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Short communications and technical notes

Novel breath-hold liver target stereotactic ablative radiotherapy using the intrafraction diaphragm registration of kilovoltage projection streaming image with digitally reconstructed radiography of the planning computed tomography

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ABSTRACT

Stereotactic ablative radiotherapy (SABR) is an emerging treatment option for patients with primary or metastatic liver tumors, particularly for those who are not eligible for surgery or transplantation. SABR is a high-precision radiation therapy that delivers a high dose of radiation to the tumor while minimizing the dose to the surrounding healthy tissues. However, the accurate targeting of the tumor is a crucial aspect of liver SABR, which requires real-time imaging and tracking of the liver and tumor motion during treatment. One of the motion management strategies for liver SABR is the repeated breath-hold technique, which involves the patient holding their breath multiple times during treatment delivery to reduce the movement of the liver and other organs due to breathing. This technique helps to improve the accuracy of the treatment and reduce the radiation dose to the healthy liver.

The current study proposes a novel approach for multiple breath-hold volumetric modulated arc therapy (VMAT) stereotactic ablative radiotherapy for liver tumors, which uses the intrafraction diaphragm registration in real time to improve the accuracy and precision of the treatment. The proposed approach is based on real-time comparison of the diaphragmatic surface location between the digitally reconstructed radiography (DRR) and intrafraction kilovoltage projection streaming images (kV-PSI) having the same beam angles. The image cross-correlation between the DRR and the intrafraction kV-PSI provides a measure of the similarity between the two images and can be used to identify and track the diaphragm position during VMAT delivery. The proposed methodology consists of several steps, including planning CT and treatment planning, reference image reconstruction, and patient positioning and immobilization. The proposed approach has the potential to improve the accuracy and precision of liver cancer VMAT SABR, thereby increasing the efficacy of the treatment and reducing the risk of radiation exposure to surrounding healthy tissues.

Introduction

Liver cancer is a significant cause of cancer-related deaths worldwide, with an estimated 0.83 million per year in 2020, and the third leading cause of cancer deaths [1]. Stereotactic ablative radiotherapy (SABR) has emerged as a promising treatment option for patients with primary or metastatic liver tumors who are not candidates for surgery or transplantation [2–4]. SABR is a high-precision radiation therapy that delivers a high dose of radiation to the tumor while minimizing the dose to surrounding healthy tissues.

A recent clinical phase II trial conducted by Kimura et al. reported that SABR for solitary primary hepatocellular carcinoma resulted in excellent local control rates of 90% at 3 years [5]. Facciorusso et al. conducted a *meta*-analysis comparing SABR with radiofrequency ablation (RFA) as a well-known standard treatment for localized liver cancer [6]. They reported that SABR had a better recurrence-free survival rate compared to RFA (hazard ratio: 0.50, 95% confidence interval: 0.33–0.76, p = 0.001). SABR has emerged as a promising alternative of

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surgical resection for liver tumors and offers the potential for local control and improved survival outcomes [7]. The key point of liver SABR is related to the accurate targeting of the tumor, since a large variation in both of interactional and intrafraction motion was reported [8].

The breath-hold technique is one of the widely used motion management strategies in liver SABR [9]. Repeated breath-hold involves having the patient hold their breath multiple times during treatment delivery to reduce the movement of the liver and other organs due to breathing. This helps to improve the accuracy of the treatment and reduce the radiation dose to healthy liver [10]. Eccles et al. recommended active breathing coordinator system provided good intrafraction reproducibility in respiratory management of liver position [11].

When using repeated breath-hold SABR for liver tumors, the patient is instructed to take a deep breath and hold it for ten to a few tens of seconds while the radiation is delivered. This process is repeated multiple times during the treatment session to ensure the accuracy of the treatment and reduce the risk of radiation exposure to surrounding healthy tissues. Volumetric modulated arc therapy with flattening filter free beam (FFF-VMAT) is often employed, thereby achieving optimized dose distributions with high dose rate in order to shorten the total irradiation time [12]. With FFF-VMAT SABR, each fractionated delivery takes about 2–3 min, and if each breath-hold lasts for about 15 to 20 s, 6 to 8 breath-holds are required to complete the VMAT delivery.

In the conventional way of repeated breath-hold VMAT, the position of the diaphragmatic surface was only confirmed by comparing digitally reconstructed radiography (DRR) images and kilovoltage X-ray projection images immediately before irradiation, as the DRR was available only at the gantry start angle [Fig. 1: Conventional method]. In this study, we have proposed a novel breath-hold liver target VMAT SABR using the intrafraction diaphragm registration in real time to improve the accuracy and precision of liver cancer VMAT SABR [Fig. 1: Current method].

Proposal of a new multiple breath-hold VMAT procedure

Our novel approach was based on a real time comparison of the diaphragmatic surface location between the DRRs and intrafraction kilovoltage projection streaming images (kV-PSI) having the same beam angles. The projection streaming license was provided under a research agreement with Elekta (Stockholm, Sweden). The DRRs were computed from the planning CT scan and provided simulated 2-dimensional X-ray projection images of the diaphragm from every gantry angle with a step of 1 degree. The image cross-correlation between the DRR and the intrafraction kV-PSI provides a measure of the similarity between the two images and can be used to identify and track the diaphragm position during VMAT delivery. The methodology consists of several steps, as outlined below [Fig. 2]:

(i) Planning CT and treatment planning

Patient CT images are acquired using a CT scanner with a slice thickness of 2 mm under expiration breath-hold. A treatment plan is created, whereby a gross target volume (GTV) is contoured by a radiation oncologist, further referencing contrast-enhanced magnetic resonance images of the patient. The clinical target volume (CTV) is defined identical to the GTV and the CTV is isotropically expanded by 5 mm to create the planning target volume (PTV). Prescription dose was 48 Gy in 4 fractions, which covered at least 50% of the PTV.

(ii) Reference image reconstruction

The DRR of the diaphragm from every gantry angle with a step of 1 degree is generated from planning CT data before the treatment delivery. The DRR is used as a reference image for comparison with the intrafraction kV-PSI provided by a cone-beam CT scanner on a linear accelerator system.

(iii) Patient positioning and immobilization

The patient is positioned on the treatment couch using an immobilization device, such as a vacuum bag. A linear accelerator (linac), VersaHD (Elekta AB, Stockholm, Sweden), having an on-board CBCT scanner with the kV-PSI research license is used. VMAT is delivered under real-time comparison of the diaphragm position by calculating cross-correlation between the kV-PSI and the DRR.

The kV-PSI has a streaming interface to an external computer with a transfer rate of 5.5 frames per second (approximately 180 msec/frame) The cross-correlation analysis is performed in real time using the external computer having another interface ~~with~~ to the linac. Supplementary video data show the pilot version software of real time comparison of diaphragm images. Displacement of the diaphragm during irradiation could be confirmed to be within 5 mm.

A treatment fraction is completed in a few breath-holds, each lasting for 15–20 s. The use of kV-PSI allows continuous imaging during treatment delivery, thereby providing additional information on the position of the diaphragm and thus the liver tumor which is invisible on the projection image.

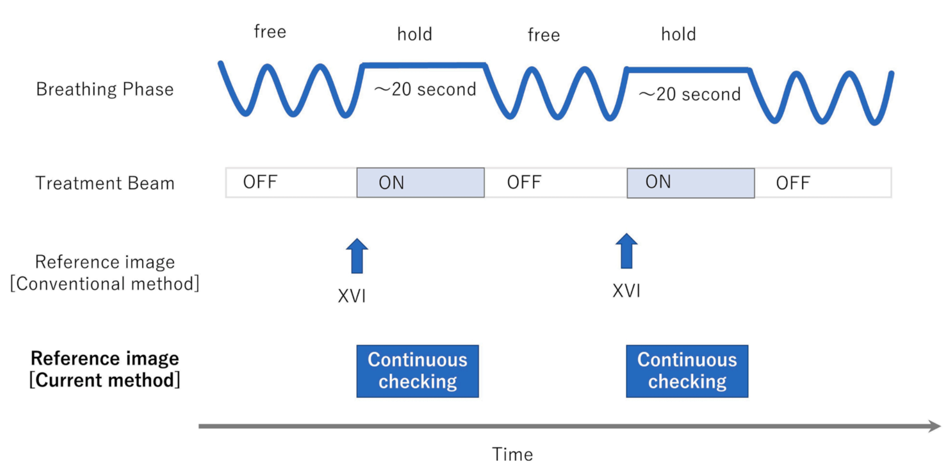

Fig. 1. Respiratory phase and beam-on time in repeated breath-hold in liver stereotactic ablative body radiotherapy Legend: In the conventional method, diaphragmatic surface was confirmed only before beam-on. In the proposed method, the diaphragmatic surface is continuously compared between kilovoltage projection streaming imaging and digitally reconstructed radiography during each beam-on period.

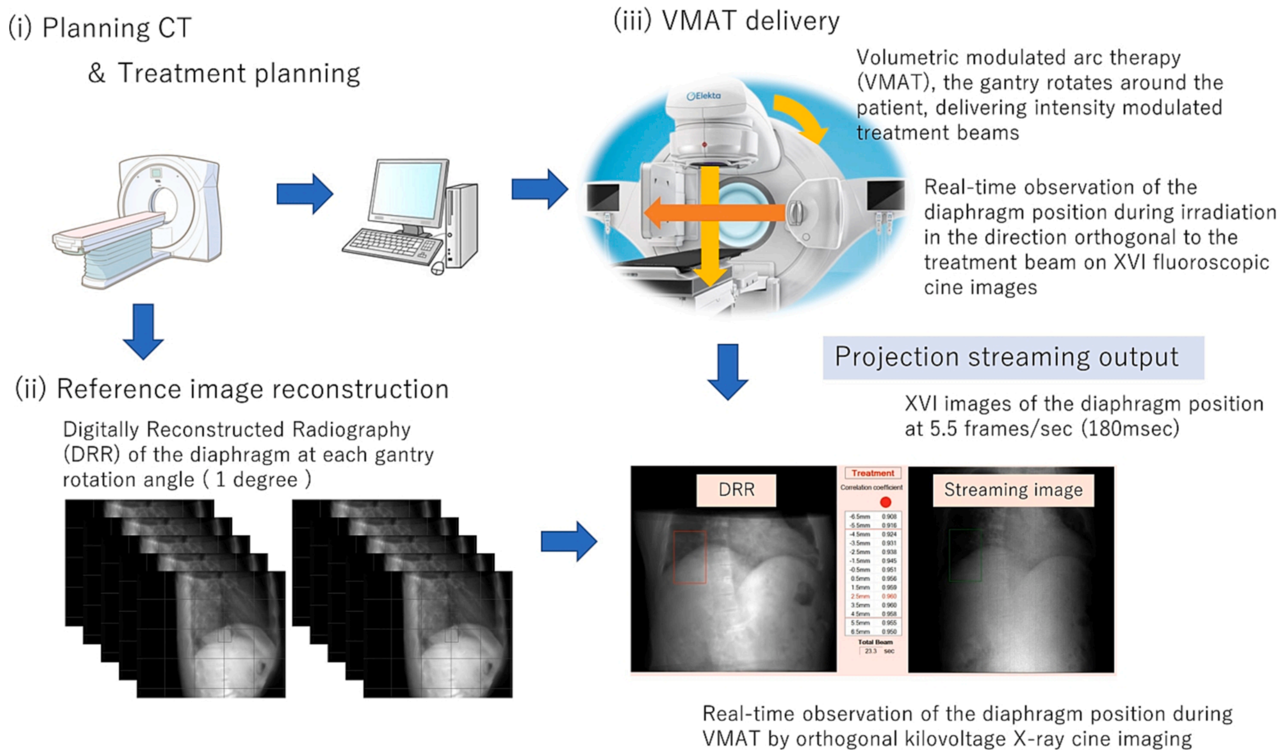

Fig. 2. Schema of the proposed breath holding radiation system. Legend: Digital reconstructed radiographies (DRRs) are reconstructed from the planning computed tomography scan and provide a simulated 2-dimensional X-ray projection image of the diaphragm from every gantry angle with a step of 1 degree. The diaphragm position registration between the DRRs and intrafraction kilovoltage projection images provides a measure of the similarity between the two images and can be used to identify and track the diaphragm position during each beam on period.

Discussion

SABR for liver tumors requires high accuracy in the targeting process with appropriate respiratory motion management. A recent clinical guideline from the American Society for Radiation Oncology strongly recommended appropriate respiratory management for patients with hepatic tumor receiving SABR [13]. The report by the German Society of Radiation Oncology also provides guidelines for safe and effective SABR of liver tumors [14]. An international survey of radiation therapy for liver tumor revealed an increasing number of referrals, with a focus on radical SABR for focal tumor, however significant variation in technology utilization and dose regimens, and the need for prospective studies or registries to optimize patient selection [15].

The novel technique presented in this study has several potential advantages over conventional respiratory management techniques of SABR treatment. Traditionally, fiducial markers are used to guide the targeting of liver tumors during SABR, but this method has limitations such as the potential for marker migration, discomfort for the patient, and additional radiation dose. Stick et al. evaluated intra-fractional fiducial marker migration during SABR in patients treated for liver metastases [16]. They concluded that the difference in marker position of up to 1.0 cm was observed during a single breath hold despite the use of a narrow external gating window and visual feedback. And, they also insisted the stability examination on pre-treatment image guidance was not sufficient to guarantee intrafraction stability. Real-time intrafraction motion monitoring is important for recent SABR [17].

Diaphragm is a good anatomical surrogate in image-guided radiation therapy for liver tumor. Kawahara et al. showed that diaphragm matching produced smaller target positioning errors compared to bone matching technique for determining liver tumor positions [18]. Lens et al. reported that exhalation breath-holds was more stable than inhalation breath-holds for abdominal organ motion [19]. In present case, we adopted expiration breath hold method for liver SBRT, according to their results of study. Our approach could be used for inspiration breath hold case in postoperative breast cancer radiotherapy.

Recently, surface-guidance radiotherapy (SGRT) is also utilized for real-time marker less position verification in breath-hold during SABR. Schönecker et al. revealed that SGRT system enabled reliable application and deep inspiration breath-hold in daily clinical use in breast cancer patients to avoid adverse cardiovascular effects [20]. However, the SGRT system can only monitor the patient surface, and therefore it is less accurate to localize deep-seated tumors. Our view is that the diaphragm is a more reliable surrogate marker for an intrahepatic tumor.

Limitation

Despite the advantages of the present technique, they also have several limitations. First, they require high-quality registration to confirm the diaphragm positioning depending on quality of images of DRRs and kV-SPI and software algorithms. Second, kV-SPI are sensitive to changes in tissue density and can be affected by organ deformation, which can result in errors in targeting. Third, patients who are unable to hold their breath for the required duration or who experience discomfort during the breath-hold phase may not be suitable candidates for this approach.

Future directions

The use of our proposed technique in liver target VMAT SABR is still in its early stages, and further studies are needed to evaluate its clinical feasibility and effectiveness. One potential direction is automatic beam control by detection of diaphragm deviation from its planned position. Response gating interface (Elekta AB, Stockholm, Sweden) on an Elekta linac allows an external system to turn the linac beam on and off. When an incidental diaphragm deviation occurred during the breath-hold, then the treatment beam could be immediately turned off.

Another potential direction is to display the intrafraction CBCT image reconstructed from the kV-PSI immediately after the treatment is completed. With this functionality, we are able to validate the treatment accuracy by comparing the liver location on the intrafraction CBCT and the planning CT images. A similar study was already reported by Brown et al, where they assessed the diaphragmatic position stability using intrafraction CBCT during liver VMAT SABR [21].

Conclusion

In conclusion, we have proposed a novel liver target VMAT SABR technique using the intrafraction diaphragm registration between the DRR and the intrafraction kV-SPI which may lead to highly conformal dose to the tumor while minimizing the dose to surrounding healthy tissues. Future studies should aim to evaluate the accuracy and the precision of this procedure and compare its efficacy with other breath-hold and free breathing VMAT SABR techniques. While we used this technical approach in a few patients, the use of a larger sample size would generalize the proposed methodology. Furthermore, potential applications to other organs with respiratory motion, such as lung, could also be explored.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: The Department of Comprehensive Radiation Oncology, to which Masanari Minamitani and Keiichi Nakagawa belong, is an endowment department, supported by an unrestricted grant from Elekta K. K. However, no funding was received for conducting this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tipsro.2023.100217.

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