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Design and 3D printing of miniaturized dialyzers for laboratory use

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Abstract: The limiting factor of extracorporeal blood purification in preclinical testing is the large volume of blood required. For this reason, developing miniaturized devices for few milliliters of patient's blood is the focus of this work. Clinical dialyzers are adapted to the sample volume by appropriate downscaling. The housings were created digitally, printed using polyjet technology and iteratively refined. A design was achieved that enables optimal potting results and homogeneous distribution of fibers within the dialyzer. Miniaturized housings with complex design and high resolution could be realized. Nevertheless, performance comparison to the clinical device is necessary for future laboratory application.

I. Introduction

The miniaturization of medical devices using 3D printing techniques is under extensive development [1]. 3D printing allows the development of complex designs that cannot be produced conventionally. Thus, enabling the investigation of highly complicated medical scenarios in a miniaturized scale before reaching the clinic. The limiting factor of extracorporeal blood purification during preclinical testing is mainly the large amount of required blood. While in vitro-dialysis experiments require at least 0.5 and up to 1 l, miniaturized setups allow such experiments to be carried out in a few millilitres of blood (Fig. 1A). Moreover, studies with patient blood simulate a physiologically similar situation in vitro, which has not been possible so far.

In this work, dialyzers used in daily clinical practice for renal replacement therapy are adapted to the sample volume by accordingly downscaling for in vitro experiments (Fig. 1B) [2].

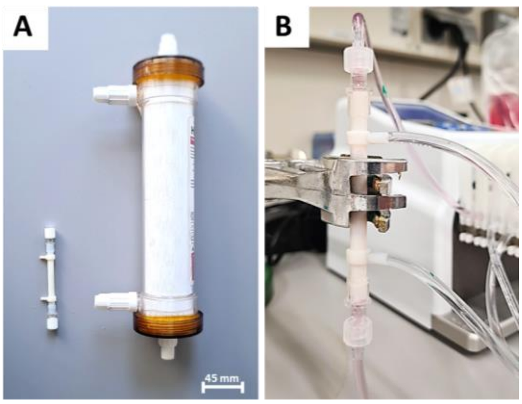

Figure 1: (A) Size comparison between a clinical (right) and a miniaturized dialyzer (left). (B) Laboratory setup of miniaturized dialysis with final dialyzer design.

3D printing technology allows many comparative tests among miniaturized dialyzers and rapid optimization of miniature housings. A high precision of fine structures and surface is required for low flow conditions. Furthermore, a stable structure of the housing improves the mounting of hollow fibres.

The main focus of this publication is the development and manufacture of 3D printed housings for miniaturized dialyzers using the polyjet technique. Particular attention is paid to the manufacturing process as well as the design. The manufacturing characteristics will be observed, such as the fitting accuracy of the components to be assembled.

II. Material and methods

In order to design a miniaturized dialyzer, all design ratios as well as the packing density of hollow fibres were determined. On the other hand, the effective surface area of the hollow fibres was used as a measure for scaling. The hollow fibres are semi-permeable and are the key component of the dialyzer. The functions of the hollow fibres include separating the blood and dialysate areas and ensuring mass transfer for small and medium molecules. Down scaling of the effective surface area is used to determine the number of fibres. As a prerequisite, all geometric sizes of the fibre as well as the packing density were known.

For a first feasibility check, a simple design was chosen (see Fig. 2A). Based on the initial experimental results, the design was then iteratively improved and further developed (see Fig. 2B, C). Due to the complexity of the internal structures, the fabrication of such miniaturized dialyzers can only be realized using additive manufacturing (AM). In addition, the AM process used enables the first prototypes to be produced quickly, which have a suitable level of accuracy and can be further processed directly.

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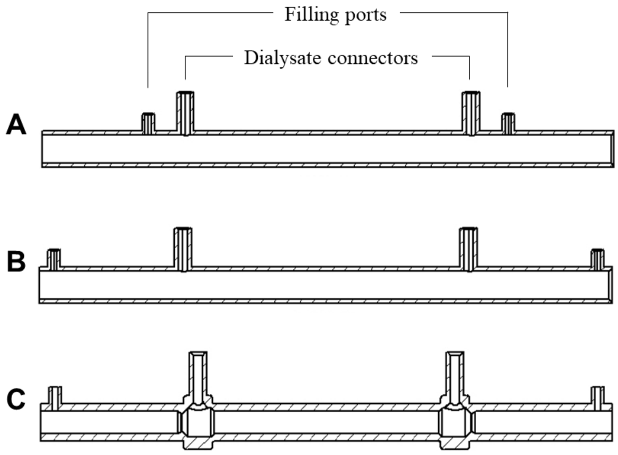

Figure 2: Section view of technical drawings: (A) initial version; (B) first optimization; (C) final design

The housings were printed according to the specifications using the polyjet principle with an Objet Connex500 printing system (Stratasys Ltd., Los Angeles, USA). For this purpose, digital computer aided design (CAD) files were first generated with the CAD program SolidWorks (Dassault Systemes, Waltham, USA) and sliced with the printer-specific slicer software ObjetStudio, version 8.0.1.3 (Stratasys Ltd.). This was followed by the additive polyjet printing process, in which acrylic resin-based photopolymers were applied in layers to a printing platform using inkjets and polymerized with ultraviolet lamps [3]. The printed parts for this study were made from VeroWhitePlus, RGD835 (Stratasys Ltd.) material. For the printing process, a second support material is required, for which the material SUP705 (Stratasys Ltd.) was used. All parts were printed horizontally with the tubes on the side. The layer thickness of all test samples was 0.016 mm with a resolution of 600 dpi in the plane and 1600 dpi in the z-direction. During post-processing, the support material was removed both mechanically and by ultrasonic treatment in an alkaline (1% sodium hydroxide) solution. Undulated polysulfones hollow fibres were inserted into the housings and bonded with the two-component polyurethane Biresin® DR404 and DH 41 (Sika AG, Zurich, Switzerland).

III. Results and discussion

All versions and repetitions are successfully printed. The high accuracy of polyjet 3D-printing produced very accurate parts without any defects like cracks or warping. Due to the complex internal structure of the final housing design (Fig. 3C), the postprocessing is more time consuming and has possibility of damaging the inner part by mechanical removal of support materials. The iterative design optimization is described in the following:

It appeared that the first version of the housing (Fig. 3A) is unsuitable for potting the hollow fibers. The distance between the dialysate ports and the material filling ports was too small, so that the dialysate ports were blocked by the potting material.

The second housing design (Fig. 3B) shows a wider distance between the two different ports, which enables potting without blocking the dialysate ports. In addition, filling the ends of the dialyzer with the potting material resulted in heterogeneous distribution of the fibres.

In the further design process, a taper of the inner housing diameter was constructed at the distal ends of the dialyzer in close proximity to the dialysate port. The final design (Fig. 3C) thus meets all the requirements for an optimal dialyzer housing: i. homogeneous coverage of the hollow fibres with potting material without blocking the dialysate ports and ii. homogeneous distribution of the fibres in the centre of the dialyzer.

Filling the dialyzer with the potting material is impeded by the opaque nature of the material used. The next steps would therefore include using a transparent printing material in addition to a biocompatible material in order to be able to carry out future in vitro dialysis tests with blood.

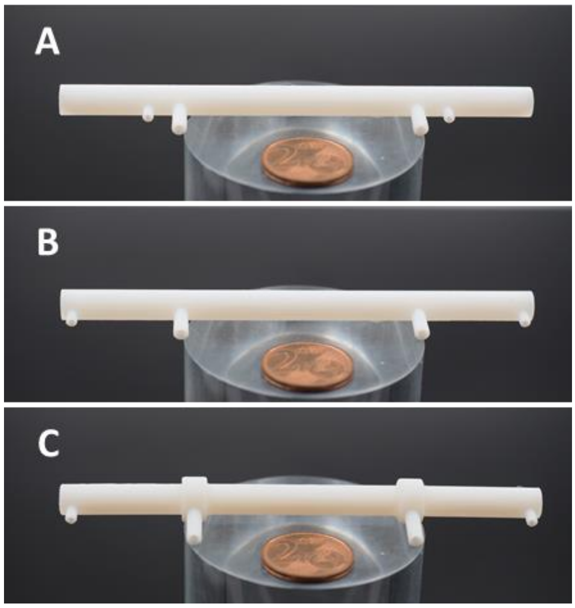

Figure 3: 3D printed housings for miniaturized dialyzers. Various design stages were printed using the polyjet process: (A) initial version; (B) first optimization; (C) final design.

IV. Conclusions

The production of a miniaturized dialyzer housing with a complex design and a high-resolution is possible by an additive manufacturing technique such as polyjet. This method provides the possibility of an iterative process to optimize the geometry due to the freedom in design and the speed of 3D printing. Afterwards, the performance characterization (clearance, sieving and ultrafiltration coefficient) of the miniaturized dialyzer will be compared to the clinical device to finally develop miniaturized in vitro renal replacement therapy.

Author's statement

The Authors state no conflict of interest. Informed consent has been obtained from all individuals included in this study.

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