Department of BIOMEDICAL ENGINEERING
THE UNIVERSITY OF UTAH

Using prognostic biomarkers for risk stratification to assign therapeutic intensity in neuroblastoma

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Sorenson Molecular Biotechnology Building (USTAR Bldg) – 2nd Floor

Abstract: Neuroblastoma is the most common extracranial solid tumor of childhood, with about 800 children diagnosed annually in North America. Clinical features and outcome for neuroblastoma are quite heterogeneous, providing opportunities to identify statistically and clinically distinct patient subgroups. Using prognostic biomarkers, patients can be classified as having low-risk, intermediate-risk, or high-risk disease. Almost all low- and intermediate-risk children can be cured of their disease with current treatment approaches, whereas children with high-risk neuroblastoma have ~60% overall survival at 3-years post-diagnosis. Treatment for patients classified as low-risk is limited to surgery and observation, while high-risk patients receive 5-6 cycles of intensive chemotherapy, radiation and MIBG, hematopoietic stem cell transplant, and immunotherapy, over a period of 18-24 months. Accurate statistical risk stratification is important so that a child is not over- or under-treated.

Event-free survival (EFS), defined as the time from diagnosis until the first occurrence of an event (disease relapse, progression, secondary malignancy, or death from any cause), has been the endpoint most frequently used to identify neuroblastoma prognostic biomarkers. Several statistical approaches for risk stratification will be presented, including, a) univariate (log rank test) and multivariable (Cox proportional hazards regression) models to identify factors prognostic of EFS; b) supervised recursive partitioning to identify statistically and clinically distinct patient subgroups; and, c) a nomogram to estimate the probability of survival at 3 years post-diagnosis. Examples of these techniques will be presented, including the International Neuroblastoma Risk Groups (INRG) classification, the Adaptive Clinical Neuroblastoma Risk Groups (ACNRG) classification, and a nomogram within high-risk neuroblastoma.

Bio: Dr. London is a Professor of Pediatrics, Harvard Medical School, and the Director of Biostatistics in the Division of Pediatric Hematology/Oncology at Dana-Farber Cancer Institute and Boston Children's Hospital. She is the Director of the Survey and Qualitative Methods Core, Dana-Farber/ Harvard Cancer Center. Dr. London was awarded her PhD in Biostatistics from Virginia Commonwealth University, Medical College of Virgina, in 1997. She has >25 years of experience in design, conduct, analysis, and reporting of clinical trials and biological studies in pediatric cancer. Dr. London serves as a member of the Children's Oncology Group (COG) Neuroblastoma Steering Committee, and was Lead Statistician for the COG Neuroblastoma Committee (1998-2014). She collaborated/designed/conducted phase 3 trials in high-risk neuroblastoma that set a new standard of care: FDA approval of the immunotherapy, dinutuximab, and superiority of two autologous stem cell transplants. Dr. London was instrumental in developing the COG Neuroblastoma Virtual Tumor Bank of specimen, biology, and outcome data, and developed automated systems for assigning risk group (treatment intensity).

Dr. London's research focuses on the identification of prognostic biomarkers in neuroblastoma, and applying them to create and improve risk stratification for the assignment of treatment intensity for children with neuroblastoma, at diagnosis and relapse. She chairs the Statistics Committee of the International Neuroblastoma Risk Groups (INRG) task force, where she collaborated to develop a global system for pre-treatment risk stratification and the INRG Data Commons.

Dr. London is a member of the Cellular, Tissue, and Gene Therapies Advisory Committee of the Food and Drug Administration (2023-27) and the NIH/NCI Therapeutic Immune Regulation (TIR) Study Section (2022-26). She served as a permanent member of the NIH/NCI Clinical Oncology Study Section (2006-10), on NIH/NCI Immunotherapy Study Section (2022-23), on NIH/NCI Subcommittee H in review of the cancer cooperative groups, and on the American Society of Clinical Oncology (ASCO) program committee (2014-16). She is a member of the editorial board of the Journal of the National Cancer Institute (2020-present), and was a member of the Journal of Clinical Oncology editorial board from 2013-2020. She has been a faculty member of the American Association for Cancer Research/American Society of Clinical Oncology (AACR/ASCO) Methods in Clinical Cancer Research Workshop since 2011, and is currently a workshop co-chair (2024-26).