Technical Note

Respiratory gated radiotherapy-pretreatment patient specific quality assurance

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ABSTRACT

Organ motions during inter-fraction and intra-fraction radiotherapy introduce errors in dose delivery, irradiating excess of normal tissue, and missing target volume. Lung and heart involuntary motions cause above inaccuracies and gated dose delivery try to overcome above effects. Present work attempts a novel method to verify dynamic dose delivery using a four-dimensional (4D) phantom. Three patients with mobile target are coached to maintain regular and reproducible breathing pattern. Appropriate intensity projection image set generated from 4D-computed tomography (4D-CT) is used for target delineation. Intensity modulated radiotherapy plans were generated on selected phase using CT simulator (Siemens AG, Germany) in conjunction with "Real-time position management" (Varian, USA) to acquire 4D-CT images. Verification plans were generated for both ion chamber and Gafchromic (EBT) film image sets. Gated verification plans were delivered on the phantom moving with patient respiratory pattern. We developed a MATLAB-based software to generate maximum intensity projection, minimum intensity projections, and average intensity projections, also a program to convert patient breathing pattern to phantom compatible format. Dynamic thorax quality assurance (QA) phantom (Computerized Imaging Reference Systems type) is used to perform the patient specific QA, which holds an ion chamber and film to measure delivered radiation intensity. Exposed EBT films are analyzed and compared with treatment planning system calculated dose. The ion chamber measured dose shows good agreement with planned dose within ± 0.5% (0.203 ± 0.57%). Gamma value evaluated from EBT film shows passing rates 92–99% (96.63 ± 3.84%) for 3% dose and 3 mm distance criteria. Respiratory gated treatment delivery accuracy is found to be within clinically acceptable level.

Key words: Gated dose delivery, pretreatment quality assurance, respiratory gating, three-dimensional imaging

Introduction

Conformal and intensity modulated radiation therapy improved the treatment outcome by delivering adequate dose to target and minimizing dose to normal structures. Organ motion are classified into inter-fraction and intra-fraction motions and they become an inevitable challenge in radiation therapy dose delivery. Lung and heart are involuntary organs, the main sources for intra-fraction tumor/organ motion. These develop artifacts in computed tomography (CT) images for planning and result in inadvertent alterations in dose distributions, which can potentially spoil the effort of intensity modulation.[1]

In spite of using advanced immobilization devices, organ motions due to physiological function of the human body

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cannot be addressed and clinical results are compromised. Studies report increased dose to normal tissue because of internal margin changes.[2] The range of lung tumor motion and its occurrence cannot be predicted by tumor position and size.[3] Modern linear accelerators have radiotherapy dose delivery techniques to reduce the setup internal margin in planned target volume (PTV).[4] A number of techniques to mitigate the effect of organ motion have been discussed in literature.[5-12] Tumor and organs in thorax and abdominal regions may be affected by the respiratory motion, cardiac motion and swallowing. Lung tumors, breast and liver tumors are more susceptible to respiratory motion.[13] The organ motion of each patient is assessed individually through four-dimensional (4D)-CT. Reproducibility and regularity of breathing pattern is crucial for respiratory gating. Respiratory gating method assumes the tumor position is a function of external surrogate position. "Breath-hold", "Respiratory gating" techniques and tumor tracking methods are widely accepted. These techniques concentrate the dose to target and avoid dose smearing. Mageras and Yorke[14] reported that "breath-hold" techniques are often poorly tolerated by patients with lung cancer.

"Respiratory gating" allows free breathing in patients. Respiratory gating enables to treat moving targets with high spatial[1] and dosimetric accuracy.[15] 4D-CT is the essential part of motion management in radiation therapy. Radiation intensity will be delivered from the machine only during preset gated window of the respiratory cycle. Managing organ motion supports dose escalation, reduces margin around target, and reduces the dose to normal structures, thereby increasing tumor control probability and decrease the normal tissue complication probability. Coaching improves the gated delivery accuracy and efficiency. Kini *et al*.[16] found that audio prompting for coaching shows less variation of breathing period than visual feedback method. Voice instruction ("breathe in… breathe out…") given to the patient to reproduce the breathing pattern comfortably, which can be maintained during intra-fraction and inter-fraction. It requires the acquisition of 4D-CT.

In our clinic, we are in the process of implementing gated dose delivery with a newly installed linear accelerator. Earlier studies recommend the need for verification method for patient specific quality assurance (PSQA).[17] A phantom study protocol with a commercially available phantom along with developed software is reported.

Materials and Methods

Computed tomography simulator image acquisition

Three patients with mobile target (two lung, one liver) are recruited for respiratory gated treatment. Recruited patients are coached for reproducible and regular breathing pattern. Siemens Somatom Sensation Open (Siemens AG, Germany) CT-Simulator, along with real-time position management (RPM) system™ (Varian Medical Systems, USA) were used to acquire 4D-CT image set. The RPM system has a six dotted marker block (surrogate), wall-mounted camera system with infrared (IR) illuminator [Figure 1], display unit (view finder) and gating software. The dots on the marker block will reflect the IR rays. The adjacent dots have a separation of 2.6 cm in the horizontal direction and 3 cm in the vertical direction. During "initialization" a calibration check is performed to validate the IR camera calibration. Patients are immobilized with appropriate immobilization device. Marker block is kept on the xiphoid process [Figure 2], where the respiratory motion is felt well. The marker block was placed on a permanent tattoo marked on the patient's skin thus improving its reproducibility. The RPM system detects the breathing pattern of the patient (by the surrogate IR reflector and IR camera), thereby monitoring the motion constantly. The RPM software assesses the reproducibility of the breathing cycle within preset tolerance value, which is regulated by normal breathing predictive filter (NBPF) setting. Recording of respiratory cycle starts only when the NBPF setting has been correctly validated. The image acquisition is based on predefined threshold setting, which is initiated by the triggering of RPM gating signal linked to the CT simulator image acquisition. Reproducibility of the breathing pattern is assessed in RPM system, and when the patient is able to reproduce the coached breathing pattern, respiratory signal from the IR camera is recorded in the RPM system. Each image in the 4D-CT raw data is tagged with respiratory signal for the purpose of treatment planning. 4D image sets are sorted into phase wise bins for every 10% of the breathing phase.

Maximum intensity projection/Minimum intensity projection generation

The images in all the phase bins together form a cine mode which can display the target trajectory. Respiratory cycle and respiration amplitude are variable depending on the parameters such as patient's age, general condition,

Figure 1: Camera system with infrared illuminator (wall-mounted) and display unit. Marker dots are seen in the monitor

diagnosis, and clinical stage. In this study, the respiratory amplitudes were in the range of 9.7–14.5 mm; respiratory cycles were in the range of 2.2–3.6 s. Phase bins with optimal motion were selected for delineation, restricting selection of phase bins within residual motion ≤0.5 cm, as an earlier report[18] indicated that 5 mm residual motion results in insignificant variation in resultant dose distribution. We have developed a prototype in-house "MATLAB (The Mathworks Inc.)" program to generate maximum intensity, minimum intensity, and average intensity projections (AvgIP) (maximum intensity projection [MIP], minimum intensity projections [MinIP], AvgIP) to adhere to the above requirement of obtaining ≤5 mm residual motion during radiotherapy execution. The workflow sequence of the MATLAB program is highlighted in [Figure 3]. All imported 4D-CT images were segregated into their respective phase bins. Selected phase (P_s) bin images were used to generate MIP and MinIP for lung and liver patients, respectively, and they were sorted out based on their "table position". For each table position, maximum, minimum, and average voxel intensity were generated. The intensity projected images were saved as Digital Imaging and Communications in Medicine (DICOM) file for subsequent procedures.

Target volume delineation

Internal target volume (ITV)[4] is delineated from MIP image set for lung patients and from MinIP image sets for liver patients. ITV delineated on MIP or MinIP is equivalent to the union of gross tumor volume delineated on selected phase bins. A setup margin of 5 mm is accounted for PTV contouring. Normal structures are drawn in central phase (P_c) bin of the selected phases.

Dynamic thorax phantom

Commercially available Computerized Imaging Reference Systems dynamic thorax phantom (CDTP) is a thorax phantom, made up of human tissue equivalent material with a lung equivalent rod. A piston arrangement gives a programmed motion electromechanically by a bipolar stepper motor using an actuator and controller. Figures 4 and 5 shows the CDTP and its components. The controller receives the program from the motion perfect software and drives the actuator.[2] Computerized Imaging Reference Systems (CIRS) phantom thereby synchronizes the piston movement to simulate chest and surrogate platform movement. Different lung equivalent rods facilitate provision for placement of ion chamber, film, and metal oxide-silicon field effect transistors (MOSFET) for dose measurements. Because of the limitation of the size of the lung equivalent rod, for film dosimetry, an EBT rectangular film of 13.3 cm × 5.3 cm size was used. Positioning accuracy of the film is assured by having three prick holes by a needle. CDTP is used for quality assurance (QA) method for "image guided dynamic dose delivery" from 4D imaging acquisition, treatment planning, and dose delivery. In-house developed MATLAB program ensures breathing pattern file from RPM system converted to CDTP compatible file. This "respiratory pattern" file is fed to the CDTP to validate the original patient respiratory pattern. The 4D-CT image set of CDTP, both for ion chamber and film holder acquired using patient breathing pattern. The basic assumption in this phantom based measurement is that the target motion and the surrogate motion are linearly correlated with each other. The respiratory pattern file obtained from RPM system represents only the surrogate motion and not the target motion. Therefore, the set up validates the motion pattern of the detector (ion chamber, film, or MOSFET) which may differ from the real target motion.

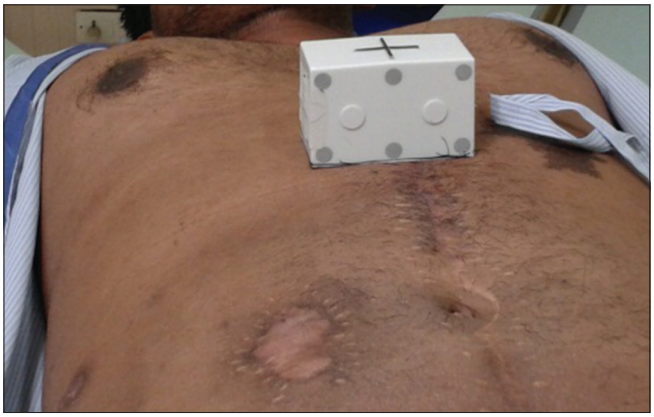

Figure 2: Marker block kept on the patient chest during four-dimensional-computed tomography acquisition (dots are in silver color)

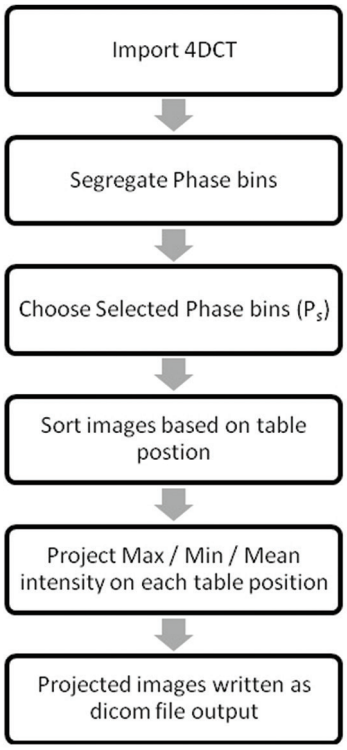

Figure 3: Generated flow of MATLAB program for maximum intensity projection/minimum intensity projections/average intensity projections

Treatment planning

The central phase bin image set of the selected phases (Ps) was used for dose calculation. All the central phase bins were in the expiratory phase (expiration 60%, expiration 60%, and expiration 100%). Dynamic intensity modulated radiotherapy (IMRT) plans were generated in Eclipse (Version 10.0) (Varian Medical Systems, Palo Alto) treatment planning system (TPS) for the three patients (two lung and one liver PTVs). Beam orientation and number of beams were chosen according to the tumor and critical structure position. Dose calculation was carried out with a 2.5 mm × 2.5 mm grid size using analytical anisotropic algorithm (AAA). Verification plans were generated on the central phase (P_c) bin image set of CDTP, for both ion chamber and film image sets.

Dynamic thorax phantom dose verification

Verification plans were delivered from linear accelerator with multi-leaf collimator (Clinac-iX, 120 Millenium MLC, Varian AG, USA) equipped with On-Board Imager (OBI) and an RPM system for gated delivery. Ion chamber and EBT film were positioned in the lung equivalent rod in the image-guided radiation therapy phantom. Respiratory gated verification plans were delivered on CDTP. Delivered dose was measured with ion chamber (CC 13, Dose 1 Electrometer, IBA Dosimetry, Germany) and also by the EBT film. Exposed films were analyzed and evaluated in film QA software (3Cognition, USA). Measured dose plane was taken as the reference and compared with the TPS calculated dose. The film dosimetry pattern obtained by the film rod in this study is shown in Figure 6. Gamma index[19] was used to evaluate the measured films. The criteria adopted for passing rate calculation was 3% dose difference and 3 mm distance to agreement. Points outside the film area were not included for gamma index calculation. Gated beam output was compared with nongated beam output to ensure the stability of gated output. For this, radiation beam was delivered in un-gated mode and in gated mode on an ion chamber kept stationary in a phantom. Gated beam is delivered with 30% and 70% duty cycles.

Results

Table 1 shows the gated beam output stability. Virtually no difference was found between gated and un-gated beam output, with maximum output difference of about 0.01%. The calculated dose by TPS was compared with ion-chamber measured dose in PSQA for these three patients and the results are given in Table 2. It can be seen that there is a good agreement between TPS and measured doses. The deviation observed between TPS calculated and measured doses was within ± 0.5% (0.20 ± 0.57%). Figure 7 shows comparison of film measured and TPS calculated isodose distribution. The gamma passing rate evaluated from EBT film were in the range of 92.4–99.9% (96.6 ± 3.8%), which is quite acceptable for treatments.

Figure 4: Computerized Imaging Reference Systems dynamic thorax phantom; (lung equivalent, actuator [black box], controller [blue box])

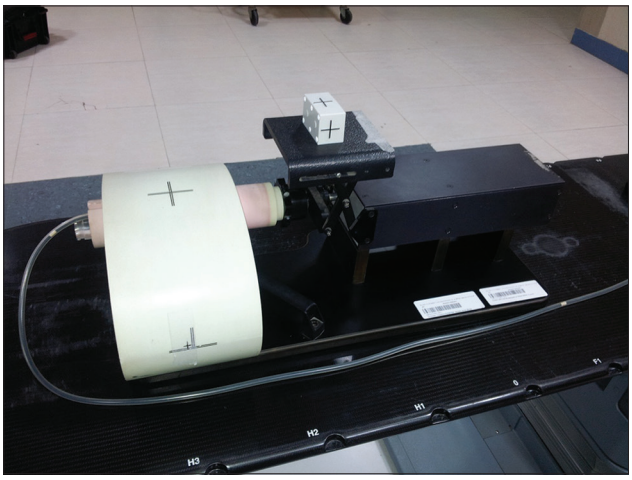

Figure 5: Computerized Imaging Reference Systems dynamic thorax phantom measurement setup with ion chamber (marker block on the phantom)

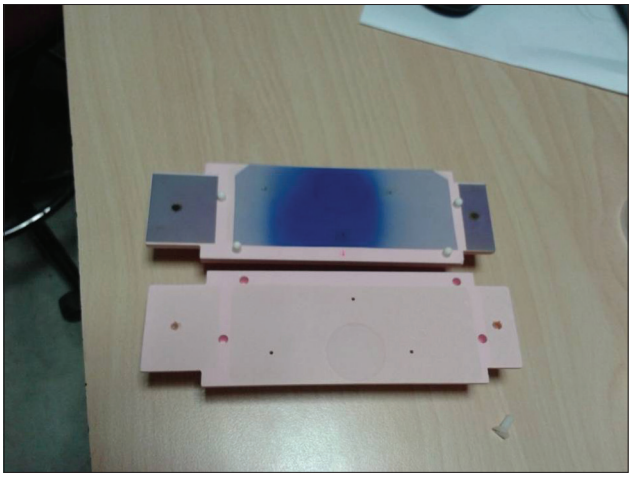

Figure 6: Exposed film rod in open condition

Table 1: Un-gated versus gated beam output for different duty cycle

Serial number	*Duty cycle (%)*	*Un gated dose output (Gy)*	*Gated dose output (Gy)*	*Difference in dose (%)*
1	30	2.1543	2.1540	0.01
2	70	2.1543	2.1540	0.01

Table 2: Comparison of TPS calculated dose and IC, film, and dose estimates

Patient serial number	*Lesion*	*TPS dose (cGy)*	*Estimate IC (CDTP) (cGy)*	*Difference in dose (%)*	*Gamma index (film) (passing rate%)*
1	Lung	812.5	816.2	0.45	99.9
2	Lung	761.4	757.4	−0.52	92.4
3	Liver	1327.5	1320.3	−0.54	97.6

IC: Ion chamber, TPS: Treatment planning system, CDTP: CIRS dynamic thorax phantom, CIRS: Computerized Imaging Reference Systems

Discussion

Respiratory gated treatments intend to reduce the internal margin and reduce the toxicity to normal tissue. Excessive volume of normal lung irradiation increases the risk of pneumonitis. Graham *et al*.[20] reported that lung V_{20} (volume of lung receiving at least 20Gy) more than 32% resulted in high grade to fatal pneumonitis. Liang *et al*.[19] reported that mean dose to normal liver >23 Gy increased the radiation induced liver disease. The amplitude or phase of the respiratory pattern used for gating should be such that the residual motion is minimum within the gating window. Cardenas *et al*.[21] reported that residual motion of 0.16–0.58 cm were observed for a group of patients who underwent respiratory gated radiation therapy. Patient coaching is an important part of QA in respiratory treatment delivery.[3] The respiratory signal from the external surrogate is not truly representing the tumor motion amplitude. External surrogate may be in phase or out of phase with the tumor motion. This is because it samples a small portion of the body surface. However, the surrogate motion is a function of tumor motion and/or respiratory motion. The nomenclatures used in RPM system and Somatom Sensation Open CT simulator are different. RPM system reads a single respiratory wave form 0% to 100%, but CT simulator reads it as 0% to 100% for inhale and 0% to 100% for exhale separately. While using systems from different vendors, the end user should be aware of the nomenclature changes to avoid any inadvertent errors in setting the gating threshold for imaging and delivery.

The impact of gating on beam output is negligible and is independent of duty cycle. Ion chamber based measurements are robust,[22] and it is used for IMRT PSQA. Saw *et al*.[23] compared the un-gated plan delivered to a stationary phantom and gated plan delivered to a moving phantom as a part of QA in respiratory gated treatment. Chen *et al*.[18] reported that ion chamber measurements at isocenter showed <2% difference even for a maximum motion of 3 cm. The author has also compared dose distribution calculated on a phantom and measured from the moving phantom with gated delivery. Our results from ion chamber measurement are not differing more than 0.54% and are comparable with earlier reports in literature. Measuring dose at isocenter alone will not show the clear picture. Sampling more points in the treatment field by ion chamber is not practicable. Therefore, complimenting with film dosimetry is carried out verifying the two-dimensional dose distributions. Our method therefore verifies spatial modulation in intensity over the target and position of the target in the temporal space. The maximum size of EBT film that can be used in CDTP is restricted by the diameter of the film rod. Hence, large size treatment field cannot be verified by the film in CDTP. The results obtained from ion chamber and film based measurements were well within clinically acceptable range. The duty cycle of the gated delivery should be chosen optimally to increase the efficiency of dose delivery, patient comfort, which is essential in a busy department. At the same time, one should keep the magnitude of the residual motion within 0.5 cm.[18]

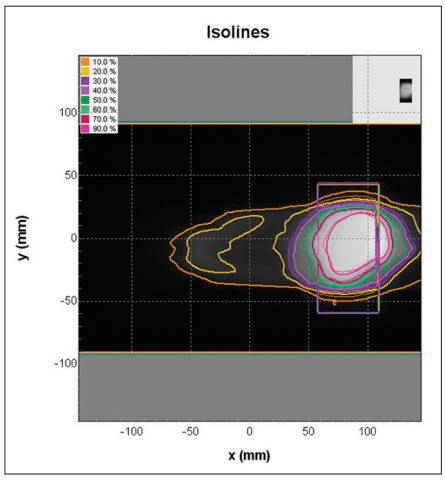

Figure 7: Isodose lines compared in film and treatment planning system calculated dose

Conclusion

The above study estimated the dosimetric accuracy of respiratory gated treatment delivery in a dynamic thorax phantom (CDTP). Both ion chamber and film measurement results were well within clinically acceptable values with verification by two independent methods. In this study, CDTP simulated tumor motion using patient breathing pattern corresponding to a single session. However, it is opined that day-to-day variation in patient breathing pattern should be paid paramount attention and corrective action must be applied appropriately because variations in patient's respiratory pattern during treatment

may jeopardise the planned dose distribution.[24] With this verification method, we could implement the image guided radiotherapy with our OBI set up.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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