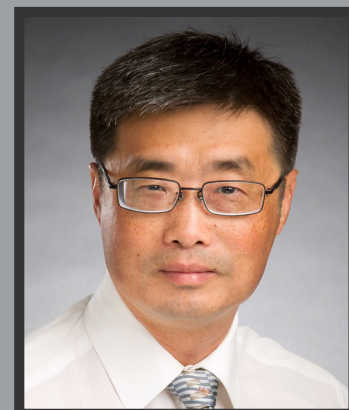


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NONPARAMETRIC FAILURE TIME ANALYSIS: THINKING OUT OF THE "COX-REGRESSION BOX" IN GENOMIC APPLICATIONS

ABSTRACT:

Genome-wide Association Study (GWAS) has become routine in oncology genomic translational research. GWAS often requires genome-wide screening to identify ordinal or continuous genomic features that are associated with long-term treatment outcome; for example, single nucleotide polymorphisms associated with time to cancer relapse. The estimated coefficient of a hazard rate regression model (HRRM, such as Cox's model) has been a popular choice for a statistic to test for such associations. It will be demonstrated in this talk that in certain circumstances one runs into trouble with the HRRM approach. Motivated by this problem, a robust, completely nonparametric approach using Pearson's or rank-based correlation has been developed. This method, called correlation profile test (CPT), is formed by the correlation profile statistic coupled with an accurate hybrid permutation test that combines permutation and asymptotic distribution. Statistical performances of CPT are compared with a few established methods by a simulation study and an analysis of a real GWAS dataset. It is shown that in cases where the proportional hazards assumption does not hold, CPT is much superior to the HRRM approach in terms of possessing higher statistical power and maintaining the nominal significance level. Only in the scenarios where the proportional hazards model holds exactly or approximately can CPT be inferior to the HRRM approach. Some analytical insight into this performance pattern will be presented. In summary, CPT is a complementary alternative to the HRRM approach in testing associations between two random variables one of which is a failure time subject to right censoring.

BIO: Dr. Cheng Cheng is a Member (Professor) of the Department of Biostatistics and the Comprehensive Cancer Center of St. Jude Children's Research Hospital. He collaborates with investigators in the Hematological Malignancies Program and academic departments by providing statistical expertise in study designs and data analyses for clinical trials, laboratory experiments, and publications in peer-reviewed journals. He received his PhD in Statistics from Texas A&M University in 1993 under the advisement of the late Emanuel Parzen, and then became a Postdoctoral Fellow at Upjohn Laboratories before joining Johns Hopkins University as an Assistant Professor in 1995. In 2000 he joined St. Jude where he continues to lead the statistical design and analyses in translational, clinical, and laboratory research of childhood leukemia. He has coauthored several high-impact publications in this area since 2000. Dr. Cheng has been a member of the Institute of Mathematical Statistics and the American Statistical Association since 1994 and was a recipient of a Team Science Award from the American Association for Cancer Research in 2009.

Thursday, November 17, 2022

11:00 AM - 12:00 PM, CST

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