IN-VITRO THROMBOGENICITY TESTING FOR ECLS OXYGENATORS – FEASIBILITY, RELIABILITY AND REPRODUCIBILITY

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Introduction

Hemostatic complications limit the maximum duration of the clinical application of ECLS, normally days or weeks. Decreasing the circuit thrombogenicity remains the Gordian Knot of the therapy and the oxygenator is a major contributor [1]. However, in-vivo-experiments are the only near-to-conclusive testing modality to evaluate the thrombogenicity of oxygenator designs, but they are expensive, slow, and ethically problematic [2]. Our group is currently developing an in-vitro-setup for referential testing of oxygenator variants.

Materials and Methods

We performed in vitro experiments with recirculating porcine whole blood. Two identical circuits were run for 5 hours using blood from the same donor animal. Each circuit comprised the oxygenator with integrated heat exchanger and centrifugal blood pump, a miniaturized blood reservoir, ports for blood sampling and pressure measurements, as well as flow meters. The oxygenators were specifically manufactured HLS 7.0 that have passed the identical production line as commercial devices but omitting the coating step. Throughout the experiment, the flow in each circuit was kept constant. We continuously measured temperature, pump rotations as well as pressures pre-pump, between pump and oxygenator, and post-oxygenator. The setup is depicted on Figure 1.

Further, we took ten blood samples from each circuit distributed over each experiment day. The samples were analyzed using ROTEM (INTEM, HepNATEM), aggregometer, hemogram, BGA, coagulometer (Fibrinogen, FXII), photometer (hemolysis). So far, in 22 experiments, we tested 44 uncoated Maquet HLS 7.0. To prove the validity of our experiment design, the last 8 experiment days were conducted entirely identical, with one exception: For 4/8 of the experiments, we deliberately omitted the usage of an advanced blood selection protocol with the intention to create negative controls, i.e. experiment runs without hemostatic events.

Results

It is feasible to create spontaneous hemostatic events in vitro and in only 5 hours experiment run time, with all logistical and resource-related benefits. Comparing parameters such as blood gases, temperature or hematocrit proves identical circuit conditions. It is also possible, to achieve these spontaneous events reliably. In the final series, we reliably achieved hemostatic events presenting on form of rising pressure differentials and validated by characteristic parameters like platelets, fibrinogen, leukocytes, etc.

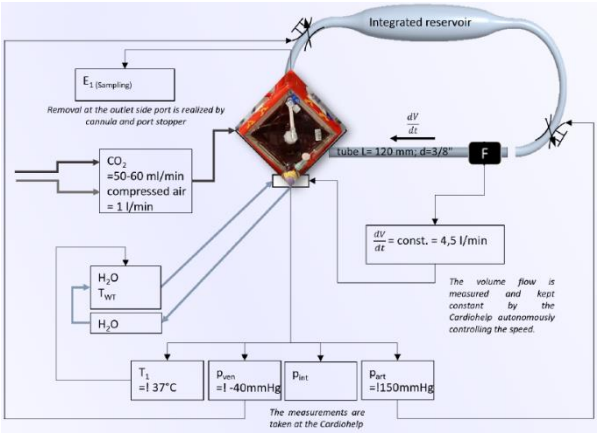

Figure 1 - Schematic of experiment setup.

4/4 experiment days with the advanced blood selection protocol yielded positive experiment course, 3/4 experiment days without the advanced blood selection protocol yielded negative controls, as intended. All paired test circuits behaved highly similar in both positive and negative experiment runs for continuous and discrete parameters, showing reproducibility.

Discussion

Our data shows that it is *feasible* to *reliably* and *reproducibly* create hemostatic events using porcine whole blood from the slaughterhouse in two identical circuits in a short time frame of only 5 hours. All measured parameters show high conformity. Thrombogenicity is difficult to quantify in form of an isolated value. As also known from similar test setups (e.g. hemolysis in heart assist systems), referential tests can, nonetheless, offer important insight.

Due to the negative controls, we can qualitatively compare readings during hemostatic events against inherent or autologous processes.

Our results are highly promising that, for the first time, such a test setup can be standardized for the thrombogenicity evaluation of ECLS oxygenators.

References

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2. Sarode DN, Roy S. In Vitro models for thrombogenicity testing of blood-recirculating medical devices. *Expert Rev Med Devices* 2019;16(7):603–16

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