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Integrated Clinico-Radiomic Nomogram for Predicting Disease-Free Survival (DFS) in Stage I and II Non-Small Cell Lung Cancer

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Background: Early stage non-small cell lung cancer (ES-NSCLC) comprises about 45% of all NSCLC patients, with 5-year survival ranging between 30-49%. Surgical resection is the standard of care curative modality in these patients but about 30-55% of patients often recur following surgery within the first 3 years. There is currently no validated method to stratify patients based on their risk of recurrence following surgery in these patients. In this project, we develop and validate a nomogram using a combination of CT-derived radiomic textural features and clinico-pathologic factors, in order to predict DFS in ES-NSCLC.

Method: This study comprised 350 ES-NSCLC patients from two different institutions who underwent surgery (75 patients relapsed). Radiomic textural features were extracted from tumor region (Intratumoral - IT) as well as from the anular ring shaped peritumoral region (PT) with 3mm as a ring thickness and extending 9 mm outside the nodule. A total of 124 features from Gabor, Laws, Laplace, Haralick and Collage feature families were extracted from IT and each PT ring for all patients. The most stable, significant and uncorrelated features were selected from D1 (N=221) and used to build a Lasso-regularized multivariate Cox-regression model to generate a Radiomic Risk Score (RRS) derived from weighted Lasso coefficients. Further, RRS was integrated with clinicopathologic variables (Lympho-vascular invasion LVI and AJCC stage) which were independently predictive on DFS in multivariate analysis to build a CT-derived model. A nomogram was constructed to visually assess the differences between the individual and integrated model.

Result: Top 6 Radiomic features included 2 IT and 4 PT features from the Haralick and Collage feature families. In predicting DFS, While QH model comprised 6 nuclear shape and graph features. In predicting DFS, While Radiomic model had a HR of 2.4 (p<0.01) with C-index of 0.74, the Radiomic and QH model yielded a C-index of 0.78 (p<0.01). After addition of prognostic clinical factors (LVI, AJCC stage) to the model, the C-index was 0.80, almost doubling either modalities alone. The constructed nomogram visualized the apparent benefits of the three models while a decision curve clearly demonstrated the increased benefit of combined integrated model.

Conclusion: Addition of prognostic clinical factors (LVI, AJCC stage) improved the performance of the Radiomic Risk Score model in order to accurately predict DFS in ES-NSCLC patients undergoing surgery.

Keywords: Early stage non-small cell lung cancer, prognostic biomarker, Radiomics

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Integrating CT Radiomic & Quantitative Histomorphometric Whole Slide Image Features Predicts Disease Free Survival in ES-NSCLC

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Background: Early-stage non-small cell lung cancer (ES-NSCLC) accounts for approximately 40% of NSCLC cases, with 5-year survival rates varying between 31-49%. Radiomic textural features from pretreatment CT scans and QH features from H&E stained WSIs have been shown to be independently prognostic of outcome. With diagnostic CT scans and surgical resection, the standard of care in ES-NSCLC, in this work we seek to take a multimodality approach using routine imaging to improve the predictive performance in determining DFS following resection.

Method: A retrospective chart review of Stage I and II (ES-NSCLC) pts undergoing surgical resection between 2005-14 with available CT and resected tissue yielded 70 pts. A total of 248 radiomic CT textural features from inside the tumor (Intratumoral—IT) and outside the tumor (Peritumoral—PT) and 242 QH features related to the nuclear shape, texture and spatial orientation and architecture from H&E WSI were extracted. We developed two risk models, Radiomic and QH using the most stable, discriminative and uncorrelated features from CT and QH respectively determined by Lasso-regularized Cox regression to predict Disease free survival (DFS). Model performances were analyzed using Hazard Ratios (HR), Concordance Index (C-index) and Decision curve analysis. We built a nomogram to calculate the DFS based around the individual models as well as an integration of the QH and Radiomic models.

Result: Top 6 Radiomic features included 2 IT and 4 PT features from the Haralick and Collage feature families. The QH model comprised 6 nuclear shape and graph features. In predicting DFS, While the Radiomic model had a HR of 2.4 (p<0.01) with C-index of 0.67, the QH model had HR = 3.1 (p<0.01) with C-index = 0.74. Integration of the Radiomic and QH model yielded a C-index of 0.78 (p<0.01). After addition of prognostic clinical factors (LVI, AJCC stage) to the model, the C-index was 0.80, almost doubling either modalities alone. The constructed nomogram visualized the apparent benefits of the three models while a decision curve clearly demonstrated the increased benefit of combined integrated model.

Conclusion: Integration of CT-derived radiomic and tissue-derived QH features was found to show improved performance in predicting DFS when compared to either radiomics or QH alone.

Keywords: ES-NSCLC, Radiomic, Pathomic

Figure: a) Nomogram representing integrated Rad-Path risk score for predicting DFS; b) Decision curve analysis showing net benefit for the integrated model. The combined Radiom-Path clinical model had the highest net benefit; c) QH nuclear shape feature and radiomic peritumoral Haralick feature heatmaps showing difference between high-risk and low-risk groups; d) Table for individual prognostic clinical factors, and integrated (Rad-Path and Rad-Path Clinical) models.