

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

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**Objectives:** Integration of computer extracted quantitative features from routine radiographic as well as pathology tissue images can provide a non-invasive way to stratify patients based on their risk of recurrence in early stage non-small cell lung cancer patients treated with curative resection.

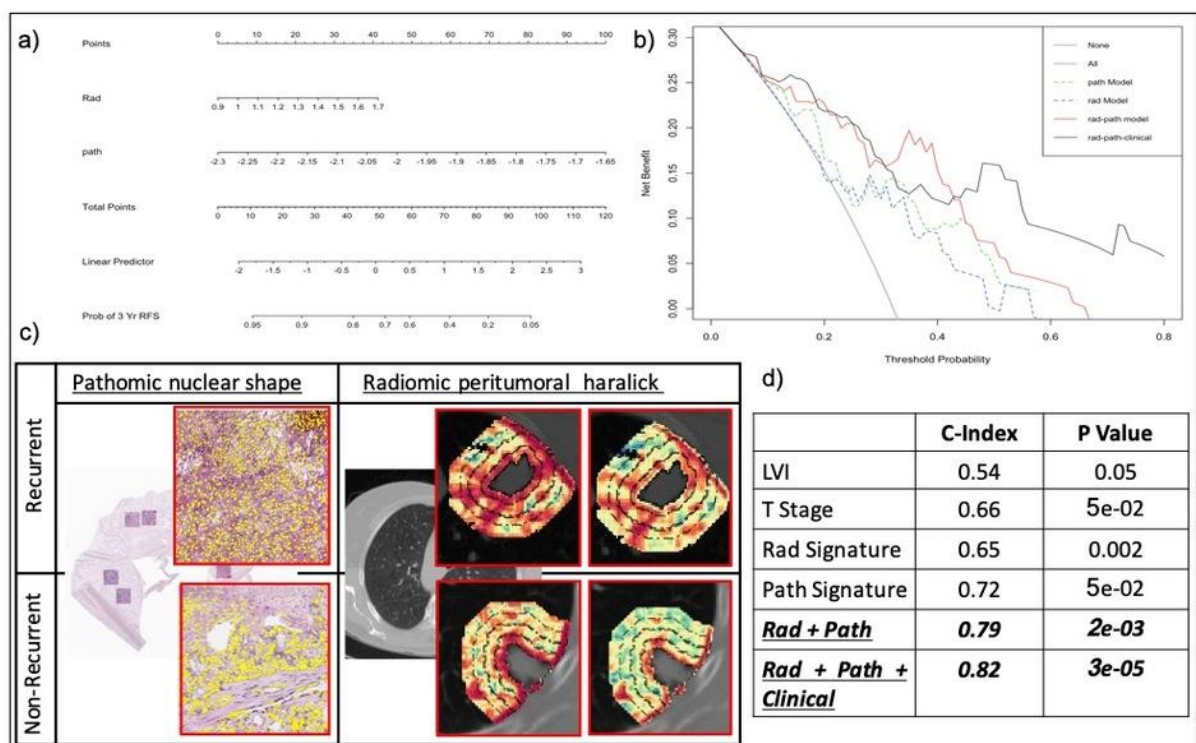
**Background:** Early-Stage non-small cell lung cancer (ES-NSCLC) accounts for approximately 40% of NSCLC cases, with 5-year survival rates varying between 31-49%. Radiomic textural features from pre-treatment CT scans and QH features from H&E stained WSIs have been shown to be independently prognostic 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.

**Methods:** 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 WSI 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.

**Results:** Top 6 Radiomic features included 2 IT and 4 PT features from the Haralick and Collage 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

– 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 RFS when compared to either radiomics or QH alone.



**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 Rad-Path-clinical model had the highest net benefit; c) QH nuclear shape feature and radiomic peritumoral Haralick feature heatmeps 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.