Bayesian analysis of physiologically based pharmacokinetics modelling of perchloroethylene in humans

Junshan Qiu

Department of Statistics, University of Georgia

E-Mail: TBP

Abstract: This study is to estimate population distributions of PBPK model parameters and to make a dose reconstruction with clinical data from uncontrolled studies. Perchloroethylene (PCE) is a widely distributed pollutant in the environment. The cancer risks of PCE at low exposures are uncertain. PCE occurs widely in the dry cleaning establishments and also can be found in indoor air. However, the concentrations of PCE are mostly below 1ppm. Therefore, it is very important to assess cancer risks at these low concentrations. A human physiologically based pharmacokinetics (PBPK) model was used to quantify tissue doses of PCE and its key metabolite, Trichloroacetic Acid (TCA) after inhalation exposures. This PBPK model was integrated with a statistical hierarchical model to acknowledge variations due to intraindividual variation, interindividual variation, measurement error and difference between study methods. A Bayesian approach, Markov chain Monte Carlo analysis, was employed to analyze clinical data obtained from controlled studies. The data are on alveolar or exhaled breath concentrations of PCE, blood concentrations of PCE and TCA, urinary excretion of TCA. The posterior distributions of PBPK model parameters were obtained. Predictive ability of posteriors was satisfactory. Posterior predictions are much better than prior fit.