A Bayesian Approach in Differential Equation Dynamic Models Incorporating Clinical Factors and Covariates

by
Yangxin Huang
University of South Florida
Department of Epidemiology & Biostatistics, College of Public Health, MDC 56
University of South Florida, Tampa, FL 33612, USA
yhuang@health.usf.edu

Abstract

A virologic marker, the number of HIV RNA copies or viral load, is currently used to evaluate antiretroviral (ARV) therapies in AIDS clinical trials. This marker can be used to assess the antiviral potency of therapies, but may be easily affected by clinical factors such as drug exposures and drug resistance as well as baseline characteristics during the long-term treatment evaluation process. HIV dynamic studies have significantly contributed to the understanding of HIV pathogenesis and ARV treatment strategies. Viral dynamic models can be formulated through differential equations, but there has been only limited development of statistical methodologies for estimating such models or assessing their agreement with observed data. This talk develops a mechanism-based nonlinear differential equation models for characterizing long-term viral dynamics with ARV therapy. In this model we not only incorporate clinical factors, but also baseline covariate into a function of treatment efficacy. A Bayesian nonlinear mixed-effects modeling approach is investigated with application to an AIDS clinical trial study. The effects of confounding interaction of clinical factors with covariate-based models are compared using the Deviance Information Criteria (DIC), designed from complex hierarchical model settings. Relationships between baseline covariate combined with confounding clinical factors and drug efficacy are explored. In addition, we compared models incorporating each of four baseline covariates through DIC and some interesting findings are presented. Our results suggest that modeling HIV dynamics and virologic responses with consideration of time-varying clinical factors as well as baseline characteristics may play an important role in understanding HIV pathogenesis, designing new treatment strategies for long-term care of AIDS patients.