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Biological in vivo Three-Dimensional Dose Distribution Verification for Lung Cancer: From Rigid-Body Model to Porcine Lung

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ABSTRACT

This study introduces a novel concept, biological in vivo three-dimensional (3D) dose distribution verification, aimed at investigating how respiratory motion affects the efficacy of lung cancer radiotherapy, representing an evolution from the current standard of rigid-body dose distribution verification.

A 3D ex vivo biological lung motion simulation device (3D-BioLungEx) was designed to replicate human respiration. A radiotherapy plan of the patient was copied to the porcine lung, which was driven by 3D-BioLungEx to simulate various respiratory patterns that occur during treatment. To ensure anatomical consistency with the patient's lung structure, during transmission, skin, skeleton, and organs were adjusted according to CT images of the porcine lung. The patient's radiotherapy plan was then adapted to the porcine lung using the Monaco treatment planning system (TPS). Next, an iterative optimization and scatter inversion-based dose distribution retro-analysis algorithm (IOSI-BLDose) was developed to calculate the dose distribution during treatment.

Gamma passing rates were used to quantify discrepancies between this dose distribution and that of the radiotherapy plan. When respiratory conditions were replicated, the passing rate reached up to 93.61%, while irregular breathing dropped it to 70%–90%, primarily due to amplitude changes. However, cycle variations had minimal impact.

Compared to conventional rigid-body dose distribution verification, our method provides real-time biological feedback and more effectively captures motion-induced deviations. Accordingly, our biological in vivo 3D dose distribution verification has potential for improving treatment precision and enabling adaptive radiotherapy in clinical practice.

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INTRODUCTION

Lung cancer remains one of the leading causes of cancer-related mortality worldwide, and radiotherapy plays an essential role in its treatment. However, respiratory motion can cause continuous displacement and deformation of lung tumors during irradiation, leading to discrepancies between the planned and delivered dose distributions.

Conventional dose verification is mainly based on static CT images or rigid-body phantoms, which cannot fully reproduce patient-specific respiratory dynamics or biological tissue deformation during treatment. To address this limitation, this study proposes a biological in vivo 3D dose distribution verification strategy for lung cancer radiotherapy.

By integrating patient CT data, 3D printing, porcine lung tissue, and a customized respiratory motion simulation system named 3D-BioLungEx, this work provides a more realistic platform for evaluating respiration-induced dose deviations.

In addition, the IOSI-BLDose algorithm was developed to reconstruct 3D dose distribution within the lung, offering a potential approach to improve dose verification accuracy and support more precise adaptive radiotherapy.

METHODS AND MATERIALS

A patient-specific biological lung motion simulation platform, 3D-BioLungEx, was developed to reproduce respiratory motion during lung cancer radiotherapy. The system included three main modules: a monitoring module for recording patient respiratory curves, a phantom module for constructing a customized thoracic model from 4D CT images, and an actuator module for driving lung motion. Fresh porcine lungs were placed inside the 3D-printed thoracic phantom to provide a biologically realistic lung model. Normal breathing and abnormal respiratory patterns, including Cheyne–Stokes breathing, yawning, and coughing, were simulated to evaluate their effects on dose delivery. The patient's radiotherapy plan was transferred and adapted to the porcine lung model using the Monaco treatment planning system. During irradiation, EPID images were collected, and the IOSI-BLDose algorithm was applied to reconstruct the 3D dose distribution inside the lung. Gamma passing rates were then calculated to compare planned and reconstructed dose distributions and quantify respiratory-motion-induced dose deviations.

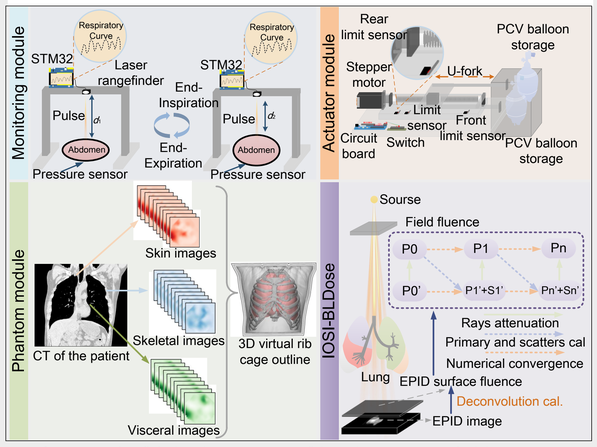

Figure 1. The fabrication process of 3D-BioLungEx and IOSI-BLDose.

RESULTS

The 3D-BioLungEx system demonstrated high accuracy in reproducing both normal and abnormal respiratory patterns. As shown in Table 1, compared with the conventional vacuum pump, 3D-BioLungEx achieved lower simulation errors across CT-simulated breathing, Cheyne–Stokes breathing, yawning, and coughing, indicating its superior ability to control respiratory amplitude and cycle.

Table 1. Performance comparison of the 3D-BioLungEx device.

Device	Pattern	Curve	MAE/mm	RMSE/mm	MAPE/%
3D-BioLungEx	Normal (n = 50)	CT-sim breathing	0.81 ± 0.08	0.98 ± 0.12	8.94 ± 1.77
	Abnormal (n = 30)	CS breathing	0.56 ± 0.15	0.79 ± 0.28	6.87 ± 1.43
	Abnormal (n = 30)	Yawning	1.21 ± 0.70	1.81 ± 0.94	16.94 ± 8.12
	Abnormal (n = 30)	Coughing	1.92 ± 0.98	2.33 ± 1.06	19.45 ± 9.19
Vacuum pump	Normal (n = 50)	CT-sim breathing	2.06 ± 0.89*	1.53 ± 0.74*	27.01 ± 8.08*
	Abnormal (n = 30)	CS breathing	1.97 ± 0.58*	1.01 ± 0.45*	24.59 ± 7.07*
	Abnormal (n = 30)	Yawning	2.85 ± 1.04*	1.95 ± 0.70*	26.94 ± 8.12*
	Abnormal (n = 30)	Coughing	3.97 ± 1.72*	2.62 ± 1.28*	39.45 ± 12.19*

Dose verification results in Figure 2 further showed that respiratory motion markedly affected dose delivery accuracy: ArcCHECK achieved the highest passing rate under static conditions, whereas patient free-breathing and irregular breathing patterns led to increased dose mismatch. In particular, coughing produced the lowest gamma passing rate, suggesting the strongest motion-induced dose deviation.

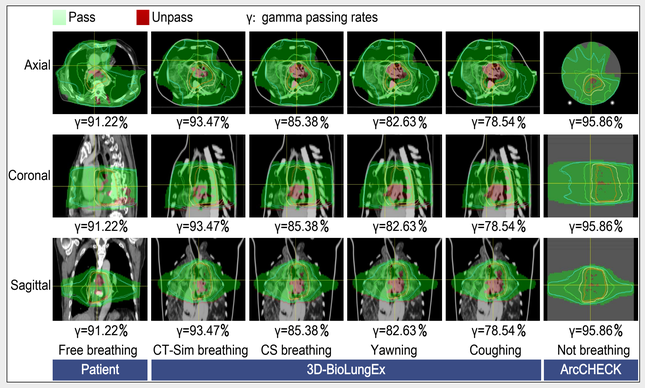

Figure 2. Quantitative Verification of Biological In Vivo 3D Dose Distribution.

As summarized in Figure 3, 3D-BioLungEx achieved a global gamma passing rate of approximately 93.61% under CT-simulated breathing, while abnormal breathing patterns progressively reduced the passing rate.

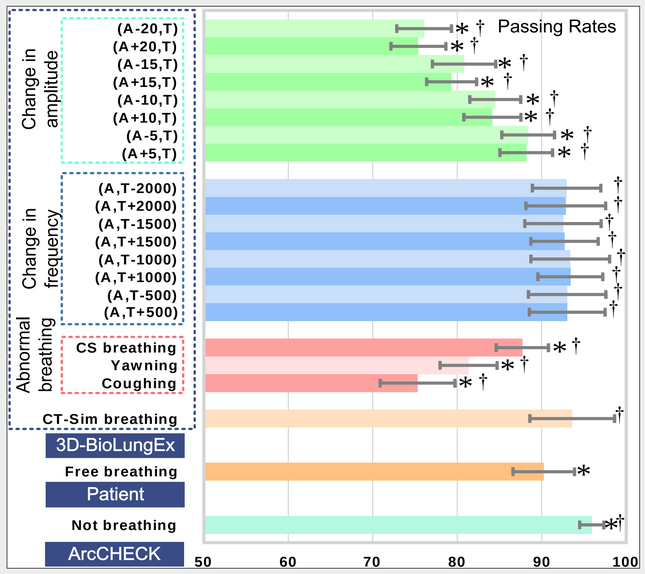

Figure 3. Gamma passing rates under different respiratory patterns.
Footnotes: *indicates $p < 0.05$.

DISCUSSION

Respiratory motion remains a major source of uncertainty in lung cancer radiotherapy, as it can alter tumor position and tissue deformation during dose delivery. The results demonstrated that static verification using ArcCHECK achieved the highest gamma passing rate, whereas patient free-breathing and irregular respiratory patterns showed reduced dose agreement. This suggests that conventional rigid-body verification may overestimate treatment accuracy because it cannot fully account for respiration-induced anatomical and dosimetric changes during actual irradiation.

The 3D-BioLungEx system provides a more realistic biological verification platform by combining patient-specific thoracic anatomy, porcine lung tissue, and controllable respiratory motion simulation. Compared with static or purely mechanical phantoms, this system better reflects the dynamic behavior of lung tissue under different breathing conditions.

The progressive decrease in gamma passing rates under Cheyne–Stokes breathing, yawning, and coughing further confirms that irregular respiration can substantially compromise dose delivery accuracy. In particular, the findings indicate that respiratory amplitude has a stronger influence on dose distribution than respiratory cycle variation, highlighting the importance of motion amplitude control during lung cancer radiotherapy.These findings support the clinical value of biological in vivo 3D dose verification for evaluating motion-induced dose errors and improving treatment precision.

By capturing dose deviations under realistic respiratory conditions, 3D-BioLungEx may help optimize treatment planning, assess plan robustness, and support adaptive radiotherapy strategies. Nevertheless, further validation with larger datasets and more complex clinical scenarios is still needed before broad clinical application.

CONCLUSIONS

Lung cancer patients often fail to replicate the respiratory pattern observed during CT simulation in actual treatment sessions, resulting in lower-than-expected gamma passing rates. Respiratory amplitude is identified as the primary factor affecting dose delivery accuracy. The proposed biological in vivo three-dimensional dose distribution verification method enables real-time dose monitoring and provides critical theoretical and practical support for dose-guided radiotherapy.

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