Title: DEVELOPING AGE-SPECIFIC BASAL CELL CARCINOMA RISK PREDICTION MODELS AMONG SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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Background and aims: Basal cell carcinomas (BCCs) represent >50% of subsequent neoplasms among long-term childhood cancer survivors. Surgical excision is the primary treatment, so late detection can result in excessive scarring and disfigurement. We aim to develop age-specific BCC risk prediction models for survivors that may inform screening periodicity.

Methods: Risk prediction models for subsequent BCCs by ages 40, 45, and 50 years were developed using data from five-year survivors in CCSS. Predictors included: demographics; cancer diagnosis/age; treatment decade; body region-specific radiotherapy (RT) doses; hematopoietic cell transplantation (HCT); and chemotherapy drugs/doses. XGBoost (eXtreme Gradient Boosting) performed best among evaluated statistical algorithms. To assure generalizability, we assessed nested cross-validated age-specific prediction performance metrics (AUROC/AUPRC: area under the receiver operating characteristic curve/precision-recall curve). We compared models with Children's Oncology Group Long-Term Follow-Up Guidelines (COG LTFU, v6.0) recommending yearly dermatologic screenings following any RT or HCT.

Results: Among 23,091 survivors, 1,148 developed BCC, with estimated prevalence of 7%, 13%, and 22% by ages 40, 45, and 50. Age-specific XGBoost algorithms showed good discrimination (AUROC=0.76-0.81) and precision (AUPRC=0.22-0.64), improving with increasing age cutoffs. Important predictors included diagnosis age, and doses of cranial/neck RT, alkylators, and anthracyclines. BCC prevalence by age 50 was 6%, 21%, and 66%, respectively, in low (<10%), medium (10-49%), and high (≥50%) model-predicted risk groups. In comparison, the COG LTFU guideline-based classification performed significantly worse across all ages (AUROC=0.61-0.65, P<0.01; AUPRC=0.09-0.27, P<0.01). Among survivors recommended for screening per COG LTFU, re-classification rates to low risk using our XGBoost model were substantial (65% at 40y; 21% at 50y). Importantly, 23% not recommended for screening by age 50 were re-classified as higher risk.

Conclusion: Once validated in the St. Jude Lifetime Cohort, implementation of our subsequent BCC risk prediction models will inform more accurate risk-/age-based screening recommendations, which are not currently available for this high-risk population.