Graziani, Rebecca; Guindani, Michele; Thall, Peter F.
Bayesian nonparametric estimation of targeted agent effects on biomarker change to predict clinical outcome.  (English) Zbl 1419.62356

Summary: The effect of a targeted agent on a cancer patient’s clinical outcome putatively is mediated through the agent’s effect on one or more early biological events. This is motivated by pre-clinical experiments with cells or animals that identify such events, represented by binary or quantitative biomarkers. When evaluating targeted agents in humans, central questions are whether the distribution of a targeted biomarker changes following treatment, the nature and magnitude of this change, and whether it is associated with clinical outcome. Major difficulties in estimating these effects are that a biomarker’s distribution may be complex, vary substantially between patients, and have complicated relationships with clinical outcomes. We present a probabilistically coherent framework for modeling and estimation in this setting, including a hierarchical Bayesian nonparametric mixture model for biomarkers that we use to define a functional profile of pre-versus-post-treatment biomarker distribution change. The functional is similar to the receiver operating characteristic used in diagnostic testing. The hierarchical model yields clusters of individual patient biomarker profile functionals, and we use the profile as a covariate in a regression model for clinical outcome. The methodology is illustrated by analysis of a dataset from a clinical trial in prostate cancer using imatinib to target platelet-derived growth factor, with the clinical aim to improve progression-free survival time.

MSC:
62P10 Applications of statistics to biology and medical sciences; meta analysis
62G99 Nonparametric inference
62F15 Bayesian inference
62N05 Reliability and life testing

Keywords:
Bayesian nonparametrics; biomarker profiles; nested Dirichlet process; receiving operating curve; survival analysis

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