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Abstract

Bringing individualized, locally drug-delivering implants from the lab to bed

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Pharmacotherapy for intracranial pathological conditions faces substantial challenges due to physiological barriers such as the blood-brain barrier (BBB). Systemic drug administration, whether oral or intravenous, typically requires very high doses to achieve sufficient drug bioavailability in cranial structures. This approach is associated with significant adverse effects and often fails to deliver adequate drug concentrations to the target area, leading to inconsistent therapeutic outcomes. A promising solution to these challenges is localized, sustained drug delivery. The development of personalized implants tailored to a patient's specific anatomy is crucial. 3D printing offers design flexibility, enabling the additive manufacturing of patient-specific drug-delivering implants.

We developed an advanced workflow designed to enhance localized pharmacotherapy for cranial conditions. The process begins with acquiring high-resolution 3D clinical scans of the target anatomical regions. These scans undergo detailed software processing, employing semi-automated segmentation techniques to accurately delineate the areas of interest. Subsequently, we apply 3D printing technology to fabricate implants from medical-grade silicone, which is preloaded with repurposed pharmacological agents. These implants are engineered for precise fit and function in specific anatomical sites such as the outer ear canal, the round window niche, and the frontal sinus. This method ensures targeted, sustained drug delivery, optimizing therapeutic outcomes while reducing systemic adverse effects.

Various critical parameters, including drug release rates, biocompatibility, bio-efficacy, accuracy, and precision, were evaluated throughout the development process. In vivo experiments using animal models were conducted to thoroughly investigate the safety and efficacy of the implants. These studies focused on monitoring pharmacokinetics, tissue response, and therapeutic outcomes over extended periods. Initial individual therapeutic applications are currently ongoing. These individualized applications are necessary to treat patients who currently cannot be helped due to the lack of approved effective treatment options. In parallel it helps to refine the technology and ensure its effectiveness and safety for broader patient populations. Based on the promising results so far we are now setting up a GMP-production and will apply for Trade Supervisory Office approval to get the permission to produce the individualized, drug delivering implants for a prospective clinical trial.

The data show encouraging results in terms of safety, patient compliance and positive therapeutic effects. Nevertheless, the therapeutic benefit for patients has to be proven in future prospective studies.

AUTHOR'S STATEMENT

Conflict of interest: Authors state no conflict of interest. Animal models: The in vivo experiments in this study were conducted in accordance with the German Animal Welfare Law and the European Directive 2010/63 and approved by the State Office for Consumer Protection and Food Safety, Dept. of Animal Welfare under the number 20/3592. Informed consent: Informed consent was obtained from all individuals included in this study. Ethical approval: The research related to human use complies with all the relevant national regulations, institutional policies and was performed in accordance with the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board.

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