Radiotherapy and Oncology 117 (2015) 491–495

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Tumor tracking

Effect of MLC tracking latency on conformal volumetric modulated arc therapy (VMAT) plans in 4D stereotactic lung treatment

James L. Bedford *, Martin F. Fast, Simeon Nill, Fiona M.A. McDonald, Merina Ahmed, Vibeke N. Hansen, Uwe Oelfke

The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, London, UK

ARTICLE INFO

Article history:
Received 3 February 2015
Received in revised form 29 July 2015
Accepted 29 July 2015
Available online 13 August 2015

Keywords:
MLC tracking
Latency
Lung
VMAT
Motion prediction

ABSTRACT

Background and purpose: The latency of a multileaf collimator (MLC) tracking system used to overcome respiratory motion causes misalignment of the treatment beam with respect to the gross tumour volume, which may result in reduced target coverage. This study investigates the magnitude of this effect.

Material and methods: Simulated superior–inferior breathing motion was used to construct histograms of isocentre offset with respect to the gross tumour volume (GTV) for a variety of tracking latencies. Dose distributions for conformal volumetric modulated arc therapy (VMAT) arcs were then calculated at a range of offsets and summed according to these displacement histograms. The results were verified by delivering the plans to a Delta^4 phantom on a motion platform.

Results: In the absence of an internal target margin, a tracking latency of 150 ms reduces the GTV $D_{95\%}$ by approximately 2%. With a margin of 2 mm, the same drop in dose occurs for a tracking latency of 450 ms. Lung V_{13Gy} is unaffected by a range of latencies. These results are supported by the phantom measurements.

Conclusions: Assuming that internal motion can be modelled by a rigid translation of the patient, MLC tracking of conformal VMAT can be effectively accomplished in the absence of an internal target margin for substantial breathing motion (4 s period and 20 mm peak–peak amplitude) so long as the system latency is less than 150 ms.

Multileaf collimator (MLC) tracking is emerging as an important method of minimising normal tissue doses in the presence of respiratory motion [1,2]. Instead of adding an internal target margin to the clinical target volume (CTV) to create an internal target volume (ITV) which encompasses the tumour at most of its cyclical positions, the leaves of the MLC are used to follow the target, thereby enabling the ITV to be small or absent and consequently sparing adjacent normal tissues [3].

However, MLC tracking is rarely perfect. There is an inherent delay in the detection of the target position, the processing of this information into appropriate MLC leaf positions and the subsequent movement of the MLC leaves to the desired updated position [4,5]. The total delay due to all of these factors is referred to as the *system latency* [6]. Typical values reported in the literature vary from 50 ms to 500 ms for different tracking systems [6–10]. If the respiratory motion is reasonably repetitive, motion prediction algorithms can be used to predict the position of the tumour at the end of the latency period and drive the MLC directly to where the tumour is expected to be [10]. In this case, any remaining latency is referred to as *residual system latency*.

The impact of system latency is to introduce an offset between the position of the CTV and the position of the treatment beam. This is expected to reduce the CTV coverage and increase the normal tissue dose. However, it is currently unclear exactly what the dosimetric impact of the latency is. This study therefore aims to quantify as accurately as possible the impact of various system latencies on the coverage of the CTV and on the surrounding normal tissue, taking into account the beam characteristics and the variation in density of the patient around the gross tumour volume (GTV). The case of stereotactic ablative body radiotherapy (SABR) for lung is considered [11], as this is a likely scenario for the use of MLC tracking. The study consists of two parts: firstly calculating the expected target coverage based on a treatment planning study, thereby allowing acceptable latency to be defined, and secondly, the verification of the results by delivering the treatment plans

* Corresponding author at: Joint Department of Physics, The Institute of Cancer Research and The Royal Marsden NHS Foundation Trust, Downs Road, Sutton, Surrey SM2 5PT, UK.

E-mail address: James.Bedford@icr.ac.uk (J.L. Bedford).

http://dx.doi.org/10.1016/j.radonc.2015.07.044
0167-8140/

to a moving phantom. The study also evaluates what *tracking ITV margin* might be necessary to overcome any residual system latency.

Materials and methods

Treatment plans

Five typical SABR lung patients were retrospectively studied, with three tumours located in the upper lobes and two in the lower lobes close to the diaphragm, and with a GTV ranging from 12.8 cm^3 to 48.5 cm^3. CT scans were acquired in breath hold using Active Breathing Coordinator (ABC) (Elekta AB, Stockholm, Sweden), with a slice thickness and spacing of 2 mm. The gross tumour was delineated and the CTV was taken to be equal to the GTV, in accord with normal practice for this type of treatment [11]. It was then assumed that the static CT scan with an isocentre at the geometric centre of the GTV represented a perfectly tracked tumour with zero system latency. To evaluate what margin might be needed to overcome the effect of latency, a series of tracking ITVs were created, consisting of the GTV plus a margin of between 0 mm and 5 mm in the superior–inferior direction and 0 mm in the other directions. The PTV was equal to the tracking ITV as no setup error was assumed present in this MLC-tracked scenario.

Treatment plans based on the tracking ITVs were generated using the AutoBeam in-house inverse planning system [12] and consisted of a single anticlockwise volumetric modulated arc therapy (VMAT) arc from 175° to 185°, with control points spaced at 5° intervals, for delivery using a 6-MV flattened beam. Collimator angle was 2° in all cases to spread out any interleaf leakage. This resulted in MLC leaf motion perpendicular to the direction of tumour motion. The apertures conformed to the beam's eye view of the tracking ITV, with zero penumbra margin, except superiorly and inferiorly, where the penumbra margin was 4 mm. The control point weights were iteratively adjusted by the inverse planning process to additionally conform the treatment plans to the tracking ITV [12]. The dose prescription was 55 Gy in 5 fractions to 95% of the tracking ITV. This planning approach resulted in a prescription isodose which was between 60% and 90% of the maximum dose in all cases, and typically around 70%.

A software application was produced to calculate the effect of the respiration on the treatment plan. Breathing motion was then taken to be purely in the superior–inferior direction:

$$z = A - 2A\sin^6[\pi t / T], \quad (1)$$

where z was positive towards the head of the patient, the peak–peak amplitude $2A$ was taken to be between 10 mm and 30 mm and the time period of motion, T, was taken to be between 2 s and 4 s [13]. Although this model was simple, its advantage was that it enabled a wide range of motions to be conveniently simulated. Tracking motion was taken to be of the form:

$$z = A - 2A\sin^6[\pi(t - \theta) / T], \quad (2)$$

where the latency θ was varied from 0 ms to 500 ms in 50 ms intervals. The same motion equations were also investigated with an exponent of two instead of six [13], for comparison purposes. The beam isocentre position relative to the centre of the GTV resulting from tracking with a system latency, was then taken as the difference between Eqs. (1) and (2). To give an indication of how the model related to real clinical breathing traces, the superior–inferior component of the high-frequency motion trace described by Sawant et al. [8], in turn based on the work of Suh et al. [14], was also used in the same way.

The difference between the beam isocentre and the centre of the GTV was used to construct a probability density function (PDF) of the proportion of time spent by the isocentre at each position, in integral numbers of mm, relative to the centre of the GTV. In order to evaluate the resulting dose distribution, the entire VMAT plan was computed on a dose grid of 2 mm × 2 mm × 2 mm in Pinnacle^3 (Philips Radiation Oncology Systems, Madison, WI) on isocentres positioned at 1-mm intervals from 20 mm superior to the centre of the GTV to 20 mm inferior to the centre of the GTV. The ±20 mm range was necessary to accommodate the worst case scenario of the beam aperture being in antiphase to the GTV. The component dose distributions were then superposed according to the value of the PDF at each position. The result represented the dose distribution that would be obtained after a number of deliveries of the VMAT plan (Fig. 1). The process was repeated for all of the plans based on each tracking ITV. The value of $D_{95\%}$ for the GTV and V_{13Gy} for normal lung was recorded for all latencies and tracking ITVs.

The calculations were repeated with $z = 0$ in Eq. (2) to indicate the outcome if treatment were performed without tracking using an isocentre located midway between the motion extrema. This was for purposes of comparison only, as the breath-hold CT scan used in this study was not strictly appropriate to this free-breathing situation.

Verification measurements

The treatment plans for zero tracking ITV margin were recalculated on an artificial dataset representing a Delta^4 phantom (ScandiDos, Uppsala, Sweden) [15], using a dose grid of resolution 2 mm × 2 mm × 2 mm. The plans were then delivered using a Synergy accelerator with Agility MLC (Elekta AB, Stockholm, Sweden) [16] and the dose was measured using the Delta^4 phantom. The Delta^4 phantom was positioned by means of the in-room lasers on a programmable motion platform [17] (Supplementary Fig. S1) and the platform set to move in the superior–inferior direction with the motion described by Eq. (1). The accuracy of setup was estimated to be ±1 mm. The motion platform reported its position every 25 ms to an in-house tracking programme, which calculated the desired MLC leaf positions and requested the accelerator to move the MLC leaves to that position [6]. Various latencies were introduced into the tracking software, so that the total system latency varied from 0 ms to 500 ms in 100 ms intervals. The system latency was 69 ms [6], so to achieve a latency of 0 ms, a linear regression motion prediction method was used, resulting in a residual latency of less than 10 ms [10]. For all the other latencies, motion prediction was turned off. The value of $D_{95\%}$ for the GTV was obtained from the dose–volume histogram reconstructed in the phantom environment by the Delta^4 software from the measurements and supplied depth dose curves. It was not possible to evaluate lung dose in the phantom study.

Results

With zero tracking ITV margin and with no latency, $D_{95\%}$ was 55 Gy as prescribed (Fig. 2a). As the latency increased, the $D_{95\%}$ dropped. It was postulated that a drop in $D_{95\%}$ of 2% to 53.9 Gy was acceptable, and for an amplitude of 10 mm and a period of 4s, this occurred at a latency of around 150 ms. In general, larger GTVs were less affected by latency than smaller GTVs, with the range of $D_{95\%}$ values being around 3 Gy at 500 ms latency. If a tracking ITV margin was used, the prescription of $D_{95\%} = 55$ Gy was given to the tracking ITV, so that the GTV $D_{95\%}$ was somewhat higher than 55 Gy due to the non-uniformity of ITV dose in this type of treatment plan. Because of the tracking ITV margin, the GTV coverage was more resilient to motion, so that the drop in GTV $D_{95\%}$ to 53.9 Gy did not occur until 350 ms (1-mm margin) or 450 ms (2-mm) margin. Corresponding results for $\sin^2(t)$ motion as opposed to $\sin^6(t)$ motion were also demonstrated (Fig. 2b).

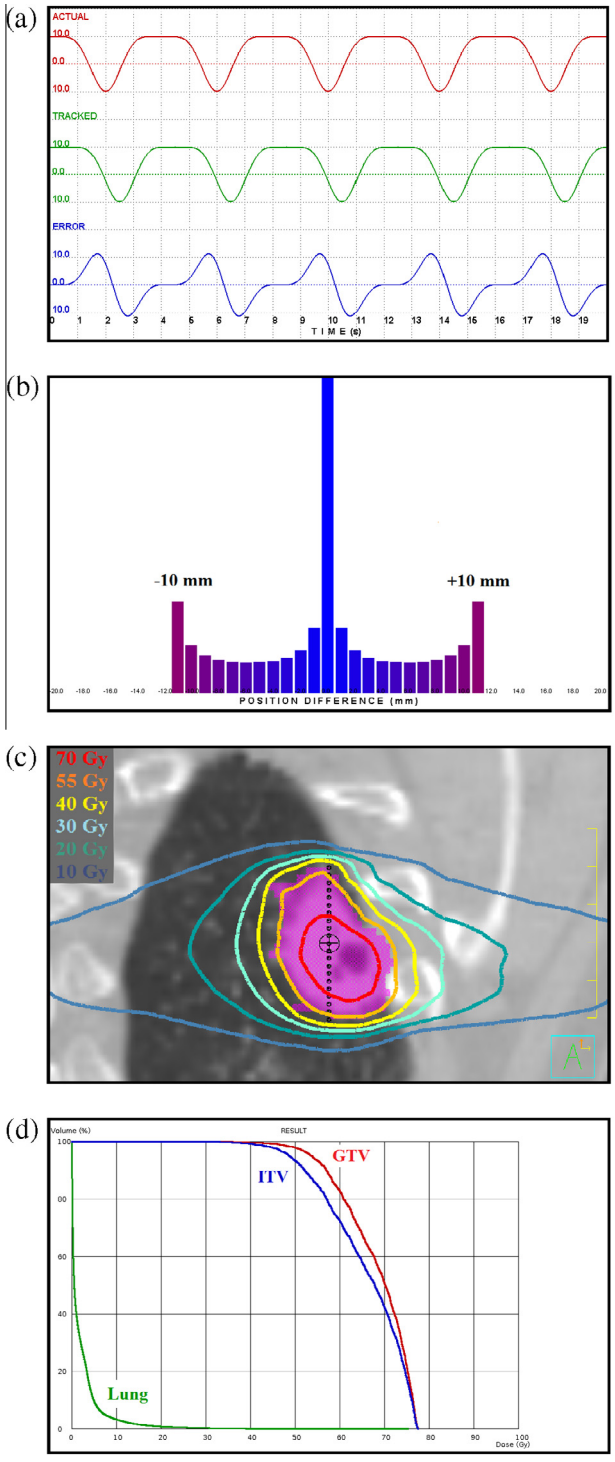

Fig. 1. Tracking model for $\sin^6(t)$ motion with 500 ms latency and 2-mm tracking ITV margin. (a) Motion traces, showing tumour position (ACTUAL), beam position (TRACKED) and difference between the two (ERROR), (b) probability density function of beam position in relation to the tumour, (c) coronal dose distribution for the VMAT treatment plan of a single patient based on an isocentre at the centre of the gross tumour volume (purple region), but with the isocentres of the complete set of dose components shown (black circles), (d) dose–volume histograms. Note that with this latency and margin, neither the tracking ITV nor the GTV receive the prescribed dose of 55 Gy to 95%.

Lung V_{13Gy} increased from 3.7% to 5.7% as the internal target margin was increased from 0 mm to 5 mm. The irradiated volume of lung was only weakly dependent on the latency and the form of breathing trace, i.e. $\sin^6(t)$ motion or $\sin^2(t)$ motion.

In general, system latency had a larger impact on GTV $D_{95\%}$ for larger amplitudes and shorter periods of breathing motion (Fig. 3). This was to be expected as the GTV moved by a larger distance in a given time for these conditions. The clinically recorded motion trajectory produced similar results to the Lujan model with an amplitude of 5 mm and a period of 4 s (Fig. 3).

If treatment was performed without tracking, GTV $D_{95\%}$ was 36.7 Gy with $\sin^6(t)$ motion and zero ITV margin, rising to 55.8 Gy with a 5-mm margin. Lung V_{13Gy} rose from 3.6% to 5.5% over the same range of margins.

The impact of system latency on the measured GTV $D_{95\%}$ in the phantom was very similar to that predicted by the model (Fig. 4). A drop in $D_{95\%}$ of 2% was observed at around 100 ms.

Discussion

The simulation study showed clearly that a tracking system latency of up to 150 ms had a negligible impact on the accuracy of conformal VMAT treatment plan delivery for larger-than-average tumour motion, while in the phantom study, a value of approximately 100 ms was obtained. The simulation took account of the inhomogeneous environment around the GTV, whereas the phantom study used a homogeneous phantom, so the simulation was likely to better represent the inhomogeneous situation present in a lung SABR treatment. On the other hand, the delivery study included practical effects such as MLC refitting.

For the Agility MLC used in this study, the MLC adjustment latency was in the order of 60–70 ms, depending on the motion trajectory, so a further latency of up to 80 ms in the motion

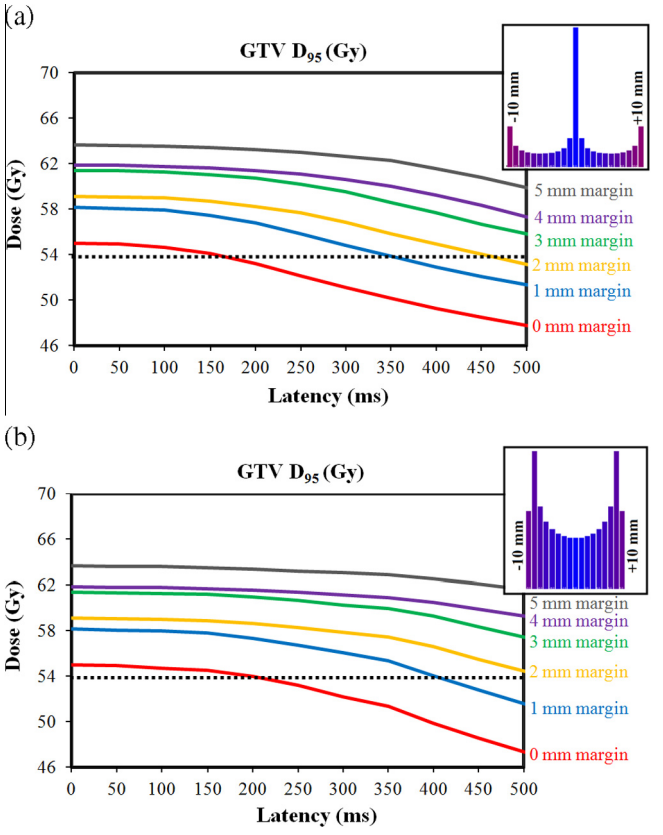

Fig. 2. Mean gross tumour volume (GTV) coverage for the five patients as a function of internal target margin and tracking system latency for amplitude 10 mm and period 4s. (a) $\sin^6(t)$ motion, (b) $\sin^2(t)$ motion. The threshold of 2% dose reduction from 55 Gy is shown as a dotted line. The inset shows the probability density function for 500 ms latency in each case.

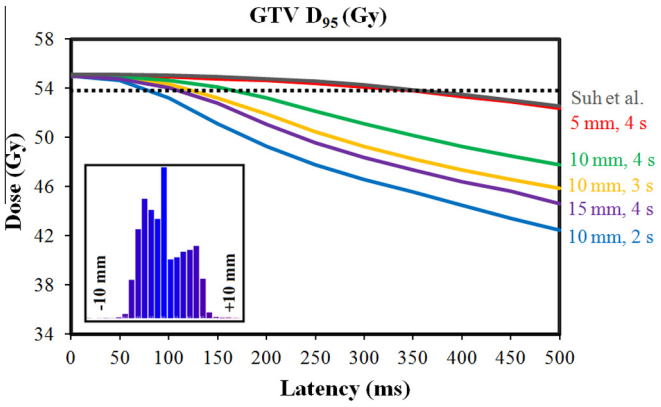

Fig. 3. Mean gross tumour volume (GTV) coverage for the five patients as a function of amplitude, period and tracking system latency for 0 mm tracking ITV margin. All curves are for $\sin^6(t)$ motion, with the exception of that marked Suh et al. (closely following that of 5 mm 4 s), which uses a recorded breathing trace from the literature. The threshold of 2% dose reduction from 55 Gy is shown as a dotted line. The inset shows the probability density function for 500 ms latency for the recorded breathing trace (Suh et al.).

detection device was permissible without using motion prediction. In practice, the likely scenario was that motion prediction would be used to obtain as low a residual latency as possible, but that if the patient were to breathe arhythmically at some point during the treatment, the prediction could be automatically switched off and/or retrained. With a system latency of less than 150 ms, this would not be problematic.

The results were slightly dependent on the form of the motion trace used for the motion model. The $\sin^6(t)$ model spent a relatively long period of time at the exhale position, so there was time for the tracking beam to catch up, even with a significant latency. However, the results for $\sin^2(t)$ were not very dissimilar. In this case, although less time was spent at the exhale position, the velocity between inhale and exhale was lower, so the tracking system was not so challenged in this time interval. The results for an exponent of four, as is often used with the Lujan model [13], were expected to lie between these two cases. The motion model used in this study also assumed superior–inferior motion in the interest of making the calculations tractable. This assumption was unlikely

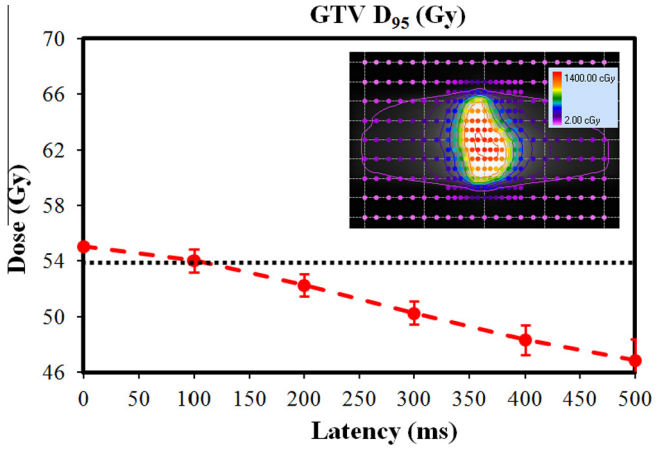

Fig. 4. Mean (±1 SD) gross tumour volume (GTV) coverage, relative to dose measured without motion and normalised to 55 Gy, for the five patients as measured by the Delta^4 phantom, as a function of tracking system latency. Shown on the same scale as Fig. 2. The inset shows the planned dose distribution (greyscale and isodoses from 10% to 100% of isocentre dose in 10% intervals) and measured dose distribution (squares coloured according to scale included) for one of the patients on the Delta^4 with 500 ms latency.

to have a significant impact on the results. In principle, there could also have been some interplay between the breathing motion and the treatment delivery, which this study neglected by summing the entire treatment plan at each superior–inferior offset, thereby giving the results expected after delivery of a number of treatment fractions. The good agreement of GTV dose in the phantom study, which consists of delivering only one fraction of treatment, with the simulation, supported this view.

The patient was assumed in this study to be a rigid body, whereas in reality it deforms between breathing phases. As the superior–inferior variation in patient contour was small over the ±10 mm of motion considered in this study, it was not thought that this significantly affected the results, but it was a source of uncertainty. The effect was likely to have less of an impact at shorter latencies, where the offset between beam aperture and GTV was small. In addition, the calculation of lung dose was limited in this study due to the rigid body model used. In a tracking treatment, the target and the beam oscillate superiorly and inferiorly, so that the dose deposition is spread out over the normal lung, influencing the irradiated volume. However, in this study, the tracked target was represented as stationary, so that this effect was not taken into account. One could estimate this effect by calculating lung dose based on the individual breathing phases. The errors were likely to be greater further from the GTV, as the lung tissue around the GTV deforms with the GTV itself during respiration, so that the currently simplified model was more relevant. Possible differential motion between the GTV and critical structures was also not taken into account by the rigid model.

The use of conformal VMAT was robust for this type of treatment planning, as it prevented the optimiser from attempting to boost the dose to the low density lung tissue surrounding the GTV, and was sufficient to provide a high-quality treatment plan. The implications for MLC tracking were twofold: firstly, the MLC fit to the PTV was generally optimum with the direction of leaf motion transaxially oriented, which was challenging when tracking superior–inferior motion, and secondly, it may have lessened the impact of any latency effects as only the periphery of the tracking ITV was affected by spatial mismatch between the GTV position and the aperture position. Other studies have investigated the use of VMAT with more complex modulation for tumour tracking [2,18] and reported on the impact of collimator orientation [18]. The simulation study assumed that the MLC leaves were able to follow the perpendicular motion accurately, with the specified latency, so that with zero latency, the leaves fitted the ITV accurately at all times. For this reason, the results of the study were expected to be applicable to other tracking methods such as couch tracking or tracking with a gimballed head. In contrast, the phantom study demonstrated tracking of motion perpendicular to the MLC leaves, where the leaves must be continually refitted to the moving target. This refitting of leaves was included in the MLC adjustment latency, which in turn formed part of the system latency.

The results were comparable to those of other studies. For example Sawkey et al. [5] calculated using realistic breathing traces that for a latency of 50 ms, a tracking ITV margin of 1.2 mm (range 0.6–2.6 mm) was needed, and that for a latency of 200 ms, a tracking ITV margin of 4.1 mm (range 2.3–7.6 mm) was needed. This was based on a requirement that the reference dose should be greater than 95%, which, when translated into individual directions, required that the reference point should be irradiated for 0.975 of the time. The present study predicted that smaller margins were adequate, probably due to the more extensive dosimetric calculation, in which the beam penumbra and inhomogeneities around the GTV were taken into account.

Similarly, Falk et al. [18] reported on delivery of RapidArc (Varian, Palo Alto, CA) for conventionally fractionated lung plans,

using an MLC tracking system with a latency of 160 ms. They used a margin estimation method in conjunction with measurements in a Delta[4] phantom to calculate that for a peak–peak amplitude of 20 mm, dynamic tumour tracking was expected to facilitate a reduction in PTV margin of 2–4 mm. Depuydt et al. [19] also investigated the potential for margin reduction based on the results of clinical SABR lung treatments using a gimballed linear accelerator. They estimated that GTV-PTV margins could potentially be reduced from 5 mm to 3 mm, but cautioned against excessive reduction in margins in view of uncertainty in geometric definition and biological distribution of the GTV, notably in microscopic disease extension.

This biological uncertainty also formed a background to the present study. In addition, there were limitations in the study itself, for example that internal motion could be modelled by a rigid translation of the patient. However, from the simulation and measurements, it was concluded that MLC tracking of conformal VMAT could be effectively accomplished in the absence of an internal target margin for substantial breathing motion (4 s period and 20 mm peak–peak amplitude) so long as the system latency was less than 150 ms. Latencies of less than this resulted in a drop in GTV $D_{95\%}$ of less than 2%. Longer latencies of up to 450 ms could be effectively mitigated by the use of a 2-mm tracking ITV margin.

Conflict of interest statement

Financial and technical support has been received from Elekta AB, Stockholm, Sweden.

Acknowledgments

We are grateful for NHS funding to the NIHR Biomedical Research Centre at The Royal Marsden and the ICR. We also thank Elekta AB, Stockholm, for making a shared accelerator available, for providing a tracking control system and funding this project. The sponsors had no part in the design or execution of the study. Submission of the manuscript for publication was part of the research agreement. Research at The Institute of Cancer Research is also supported by Cancer Research UK under Programme C46/A10588 and C33589/A19727.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.radonc.2015.07.044.

References

[1] Korreman SS. Motion in radiotherapy: photon therapy. Phys Med Biol 2012;57:R161–91.
[2] Keall PJ, Colvill E, O'Brien R, et al. The first clinical implementation of electromagnetic transponder-guided MLC tracking. Med Phys 2014;41:020702.
[3] McQuaid D, Partridge M, Symonds-Tayler JR, Evans PM, Webb S. Target-tracking deliveries on an Elekta linac: a feasibility study. Phys Med Biol 2009;54:3563–78.
[4] Poulsen PR, Cho B, Sawant A, Ruan D, Keall PJ. Detailed analysis of latencies in image-based dynamic MLC tracking. Med Phys 2010;37:4998–5005.
[5] Sawkey D, Svatos M, Zankowski C. Evaluation of motion management strategies based on required margins. Phys Med Biol 2012;57:6347–69.
[6] Fast MF, Nill S, Bedford JL, Oelfke U. Dynamic tumor tracking using the Elekta Agility MLC. Med Phys 2014;41:111719.
[7] Depuydt T, Verellen D, Haas O, et al. Geometric accuracy of a novel gimbals based radiation therapy tumor tracking system. Radiother Oncol 2011;98:365–72.
[8] Sawant A, Dieterich S, Svatos M, Keall P. Failure mode and effect analysis-based quality assurance for dynamic MLC tracking systems. Med Phys 2010;37:6466–79.
[9] Hoogeman M, Prévost J-B, Nuyttens J, Pöll J, Levendag P, Heijmen B. Clinical accuracy of the respiratory tumor tracking system of the Cyberknife: assessment by analysis of log files. Int J Radiat Oncol Biol Phys 2009;74:297–303.
[10] Krauss A, Nill S, Oelfke U. The comparative performance of four respiratory motion predictors for real-time tumour tracking. Phys Med Biol 2011;56:5303–17.
[11] Timmerman R, Paulus R, Galvin J, et al. Stereotactic body radiation therapy for inoperable early stage lung cancer. JAMA 2010;303:1070–6.
[12] Bedford JL. Treatment planning for volumetric modulated arc therapy. Med Phys 2009;36:5128–38.
[13] Lujan AE, Larsen EW, Balter JM, Ten Haken RK. A method for incorporating organ motion due to breathing into 3D dose calculations. Med Phys 1999;26:715–20.
[14] Suh Y, Dieterich S, Cho B, Keall PJ. An analysis of thoracic and abdominal tumour motion for stereotactic body radiotherapy patients. Phys Med Biol 2008;53:3623–40.
[15] Bedford JL, Lee YK, Wai P, South CP, Warrington AP. Evaluation of the Delta[4] phantom for IMRT and VMAT verification. Phys Med Biol 2009;54:N167–76.
[16] Bedford JL, Thomas MDR, Smyth G. Beam modeling and VMAT performance with the Agility 160-leaf multileaf collimator. J Appl Clin Med Phys 2013;14(2):172–85.
[17] Davies GA, Clowes P, Bedford JL, Evans PM, Webb S, Poludniowski G. An experimental evaluation of the Agility MLC for motion-compensated VMAT delivery. Phys Med Biol 2013;58:4643–57.
[18] Falk M, Munck af Rosenschöld P, Keall P, et al. Real-time dynamic MLC tracking for inversely optimized arc radiotherapy. Radiother Oncol 2010;94:218–23.
[19] Depuydt T, Poels K, Verellen D, et al. Treating patients with real-time tumor tracking using the Vero gimbaled linac system: implementation and first review. Radiother Oncol 2014;112:343–51.