



UNC
GILLINGS SCHOOL OF
GLOBAL PUBLIC HEALTH

BIOSTATISTICS
AWARDS DAY
and Seminar

James E. Grizzle Distinguished Alumni Award

Guosheng Yin
M. D. Anderson Cancer Center, University of Texas

**Bayesian Adaptive Designs for Early-phase
Clinical Trials**

The continual reassessment method (CRM) is a popular dose-finding design for phase I clinical trials. This method requires practitioners to prespecify the toxicity probability at each dose. Such prespecification can be arbitrary, and different specifications of toxicity probabilities may lead to very different design properties. We propose using multiple parallel CRM models, each with a different set of prespecified toxicity probabilities. We assign a discrete probability mass to each CRM model as the prior model probability. The posterior probabilities of toxicity can be estimated by the Bayesian model averaging (BMA) approach. Dose escalation or de-escalation is determined by comparing the target toxicity rate and the BMA estimates of the dose toxicity probabilities. Simulations show that the BMA-CRM is competitive, robust, and eliminates the arbitrariness of the skeleton. Treating patients with a combination of agents is becoming common-place in cancer clinical trials, with biochemical synergism often the primary focus. In a typical drug combination trial, the toxicity profile of each individual drug has already been thoroughly studied in the single-agent trials, which naturally offers rich prior information. We propose Bayesian adaptive designs for dose finding, which include the copula-type regression, latent contingency table approach and sequential CRM. To search for the maximum tolerated dose combination, we continuously update the posterior estimates for the toxicity probabilities of the combined doses. By reordering the dose toxicities in the two-dimensional probability space, we adaptively assign each new cohort of patients to the most appropriate dose. We illustrate the proposed methods under various practical scenarios based on recent clinical trials at M. D. Anderson Cancer Center.

Wednesday, April 15, 2009
1301 McGavran-Greenberg
3:30 – 4:30 PM

Reception to follow, 3rd Floor McGavran-Greenberg