Seminar on Confirmatory statistical analysis for cancer immunotherapy trials

日時：2019年12月13日（金）13：30-16：30（開場 13:15）

会場：大阪大学 最先端医療イノベーションセンター
1階マルチメディアホール　http://www.comit.med.osaka-u.ac.jp/

13:30-14:45

Zhenzhen Xu (U.S. Food and Drug Administration)

Designing cancer immunotherapy trials with random treatment time-lag effect

15:00-16:15

Hajime Uno (Dana-Farber Cancer Institute/Harvard Medical School)

Adaptive long-term restricted mean survival time approach to compare time-to-event outcomes in randomized controlled trials for immunotherapy

詳細はホームページをご覧ください。http://www2.med.osaka-u.ac.jp/biostat/

主催：大阪大学大学院 医学系研究科 医学統計学教室
大阪大学大学院 医学系研究科 先導的学際研究の推進による新学術領域での世界最高水準の研究拠点形成事業「医学研究の高度化を支える疫学・統計学・生物情報科学・医療情報学の融合研究 －メディカルデータサイエンス研究拠点の形成－」（研究代表者：磯博康）
大阪大学大学院 医学系研究科 新研究分野創生事業「臨床疫学データの構築・解析からリバーストランスレーショナルリサーチへの展開とその担い手育成プロジェクト」（研究代表者：磯博康）

【問い合わせ】
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Designing cancer immunotherapy trials with random treatment time-lag effect

Zhenzhen Xu (U.S. Food and Drug Administration)

In some clinical settings such as the cancer immunotherapy trials, a treatment time-lag effect may be present and the lag duration possibly vary from subject to subject. An efficient study design and analysis procedure should not only take into account the time-lag effect but also consider the individual heterogeneity in the lag duration. In this paper, we present a Generalized Piecewise Weighted Logrank (GPW-Logrank) test, designed to account for the random time-lag effect while maximizing the study power with respect to the weights. Based on the proposed test, both analytic and numeric approaches are developed for the sample size and power calculation. Asymptotic properties are derived and finite sample efficiency is evaluated in simulations. Compared with the standard practice ignoring the delayed effect, the proposed design and analysis procedures are substantially more efficient when a random lag is expected; further, compared with the existing methods by Xu et al (2017) considering the fixed time-lag effect, the proposed approaches are significantly more robust when the lag model is mis-specified. An R package (DelayedEffect.Design) is developed for implementation.

講師略歴：

Zhenzhen Xu is a mathematical statistician in the center for Biologics evaluation and research at the FDA and the recipient of the FDA Chief Scientist Publication Award. Prior to joining the FDA, she spent two years working in the pharmaceutical industry. Dr. Xu holds a Ph.D. in Biostatistics from the University of Michigan and a Master degree in Statistics from Harvard University. Her research develops novel methods for the design and analysis of clinical trials, particularly cancer immunotherapy trials and cluster randomized trials.

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Adaptive long-term restricted mean survival time approach to compare time-to-event outcomes in randomized controlled trials for immunotherapy

Hajime Uno
Dana-Farber Cancer Institute/Harvard Medical School

Logrank/hazard ratio (HR) test/estimation approach has been routinely used in almost all cancer clinical trials with time-to-event outcomes. Although the logrank test is an asymptotically valid nonparametric test, it is not the most powerful test when the pattern of the difference is non-proportional hazards (PH). Also, interpretation of the HR is not obvious when the PH assumption does not hold. For immunotherapy trials, we often see a delayed difference pattern, where the conventional logrank/HR approach is not appropriate for testing equality nor estimating the magnitude of the treatment effect. Restricted mean survival time (RMST)-based analysis has been proposed as an alternative to the logrank/HR approach. It provides a robust and interpretable summary of the treatment effect. However, it is known that the standard RMST-based approach offers lower power than the logrank/HR approach in delayed difference scenarios. We propose a new prespecified RMST-based test and a corresponding treatment effect estimation procedure, particularly when a delayed difference pattern is expected at the design stage. Simulation studies show how effectively the proposed method can detect the treatment difference, compared to the logrank test, various weighted logrank tests, MaxCombo test, standard RMST-based tests, and so on.

講師略歴：

Hajime Uno is an assistant professor at Division of Data Sciences, Dana-Farber Cancer Institute/Harvard Medical School. He has also been appointed in Division of Biomedical Statistics, Department of Integrated Medicine, Osaka University, as an adjunct faculty member, since April 2019. He has more than nine years of work experience in pharmaceutical industry in Japan. After he received Ph.D. in Biostatistics in 2003, he completed post-doctoral training at Harvard University for two and a half years. He has been working on various methodological and clinical research projects. His methodological research work has been published in high-tier journals of statistics such as JASA, Biometrika, Biometrics, and so on. One of his notable contributions is C-statistics (Uno et al. Statistics in Medicine 2011). This paper was ranked in one of the 10 most cited Statistics in Medicine papers in Year ’12-’13. This method has been called “Uno’s C” and employed in SAS/PHREG procedure (CONCORDANCE=UNO option). One of his current research interests is to improve the routine practice of survival data analysis and to disseminate better alternatives for enhancing the quality of informed treatment decision making. His contributions in this area are seen in major medical journals (e.g., Journal of Clinical Oncology 2014, Annals of Internal Medicine 2015), in several invited lectures (e.g., U.S. Food and Drug Administration in 2016), and in developed software (e.g., contributed R package survRM2).

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