

Predictive modelling for radiation pneumonitis using mid-treatment functional information

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Significance

- Radiation-induced pneumonitis (RP) reduces quality of life for non-small cell lung cancer (NSCLC) patients treated with radiation therapy.
- Improvements in toxicity predictions may lead to reduced rates of RP.
- Limitations of current clinical toxicity models^{1,2}:
 - Lack of functional information
 - Assumed relative biological effectiveness (RBE) of 1.1 for proton therapy patients despite evidence of variable RBE

Hypothesis: Predictive models for RP will demonstrate improved accuracy when variable RBE and lung functional information are incorporated.

Approach

Patient cohort:
72 photon (n=12 with G2+ RP)
38 proton (n=8 with G2+ RP)

Re-calculate proton physical dose using variable RBE using image density change from pre-treatment to post-treatment follow-up CTs

Figure 1 shows a scatter plot of Image Density Change (HU) on the y-axis (ranging from -25 to 150) versus Dose (Gy) on the x-axis (ranging from 0 to 75). Two data series are plotted: PSPT (red dots) and IMRT (blue dots). Both series show a positive linear relationship, with PSPT having a steeper slope than IMRT.

Figure 2 illustrates the workflow for generating voxel-wise ventilation maps. It shows two time points: Planning week (T0 to T5) and Mid-treatment (T0 to T5). For each time point, CT scans are processed through DIR (Deformable Image Registration) to produce ventilation maps. The mid-treatment maps are then used to calculate the change in ventilation from the planning week maps.

Figure 3: Model training and validation workflow for 7/6-fold nested cross validation. The workflow involves Training data and Validation data, leading to Feature selection, Training, Model, Hyper-parameter tuning (grid search), Evaluation, and Results. The process is repeated 6 times for training and 7 times for validation.

Results

Table 1: Model training data for 110 patients and corresponding cross-validation results for area under the curve (AUC) and standard deviation (std) across folds, F1 score, accuracy, sensitivity, and specificity.

Model Name	Training Data	AUC ± Std	F1 Score	Accuracy	Sensitivity	Specificity
CT+Dose	Planning CT Original dose map	0.75 ± 0.08	0.44	0.60	0.90	0.57
CT+RBE	Planning CT Variable RBE-weighted dose map	0.76 ± 0.08	0.42	0.63	0.80	0.62
CT+RBE+VC	Planning CT Variable RBE-weighted dose map Ventilation change data	0.78 ± 0.10	0.45	0.71	0.75	0.77

Final 6 features that demonstrated highest stability:

- V40
- V70
- Mean HU within lung
- First-order entropy within lung CT
- First-order mean absolute deviation within lung CT
- First-order entropy of ventilation change at mid-treatment (excluded from CT+Dose and CT+RBE models)

Random Forest models demonstrated highest performance across all 3 model types

Figure 4 displays Receiver Operating Characteristic (ROC) curves for three models: (a) CT+Dose Model, (b) CT+RBE Model, and (c) CT+RBE+VC Model. Each plot shows the True Positive Rate (Y-axis) versus the False Positive Rate (X-axis). The optimal threshold and AUC values are indicated for each model.

Model	Optimal threshold	AUC
(a) CT+Dose Model	0.36	0.74 ± 0.08
(b) CT+RBE Model	0.39	0.75 ± 0.08
(c) CT+RBE+VC Model	0.49	0.77 ± 0.1

Figure 5 displays Confusion Matrices for three models: (a) CT+Dose Model, (b) CT+RBE Model, and (c) CT+RBE+VC Model. The matrices show the relationship between True Labels (Non-RP, RP) and Predictions (Non-RP, RP).

Model	True \ Predicted	Non-RP	RP
(a) CT+Dose Model	Non-RP	51	39
	RP	2	18
(b) CT+RBE Model	Non-RP	56	34
	RP	4	16
(c) CT+RBE+VC Model	Non-RP	69	21
	RP	5	15

Conclusion

- Demonstrated potential of functional information and variable RBE for improving prediction modeling for pneumonitis.
- Existing studies on predictive modeling with lung functional information mostly focus on incorporating pre-RT ventilation; the use of mid-treatment information may allow for interventions during treatment such as adaptive replanning.
- Future work will incorporate lobe-wise ventilation information and tumor response into predictive models.

References

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