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Evaluation of reproducibility of tumor repositioning during multiple breathing cycles for liver stereotactic body radiotherapy treatment

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ABSTRACT

Aim: To evaluate the tumor repositioning during gated volumetric modulated arc therapy (VMAT) for liver stereotactic body radiotherapy(SBRT) treatment using implanted fiducial markers and intrafraction kilovoltage (kV) images acquired during dose delivery.

Materials and methods: Since 2012, 47 liver cancer patients with implanted fiducial markers were treated using the gated VMAT technique with a Varian Truebeam STx linear accelerator. The fiducial markers were implanted inside or close to the tumor target before treatment simulation. They were defined at the maximum inhalation and exhalation phases on a 4-dimensionnal computed tomography (4DCT) acquisition. During the treatment, kV images were acquired just before the beam-on at each breathing cycle at maximum exhalation and inhalation phases to verify the fiducial markers positions. For the five first fractions of treatment in the first ten consecutive patients, a total of 2705 intrafraction kV images were retrospectively analyzed to assess the differences between expected and actual positions of the fiducial markers along the cranio-caudal (CC) direction during the exhalation phase.

Results: The mean absolute intrafractional fiducial marker deviation along the CC direction was 1.0 mm at the maximum exhalation phase. In 99%, 95% and 90% cases, the fiducial marker deviations were ≤4.5 mm, 2.8 mm and 2.2 mm, respectively.

Conclusion: Intrafraction kV images allowed us to ensure the consistency of tumor repositioning during treatment. In 99% cases, the fiducial marker deviations were ≤4.5 mm corresponding to our 5 mm treatment margin. This margin seems to be well-adapted to the gated VMAT SBRT treatment in liver disease.

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1. Background

Stereotactic Body Radiation Therapy (SBRT) is an effective treatment procedure allowing the delivery of high radiation doses in a few fractions leading to a high biological effective dose.[1] The delivered doses are strictly conformed to the target with a rapid fall-off away from the tumor, protecting the surrounding tissue, and the administration of high doses thus requires a very accurate dose delivery to the tumor. For abdominal tumors, the intrafraction motion provides some imprecision in the dose delivery. In liver SBRT, the main challenge is to take into account these motions. Liver motion is complex, consisting of translations, rotations and hysteresis. It is mostly related to breathing and is usually the largest in the cranio-caudal (CC) direction.[2] Kitamura et al. analyzed the liver tumor motion under tidal breathing and showed a tumor motion up to 4 mm (range 1–12 mm), 9 mm (range 2–19 mm) and 5 mm (range 2–12 mm) in the left–right (LR), CC and anterior–posterior (AP) directions, respectively.[2,3]

Several techniques can be used to manage tumor motion, such as active breath control, abdominal compression, respiratory gating and real-time tumor tracking.[4–9] In this study, we used the respiratory gating technique with an external surrogate placed on the patient's abdominal wall associated with implanted fiducial markers to manage liver motion.[5,10] The aim of this technique is to limit the radiation exposure during specific phases of the breathing cycle and to create a correlation model between the internal target motion and the external surrogate (skin surface), and finally to control the radiation beam delivery thanks to the external surrogate signal.

Previous studies have shown that the position of the tumor changes both between the treatment fractions (interfraction) and within a single treatment fraction (intrafraction).[11–15]

Park et al. analyzed the interfraction and intrafraction liver motion variability constructing a 3-dimensional motion trajectory of the fiducial markers implanted, at different sites in the liver and as a function of the breathing cycle. They reported, for 20 patients, a range of motion of 3.0 ± 2.0 mm, 5.1 ± 3.1 mm and 17.9 ± 5.1 mm using the planning 4-dimensionnal computed tomography (4DCT), and of 2.8 ± 1.6 mm, 5.3 ± 3.1 mm, and 16.5 ± 5.7 mm using the cone-beam computed tomography (CBCT), for the LR, AP and CC directions, respectively. The authors found that the breathing-induced AP and CC motions were highly correlated. They also reported a significant variation during the interfractional gating window, with the largest having 29.4–56.4% range between fractions.[12] Worm et al. described mean 3D intrafraction and intrafield motion ranges of internal markers during liver SBRT of 17.6 mm (range 5.6–39.5 mm) and 11.3 mm (range 2.1–35.5 mm), respectively, using standard X-ray imagers.[13]

In a recent study, Poulsen et al. used intrafraction kilovoltage (kV) imaging during volumetric-modulated arc therapy (VMAT) liver SBRT to estimate the intra-treatment target motion and to reconstruct the delivered target dose. They estimated that the intrafraction motion caused a mean 3D target position error of 2.9 mm and a mean D_{95} reduction of 6.0%.[14]

Interfraction uncertainties have been well reduced thanks to the daily use of image-guided setup techniques, such as kV imaging, fluoroscopy and kV CBCT. Intrafractional target motion verification is the new challenge to achieve. Indeed, it is crucial to make sure that the tumor always stays inside the planning target volume (PTV) when the radiation beam is turned on during the dose delivery. Because liver tumors cannot be visualized by kV images, intrafractional target motion verification relies on implanted fiducial markers. These can be used during the patient's setup and for the tumor motion verification as they are implanted inside or close to the target.[16] Recent report evaluated the geometric accuracy of the surrogate-based gated VMAT with a respiratory phantom and also on real patients cases including liver tumors.[17] Li et al. showed in a phantom study a high geometric accuracy (average error of 0.8 mm in the CC direction) when no target-surrogate relation changes occurred during the treatment. However, including a phase shift of 5% and 10% increased the average errors to 2.3 and 4.7 mm, respectively. The same authors obtained similar trend with real human respiratory curves. For the patient study, they obtained an average intrafraction positioning errors of 0.8, 0.9, and 1.4 mm in the LR, AP and CC directions, respectively.[17]

In our study, data sets of kV images acquired during the dose delivery using the Varian Novalis Truebeam Stx Linac and the Intrafraction Motion Review software (IMR) (Varian Medical Systems, Palo Alto, CA, USA) were used to evaluate the reproducibility of tumor repositioning during multiple breathing cycles during the liver SBRT treatment. The purpose of this evaluation was to determine if the internal target volume (ITV)/PTV safety margin used in our institution was appropriate and if it could be reduced.

Table 1 – Patients characteristics.

Patient index	Sex	Age (y)	PTV dose (Gy)	V_{PTV} (cm^3)
1	F	85	5 × 10	106.3
2	F	59	5 × 10	66.7
3	M	62	5 × 10	55.7
4	F	82	8 × 5	224.3
5	M	70	10 × 5	141.2
6	M	56	10 × 5	367.2
7	M	63	10 × 5	83.5
8	F	64	5 × 10	18.9
9	F	81	5 × 10	93.4
10	M	65	5 × 10	39.1

2. Materials and methods

2.1. *Patients, treatment simulation and planning*

Since 2012, 47 liver cancer patients with implanted fiducial markers were treated using the gated VMAT SBRT technique delivered using a Novalis Truebeam STx Linac. The present study was based on intrafraction kV images data from the first 10 patients treated with this technique (Table 1).

The fiducial markers were implanted inside or close to the tumor target before the treatment simulation. Most of the patients had two to three fiducial markers implanted (Visicoil, IBA) and some of them presented with multiple surgical clips or prostheses due to a previous surgery. The implantation procedure was made 1–2 weeks before the planning scan allowing

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