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Abstract

Anisotropic blood contactor module with immobilized enzyme to treat septic AKI

L. T. Hirschwald[1*], F. Hagemann[2], M. Restrepo[1], P. Peric[1], T. Höhs[1], M. Tillmann[1], F. Neuhaus[1], J. Linkhorst[1], and M. Wessling[1,2]

[1] *Chair of Chemical Process Engineering, RWTH Aachen University, Aachen, Germany*
[2] *DWI – Leibniz Institute for Interactive Materials e.V., Aachen, Germany*
[*] *Corresponding author, email: lukas.hirschwald@avt.rwth-aachen.de*

Worldwide, more than 3 million people yearly suffer from severe acute kidney injury (AKI), which, combined with sepsis, leads to high mortality. Dialysis is the therapeutic approach to treat AKI and is, therefore, a clinically and economically significant indication for blood treatment procedures. In 2018, Pickkers et al. showed in a study involving 301 patients with septic AKI that repeated intravenous application of the enzyme alkaline phosphatase (ALP) led to a significantly better survival rate for those affected than the administration of a placebo [1]. However, studies with healthy volunteers show that the ALP concentration in the blood drops to below 10 percent of the initial peak concentration only 4 hours after intravenous infusion [2]. Therefore, high infusion doses are needed to continuously exceed the therapeutically effective minimum concentration of the enzyme in the blood [1].

In this work, we immobilize the enzyme ALP on a blood-accessible surface [3]. As the enzyme is no longer freely available in the body, degradation is inhibited, a smaller amount of drug is required, and as tissues and organs are less exposed to the enzyme, side effects are reduced. Three geometrically distinct modules with identical fluid volume and internal surface area were fabricated from a hemocompatible material using digital light processing. The investigated internal module geometries are (a) straight tubes similar to a dialyzer (tube module), (b) isotropic triply periodic minimal surface structures (iTPMS module), and (c) anisotropic TPMS structures (aTPMS module). The convoluted TPMS structure provides an optimal, continuous surface geometry for blood without sharp edges and corners, thus reducing hemolysis and coagulation. In flow MRI measurements and tracer experiments, the perfusion and residence time distribution are determined and used to validate the performed CFD simulations.

In comparison to the tube module, the iTPMS and aTPMS modules are expected to significantly improve the enzymatic conversion of toxins in the blood due to intrinsic mixing induced by the TPMS structure.

Author's statement

All authors state no conflict of interest. Informed consent has been obtained from all individuals included in this study. M. Wessling acknowledges DFG funding through the Gottfried Wilhelm Leibniz Award 2019 (WE 4678/12-1). This work was supported by the German Federal Ministry of Education and Research (BMBF) under the project "ALP" (FKZ 13XP5160).

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