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Intrafraction Verification of Gated RapidArc using Beam-Level Kilovoltage X-Ray Images

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Abstract

Purpose—To verify the geometric accuracy of gated RapidArc treatment using kV images acquired during dose delivery.

Methods and Materials—Twenty patients were treated using the gated RapidArc technique on a Varian TrueBeam STx Linac. One to seven metallic fiducial markers were implanted inside or near the tumor target before treatment simulation. For patient setup and treatment verification purposes, the internal target volume (ITV) was created corresponding to each implanted marker. The gating signal was generated from the RPM system. At the beginning of each fraction, individualized respiratory gating amplitude thresholds were set based on fluoroscopic image guidance. During the treatment, we acquired kV images immediately before MV beam-on at every breathing cycle, using the on-board imaging system. After the treatment, all the implanted markers were detected and their 3D positions in the patient were estimated using in-house developed software. The distance from the marker to the corresponding ITV was calculated for each patient by averaging over all markers and all fractions.

Results—The 3D distance between the markers and their ITV is 0.8 ± 0.5 mm on average (range: 0 to 1.7 mm), and is 2.1 ± 1.2 mm at 95th percentile (range: 0 to 3.8 mm). On average a margin of 0.6 mm (left-right), 0.8 mm (anterior-posterior), 1.5 mm (superior-inferior) is required to account for 95% of the intrafraction uncertainty in RPM-based RapidArc gating.

Conclusion—To our knowledge, this is the first clinical report on intrafraction verification of respiratory gated RapidArc treatment in SABR. For some patients, the markers deviated significantly from the ITV by more than 2 mm at the beginning of the MV beam on. This

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CONFLICTS OF INTEREST NOTIFICATION

The authors declare no conflict of interest.

emphasizes the need for gating techniques with beam-on/off controlled directly by the actual position of the tumor target instead of external surrogates such as RPM.

Keywords

intrafraction; treatment verification; respiratory gating; gated RapidArc; beam-level images

INTRODUCTION

The motion of thoracic and abdominal tumors represents a major challenge in radiation therapy. Respiratory gating limits the radiation to certain parts of the breathing cycle, thereby allowing dose escalation to the tumor and/or dose reduction to organs at risk [1–2]. Currently, the standard clinical practice is to correlate the internal target motion with some external surrogate (*e.g.*, skin surface, abdominal pressure, tidal volume) and control the radiation beam on/off based on the external surrogate signal. However, it has been demonstrated that the relationship between the internal target motion and external surrogate signal is subject to change both inter- and intra-fractionally [3]. It is therefore important to verify that the moving tumor stays inside the planning target volume (PTV) whenever the beam is enabled during treatment delivery. With the recent development and clinical implementation of stereotactic ablative radiotherapy (SABR) [4–5], which is characterized by steep dose gradients and large fractional dose, treatment verification becomes all the more important since even small geometric errors can cause large deviations in delivered dose distributions [6–7].

There have been extensive studies on the use of both in-room and on-board imaging for treatment verification, mostly for pre-treatment patient setup. These imaging modalities include MV portal, kV radiograph and fluoroscopy, kV and MV CBCT, 4D CBCT *etc.* [8–12]. On the other hand, the study on intrafraction verification during treatment delivery has been limited. Recently, Adamson and Wu [13] assessed prostate intrafraction motion using kV fluoroscopy during IMRT treatment delivery. Two studies have reported on the use of electronic portal imaging device in *cine* mode or MV fluoroscopy for gated treatment delivery verification [14–15]. However, target localization in MV portal images remains a challenging task, due to the inherently low contrast and degraded image quality compared with their kV counterpart. In addition, the blockage of anatomy or markers by the multi-leaf collimators during beam modulation presents another potential problem for target localization in MV images [16].

The TrueBeam system (Varian, Palo Alto, CA) is capable of external marker-based gated volumetric modulated arc therapy (VMAT; RapidArc, Varian, Palo Alto, CA). Furthermore, kV images can be acquired immediately before MV beam on or after MV beam off at every breathing cycle during treatment delivery. For this study, all kV images were taken before the MV beam on. These triggered or so called “beam-level” kV images are valuable for verifying the intrafraction geometric accuracy of gated treatment. In this study, we report our initial clinical experience in using the beam-level kV images for treatment verification. To our knowledge, this is the first clinical report on intrafraction verification of respiratory

gated RapidArc SABR. Details about patient simulation, setup, treatment delivery, image acquisition, and quantitative analysis will be discussed in the following sections.

METHODS AND MATERIALS

Patient characteristics

Twenty patients treated with the gated RapidArc technique were enrolled in the current study. The mean ($\pm$ SD) age of all 20 patients was 69 ± 10 years (range: 57–87 years). Among the 20 patients, 2 had lung cancer, 7 had liver tumors, and 11 had pancreatic cancer. All 20 patients received SABR in three to five fractions. The patient and treatment characteristics are summarized in Table 1. A flowchart for the overall methods of this study is shown in Fig. 1, including the clinical workflow and image/data analysis.

Patient simulation, setup and verification prior to treatment

For patient simulation, four-dimensional (4D) CT scans were acquired in cine mode with an 8-slice GE LightSpeed™ CT scanner. The cine images were sorted into 10 respiratory phases according to phase. The CT axial slice thickness was 1.25 mm. To facilitate patient setup and treatment verification, one to seven gold fiducial markers were implanted inside or near the tumor target before treatment simulation. One patient with a liver tumor (#9) had surgical clips for localization. To prevent marker migration, platinum coils instead of cylindrical gold markers were implanted in the patients with a lung tumor [17]. The gross tumor volume (GTV) was contoured to correspond to the exhale phase for gating at exhale. The “gated” internal target volume (ITV) for each marker was contoured in the planning CT. The ITV was contoured in the maximum intensity projection of the 4D CT phases within the gating window. In contrast to a conventional motion inclusive ITV that is often constructed to encompass the full range of motion determined by 4-D CT, the gated ITV is an allowance for residual motion within the respiratory gating window. An additional setup margin of 5 mm was added to form the final planning target volume (PTV).

A point structure was created in the treatment planning system software as a reference for each marker. The virtual software reference marker was placed at the boundary of the ITV (the centroid of the most inferior slice) so that they lie exactly at the gating threshold of the planned treatment, assuming gating at exhale. At each treatment fraction, after patient alignment, the gating window would be manually adjusted so that the MV beam-on occurs at the same time when the markers coincide with or move sufficiently close to the reference in orthogonal kV fluoroscopy. This pre-treatment verification procedure based on fluoroscopic images is intended to ensure that when the MV beam is enabled, the markers (or target) stay inside their respective ITVs. In practice, this is realized by projecting the ITVs onto the fluoroscopic images at the treatment console and visually checking the relative positions of the markers and the lower boundary of their ITVs at the beginning of beam on by the clinicians.

Treatment delivery and beam-level kV image acquisition

The gated RapidArc treatment was delivered by a TrueBeam™ STx Linac. An RPM block was placed on the patient’s abdominal surface and the gating signal was generated from the

RPM system, which is currently the only commercially available solution in our clinic. During the treatment, we acquired kV images immediately before MV beam-on at every breathing cycle, using the on-board imaging system. Intrafraction kV images were acquired from one treatment fraction for all patients, except for patients 2, 5, 13 and 14. Depending on the specific breathing patterns, the total number of kV images ranged from 11 to 40 in one fraction. Figure 2 shows one of the beam-level kV images acquired during a gated RapidArc treatment for patient 1. All three fiducial markers are clearly visible in the kV image.

Marker detection and 3D position estimation

After the treatment, all the implanted markers were automatically detected in each beam-level kV image using in-house software using intensity and geometry based approach. Because the detected markers are in the 2D imager coordinate, their full 3D position in the patient coordinate system needs to be estimated. For this purpose, a recently proposed 3D Bayesian real-time tracking algorithm [18] was adopted, which is based on the effective use of patient- and session-specific prior information of the target motion and has been shown to achieve a sub-mm accuracy when tested on real (lung and pancreas) patient breathing traces.

Verification of gated target coverage

Because the beam-level kV images were acquired immediately before MV beam-on at every breathing cycle, they can be used to verify the target coverage during gated treatment, by comparing the marker position estimated from the kV images during delivery with the ITV defined in the planning CT. Since the beam should be on only while the marker is within its respective ITV, any discrepancy between the two may be characterized as a “gating miss” (except for uncertainties of the mechanical and imaging systems which are used to detect the markers in the patients). We calculated the distance from the marker to the corresponding ITV in the superior-inferior (SI), left-right (LR), anterior-posterior (AP) direction as well as the 3D distance. When the marker is inside the ITV, the gating error was defined to be zero. This procedure was repeated for each kV image acquired during dose delivery and the final results were obtained by averaging over all markers and all fractions for each patient.

RESULTS

Figure 3 shows the 3D position of one of the markers estimated from the beam-level kV images and the corresponding reference position for patients 1 and 12. There appears to be no distinct patterns of the marker position: the movement of the marker when the MV beam is enabled is quite random from one breathing cycle to the next. The maximum deviation of the marker from the corresponding reference position is about 2 and 3 mm in the SI direction for patient 1 and 12, respectively. For patient 1, the marker is centered around the reference position, while for patient 12, there seems to be a 1–2 mm baseline shift of the marker in the AP and SI directions.

Of note, the gating errors measured in this study are small relative to the additional 5 mm margin added to the gated ITV to form the final PTV, indicating there were no geometric misses in this patient cohort using our technique of pre-treatment fluoroscopic verification

of the gating thresholds. However, if smaller margins are used or if fluoroscopic image guidance is omitted, our study demonstrates the clear potential for geometric misses using conventional surface marker based gating.

Figure 4 shows the 3D position of one of the markers for patients 2 and 5, with beam-level kV images from multiple treatment fractions. Similarly as patients 1 and 12, there are no distinct patterns of the marker position within one fraction. However, for patient 2, there does appear to be a distinct pattern in the SI direction between different fractions, *i.e.*, a shift in the mean marker position. For instance, there is a 3 mm shift ($p < 0.0001$, unpaired *t*-test) in the mean marker position between the first and second fraction for patient 2. The intrafraction variation of the marker position is generally smaller than the interfraction variation, especially in the SI direction. For instance, the SI intrafraction variation is mostly around 1 mm for patient 2, while the interfraction variation is as large as 2–3 mm. For patient 5, the shift in the mean marker position between different fractions is less apparent, and the intrafraction variation of the marker position is comparable to the interfraction variation.

Table 2 summarizes the results for all the patients. In particular, the mean 3D distance between the markers and ITV is 0.8 ± 0.5 mm on average, and is 2.1 ± 1.2 mm at 95th percentile. The average 95th percentile distance between the markers and ITV is 0.6, 0.8, and 1.5 mm in the LR, AP, and SI direction, respectively. The difference in marker positioning errors between different patients is larger: the mean 3D error ranges from 0 mm (for patient 10) to 1.7 mm (for patient 12); while the 95th percentile ranges from 0 mm (for patient 10) to 3.8 mm (for patient 3). In most patients, the main source of error is along the SI direction, with a few notable exceptions, *e.g.*, in patients 3, 5, and 8.

DISCUSSION

In this paper, we have reported our initial findings on intrafraction verification of respiratory gated RapidArc SABR treatments. From a group of 20 patients with tumors in multiple anatomical sites, it was found that on average an additional margin beyond the gated ITV of 0.6 mm (left-right), 0.8 mm (anterior-posterior), 1.5 mm (superior-inferior) is required to account for 95% of the gating uncertainty in RPM-based RapidArc gating. In addition, the markers and beam-level images provide a method to verify the gating window, and if needed, it can be adjusted prior to or during treatment. Narrowing the gating window can reduce the chance of “gating miss.” For some patients, the markers were outside the ITV by more than 2 mm at the beginning of the MV beam on, indicating that further investigation is needed to ensure that the target remains within the ITV. This also emphasizes the need for gating techniques with beam-on/off controlled directly by the actual position of the tumor target instead of external surrogates such as RPM [19–20]. The relatively larger differences in marker positioning errors between different patients call for individualized margins for SABR.

Sources of marker positioning uncertainty in this study include the uncertainties due to both hardware (*e.g.*, the mechanical and x-ray imaging systems) and software (*e.g.*, marker detection and 3D tracking). According to the vendor specification and our recent end-to-end

test of the system, the TrueBeam Linac has a sub-mm mechanical and imaging accuracy. The marker detection and 3D tracking algorithms have also been demonstrated to have a sub-mm accuracy [18]. These uncertainties are generally smaller than the gating errors found in this study and therefore are unlikely to alter the conclusions. On the other hand, the apparent gating errors also include uncertainties due to contouring of fiducial markers and placement of reference markers in the planning CT as well as possible marker migration in the patient throughout the treatment course. In addition, since most patients had multiple implanted fiducial markers, there may be some variability in apparent gating errors between different markers. This is evident from Fig. 2, where two of the markers are very close to their respective reference positions, while the third marker is relatively farther from its reference. The uncertainties due to marker migration and/or inter-marker variations could affect the clinical decision for setup and verification purposes, and thus deserve further investigation. Since the effects of all those factors are random and independent, the apparent gating error is mainly affected by the dominant factor, which is the target motion caused by patient's breathing.

Due to the limited population size with multiple fractions of beam-level images (in 4 patients), the interplay between interfraction and intrafraction variations is not systematically analyzed in this study, which could otherwise offer more insight into the marker positioning uncertainty. For instance, the shift in the mean marker position between different fractions in patient 2 indicates either a setup error, or target shift after setup and before start of the treatment. The interfraction and intrafraction variations will be investigated in our future study.

Although the gating errors were reported in all three directions, they may carry different significance. Since the MV treatment beam is (almost) always perpendicular to the SI direction, SI errors at any gantry angle could contribute to measureable dosimetric errors in the delivery process. On the other hand, the dose distributions may be more tolerant to in-line (with MV beam) positioning errors, *i.e.*, a combination of errors along the AP and LR directions, depending on the specific gantry angle. However, this only applies to occasional and random errors. If there are persistent and systematic positioning errors along the AP or LR directions, the resultant dosimetric errors would have similar magnitude with that caused by SI positioning errors. This pertains to a more fundamental aspect of this study, where we have focused on the intrafraction verification of geometric accuracy instead of dosimetric accuracy, which would have a more direct clinical endpoint.

Conclusion

In this study, we have reported our initial clinical experience in using intrafraction kV images for treatment verification. To our knowledge, this is the first clinical report on intrafraction verification of respiratory gated RapidArc. Based on a cohort of 20 SABR patients, it was found that on average a margin of 0.6 mm (LR), 0.8 mm (AP), and 1.5 mm (SI) is required to account for 95% of the intrafraction uncertainty in RPM-based RapidArc gating. For some patients, the markers deviated significantly from the ITV by more than 2 mm at the beginning of the MV beam on. This emphasizes the need for gating techniques

with beam-on/off controlled directly by the actual position of the tumor target instead of external surrogates such as RPM.

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Fig. 1.
Flowchart for the overall methods including the clinical workflow and image/data analysis.

Fig. 2.
One of the beam-level kV images acquired during a gated RapidArc treatment for patient 1. All three fiducial markers were present in the kV image and are clearly visible. The projections of the PTV and fiducial marker ITV contours as well as the reference markers (shown as circles) are superimposed on the image using in-house software.

Fig. 3. 3D position (circles) of one of the fiducial markers estimated from the beam-level kV images acquired during a gated RapidArc treatment for: (a), patient 1; (b), patient 12. The horizontal line indicates the reference position of the marker defined in planning CT.

Fig. 4. 3D position (circles) of one of the fiducial markers estimated from the beam-level kV images acquired during a gated RapidArc treatment for patients with multiple fractions: (a), patient 2; (b), patient 5. The horizontal line indicates the reference position of the marker defined in planning CT.

Table 1

Patient and treatment characteristics.

Patient Index	Age (years)	Gender	Tumor site	Prescription	# of fractions of images acquired	# of markers implanted
1	78	F	Liver	10 Gy × 5	1	3
2	62	M	Pancreas	6.6 Gy × 5	4	3
3	57	M	Liver	8 Gy × 5	1	4
4	65	F	Liver	15 Gy × 3	1	5
5	64	M	Pancreas	6.6 Gy × 5	3	5
6	62	F	Pancreas	6.6 Gy × 5	1	3
7	69	M	Pancreas	6.6 Gy × 5	1	3
8	68	M	Pancreas	8.5 Gy × 5	1	3
9	59	F	Liver	9 Gy × 5	1	4
10	65	F	Lung	12.5 Gy × 4	1	4
11	62	M	Liver	18 Gy × 3	1	7
12	87	M	Pancreas	6.6 Gy × 5	1	1
13	81	M	Liver	10 Gy × 5	2	6
14	74	F	Pancreas	6.6 Gy × 5	2	5
15	64	M	Pancreas	6.6 Gy × 5	1	1
16	83	F	Pancreas	6.6 Gy × 5	1	2
17	66	F	Liver	12 Gy × 3	1	4
18	79	M	Lung	10 Gy × 5	1	4
19	84	M	Pancreas	6.6 Gy × 5	1	3
20	57	F	Pancreas	6.6 Gy × 5	1	3

Table 2

Mean and 95th percentile distance between the markers and their ITV (the distance is defined to be zero if the marker is inside ITV).

Patient Index	Mean (mm)				95 th percentile (mm)			
	LR	AP	SI	3D	LR	AP	SI	3D
1	0	0	0.7	0.7	0	0	2.2	2.2
2	0.7	0.5	0.5	1.4	2.1	2.2	2.0	2.7
3	0.2	0.6	0.1	0.7	1.1	3.7	0.5	3.8
4	0	0.1	1.3	1.3	0	0.2	3.4	3.5
5	1.1	0.3	0.1	1.2	3.6	1.3	0.5	3.7
6	0.5	0.2	0.7	1.0	1.6	0.6	1.7	2.1
7	0	0.1	0.8	0.9	0	0.3	2.3	2.3
8	1.3	0	0.4	1.6	2.6	0.1	1.5	2.6
9	0	0.1	1.1	1.1	0	0.1	2.5	2.6
10	0	0	0	0	0	0	0	0
11	0	0.1	0	0.1	0.3	0.4	0.2	0.5
12	0	0.8	1.5	1.7	0	1.2	2.6	2.7
13	0	0.1	0.8	0.9	0.2	0.8	3.5	3.5
14	1.1	0.5	0.4	0.7	0.4	3.0	1.3	3.1
15	0.1	0	0.5	0.5	0.4	0.1	1.6	1.6
16	0.1	0	0	0.1	0.4	0	0	0.4
17	0	0	0.1	0.1	0.2	0	0.7	0.9
18	0.1	0.6	0.4	0.9	0	1.3	1.4	2.0
19	0	0	0.2	0.2	0	0	1.1	1.1
20	0	0	0.3	0.3	0	0	1.0	1.0
Population	0.2 ± 0.4	0.2 ± 0.3	0.5 ± 0.4	0.8 ± 0.5	0.6 ± 1.0	0.8 ± 1.1	1.5 ± 1.0	2.1 ± 1.2