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A cGAN-based Spatially-Resolved Prediction of Lung Tumor Response to Chemoradiation

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ABSTRACT

Purpose: To develop a voxel-wise, spatially resolved model for predicting mid-chemoradiation metabolic response in lung tumors using pre-treatment PET SUV and radiotherapy dose distributions.

Methods: PET/CT images and dose distributions from 25 patients with locally advanced NSCLC were retrospectively analyzed. Masked tumor volumes were sliced along the z-axis, and PreSUV and dose maps were fused as dual-channel inputs for a cGAN model designed to synthesize MidSUV maps.

Results: Across leave-one-out cross-validation, the proposed cGAN achieved a mean SUV MSE of 2.29, RMSE of 1.34, and Spearman correlation of 0.86. Ablation analysis confirmed that residual blocks and adversarial training improved prediction accuracy.

Conclusion: The proposed framework robustly predicts spatially resolved tumor response and may support dose optimization for biologically adaptive radiotherapy.

INTRODUCTION

- Lung cancer remains a leading malignancy worldwide[1], and radiotherapy is a critical treatment modality for locally advanced non-small cell lung cancer.
- Early assessment of tumor response during chemoradiation can provide actionable information for adapting treatment strategies and reducing unnecessary toxicity[2].
- FDG-PET/CT provides functional information on tumor metabolism, while radiation dose distributions describe spatial treatment delivery. Their integration may better characterize heterogeneous tumor response[2].
- Current radiotherapy planning and response assessment still rely heavily on physician experience and global response indicators, which may overlook voxel-level spatial variation within tumors.
- This study proposes a cGAN-based framework to predict spatially resolved MidSUV maps from pre-treatment PET SUV and dose distributions, aiming to support biologically adaptive radiotherapy.

METHODS AND MATERIALS

Patient Cohort and Imaging Data

- PET/CT images and radiotherapy dose distributions from 25 patients with locally advanced NSCLC were retrospectively analyzed.
- Pre-treatment PET SUV maps, mid-treatment PET SUV maps, and dose distributions were spatially aligned within masked tumor volumes.

Data Preprocessing (Figure 1)

- Masked tumor volumes were sliced along the z-axis to generate 2D samples.
- PreSUV, MidSUV, and dose maps were individually normalized.
- PreSUV and dose were fused as model inputs, with PreSUV mapped to the red channel and dose mapped to the green channel.

cGAN Framework (Figure 2)

- A residual U-Net generator synthesized MidSUV maps from fused PreSUV–Dose inputs.
- Residual blocks were incorporated to improve feature propagation and preserve spatial details during image generation.
- A contrast-enhancement module was added at the output stage to sharpen local tumor textures and boundaries.
- A PatchGAN discriminator evaluated local realism by distinguishing real MidSUV maps from synthesized MidSUV maps.

Training and Evaluation (Table 1)

- The generator was optimized using voxel-wise MSE loss combined with weighted adversarial loss.
- A 25-fold leave-one-out cross-validation strategy was used, with 21 training, 3 validation, and 1 testing patient per fold.
- Performance was assessed using SUV-based metrics, response-ratio metrics, and ablation variants of the proposed architecture.

RESULTS

- The proposed cGAN achieved strong overall MidSUV prediction, with SUV MSE of 2.29, RMSE of 1.34, and Spearman correlation of 0.86, indicating good voxel-wise agreement with ground truth (Table 1).
- Stratified results showed response-dependent performance: the high-response group achieved the lowest Ratio MSE of 0.03, while the low-response group achieved the lowest SUV MSE of 1.76 (Table 1).
- Ablation analysis confirmed the value of the proposed design. Removing residual blocks increased SUV MSE to 2.42, while removing adversarial training further increased SUV MSE to 3.08 and reduced SUV correlation to 0.74 (Table 1).
- Visual comparisons further supported the quantitative findings. Predicted MidSUV maps closely matched ground-truth maps across Low, Medium, and High response cases, with preserved metabolic hotspots and tumor boundaries (Figure 3).

Table 1. Quantitative performance and ablation analysis.

Variant	Group	SUV MSE	SUV RMSE	SUV Cor	Ratio MSE	Ratio RMSE	Ratio Cor
Proposed cGAN	All	2.29	1.34	0.86	0.07	0.24	0.15
Proposed cGAN	High	3.12	1.51	0.85	0.03	0.17	0.18
Proposed cGAN	Mid	1.96	1.32	0.86	0.06	0.25	0.24
Proposed cGAN	Low	1.76	1.20	0.87	0.10	0.30	0.08
w/o residual blocks	All	2.42	1.38	0.84	0.07	0.25	0.12
w/o adversarial loss	All	3.08	1.51	0.74	0.08	0.27	0.09

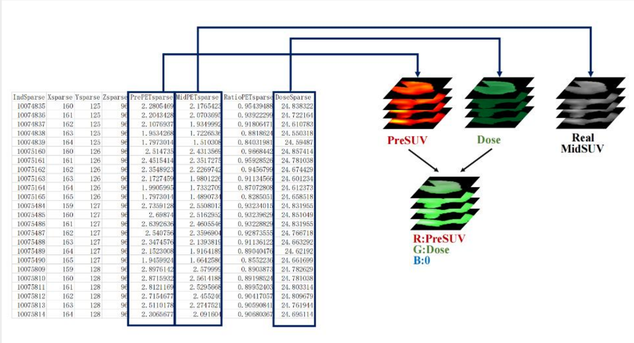


Figure 1. Data preprocessing workflow. PET/CT and dose data were sliced, normalized, and fused into PreSUV–Dose inputs for cGAN training.

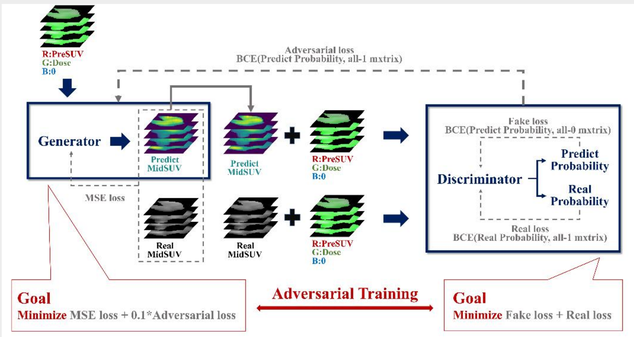
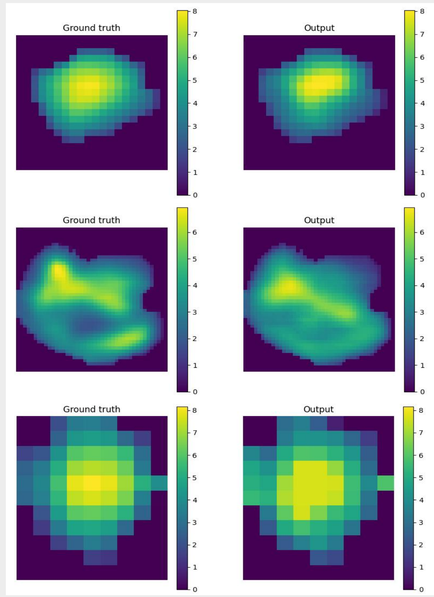


Figure 2. Proposed cGAN architecture. A residual U-Net generator synthesized MidSUV maps, while a PatchGAN discriminator evaluated real and generated outputs.

DISCUSSION

- By leveraging both PET-derived metabolic information and radiation dose distributions, the proposed cGAN captures complementary features associated with heterogeneous tumor response.
- The residual U-Net generator helps preserve spatial details during MidSUV synthesis, while adversarial training reduces over-smoothed predictions and improves visual fidelity.
- Stratified results suggest that model performance varies across response groups, indicating the importance of evaluating both absolute SUV prediction and relative response-ratio estimation.
- From a clinical perspective, voxel-wise MidSUV prediction may provide more detailed response information than global metrics and support early treatment evaluation and adaptive dose optimization.

Figure 3. Ground-truth vs. predicted MidSUV maps. Representative Low, Medium, and High response cases are shown from top to bottom. Predictions preserve major metabolic hotspots and tumor boundaries.



CONCLUSIONS

- We developed a cGAN-based framework for voxel-wise prediction of mid-chemoradiation metabolic response in locally advanced NSCLC.
- The model synthesized spatially resolved MidSUV maps from pre-treatment PET SUV and dose distributions, achieving SUV MSE of 2.29, RMSE of 1.34, and Spearman correlation of 0.86 under leave-one-out cross-validation.
- Ablation studies demonstrated that both residual connections and adversarial training contributed to improved prediction performance.
- This framework provides a data-driven tool for early treatment response assessment and may support biologically adaptive radiotherapy.

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