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Abstract

Additive manufacturing of a miniaturized ceramic implant for animal studies on the treatment Alzheimer's disease

P. Töllner[1*], J. Hofrichter[2], B. Jenßen[1], H. Krüsemann[2], and H. Seitz[1]

[1] *Chair of Microfluidics, Mechanical Engineering and Marine Technology, University of Rostock, Rostock, Germany*
[2] *Fraunhofer IZI, Rostock, Germany*
[*] *Corresponding author, email: philip.toellner@uni-rostock.de*

Neurodegenerative diseases such as Alzheimer's dementia (AD) represent one of the greatest medical and socioeconomic challenges, with an increasing trend. Extracorporeal blood purification procedures such as plasma exchange can induce AD stagnation and improve patients' quality of life [1]. The present work goes a step further and aims to remove AD-specific target proteins directly from the brain via cerebrospinal fluid (CSF) exchange. To provide proof-of-concept, miniaturized implants for ventricular puncture in mice must be fabricated under stringent requirements. E.g., the implant requires two separate rectangular channels for gluing cannulas and tubing with minimum channel diameter of 210 µm.

Lithography-based ceramic manufacturing (LCM) enables the fabrication of miniaturized ceramic implants made of aluminum oxide (Al_2O_3) ceramics that meet the required properties in terms of biocompatibility and long-term stability (> 6 months). However, photopolymerization in the LCM process requires a certain degree of overcuring to achieve good layer adhesion, but this compromises detail accuracy, which is amplified by scattering effects of light on ceramic particles [2]. In addition, the pixel-based LCM process provides a lateral accuracy of 40 µm, which is only one-fifth of the required minimum channel diameter. The multi-step manufacturing process, which includes printing, debinding, and sintering, also results in anisotropic shrinkage of the ceramic components.

In order to obtain precisely miniaturized ceramic implants, all these challenges must be taken into account in the design of the implant with the help of additional scaling factors. Therefore, benchmark parts with different channel diameters, lengths and wall thicknesses were designed in several variants in terms of layer heights and build orientations. After sintering, all geometric features were analyzed optically. Overcuring scaling factors were calculated for the different diameters and orientations. The typical staircase effect as well as the pixel effect of the additively manufactured parts require an additional scaling factor, which was set to 10% in addition to the overcuring scaling factor. Finally, a miniaturized implant for ventricular puncture in mice with all necessary functional channels was designed, 3D printed and sintered. Initial circulation tests on a skull of a dead mouse were successfully performed. The results of the benchmark study and the initial circulation test demonstrated that an Al_2O_3 implant can be fabricated with LCM that meets all the requirements for an in vivo study in a mouse model.

AUTHOR'S STATEMENT

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

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