Parameter estimation for liver function analysis with indocyanine green fluorescence measurements

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The evaluation intra-operatively of liver function is an important clinical question, because liver surgery complications are related to a poor liver function. Presently, the liver function is estimated with blood sample analysis (level of bilirubin) and indocyanine green clearance (plasma disappearance rate), since indocyanine green is a fluorescent dye, exclusively removed from the blood by liver cells. The previous methods are not intra-operatively available and they provide only combined information on possible liver perfusion and functions dysfunction. Mathematical model based on indocyanine green fluorescence dynamics in liver tissue and its parameters estimation may enable a precise quantification of the exchange between the different liver tissues. Therefore information on the perfusion and the different hepatic functions may be obtained. In this work, we present pharmacokinetic models of the processing of indocyanine green by the liver as well as its parameters estimation.

The mathematical models, based on ordinary differential equations, are built with the fluorescence measurements obtained during pig liver surgeries. Then, the sensitivity of model observables to parameters is studied. Two sensitivity analysis are performed, the traditional sensitivity and generalized sensitivity analysis. Traditional sensitivity quantifies how sensitive the model observables are to the parameters of interest, and generalized sensitivity informs on parameter correlation and on the distribution in time of the information on the parameters contained in the observable [1, 2, 3]. Next, the parameter estimation is performed using Monolix software [4], with indocyanine green fluorescence from pig surgeries. A population approach is used, assuming individual parameters are composed of a fixed effect (from the population) and a random effect (inter-individual variability). This approach allows the estimation of sub-population parameters as well as individual parameters. The parameters for different groups, control, after 75% liver ablation and after 90% liver ablation, are then estimated and compared. The link between the models parameters and liver function is investigated. The first results indicate that after liver partial ablation the exchanges between liver tissues are reduced. The proposed framework may lead to a new method for intra-operative estimation of the hepatic function(s).

References

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