Optimization of haemodialysis treatment for patient's haemodynamic stability – *in silico* simulation study

The aim of this project is to use mathematical and simulation tools to investigate the possibilities of optimizing the haemodialysis treatment in patients experiencing blood pressure drops during dialysis sessions.

It is estimated that over 4 million people around the world suffer from end-stage renal disease. Most of them (over 80%) receive regular dialysis treatment to substitute the most important functions of the kidneys, i.e. to remove from the body the excess water, waste products of metabolism and toxins, as well as to maintain the electrolyte and acid-base balance. The most common dialysis technique is haemodialysis, which is an extracorporeal technique of purifying blood and removing the excess water in a dialyzer.

Despite being a life-sustaining treatment, HD puts a significant stress on the cardiovascular system. During a typical dialysis session, a few litres of water and solutes are removed from the body in a relatively short period of time (typically 3-5 hours), which typically leads to a decrease in blood volume. The proper function of the cardiovascular system relies then on the transcapillary absorption of fluid from the tissues and the activity of blood pressure regulatory mechanisms. Unfortunately, in many dialysis patients these mechanisms work improperly or insufficiently, which results in a drop in blood pressure (hypotension) and the associated dizziness, muscle cramps, nausea, vomiting and possibly even a loss of consciousness. Intradialytic hypotension is not only uncomfortable for patients but also significantly hinders the work of medical personnel and the delivery of the prescribed dialysis dose. Moreover, the repetitive hypotension has a negative effect on the brain, heart and other organs, thus worsening the patients' prognosis and the quality of life. The mechanisms behind intradialytic hypotension are complex, patient-specific and still not fully understood.

There are several methods of preventing intradialytic hypotension consisting in the adjustments of treatment parameters or their modification during the dialysis procedure (e.g. the use of a variable rate of water removal from blood in the dialyzer). However, there is no one-size-fits-all method that can be applied to all patients, and there are no guidelines as to which method should be used in a given patient or how exactly it should be performed. Moreover, a decrease in blood volume during dialysis is not always associated with a decrease in blood pressure, and individual patients may have very different patterns of blood volume and blood pressure changes during dialysis.

In this project, we plan to develop a new, comprehensive computational model of the cardiovascular system and its regulatory mechanisms combined with the transport of water and various substances (electrolytes, urea, creatinine and proteins) within the patient's body during haemodialysis, and then use it to investigate various patterns of blood volume and blood pressure changes observed in dialysis patients and to simulate and evaluate different possible haemodialysis scenarios (with different treatment parameter values, including their temporal modification).

The results of this simulation study will allow to determine which treatment scenarios are most suitable for different types of patients, thus forming the basis for future clinical studies and for the development of a clinical decision support system for the choice of optimal parameters of haemodialysis treatment for keeping the patients haemodynamically stable.