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Extending CT ventilation imaging to 4D using time-varying velocity fields validated with Galligas PET

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INTRODUCTION AND PURPOSE

Radiation pneumonitis is a severe complication in radiotherapy for lung cancer patients, with an incidence rate of approximately 30%, and fatal cases having been reported. Consequently, functional avoidance radiation therapy using computed tomography (CT)-based pulmonary ventilation imaging (CTVI) has recently gained attention as a novel approach to avoid dose concentration in healthy lung tissue. CTVI is a functional imaging technique that creates local ventilation maps by combining four-dimensional CT (4DCT) with deformable image registration (DIR) to measure volume or density changes throughout the respiratory cycle [1, 2]. The method offers distinct advantages over conventional ventilation imaging modalities such as single-photon emission computed tomography, including higher resolution, faster acquisition, and lower cost.

Its clinical use is being studied in ongoing trials. For example, a phase II study (NCT02528942) showed that using 4DCT-ventilation in treatment planning can reduce radiation to healthy lung areas without increasing side effects [3].
CTVI typically utilizes deformable image registration (DIR) based on Displacement Vector Fields (DVF). However, conventional 3D approaches using Displacement Vector Fields (DVF) assume a linear trajectory between peak-exhale and peak-inhale phases, potentially underestimating actual respiratory motion.

PURPOSE

The purpose of this study is to evaluate the feasibility of 4D-CTVI using Time-Variant Fields (TVF), which model deformation as a temporal velocity field, and to compare it with conventional DVF-based 3D-CTVI.

METHODS AND MATERIALS

1. Patient Data

- High-quality datasets consisting of 4DCT and Galligas PET images from 5 lung cancer patients were retrieved from The Cancer Imaging Archive (TCIA) to serve as the baseline data for this study.
- To prevent noise and measurement errors in ventilation calculation and to improve evaluation accuracy, lung masks were generated to precisely exclude anatomical structures such as the trachea and major vessels.

2. Deformable Image Registration (DIR)

- To track the dynamic deformation of the lungs caused by respiratory motion, DIR was performed between peak-exhale and peak-inhale CT images using the Advanced Normalization Tools (ANTs) toolkit.

3. CT Ventilation Image (CTVI) Generation

- Two advanced approaches with different dimensions and deformation modeling, namely 3D-CTVI and 4D-CTVI, were implemented and comprehensively compared for generating CT ventilation images.
- For the 3D-CTVI approach, ventilation was calculated based on Displacement Vector Fields (DVF) obtained by applying the Symmetric Normalization (SyN) algorithm to evaluate the static deformation between two respiratory phases.
- For the 4D-CTVI approach, ventilation was derived using Time-Varying Velocity Fields (TVF), which more faithfully model the respiratory deformation as a continuous spatiotemporal velocity field over time.
- In both methods, the final ventilation images were calculated using the Jacobian determinant of the resulting deformation fields to quantitatively and physically evaluate the local volumetric change.

4. Quantitative Analysis

- To objectively evaluate the spatial accuracy and physiological validity of the generated CTVIs, Galligas PET images—the clinical gold standard for ventilation imaging—were utilized as the ground truth.
- To appropriately evaluate spatial consistency while smoothing local image mismatches, a block-averaged analysis was applied to calculate Spearman's rank correlation coefficients between the CTVIs and Galligas PET images for rigorous statistical evaluation.

RESULTS AND DISCUSSION

1. Visual Comparison of CTVIs

- Figure 1 displays coronal images arranged by patient case from top to bottom (Cases 1–5), featuring the reference Galligas PET (left column), 3D-CTVI (middle column), and 4D-CTVI (right column) for visual comparison.
- Visual assessment reveals that the proposed 4D-CTVI generally exhibits an increased extent of high-ventilation regions compared to the conventional 3D-CTVI.
- This superior visual agreement suggests that modeling deformation as a continuous TVF captures physiological ventilation more accurately than static two-phase DVF.

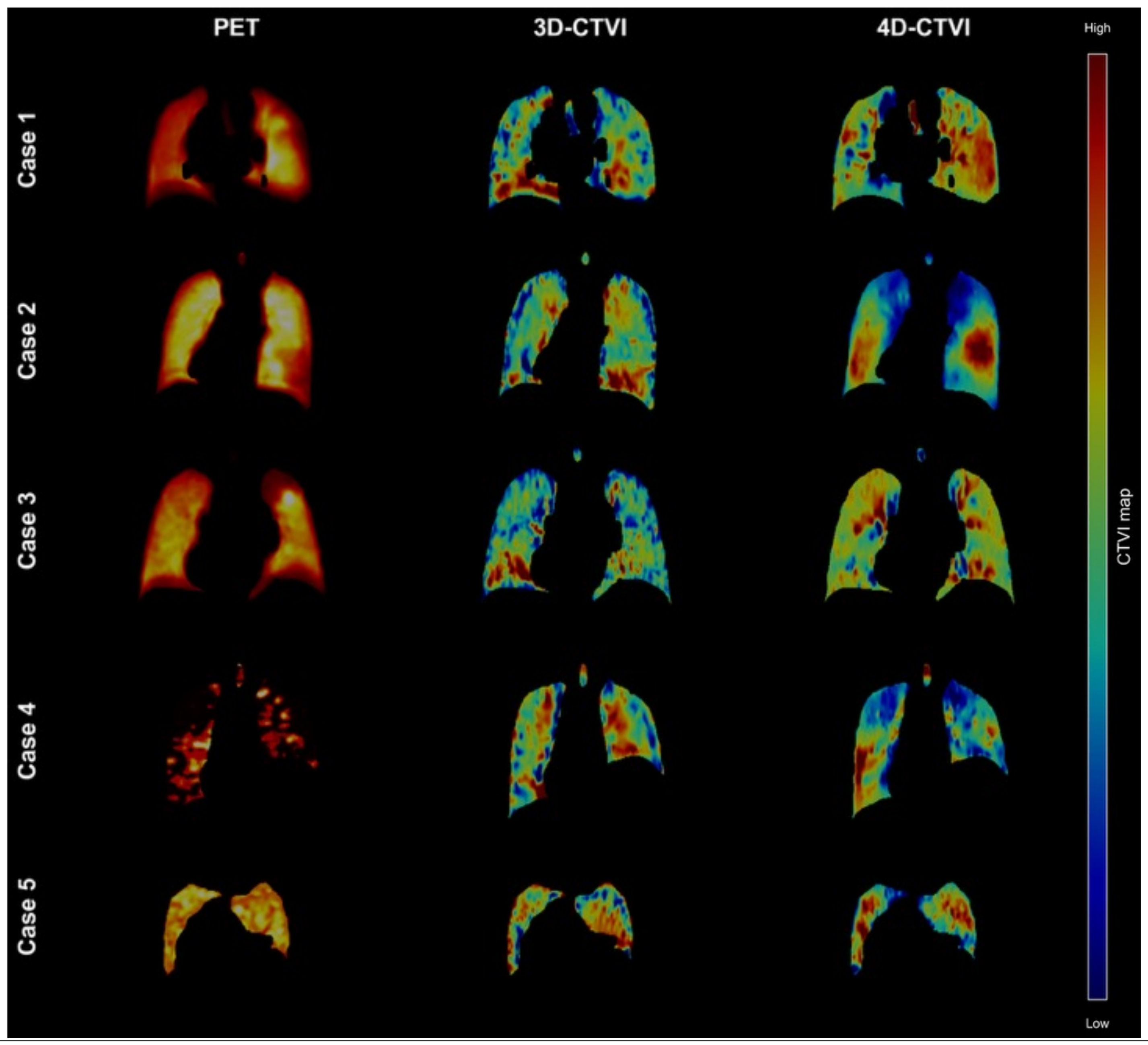

Figure 1 Visual comparison of CT-based ventilation imaging maps with Galligas PET.

2. Quantitative Analysis

- Table 1 lists the Spearman's rank correlation coefficients (R) for all five evaluated patients (Cases 1–5).
- For Cases 1 and 2, which already exhibited high baseline correlations in the 3D method, the 4D approach achieved further enhancement.
- For Cases 3 and 4, which suffered from lower baseline correlations in 3D, the 4D-CTVI demonstrated increases, while Case 5 remained comparable between the two methods.
- Overall, the proposed 4D-CTVI achieved a mean Spearman's rank correlation coefficient of 0.51 ± 0.30, which was significantly higher than the 0.38 ± 0.31 obtained by the conventional 3D-CTVI ($p < 0.05$).
- These quantitative results demonstrate that the 4D-CTVI approach provides statistically significant improvements in spatial accuracy and reliability for lung ventilation imaging.

Table 1 Comparison of Spearman's rank correlation coefficients between generated CTVIs and reference Galligas PET images for five lung cancer cases.

Case ID	Case 1	Case 2	Case 3	Case 4	Case 5	P-value
3D-CTVI	0.72	0.72	0.16	0.16	0.14	< 0.05
4D-CTVI	0.84	0.79	0.25	0.50	0.17	

CONCLUSIONS

4D-CTVI using TVF is feasible and demonstrated improved spatial correlation with functional PET compared to the conventional DVF-based 3D approach. Further accuracy improvements and validation are expected through the utilization of all respiratory phases, optimization of DIR parameters, and an increase in the number of cases.

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