Inter-Fractional Spatiotemporal Dosiomics Improves the Prediction of Local Progression for Patients with Small Cell Lung Cancer / Speaker Center

Xinhui Fu1, Yibao Zhang1, Dawei Liang1 and Jiayi Yu1,
(1)Laboratory Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department of Radiation Oncology, Peking University Cancer Hospital & Institute, Beijing 100142 China, Beijing, China

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ABSTRACT

Purpose: To evaluate whether incorporating inter-fractional spatiotemporal dose variations improves the prediction of local progression in patients with small cell lung cancer (SCLC).

Methods: A total of 144 patients from a registered phase III trial were analyzed. Six weekly cone-beam CTs (CBCTs) per patient were used to generate registered CTs and recalculate fraction-specific dose distributions. Dosiomics features were extracted from the planned and recalculated dose maps. Delta-dosiomics represented feature changes relative to the planned dose, and the six delta matrices were stacked to construct an accumulative spatiotemporal signature. Following feature selection and principal component analysis, logistic regression models were evaluated using five-fold cross-validation. Local progression-free survival (LPFS) was assessed using Kaplan–Meier analysis.

Results: The accumulative delta-dosiomics model achieved an AUC of 0.81 ± 0.08 and a PR_AUC of 0.76 ± 0.08, outperforming the planned-dose model with an AUC of 0.73 ± 0.11 and a PR_AUC of 0.65 ± 0.14. Both signatures significantly stratified LPFS risk groups ($p < 0.001$), with greater separation using the accumulative model.

Conclusion: Inter-fractional spatiotemporal dosiomics improves local progression prediction and may support adaptive radiotherapy and individualized follow-up.

CONTACT

Zhang Yibao
Laboratory Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education/Beijing), Department of Radiation Oncology, Peking University Cancer Hospital & Institute, Beijing, China,
zhangyibao@pku.edu.cn
(010)-88196218

INTRODUCTION

Planned dose distributions do not account for anatomical changes occurring during multi-fraction radiotherapy. These changes may cause clinically relevant deviations between planned and delivered dose distributions, potentially limiting the prognostic value of conventional dosiomics. Serial CBCT provides temporal anatomical information throughout treatment. We therefore developed an accumulative delta-dosiomics approach to quantify spatiotemporal dose changes and evaluated its ability to predict local progression in SCLC.

METHODS AND MATERIALS

This retrospective study included 144 patients with SCLC from a registered phase III clinical trial. Patients were divided into training and testing cohorts at an 8:2 ratio, and five-fold cross-validation was used to evaluate model robustness.

For each patient, six weekly CBCT scans were used to generate registered CTs representing inter-fractional anatomical changes. The original treatment plan was recalculated on each registered CT. A common overlapping region across all CBCT scans was used as the region of interest.

A total of 1,316 dosiomics features were extracted from the planned and fraction-specific dose distributions. Delta-dosiomics features were calculated as the differences between each recalculated dose map and the planned dose map. The six delta feature matrices were subsequently stacked to construct the accumulative spatiotemporal signature.

Features were standardized, filtered using correlation analysis and univariate statistical testing, and reduced using principal component analysis. Logistic regression models were evaluated using AUC and PR_AUC. Kaplan–Meier and log-rank analyses were used for LPFS risk stratification.

Table 1. Patient characteristic and follow-up outcome.

Status	Total (%)	Male	Female	Age (years)	LPFS (months)
Total	144	105	39	64(58~70)	33.00±19.33
LPFS (0)	88 (61%)	61	27	62(56~68)	40.73±18.00
LPFS (1)	56 (39%)	44	12	66(59~74)	20.86±14.58

Abbreviations: LPFS= Local Progression-Free Survival. No local progression is marked as 0, while the occurrence of local-regional recurrence or death is marked as 1.

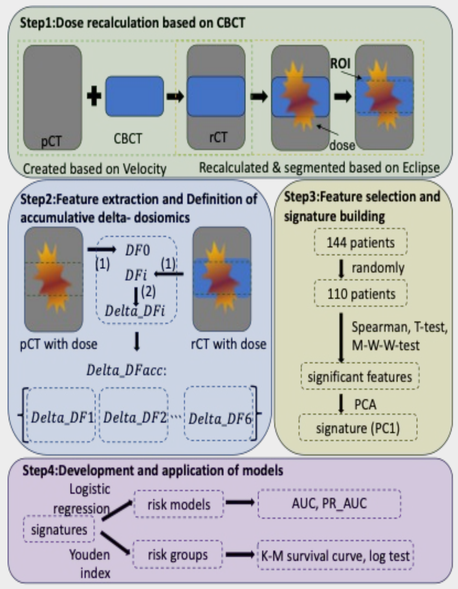

Figure 1. The flow chart of this study. (1) represents the extraction of dose distribution within the ROI based on the pyradiomics package; (2) represents the derivation of Delta-DF based on the defined formula, by acquiring DF within the ROI on pCT and rCT.
Abbreviations: DF0 = dosiomics features from dose map based on pCT; DFi = dosiomics features from dose map based on the i-th rCT; M-W-W-test = Mann-Whitney-Wilcoxon test; PCA = principal component analysis; pCT = planned CT; rCT = registered CT.

RESULTS

Among the 144 patients, 56 patients experienced local-regional progression or death, whereas 88 remained free from local progression during follow-up.

The accumulative delta-dosiomics model achieved the highest predictive performance, with an AUC of **0.81 ± 0.08** and a PR_AUC of **0.76 ± 0.08**. In comparison, conventional dosiomics based on the planned dose distribution achieved an AUC of **0.73 ± 0.11** and a PR_AUC of **0.65 ± 0.14**.

The accumulative model also outperformed all six individual fraction-specific delta-dosiomics models, whose AUCs ranged from 0.72 to 0.78.

Both the accumulative and conventional signatures significantly separated patients into high- and low-risk LPFS groups (log-rank $p < 0.001$). Greater risk-group separation was observed with the accumulative signature, with an HR of 0.222 compared with 0.291 for the planned-dose signature.

Table 2. Model performance using various significant features.

Single Model	Significant features	AUC	PR_AUC
DF0	21	0.73±0.11	0.65±0.14
Delta_DF1	37	0.72±0.05	0.61±0.10
Delta_DF2	50	0.73±0.05	0.67±0.07
Delta_DF3	33	0.73±0.13	0.66±0.11
Delta_DF4	43	0.78±0.08	0.71±0.07
Delta_DF5	35	0.74±0.10	0.64±0.04
Delta_DF6	62	0.74±0.10	0.67±0.09
Delta_DFacc	260	0.81±0.08	0.76±0.08

Abbreviations: AUC = Area Under the Curve, PR_AUC = Area Under the Precision-Recall Curve.

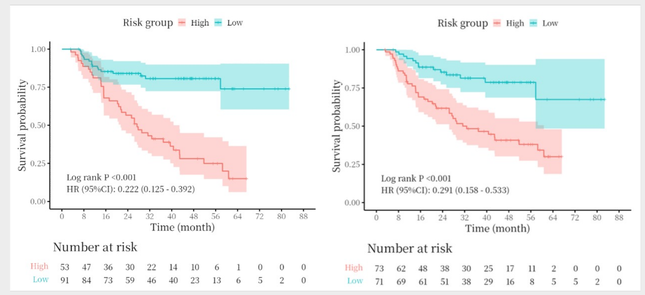

Figure 2. Local progression-free survival curves of the high- and low-risk groups stratified by the different signatures in different risk groups.
(a) accumulative delta dosiomics signature; (b) conventional dosiomics signature based on planned dose distribution.

DISCUSSION

The findings demonstrate that inter-fractional dose variations contain prognostic information that is not captured by the planned dose distribution alone. Accumulating dose-feature changes across the treatment course provided better predictive performance than either conventional planned-dose dosiomics or any single fraction-specific model.

This approach may help identify patients at increased risk of local progression who could benefit from adaptive radiotherapy, intensified treatment, or closer post-treatment surveillance. However, further validation using independent multicenter cohorts is required. Additional limitations include the weekly CBCT acquisition frequency and the restricted CBCT field of view, which may limit complete dose reconstruction.

CONCLUSIONS

Accumulative delta-dosiomics based on serial CBCT dose reconstruction improved local progression prediction and LPFS risk stratification in SCLC compared with conventional planned-dose dosiomics. Inter-fractional spatiotemporal dose changes may serve as a practical biomarker for precision radiotherapy and personalized follow-up.

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