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SBRT of lung cancer

An analysis of patient positioning during stereotactic lung radiotherapy performed without rigid external immobilization

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ABSTRACT

Background and purpose: Intra-fraction patient motion is incompletely understood and the optimum amount of support or immobilization during stereotactic body radiotherapy (SBRT) is unclear. Rigid immobilization is often advocated, but motion still occurs. In contrast, we deliver the vast majority of SBRT using simple supporting devices, simultaneously emphasizing comfort, frequent position checks and progressive reduction in treatment times. We report spine stability during lung SBRT.

Materials and methods: Patients lie on a thin mattress with arms supported above their head and below-knee support. Stereoscopic spine X-rays before and after fraction delivery identified motion in three translational and three rotational directions.

Results: Images from 109 fractions in 30 patients resulted in 327 translational and 327 rotational pre- and post-fraction comparisons. Mean RapidArc® delivery time for variable fraction dose was 4.2 min (SD = 1.4). 92% and 97% of translational and rotational differences were $\leqslant$1 mm and $\leqslant$1° in any direction and 98% of translational differences were $\leqslant$1.5 mm. Mean vertical, longitudinal and lateral motion was 0 mm (SD = 0.4), 0 mm (0.6) and 0 mm (0.6). 84% and 94% of the 109 fractions were delivered with $\leqslant$1 and $\leqslant$1.5 mm translation in all three directions and 93% with $\leqslant$1° of rotation. Two patients accounted for 10/17 fractions with >1 mm translational motion.

Conclusions: Based on pre and post-fraction X-ray imaging during fast lung SBRT, simple support devices can result in spine stability that is comparable to that reported with rigid external immobilization.

Stereotactic body radiotherapy (SBRT) is a high precision extracranial treatment technique that is being used to exploit the ablative potential of high-dose hypo-fractionated dose-fractionation schedules [1]. Fraction sizes of 1.8–4 Gy are typically used for conventional to moderately hypo-fractionated radiotherapy, which contrasts with 5–18 Gy or more in SBRT. Many organs at risk (OAR) are intolerant of SBRT doses and so it is necessary to keep the treatment volume as small as possible. This means that margins for microscopic disease are frequently omitted, there is rapid dose fall-off outside the target and image-guidance is used to reduce margins for positioning uncertainty.

To reduce uncertainty in targeting, important technical considerations in SBRT include: (1) stable and reproducible patient positioning, (2) high-quality imaging for treatment planning, (3) accurate target and OAR delineation, (4) advanced treatment planning algorithms, (5) image-guidance systems capable of performing in the sub-millimeter range, and (6) robust quality assurance (QA) methods [2]. Excessive intra-fraction patient motion risks compromising the target and OAR dose distribution [3]. This has led to the use of a variety of external immobilization devices to try to physically suppress or limit patient motion, however patients can still move in these [4,5]. Furthermore, the characteristic features and determinants of patient motion during radiotherapy are incompletely understood and the optimum 'amount' of immobilization or support that is required to maintain individual patient stability during SBRT is uncertain [5]. A recent report identified that the capital cost of obtaining an immobilization system may be one of the major treatment-dependent obstacles to implementing SBRT in some countries [6].

Against this background, we describe a simple approach to patient positioning that has been routinely used at our institution for several years [7] and is currently used for the majority of SBRT patients (excluding for example some cervical/upper thoracic spine SBRT patients who are immobilized in a mask). It forms part of a more comprehensive SBRT delivery strategy that emphasizes several variables and exploits advances in technology to manipulate them, including: simplicity, patient comfort, time taken for initial positioning and target localization, beam-on time and the frequency and mode of intra-fraction positional verification. The aim of this work is to report the intra-fraction stability of patients undergoing lung SBRT.

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Materials and methods

This manuscript reports anonymous clinical QA data that was acquired during the routine treatment of a cohort of patients with lung SBRT for the purpose of assuring the integrity of treatment delivery. These patients were treated according to our standard lung SBRT protocol that has been previously described [8]. Briefly, patients were imaged using free-breathing, non-coached 4-dimensional computed tomography (CT) performed on a 16 slice CT scanner (GE Healthcare, USA) fitted with the Real-time Position Management™ (RPM) system (Varian Medical Systems Inc., USA). As far as possible patients were positioned comfortably, lying supine on a thin foam mattress. Their arms were supported above the head (Posirest, CIVCO Medical Solutions, USA) and a foam support was placed under the knees (CIVCO).

Patients received treatment with one of several dose-fractionation schedules, risk-adapted according to factors such as tumor size and location [7]. Treatment was delivered using two volumetric intensity-modulated arcs that incorporated avoidance sectors to spare the contra-lateral lung (volumetric modulated arc therapy, performed with RapidArc®, Varian Medical Systems Inc., USA) [9]. The data in this report was acquired from patients treated on a Novalis Tx™ platform (Varian Medical Systems Inc., USA and Brainlab AG, Germany) using a maximum dose rate of 1000 MU/min [10].

In our institution initial positioning for patients treated on the Novalis Tx is typically performed using external skin marks combined with the ExacTrac® infrared-based external marker system, and in some patients the ExacTrac® X-ray 6D system (Brainlab AG, Germany). On-line automated ± manual target localization is then performed based on the planning target volume (PTV) structure plus a margin and by matching the average-intensity reconstruction of the planning CT and the cone-beam CT images (On-Board Imager®, Varian Medical Systems Inc., USA). This generates an on-line couch shift in four directions (three translational and one rotational). In these patients, after target positioning but before the start of treatment delivery, stereoscopic X-rays were acquired of the spine (Brainlab X-ray 6D system), and an automatic registration generated the 6D deviation of the spine position with respect to the planning CT-scan. No shifts were performed based on these ExacTrac images. In those cases where the target tumor was located very laterally, one of the stereoscopic X-rays may not have been able to image part of the spine, making stereoscopic matching impossible. Therefore, this analysis only included those patients where such a match was possible. During treatment delivery, patient position was monitored using the infrared marker system. Immediately after the end of the last arc another set of stereoscopic spine X-rays was acquired and automatically registered and the difference between the registration before and after fraction delivery was used to determine the intra-fraction stability of the patient in three translational (vertical, longitudinal, lateral) and three rotational (yaw/rotation, roll, pitch) directions.

All ExacTrac bone matches were performed automatically with a visual check of the alignment between the stereoscopic X-rays and the digitally reconstructed radiographs derived from 2.5 mm thick CT slices. No manual adjustments were made. We have previously reported the accuracy of the ExacTrac X-ray system to be approximately 0.3 mm (1 standard deviation) in any direction when used for intra-cranial radiosurgery [11] and have found 2.5 or 1.25 mm CT slice thickness to be comparable in this scenario. None of the patients were repositioned between the arcs based on the infrared marker monitoring during treatment delivery.

Additional information that was collected included patient age and sex, time from start of the CBCT acquisition to beam-on (includes acquisition of pre-treatment stereoscopic X-rays) and between first beam-on and last beam-off (post-treatment stereoscopic X-rays were taken immediately after this). Data is reported in graphic form with the aid of descriptive and summary statistics (mean, median, range, standard deviation [SD], Pearson correlation coefficient).

Results

A total of 109 SBRT fractions from 30 patients were analyzed (median 4 fractions/patient, range 1–8). There were 23 male and 7 female patients, with median age 72 years (range 38–90). Dose fractionation schedules were 3 fractions of 18 Gy ($n = 6$), 5 fractions of 11 Gy ($n = 8$), 8 fractions of 7.5 Gy ($n = 11$), and 12 fractions of 5 Gy ($n = 5$). Data on fraction time was available for 108 fractions. The mean time from start of initial CBCT acquisition to first arc 'beam-on' was 6.2 min (range 4.0–27.6 min, SD = 2.7 min). The mean time from first arc beam-on to the end of the last arc was 4.2 min (range 3.0–10.1 min, SD = 1.4 min). Mean time from start of initial CBCT acquisition to end of last arc was 10.3 min (range 7.1–31.3 min, SD = 3.1 min).

From 109 fractions, 327 translational and rotational data pairs were generated for comparison resulting in 327 observations for intra-fraction translation and rotational displacement. These represented the total number of positional changes derived from the stereoscopic X-ray images immediately before the first and after the last arcs in three translational (vertical, longitudinal and lateral) and three rotational (yaw/rotation, roll and pitch) directions. 92% of translational and 97% of rotational comparisons differed by $\leqslant$1 mm and $\leqslant$1°, 98% and 99% by $\leqslant$1.5 mm and $\leqslant$1.5° and 99.7% and 99.7% by $\leqslant$2 mm and $\leqslant$2°, respectively (Figs. 1 and 2).

For all 109 fractions, mean vertical, longitudinal and lateral motion, was 0.0 mm with 1SD equal to 0.4, 0.6 and 0.6 mm, respectively. Maximum absolute motion in the three translational directions was 1.2 mm vertical, 2.8 mm longitudinal and 2 mm lateral. Mean change in yaw/rotation, roll and pitch was 0.0°, 0.0° and −0.1° respectively with 1SD equal to 0.4°, 0.5° and 0.3°, respectively, and maximum absolute motion in any of the three rotational directions was 1.7° rotation, 2.3° roll and 1.1° pitch.

The mean translational motion vector was 0.8 mm (SD = 0.6 mm) and the vector was $\leqslant$1.7 mm (corresponding to a tolerance of 1 mm in the vertical, longitudinal and lateral directions) in 101/109

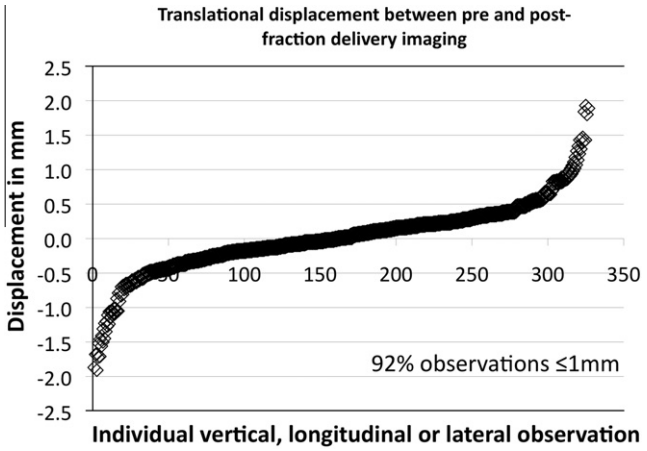

Fig. 1. Translational displacement of the spine as assessed with stereoscopic X-rays before and after the first and last arcs of stereotactic lung radiotherapy. Data presented in ascending order for 109 fractions. This resulted in 327 total observations made up of 109 pre and post-fraction comparisons in each of the three translational directions (lateral, longitudinal, vertical). 302/327 (92%) observations were $\leqslant$±1 mm with 15/25 observations >1 mm coming from 2 patients.

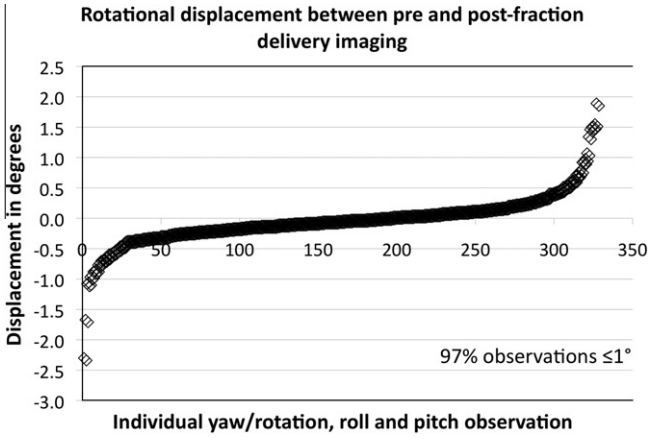

Fig. 2. Rotational displacement of the spine as assessed with stereoscopic X-rays before and after the first and last arcs of stereotactic lung radiotherapy. Data presented in ascending order for 109 fractions. This resulted in 327 total observations made up of 109 pre and post-fraction comparisons in each of the three rotational directions (yaw/rotation, roll, pitch). 316/327 (97%) observations were $\leqslant \pm 1^\circ$ with 8/11 observations >1° coming from 2 patients.

fractions (93%) (Fig. 3). When assessed per fraction, 84% of the fractions were delivered with $\leqslant$1 mm translation and 93% with $\leqslant 1^\circ$ rotation in all three translational or rotational directions. 94% and 97% were delivered with $\leqslant$1.5 mm and $\leqslant 1.5^\circ$ translation and rotation respectively. The translational motion vector did not correlate with (1) time from the start of the first arc to the end of the last arc ($r = 0.32$), (2) time from the start of CBCT acquisition to the end of the last arc ($r = 0.1$) (Fig. 4), (3) time from the start of CBCT acquisition to the start of the first arc ($r = -0.05$), or (4) patient age ($r = 0.11$).

Of the 17/109 fractions with >1 mm motion in at least one translational direction, 2/30 patients accounted for 10 of these and 1 patient accounted for 5/7 fractions with >1.5 mm displacement. One of these patients contributed data for 8 fractions and accounted for 7 fractions associated with a displacement >1 mm in one direction, and for 6 fractions with a rotational displacement (yaw/rotation, roll or pitch) of >1°. If these 2 patients were excluded from the analysis (thereby excluding 14 fractions), then 93% of fractions would have been delivered with $\leqslant$1 mm translational motion and 94% with $\leqslant 1^\circ$ change in rotation in all three translational or rotational directions.

Discussion

The main finding is that a routine strategy of not using rigid external immobilization results in satisfactory stability, as determined by the position of the spine before and after treatment delivery, for the majority of patients undergoing lung SBRT. Acknowledging differences in methodology and imaging systems (e.g. stereoscopic X-rays and cone-beam computed tomography), these data on intra-fraction stability of the spine are comparable with other published results, including those with or without external immobilization systems, and for both stereotactic lung and spine treatments [5,12–15]. They are also consistent with recommendations for performing SBRT [2] and further support the concept of frameless SBRT [5,15]. Currently we use external immobilization for a relatively small group of spine SBRT patients who are considered to be more susceptible to set-up variation and motion (for example upper thoracic/cervical spine SBRT), or for individuals with excessive motion under frameless conditions.

Although we observed maximum displacements of <3 mm in any translational direction between pre and post-fraction imaging it is important to note that the present report does not evaluate spine position between the X-rays. The lack of information on stability during beam-on time is a common limitation in reports describing intra-fraction motion and reflects what is technically possible on most treatment platforms during beam delivery. This is only partially addressed by tracking external surrogate markers that have an uncertain relationship to internal structures such as the spine. Nonetheless, we do use such technology in conjunction with observation of the patient on the in-room cameras with the aim of identifying larger deviations. Ongoing work is investigating whether it is feasible to accurately track spine position itself during irradiation using digital tomosynthesis [16]. In addition, we have not aimed to characterize intra-fraction motion of the lung tumor. The latter point means that even with a very stable spine position, a mobile lung tumor susceptible to influences such as change in breathing characteristics could move to a different position, with dosimetric implications for the target [17]. There are several ways of trying to manage tumor motion, including for example abdominal compression, various breath-hold techniques, target tracking and gating. This highlights the importance of considering both the patient and the target tumor when designing an image-guidance and motion-management strategy for high-precision radiotherapy.

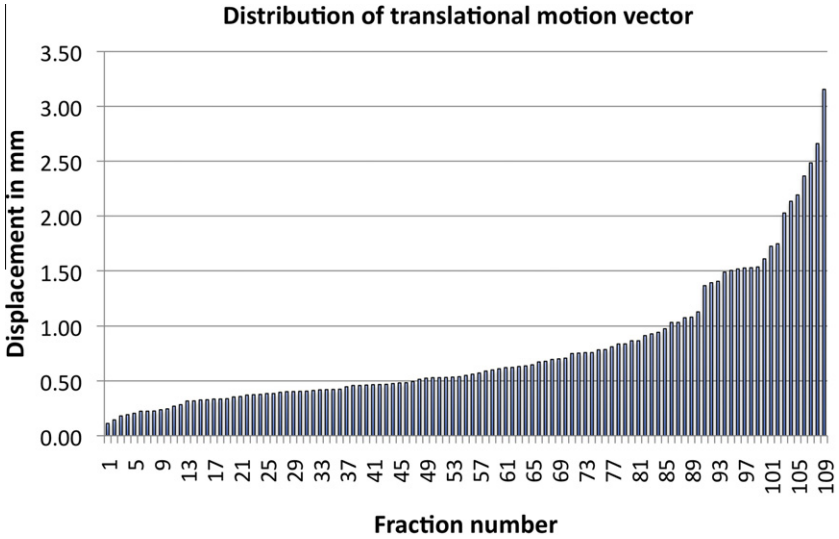

Fig. 3. The distribution of the translational motion vectors in ascending order for 109 fractions.

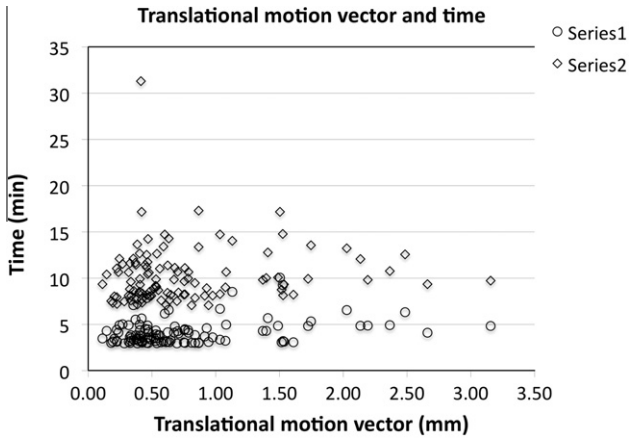

Fig. 4. The relationship between translational motion vector determined by imaging pre and post lung SBRT delivery versus (i) the time from start of first arc to end of the last arc (series 1) and (ii) the time from start of cone-beam computed tomography (CBCT) to end of the last arc (series 2).

Despite the use of fraction sizes varying between 5 and 18 Gy, average radiation delivery time using high dose rates and 2 arcs was just over 4 min, with an average time from the start of initial CBCT acquisition to the end of the last arc of approximately 10 min (note that this does not include initial positioning with skin marks and the ExacTrac optical system). These times are relatively short compared with some reports in the literature [5,18,19] and they are decreasing further as higher maximum dose rates become available [20] and as imaging routines become more efficient. One hypothesis for the lack of correlation between time and motion in this report is that treatment was relatively fast. Although not a feature of the methods used in this study, the relationship between treatment time and motion might also be affected by the frequency of imaging and correction. Imaging patients frequently during SBRT (e.g. every few minutes or less) effectively turns a long single fraction into discrete sub-fractions and provides additional opportunities for positional correction.

The treatment method described in this report emphasizes simplicity, patient comfort, opportunities for re-imaging and reductions in overall treatment time. The importance of this is that patient positioning is not seen in isolation of other variables. The data presented on treatment time demonstrate that with high dose rate delivery beam-on time may account for a minority of the overall fraction time, with the majority being taken up by initial positioning and image guidance. This points to where additional efficiency gains may be possible. It also highlights that as treatment delivery times shorten further, dose-time density increases. This means that positional verification during treatment delivery becomes even more desirable in order to identify and mitigate the potential dosimetric consequences of incorrect positioning even for short periods.

We observed that a small number of patients accounted for a disproportionately large number of deviations. When the two most mobile patients were removed from the analysis, 93% of fractions were delivered with a tolerance of 1 mm in all three translational directions and 94% with $\leqslant 1^\circ$ change in all three rotational directions. This illustrates that it would be attractive to be able to characterize a priori individual patient motion and its determinants [5]. It is also important to identify early on in treatment those patients susceptible to more motion, so that their image-guidance or immobilization strategy can be adapted as necessary (e.g. imaging during or between the 2 arcs, or considering a trial of external immobilization, for example with a vacuum bag). For those patients with pain, anxiety, or discomfort in the treatment position attention needs to be paid to adequate analgesia, explanation and reassurance, and optimal patient positioning at the time of simulation.

Although intra-fraction patient motion is still incompletely understood, these data support our current SBRT positioning strategy of (1) using an arm and knee support, for the majority of patients, (2) emphasizing patient comfort, (3) performing frequent positional monitoring and (4) striving for efficient delivery. We consider each of these elements to be important. It is therefore insufficient to adopt a patient support or immobilization system without considering the wider treatment and verification strategy. In addition we advocate that individual institutions need to evaluate their own positioning strategy by determining the stability of patients under clinical SBRT conditions.

Conflicts of interest statement

Department of Radiation Oncology, VU University medical center has research collaborations with Varian Medical Systems Inc., USA and Brainlab AG, Germany.

M.D. has received travel support from Varian Medical Systems Inc., and Brainlab AG and honoraria from Varian Medical Systems Inc.

W.V. has received travel support and honoraria from Varian Medical Systems Inc.

B.S. has received travel support and honoraria from Varian Medical Systems Inc., and Brainlab AG and has served as a consultant.

S.S. has received travel support and honoraria from Varian Medical Systems Inc. and served as a consultant.

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