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Assessment of Dosimetric Uncertainties in Liver Stereotactic Body Radiation Therapy using kilo-voltage Cone-Beam CT

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ABSTRACT

Introduction: Liver stereotactic body radiation therapy (SBRT) presents distinct challenges caused by respiratory and gastrointestinal motion. While deep inspiration breath hold (DIBH) reduces respiratory motion, gastrointestinal movement and variability in breath-hold consistency can lead to inaccuracies in tumor localization and sparing of critical organs. This study examines dosimetric uncertainties in liver SBRT with DIBH using kilo-voltage cone-beam computed tomography (kV-CBCT).

Material and Methods: In this study, twenty-five liver stereotactic body radiation therapy (SBRT) cases were evaluated retrospectively. All patients underwent treatment with volumetric modulated arc therapy (VMAT) in five fractions. The Varian real-time position management™ (RPM) system was employed for image acquisition and delivery with a 5 mm amplitude interval. Treatment plan verifications were performed using daily CBCT at the treatment isocenter. The Varian SmartAdapt automatic deformable image registration tool was utilized for contour propagation. Different dosimetric parameters, including the planning target volume (PTV) mean dose, maximum dose to the spinal canal, liver 21 Gy sparing volume, maximum dose to luminal organs, and dose received by 10 cc, were compared. Paired t-tests were employed to evaluate significant dosimetric changes with a P-value of less than 0.05 considered statistically significant.

Results: Among the 25 patients, the PTV D_{mean} (mean dose) decreased in all cases, with an average reduction of 2.2% (P<0.001). Random deviations were noted in the 21 Gy sparing volume of the liver (P: 0.374). On average, the maximum dose to the spinal canal decreased by 1.5% (P<0.001), even with target-based matching. The luminal organ's maximum dose and the dose to 10 cc exceeded the planned values by an average of 6% (P<0.001) and 6.9% (P: 0.017), respectively.

Conclusion: Dosimetric uncertainties are influenced by liver deformation from respiratory motion and the unpredictable positions of luminal organs. Even with 5mm interval amplitude gating, liver deformation remains significant.

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Introduction

In stereotactic body radiation therapy (SBRT), high doses are delivered in a limited number of fractions (hypo-fractionated radiotherapy), resulting in a high biological effective dose (BED). SBRT demands a high level of dosimetric accuracy to minimize normal tissue toxicity through rapid dose fall-off [1]. Liver movement due to respiration and its complex anatomy present significant challenges in delivering the intended dose accurately. In the liver, both intra-fractional and inter-fractional motion are caused by respiration and the gastrointestinal system. Respiratory motion significantly affects the thoracic and abdominal regions; Suramo et al. [2] reported a 2.5 cm liver motion during normal respiration. There are several techniques for managing respiratory motion, including motion-encompassing, respiratory gating, breath-hold, and respiration-synchronizing methods [3]. The Varian real-time position management™ (RPM) system employs a self-held breath hold technique with respiratory monitoring, which requires patients to voluntarily hold their breath. According to Wagman et al. [4], Varian RPM respiratory gating effectively reduces the liver planning target volume (PTV) margin, enabling dose escalation. Lu et al. [5] explored the impact of breath-hold reproducibility on liver motion.

The cone-beam computed tomography (CBCT) imaging system is essential in image-guided radiotherapy (IGRT). Dose calculation using CBCT images accounts for daily variations in treatment. In 2006, Yoo et al. [6] explored the feasibility of dosimetry using CBCT images, which generated substantial research interest in the field [7, 8]. Over time, various techniques such as site-specific calibration, Hounsfield unit (HU) override, dose deformation, and deep learning-based approaches have been developed to enhance accuracy [9-11]. IGRT has facilitated the advancement of adaptive radiotherapy (ART) by enabling the integration of patients' anatomical variations into treatment plans

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and optimizing dose delivery. Deformable image registration (DIR) is a crucial component of an adaptive radiotherapy program. DIR is essential for managing inter- and intra-fractional changes in patient anatomy relative to their treatment plans. In the Eclipse™ treatment planning system (Varian, Palo Alto, CA), SmartAdapt (V 13.6) is offered as a DIR tool [12].

Huang et al. [13] explored the dosimetric variations in liver radiotherapy by utilizing deformable registration between planning CT and cone-beam CT in conjunction with conventionally fractionated three-dimensional conformal radiation therapy. Their study aimed to examine the dosimetric impact on normal liver tissue for treatment plans with relatively lower dose gradients. In liver SBRT, the likelihood of deviations from the initial treatment plan is high due to the steep dose gradient, respiratory motion variability, and involuntary movements. Our study aimed to evaluate dosimetric uncertainties in liver SBRT on deep inspiration breath hold (DIBH) by utilizing kV-CBCT images.

Materials and Methods

In this study, a retrospective evaluation was conducted on twenty-five liver SBRT patients who were treated with DIBH. All patients received treatment using volumetric modulated arc therapy (VMAT) in 5 fractions, employing two complete coplanar split arcs (Figure 1). The CT images, with a slice thickness of 2 mm, were acquired using the Biograph Horizon PET/CT scanner (Siemens Healthcare Private Limited, India). Treatment planning was performed using the Varian Eclipse external beam planning system with the analytic anisotropic algorithm (AAA, v13.7.16). A planning target volume (PTV) margin of 7 mm was used. For all calculations, the dose calculation grid size was set to 2 mm. Treatment was administered using a TrueBeam linear accelerator with a 6 MV un-flattened beam and a maximum dose rate of 600 MU/min. CBCT images were obtained using the on-board imaging system from Varian Medical Systems (Palo Alto, CA) [14]. These CBCT images were utilized for patient positioning and plan verification.

Respiratory motion management

The DIBH technique was employed to control respiratory motion. The Varian RPM system was used to monitor the breathing pattern during both image acquisition and treatment delivery. The TrueBeam infrared reflector marker was placed at the level of the patient's diaphragm, and the three-dimensional amplitude was tracked with an infrared camera. A 5 mm amplitude gating window was defined for DIBH.

CBCT based plan verification

CBCT calibration was performed using the CTP404 module in the Catphan® 504 [15] (The Phantom Laboratory, USA). A protocol-specific calibration curve was created using 125 kVp, 1074 mAs, and half fan settings, relating relative electron density (RED) to HU values. The Varian SmartAdapt (version 13.6) automatic DIR tool was utilized to register and propagate contours between CBCT and planning CT. Treatment plan verifications were conducted using daily CBCT at the treatment isocenter. Comparisons were made between the mean dose to the PTV, the maximum dose to the spinal canal, the liver's 21 Gy sparing volume (normal liver volume - volume of the liver receiving 21Gy), the maximum dose to the planning organ at risk volume (PRV) of the luminal organ, and the dose received by 10 cc.

Statistical Analysis

Statistical analyses were conducted using SPSS software (version 21.0, SPSS Inc., Chicago, IL, USA).

Paired t-tests were employed to evaluate significant dosimetric changes, with a P-value of less than 0.05 considered statistically significant.

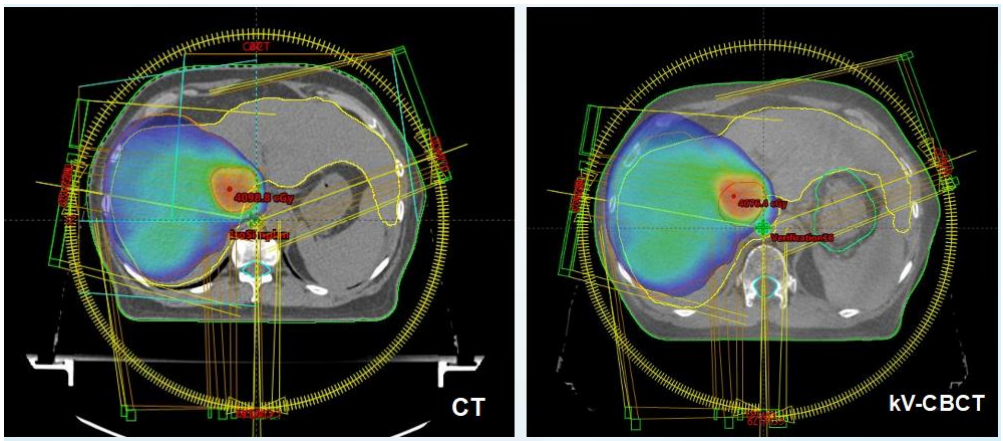

Figure 1. Stereotactic body radiation therapy (SBRT) plan on simulation CT and kilo-voltage cone-beam CT (kV-CBCT)

Results

The comparison of dosimetric parameters between the simulation CT plan and the verification CBCT plan is presented in Table 1. Among the 25 patients, the PTV D_{mean} decreased in all cases, with an average reduction of 2.2% (Figure 2). On average, the maximum dose to the spinal canal was reduced by 1.5%, remaining well within tolerance limits. Improved sparing of the spinal canal was observed, even with target-based matching. Random deviations were noted in the 21 Gy sparing volume of the liver. The PRV-luminal organ's maximum dose and the dose to 10 cc exceeded the planned values by an average of 6% and 6.9%, respectively. The luminal organ D_{max} exceeded tolerance in 23 out of 25 patients, while $D_{10\ cc}$ exceeded in 16 out of 25 patients (Figures 3 and 4).

Table 1. Comparison of dosimetric parameters between simulation CT plan and verification CBCT plan for 25 cases

DVH Parameter	Simulation CT Plan	Verification CBCT Plan	P Value
PTV Dmean (Gy)	40.2(39.25-41)	39.33 (38.13-40.40)	<0.001
Spinal canal Dmax (Gy)	14.55 (8.25-22)	14.33 (8.26-21.54)	<0.001
Liver Vs21Gy (cc)	917 (703-1240)	921 (720-1264)	0.374
Luminal organ Dmax (Gy)	31.16 (27.80-35.31)	33.03 (27.88-38.13)	<0.001
Luminal organ D10 cc (Gy)	23.67 (17.6-29.88)	25.31 (16.39-31.67)	0.017

PTV: planning target volume; Vs21Gy

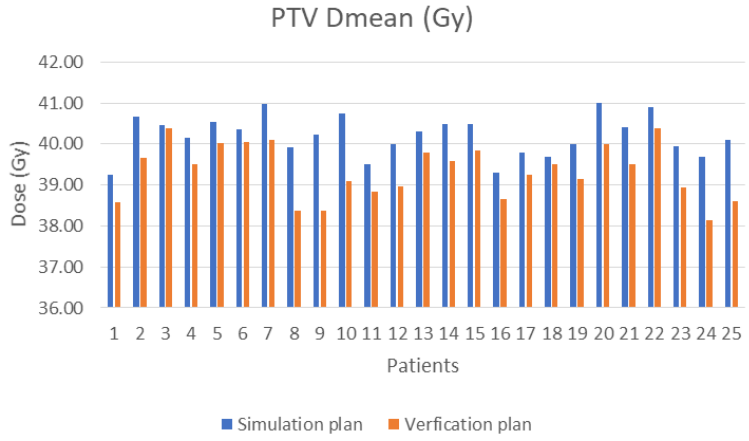

Figure 2. Patient specific deviations in the planning target volume (PTV) mean dose between simulation plan and verification plan

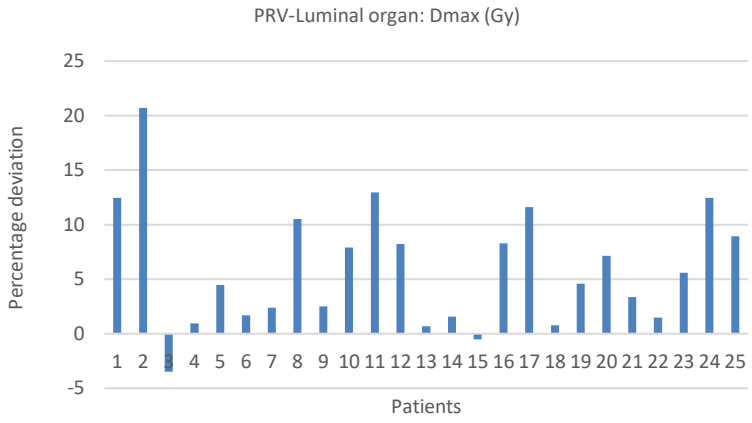

Figure 3. Patient specific deviations in maximum dose to the planning organ at risk volume (PRV)-luminal organ between simulation plan and verification plan

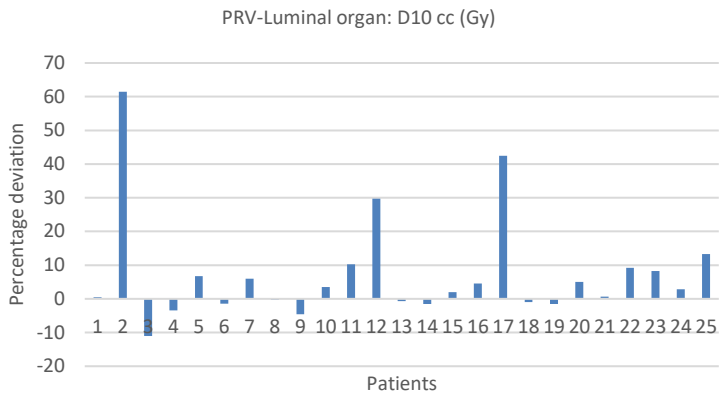

Figure 4. Patient specific deviations in dose received by 10 cc of the planning organ at risk volume (PRV)-luminal organ between simulation plan and verification plan

Discussion

Effectively managing geometric uncertainties in liver SBRT is crucial for optimizing treatment outcomes [16]. Suresh et al. [17] found that VMAT was particularly effective among delivery techniques in reducing intra-fraction motion in the liver. Our study highlights the impact of geometric uncertainties on achieving dose conformity to the target and sparing normal tissues. Thaper et al. [18] reported a significant reduction in the probability of normal liver complications when transitioning from free-breathing to breath-hold liver SBRT. However, significant liver deformation was observed with a 5 mm interval amplitude gating. Oliver et al. [19] also identified reproducibility issues and random errors associated with DIBH. Also, the random positions of the luminal organ are not predictable. Mesbahi et al. [20] investigated dosimetric uncertainties in prostate cases using CBCT-based planning and identified significant geometric inaccuracies.

In our study, we performed deformable image registration (DIR) between the planning CT and daily CBCT scans to evaluate dose distributions. We observed a significant reduction in the PTV mean dose and an increase in dose to the luminal organ. Variability in breath-hold reproducibility impacted PTV coverage and caused random deviations in normal liver sparing. Additionally, unpredictable gastrointestinal motion was evident, leading to excessive exposure of the luminal organ. Sarria et al. [21] observed a 1.76% reduction in the mean dose to the GTV (gross tumor volume) when recalculated using CBCT for neoadjuvant gastric irradiation. Huang et al. [13] reported an increase of up to 4.7% in the dose to 50% of the normal liver and up to a 4% rise in the mean dose to the normal liver, leading to radiation-induced liver disease. Lu et al. [5] also reported considerable variations in breath-hold consistency, which resulted in significant dosimetric differences.

Magnetic resonance (MR)-guided online adaptive radiotherapy has recently emerged as an effective solution. The study by Padgett et al. [22] revealed PTV under-dosage in 68% of cases when verified using MR-based techniques. Additionally, the duodenum exceeded dose tolerance in 5 out of 23 fractions, and the bowel exceeded tolerance in 5 out of 34 fractions. Weykamp et al. [23] found that stereotactic MR-guided online adaptive planning significantly outperformed the predicted plan in terms of planning target volume (PTV) coverage and adherence to organ-at-risk (OAR) dose constraints.

Since CBCT images are susceptible to artifacts, improvements in image quality through software or hardware can help enhance verification accuracy [24-26] and facilitate their use in adaptive planning. Techniques like advanced imaging, highly reproducible motion management, and adaptive planning are essential to improve the outcome.

Conclusion

Dosimetric uncertainties are impacted by liver deformation resulting from respiratory motion and the unpredictable positioning of luminal organs. Notable liver deformation occurs with a 5 mm interval amplitude gating, leading to a reduction in the mean dose to the PTV and random variations in the liver's 21 Gy sparing volume. The unpredictable positions of luminal organs caused exceedances in both the maximum dose and the dose to the 10 cc volume.

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