Could Simplified Deep Learning be More Generalizable? Predicting Recurrence-Free Survival in Head and Neck Cancer With and Without Tumor Segmentation

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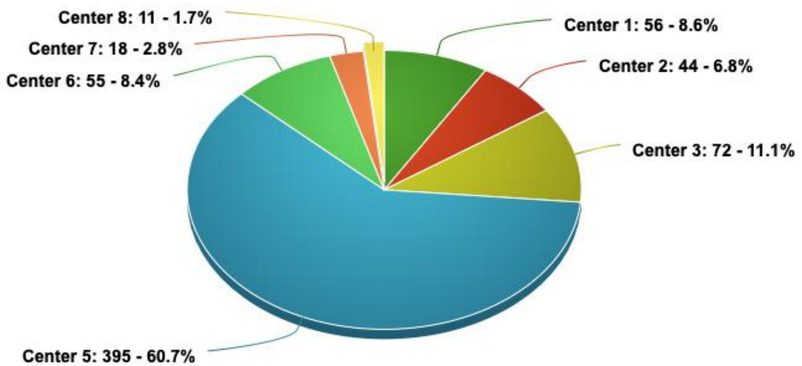
Introduction

- Head and Neck Cancer (HNC) accounts for over 900,000 new cases and 400,000 deaths annually worldwide, making it one of the most prevalent malignancies.
- Despite advances in radiotherapy and chemotherapy, recurrence rates remain high (30–50%), emphasizing the need for accurate recurrence-free survival (RFS) prediction.
- RFS prediction can help tailor care where low-risk patients may benefit from reduced chemotherapy or surveillance while high-risk patients can receive closer monitoring and timely intervention.
- Many deep learning models rely on segmentation-derived tumor features which require expert annotation. This study investigates whether a simplified multimodal model using only PET/CT and clinical data can achieve comparable predictive performance while improving generalizability.

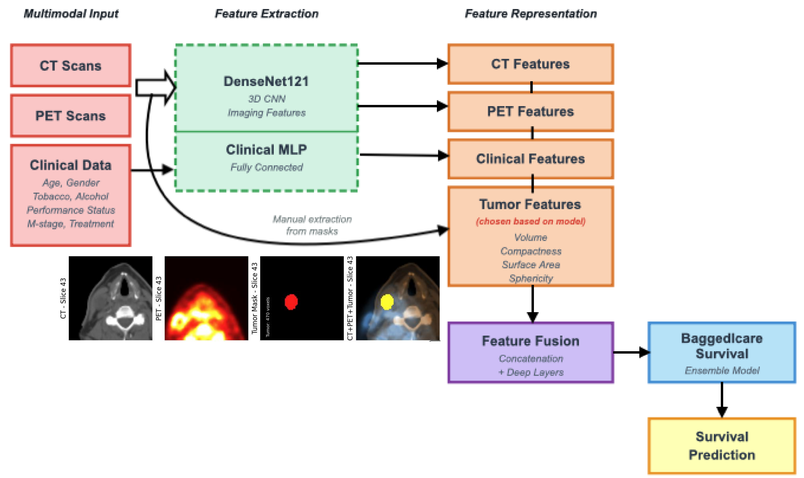
Dataset Description

- The dataset was obtained from the HECKTOR 2025 Challenge, including 651 FDG-PET/CT scans and clinical data from 7 international centers.
- PET and CT images were co-registered, resampled to 1 mm, cropped around tumors, and z-score normalized.
- Clinical variables included age, gender, tobacco, alcohol, performance status, M-stage, HPV status, treatment, and all were standardized.
- Performance status was grouped as Functional (ECOG 0–1 / Karnofsky 80–100) or Restricted (ECOG 2–4).
- Tumor features such as volume, surface area, compactness, and sphericity were extracted from segmentation masks and min–max normalized.
- The cohort had a 20.3% event rate, with 132 relapses and 519 censored cases, providing a balanced 4:1 ratio suitable for survival analysis.

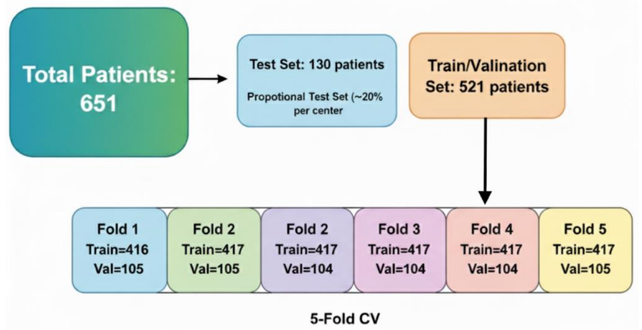


Methodology

We developed a four-stage multimodal deep learning pipeline integrating CT, PET, and clinical data for recurrence-free survival prediction, combining feature extraction, fusion, and ensemble survival modeling to capture both anatomical and clinical prognostic information.



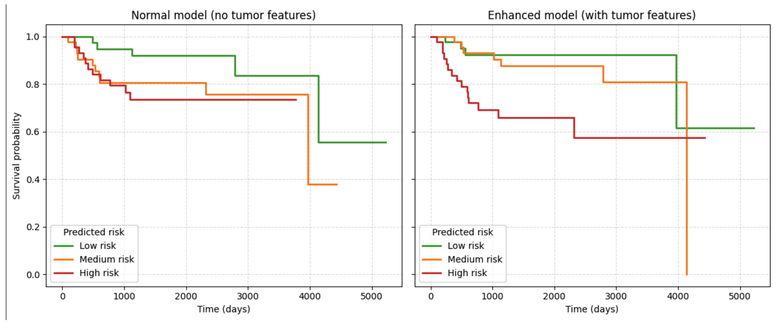
- **Stage 1** – *Multimodal Input*: Integrated co-registered FDG-PET/CT scans with key clinical variables (age, gender, tobacco, alcohol, performance status, M-stage, treatment, HPV status).
- **Stage 2** – *Feature Extraction*: Imaging features were derived using DenseNet121 (3D CNN) and clinical features via a fully connected MLP, with tumor features manually extracted from segmentation masks.
- **Stage 3** – *Feature Fusion & Representation*: Extracted CT, PET, clinical, and tumor features were concatenated to form a unified deep representation.
- **Stage 4** – *Survival Prediction*: The fused features were used in a Bagged ICARE survival ensemble for patient-level recurrence-free survival estimation.
- A stratified center-wise split ensured ~20% of patients per center in the test set (130 total) and 5-fold cross-validation on 521 remaining patients for robust evaluation.



Results

- Model performance was evaluated using the Concordance Index (C-index) and Kaplan–Meier (KM) survival curves.
- The C-index measures how well the model ranks patients by recurrence risk where higher values indicate better agreement between predicted and actual survival orderings.
- The Kaplan–Meier curves visualize patient survival over time, grouped into low, medium, and high predicted-risk tertiles. Greater vertical separation between curves reflects stronger discrimination.

Model type	Mean Validation C-index	Mean Test C-index	Best Validation C-index	Best Test C-index
With Tumor Features	0.6644	0.6603	0.7248	0.6791
Without Tumor Features	0.6371	0.5533	0.6968	0.6367



- ✓ The enhanced model (with tumor features) achieved higher mean C-index values and clearer high-risk separation on KM plots, showing improved early recurrence prediction.
- ✓ The simpler model (without tumor features) remained competitive and more generalizable across centers despite slightly lower C-index performance.

Conclusion

Tumor features enhanced recurrence-free survival prediction and improved the C-index, confirming their prognostic value. However, the simpler PET/CT + clinical model achieved comparable performance and remains more generalizable for real-world clinical deployment where segmentation data may be unavailable.