# Prediction of Radiation Pneumonitis Using Deep Learning Applied to Dose–Function Metrics

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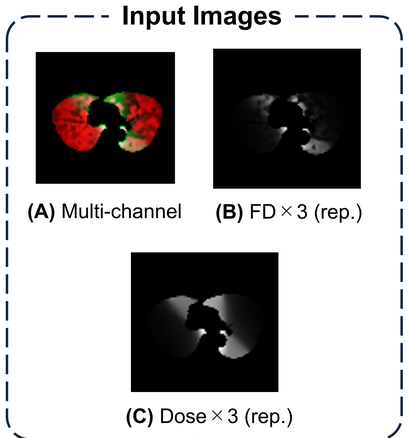
## INTRODUCTION

✓ **Clinical Problem**
- Radiation pneumonitis (RP) occurs in ~30% of lung cancer patients receiving RT [1].
- Grade ≥2 RP mandates ICI discontinuation
  → directly compromises survival [2]

✓ **Research Gap**
- Conventional dose–volume metrics fail to capture spatial dose–function relationships.
- Deep learning models integrating CTVI are promising, but the optimal input strategy remains unestablished [3]

## MATERIALS AND METHODS

✓ **Patient cohort**
- Retrospective study at Komagome Hosp. (IRB No. 2930) and Komazawa Univ. (No. 22-26)
- 95 NSCLC patients (Stage IB–IIIC); 26 (27.4%) developed CTCAE grade ≥2 RP




✓ **Image preprocessing**
- CT ventilation image : Jacobian method
- Down sampling -> Isotropic 4 mm voxel
- Functional dose (FD) = CT ventilation value × Dose

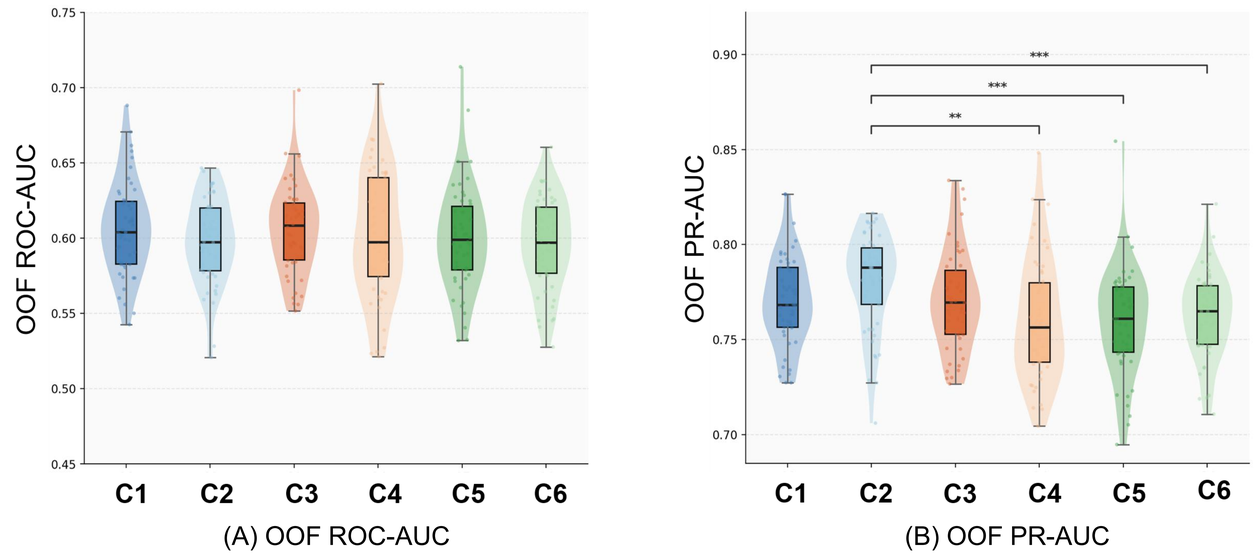
✓ **Input channels** (A)(B)(C)
- Multi-channel model: CT ventilation / Dose / FD
- Single-channel model: FD × 3 (replicated) and Dose × 3 (replicated)

✓ **Deep learning model**
- pretrained on the combined dataset with Kinetics-700 and Moments in Time [4].
- Fine-tuning: layer 3 + layer 4 + Fully connected (FC) layer with Focal Loss (γ = 1.5), Adam, Learning rate = $10^{-5}$ and early stopping (10 epochs, patience = 5)
- Fixed model (ImageNet weights frozen) vs Fine-tuned model

✓ **Classifier**
- FC layer used in fine-tuning only for training the CNN (for Loss / AUC); bypassed afterward
- Features taken up to Layer 4 → Logistic Regression (classical ML)

✓ **Evaluation**
- 50-repeat × 5-fold cross validation
- ROC-AUC, PR-AUC

## RESULTS




(A) OOF ROC-AUC (B) OOF PR-AUC

**Deep learning model training conditions**

| Condition | Input | Fine-tuning |
|---|---|---|
| C1 | CTVI + Dose + FD (3ch) | Fine-tuning |
| C2 | CTVI + Dose + FD (3ch) | None |
| C3 | FD × 3 (rep.) | Fine-tuning |
| C4 | FD × 3 (rep.) | None |
| C5 | Dose × 3 (rep.) | Fine-tuning |
| C6 | Dose × 3 (rep.) | None |

Figure shows violin plots with individual repeat values (n=50) for Out-Of-Fold (OOF) ROC-AUC (A) and OOF PR-AUC (B) across six conditions (C1–C6, defined in the table below) evaluated with Logistic Regression. Box-and-whisker overlays indicate median, interquartile range, and 1.5×IQR. Dashed lines indicate random-classifier baselines (ROC-AUC = 0.50; PR-AUC = 0.274, prevalence). Mean ± SD are shown below each condition. Significance brackets indicate Bonferroni-corrected paired t-tests (30 total comparisons).

**KEY FINDINGS**
- OOF ROC-AUC: 0.596–0.606 across all conditions — **no significant differences** found.
- OOF PR-AUC: C2 (CTVI+Dose+FD, fixed; 0.780 ± 0.026) was significantly higher than C4 (0.760), C5 (0.759), C6 (0.763)
- All conditions exceeded random baselines (ROC-AUC 0.50; PR-AUC 0.274).

## DISCUSSION

- The narrow ROC-AUC range across all conditions suggests a **biological ceiling**; neither input channel nor fine-tuning strategy significantly altered overall discrimination.
- Fine-tuning **reduced PR-AUC**, likely due to overfitting to RP-positive cases. Fixed ImageNet (video-pretrained) features (C2) achieved the highest precision–recall performance without domain-specific training.
- Dose-only inputs (C5, C6) showed the lowest PR-AUC, confirming the **added value of CT ventilation value** beyond dosimetric features alone.
- FD×3ch was equivalent to CTVI+Dose+FD, as FD encodes the **joint functional-dose distribution**, simplifying the preprocessing pipeline without performance loss.

## CONCLUSIONS

- Fixed 3D ResNet-50 (video-pretrained) with CTVI+Dose+FD input achieved **OOF PR-AUC = 0.780**, well above the random baseline (0.274), demonstrating clinical potential for pre-treatment RP risk stratification.
- Functional dose (FD) as a **single-channel input** provides equivalent performance to full 3ch fusion, offering a streamlined pipeline for clinical implementation.
- External validation with larger, multi-institutional cohorts is required before clinical translation (proof-of-concept, n = 95).

## REFERENCES

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