Individualising model-based predictions of neutropenia for decision support in oncology using sequential Bayesian data assimilation

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OBJECTIVES:
One of the major side effects of cytotoxic anticancer treatment is neutropenia, a severe reduction of neutrophils (white blood cells) that puts patients at high risk of life-threatening infections. Reliable predictions of the time course of neutropenia can help to early identify patients at risk and support individualised dosing schedules. Novel digital health care devices, allowing for frequent neutrophil monitoring, require new recursive data processing methods that enable decision support in ongoing treatment. Recursive data processing is well established in meteorology, called sequential data assimilation (DA). The objective was to investigate the benefits of sequential DA methods in systems pharmacology based on the example of neutropenia.

METHODS:
In sequential DA methods the posterior is iteratively updated via Bayes' formula by combining computer-generated Bayesian forecasts with data in real time [1]. In systems pharmacology, particle filter algorithms are particularly suitable, as they allow for nonlinear structural models and non-Gaussian error models.
The Bayesian forecasts of the particle filter were generated using models for neutropenia [3,4], based on prior knowledge about model parameters from population analysis of [2,4] of clinical studies. The update step employed patient-specific data, which was generated in silico. For comparison, a maximum a-posteriori (MAP) estimation was performed similar to prior work [5].

RESULTS:
Based on the weighted mean as posterior expectation, the particle filter has reasonable root mean squared errors in the parameter estimates and in the summary statistics, e.g. time to recovery. The uncertainty of these statistics is also comprehensively quantified by estimating the full posterior distribution, which leads to much more informative results and facilitates interpretability. Additionally, this recursive framework is very efficient for multiple cycle therapy as only the current data point is processed in the update step.

CONCLUSIONS:
Using neutropenia as an example, we demonstrated that sequential Bayesian DA methods provide an efficient framework to recursively process patient data, which allows to support decision-makers in ongoing treatment. With the development of novel digital healthcare devices this is becoming increasingly important. The comprehensive uncertainty quantification, sequential data processing and easy-to-interpret results of sequential DA methods are crucial for rational and individual decision-making in oncology.

References:

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