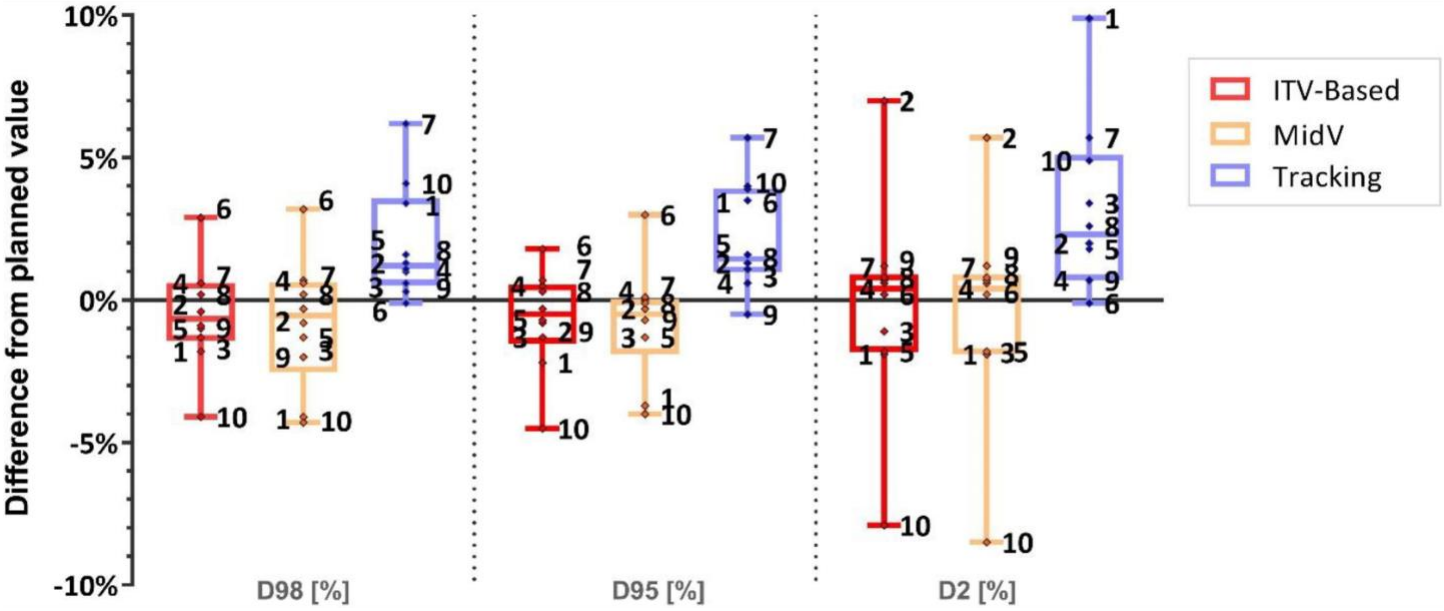


Fig. 3. Reconstructed GTV dose coverage (D98%, D95% and D2%) for ITV-based (red), midV (orange) and tracking (red) delivery. Individual patient numbers are shown on the boxplots. The box plots depict the minimum and maximum values, the upper and lower quartiles and the median (line).

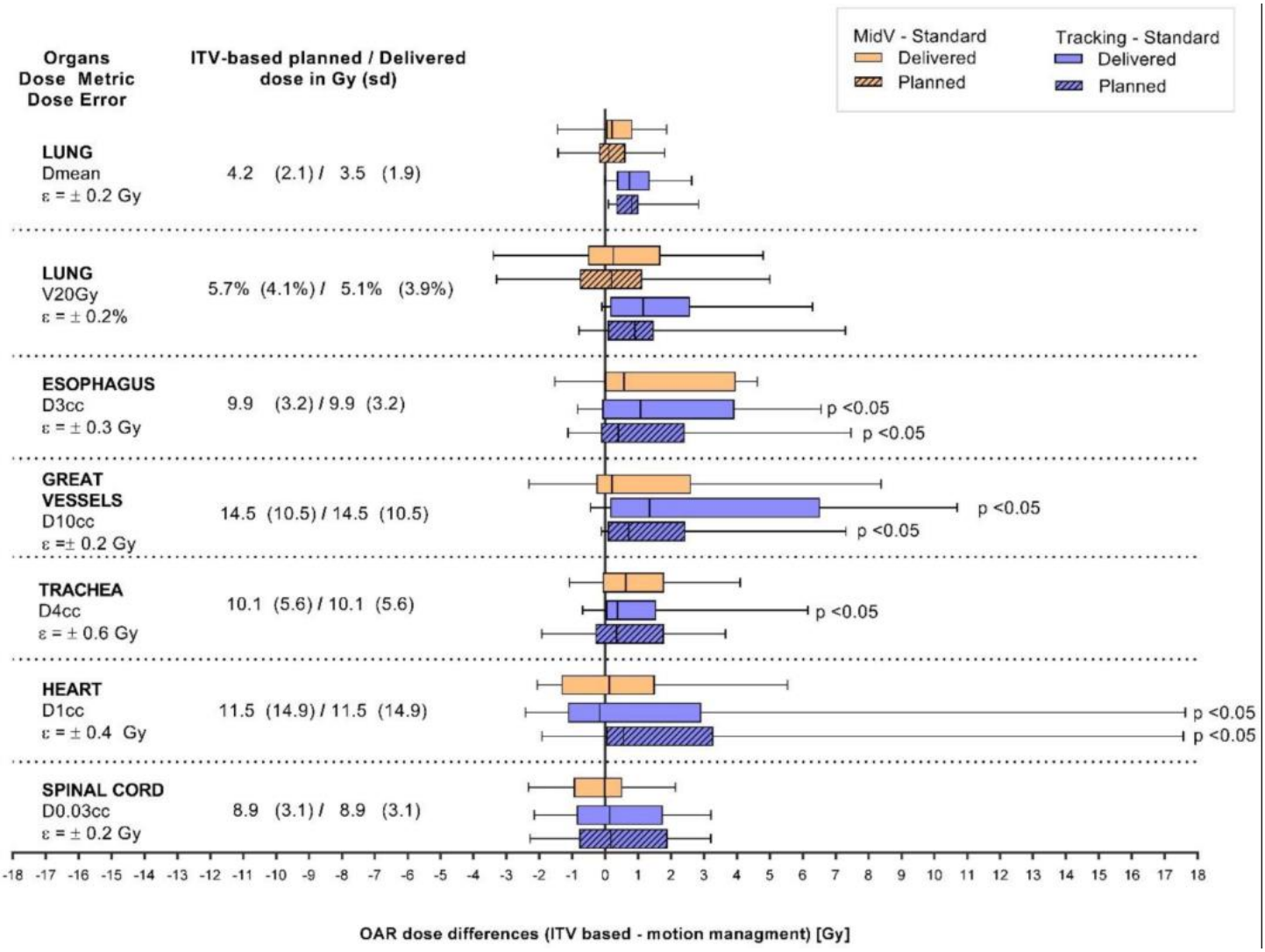
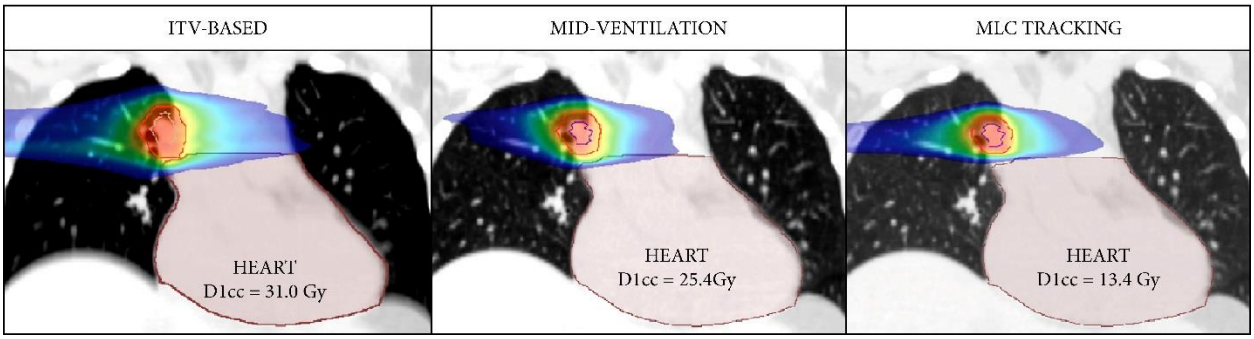


Fig. 4. OAR dose differences for midV and tracking strategies compared with ITV-based planning for the given dose metrics. The doses planned or delivered with the midV or tracking strategies were subtracted from the ITV-planned doses to obtain the OAR dose difference. Positive values signify a dose reduction during tracking or mid-ventilation based on specific dose metric. The horizontal boxplots show the minimum and maximum values, the upper and lower quartiles and the mean. Average values from the tracking plan at end-of-inhale to show the range of dose seen from the 4D-CT plan. OAR dose differences that were significantly different to the ITV-planned doses are denoted by $p < 0.05$.



Supplementary Figure

Dose reconstruction of a patient with significant dose reduction to the heart using mid-ventilation and MLC tracking. In the ITV-based dataset, the PTV is almost overlapping with the heart. Using mid-ventilation and MLC tracking, the PTV volume was reduced in both cases with subsequent reduction to the dosage received by the heart.