

# An AI-Driven Random Survival Forest Model for Predicting Cancer-Specific Survival in Pediatric Neuroblastoma: A SEER Analysis

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## Background

- Neuroblastoma (NB) is one of the most common extracranial solid tumors in children, affecting about 1 per 10,000 children annually and accounting for about 15% of pediatric cancer deaths.<sup>1-3</sup>
- Considerable tumor and outcome heterogeneity characterize NB.<sup>1-4</sup> The 5-year survival rate ranges from 75-98% for patients with low- and intermediate-risk disease, while for those with high-risk disease, it is less than 50%.<sup>1,2</sup>
- Despite this heterogeneity, conventional risk stratification methods are limited and consider few clinical factors.<sup>2,4</sup>
- This study aimed to develop an artificial intelligence (AI)-based random survival forest (RSF) model to predict survival in pediatric NB.

## Methods

- Data Source:** Surveillance, Epidemiology, and End Results (SEER) registry from 2004-2022.
- Analytic Sample:** Children aged less than 18 years with a histologically confirmed, primary diagnosis of NB or ganglioneuroblastoma (GNB).
- Outcome:** Survival at 1, 3, and 5 years.
- Features:** Demographic factors, clinical characteristics, and treatment history (Table 1).
- Feature Engineering:** One-hot encoding (categorical), unknown/missingness flags, harmonization (tumor size, grade), discretization (tumor size), category grouping (primary site, tumor stage, radiation, surgery).
- Models:** RSF vs. Cox proportional hazards (CoxPH)
- Model Tuning:** 80%/20% train/test split, followed by hyperparameter tuning and 5-fold cross-validation using Python.
- Evaluation Metrics:** Concordance index (C-index), area under the receiver operating characteristic curve (AUROC), integrated Brier score, and decision curve analysis (DCA).
- Sensitivity Analysis:** RSF complete-case analysis.

Table 1. Model Features

Feature Type	Feature
Demographic factors	<ul style="list-style-type: none"> <li>Age (0-17 years)</li> <li>Race/ethnicity (Non-Hispanic white, Non-Hispanic black, Non-Hispanic other, Hispanic)</li> <li>Sex (male, female)</li> </ul>
Clinical characteristics	<ul style="list-style-type: none"> <li>Primary site (adrenal, mediastinum/other respiratory, retroperitoneum, soft tissue, other)</li> <li>Tumor grade (1-4, unknown)</li> <li>Tumor size (≤5 cm, 5.1-10cm, 10.1-15cm, &gt;15cm)</li> <li>Summary stage (localized, regional, distant, unknown)</li> </ul>
Treatment history	<ul style="list-style-type: none"> <li>Chemotherapy (yes, no evidence of)</li> <li>Radiation (yes, no evidence of)</li> <li>Surgery – primary site (tumor resection, local tumor destruction, surgery not otherwise specified [NOS], none)</li> <li>Surgery – regional lymph nodes (1-3, &gt;4, none, other [biopsy, unknown])</li> <li>Surgery – other (yes, no, unknown)</li> </ul>

## Results

- 3,557 pediatric patients with NB CI were included in the study.
- The RSF model outperformed the CoxPH model in terms of C-index, AUROC, and integrated Brier score (Table 2, Figure 1).
- Furthermore, DCA revealed that the RSF model demonstrated positive clinical utility in predicting 1-, 3-, and 5-year survival compared to the CoxPH model (Figure 2).

Table 2. Performance Evaluation: RSF vs. CoxPH

Evaluation Metric	C-index	1-year AUROC (95% CI)	3-year AUROC (95% CI)	5-year AUROC (95% CI)	Integrated Brier score
RSF	0.80	0.80 (0.75-0.86)	0.79 (0.76-0.83)	0.80 (0.77-0.83)	0.12
CoxPH	0.77	0.76 (0.70-0.82)	0.76 (0.72-0.79)	0.78 (0.75-0.81)	0.13
RSF (Sensitivity)	0.79	0.79 (0.70-0.88)	0.77 (0.71-0.83)	0.78 (0.73-0.84)	0.12

Figure 1. Survival Prediction Accuracy: RSF vs. CoxPH

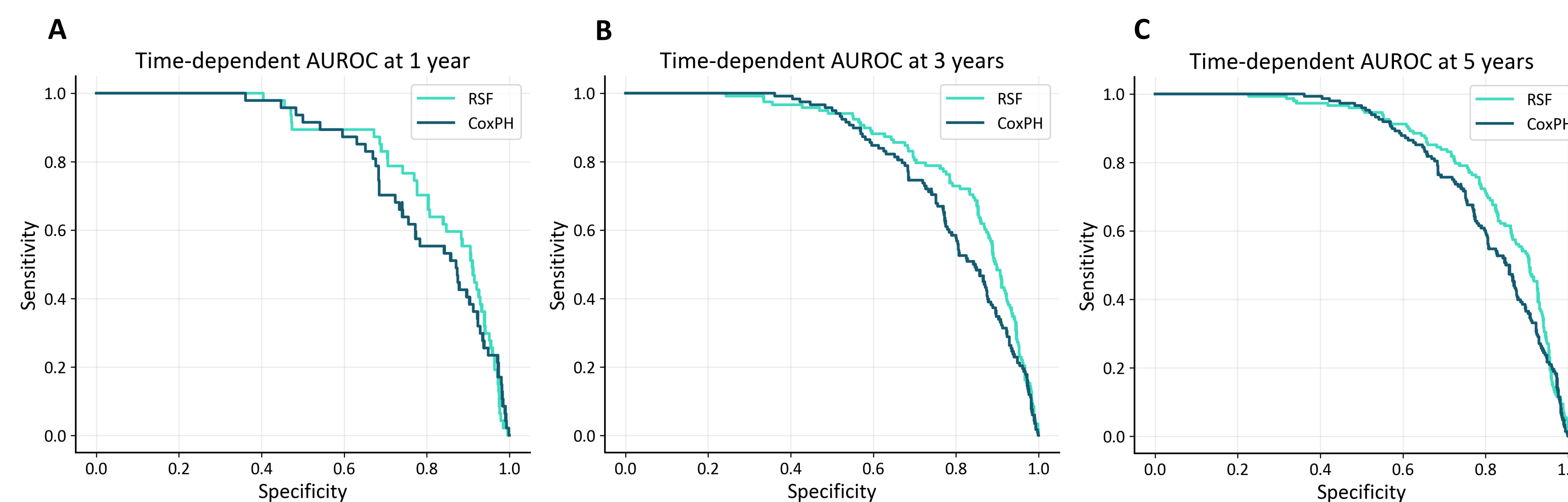


Figure 2. Clinical Utility: RSF vs. CoxPH

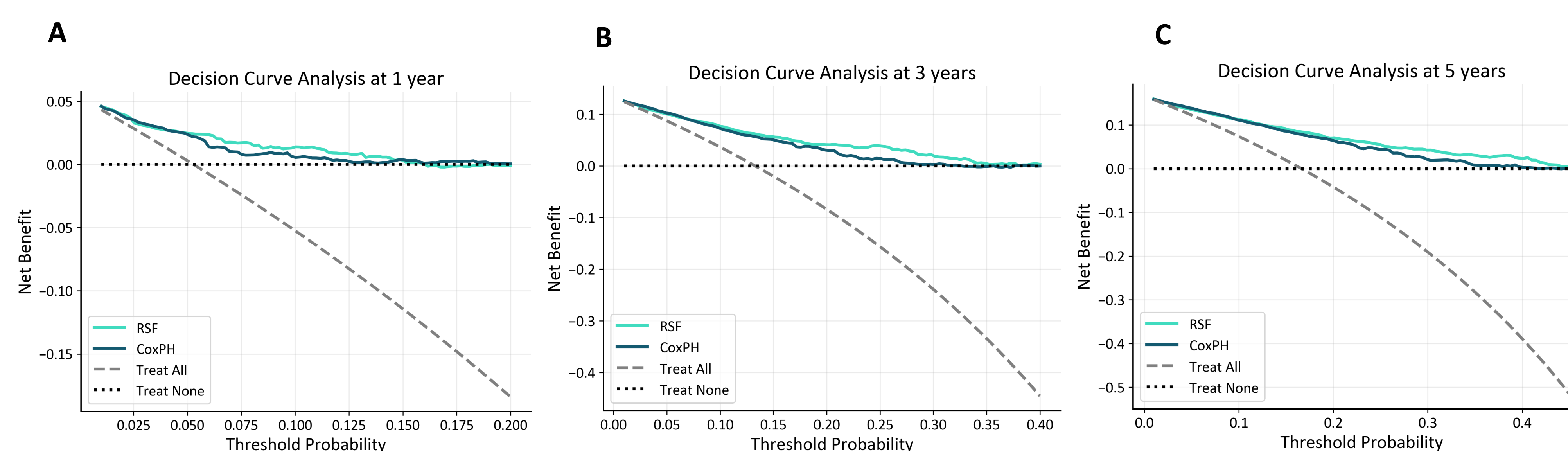
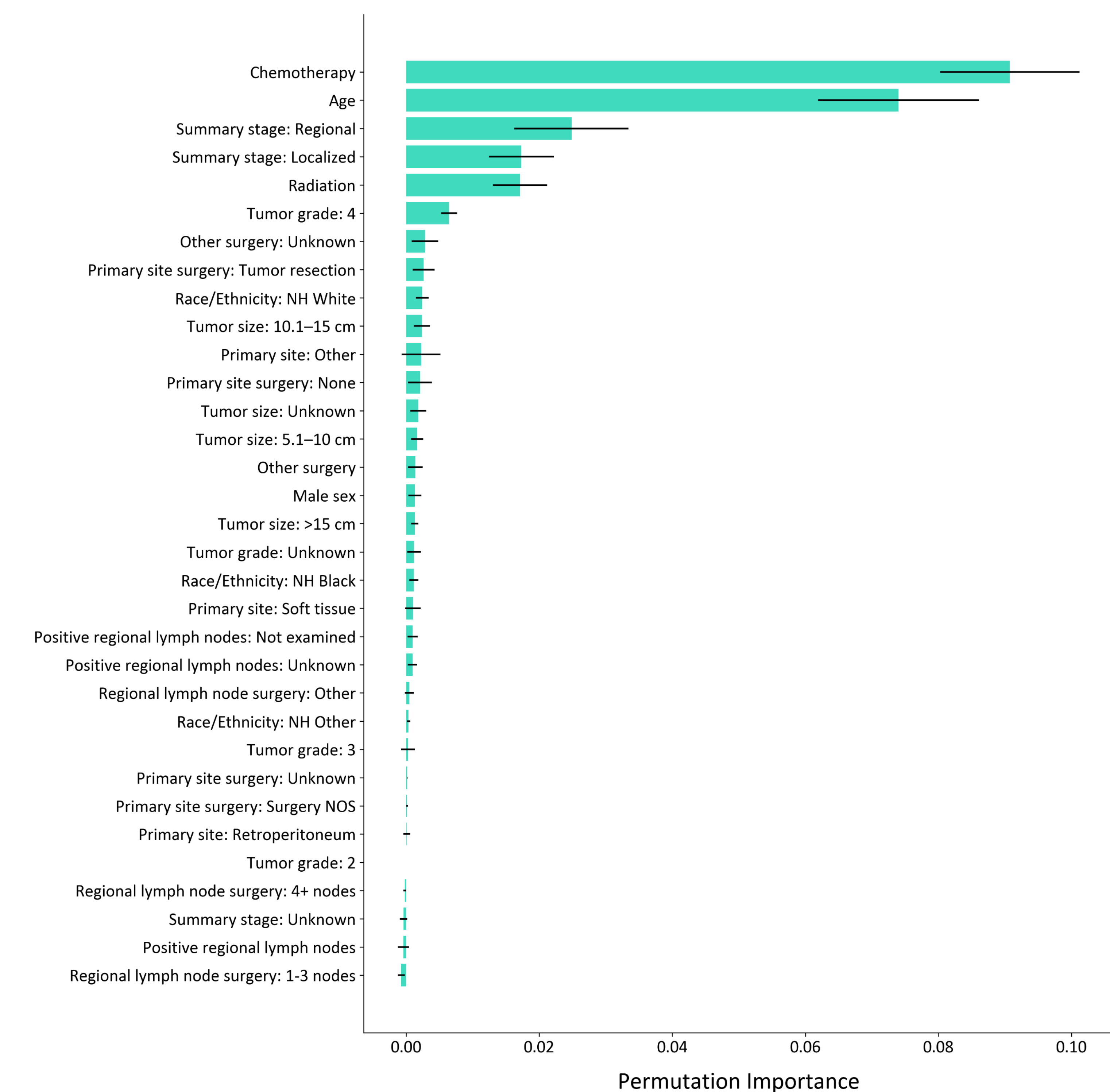


Figure 3. RSF Permutation Importance



Note: Error bars represent standard deviation of permutation importance across multiple shuffles. NH: Non-Hispanic; NOS: not otherwise specified.

- Permutation feature importance revealed that chemotherapy status was most predictive of survival, followed by age, summary stage, radiotherapy status, and tumor stage (Figure 3).

## Conclusions

- Despite marked heterogeneity in the clinical presentation and prognosis of pediatric NB, existing approaches to risk stratification are limited.
- This study demonstrates the potential of AI-based approaches using publicly available data to predict pediatric NB survival.
- Initial data suggest the potential superiority of RSF over CoxPH.
- With external validation, RSF models could inform clinical decision-making and improve patient outcomes.

## References

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