Indiana University-Purdue University Indianapolis

Department of Mathematical Sciences

STATISTICS SEMINAR

12:15pm—1:15pm, Tuesday, Jan. 30, 2018
SL 137

Speaker: **Dr. Yong Zang** (Assistant Professor)
Department of Biostatistics, School of Medicine, Indiana University

Title: **Dose-finding Clinical Trial Designs for Molecularly Targeted Agent and Immunotherapy**

Abstract:

Traditionally, the purpose of a dose-finding design in cancer is to find the maximum tolerated dose based solely on toxicity. However, for molecularly targeted agents (MTA) and immunotherapy (IT), little toxicity may arise within the therapeutic dose range and the dose-response curves may not be monotonic. This challenges the principle that more is better, which is widely accepted for conventional chemotherapy.

In this talk, we propose two Bayesian adaptive dose-finding designs for clinical trials evaluating MTA and IT, for which the dose-response curves are unimodal or plateaued. The goal of these designs is to find the optimal biological dose. The first proposed design is an efficacy driven design and uses the isotonic regression and locally logistic regression model to fit the data and guide the dose escalation. The second proposed design is a two-stage seamless design. In the first stage, we use the Bayesian model averaging continual reassessment method to monitor the toxicity outcomes and use the proposed isotonic regression method to guide dose escalation. When the first stage ends, we use the Dirichlet-multinomial distribution to jointly model the toxicity and efficacy outcomes and pick the candidate doses based on a three-dimensional volume ratio. The selected candidate doses are then seamlessly advanced to the second stage for dose validation. We conduct simulation studies to examine the operating characteristics of the proposed designs.