Flow simulation through porous ceramics used as a throttle in an implantable infusion pump

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Abstract

Pain alleviation is one of the most important therapies for chronic or incurable diseases. Consequently, implantable infusion pumps are challenged to provide long-term medication with extended check intervals. With the aim of a treatment serving each patient’s individual symptoms pattern, current research focuses especially on the possibilities of adjustable drug flow implementation. Programmable electronic devices are already capable of this performance; yet, they still require several surgeries for exchange of the power source.

Against this background, a throttle system for a gas-driven infusion device is being investigated in-silico. The system's centerpiece consists of a nanoporous ceramic throttle unit, yielding flows in the range of micro- to nanoliters per minute. The simulations shall provide information about advantages and drawbacks of variations in the geometric setup. Based on the project’s results, the most promising throttle geometries will be chosen for laboratory testing, aiming at a final application to the infusion system.

1 Introduction

Implantable infusion pumps have proven themselves in practice for intrathecal application of drugs like muscle relaxant agents and analgesics to treat spasticities and chronic pain. This therapy holds the advantage of a significant dosage reduction compared to oral and intravenous application. Intrathecal therapy may decrease the required amount of medication up to a ratio of 300 : 50 : 1 (i.th. : i.v. : oral) [1].

In general, two different types of implantable infusion pumps are available on the market. These designs differ in the type of driving force, namely gas-driven and electronic. The electrical type is telemetrically programmable, which holds the advantage that individual dosages can be adjusted without removal. Nevertheless, the power source requires replacement over time, resulting in additional surgeries. The gas-driven types are as reliable as the electrical ones, but can only provide constant flow rates. However, at proper usage, gas driven pumps do not require removal.

Further development now focuses on possibilities for adjustable flow rates with low energy consumption and small frame sizes in terms of miniaturization. In this paper, the aim, integration and benefits of the performed flow simulations shall be outlined, which contribute to the refinement of Tricumed’s intrathecal infusion device by the incorporation of a porous ceramic throttle unit for adjustable flow.

1.2 Theory

Mostly applied in geophysics, special laws govern the applicable equations for flow through porous media. In fact, the most important finding for these cases is that the fluid velocities in porous media are significantly small enough to be disregarded. Because the Reynolds number is directly related to the velocity, the flow will proportionally decrease below a value of one. As can be shown in Currie, 2005 [2], the scaling of the Navier-Stokes equations proves the Reynolds number to represent the ratio between inertia and viscous forces. Consequently, for very small Reynolds numbers, the inertia forces can be neglected, simplifying the Navier-Stokes equations to Stokes flow, also referred to as creeping flow.

H.C. Brinkman extended the equations for flow through porous media by adding a characteristic material constant [3]. These equations implemented the intrinsic permeability \( \kappa \), which had been empirically proven by Henry Darcy in 1856 [4].

\[
\kappa = \frac{\mu \cdot \eta \cdot \Delta x}{\Delta p}
\]

The intrinsic permeability is a constant depending on the ratio between velocity \( u \), dynamic viscosity \( \eta \) and the respective length of the fluid path through the porous media \( \Delta x \) to the pressure difference \( \Delta p \) measured before and after the media.

As a result, the Stokes-Brinkman equations are able to describe a complete fluidic system.

\[
\nabla p = -\eta \kappa^{-1}u + \nabla \cdot \eta_{\text{effective}}(\nabla u + \nabla u^T)
\]

In the permeable regions, the equation is governed by Darcy flow, whereas in large voids or complete free flow regions, \( \kappa \) tends to infinity, reducing equation 2 (in vector notation) to Stokes flow [5].

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2 Material and Methods

Two types of porous ceramics, zirconia and alumina, constitute the centerpiece of two throttle concepts. For a general reduction of the flow rate, the concepts use the materials resistive ability when applied to a flow system. Simulations were performed in GeoDict, a CFD software developed at the Fraunhofer ITWM Kaiserslautern. The projects methodology is sectioned in two main parts. Initially, samples of the ceramics were tested in flow experiments to determine the associated permeability constants. For the subsequent simulations, the results from the measurements are implemented as input parameters.

2.1 Ceramics

The ceramic samples used in the throttle design varied in type, pores sizes and geometric shape, to implement different ranges of possible flow modulation in the final throttles.

2.1.1 ZrO$_2$

The tested zirconia specimen was pure ZrO$_2$ type with porosities of about 30%. The grain sizes of the single-phased structure are in a range of 1-2 µm and the grains distribute homogenously, characterizing the ceramic as isotropic. The ZrO$_2$ cylinders are produced by the company Metoxit in Switzerland. The mean diameter was found to be 0.17 µm by Hg-porosimetry.

2.1.2 Al$_2$O$_3$

For the experimental testing of the alumina (Al$_2$O$_3$) ceramic, three variants of specimen tubes produced at the Fraunhofer IKTS Hermsdorf were used, differing in mean pore sizes of 0.41, 0.2 and 0.11 µm. In addition, each of the respective variations was altered by infiltration of a different type of ceramic with grain sizes in the range of nanometers. As for the ZrO$_2$ specimen, the Al$_2$O$_3$ used is single phased, isotropic, with porosities around 30%.

2.2 Software

The CFD software GeoDict is especially designed for porous media and composite materials. GeoDict is the abbreviation for Geometric material designer and material property preDictor. It offers a complete approach for both the virtual generation of structures and numerical prediction for different physics laws (www.geodict.de). In particular, GeoDict was chosen for the simulations in this project because it offers a unique explicit finite volumes solver for a fast and accurate numerical solution of the Stokes-Brinkman equations [6, 7].

Due to the largely varying scales between the throttle dimensions and the ceramics' pore and grain sizes, the problem arises to virtually imitate the complete structures down to the nanoscale level; at reasonable resolutions, this results in excessive computational requirements or times. Using GeoDict, this difficulty can be circumvented by the fact that the intrinsic permeability can directly be assigned to a virtual material.

2.3 Design

Two types of porous ceramics, zirconia and alumina, constitute the centerpiece of the two throttle concepts. For a general reduction of the flow rate, the concepts use the materials resistive ability when applied to a flow system.

2.3.1 ZrO$_2$

In this concept, a cylindrical ceramic body made from pure zirconia, with an outer diameter of 1.15 mm and 11 mm length, was melted into a glass capillary. Bore holes of about 350 µm were placed on one side of the glass capillary with an excimer laser. The assembly was coated with a loose fitting silicone hose. As shown in Figure 1, this seal leaves a bypass gap in distance to the capillary. A pin, moving along the axis of the bore holes location, was used to press the seal tightly onto the holes. Unsealed holes offered the possibility for the fluid to bypass the highly resistive zirconia, moving through the less decelerating gap instead. Consequently, the flow was adjustable, stepwise. The measured flow range of this construction was found to be in the range of 80 to 240 nL per minute.

![Figure 1 ZrO$_2$-concept. Case A: All holes opened, maximum flow rate. Case B: All holes sealed, fluid forced to move through complete ceramic specimen.](Image)

2.3.2 Al$_2$O$_3$

For the second concept, a porous alumina tube made up the core of the construction. As shown in Figure 2, the interior of the ceramic tube is lined with a loose fitting hollow silicone seal.

An adhesive casing around the outer surface fixed the ceramic tube within the construction. As a result, the outermost layer of pores was sealed with exception of the final outlet area. The fluid entered the unit moving through the gap between the inner diameter of the ceramic and the outer diameter of the silicone seal. A metal pin, slightly larger in its dimensions than the inner diameter of the seal, was inserted and moved within the silicone seal. The over-dimensioning of the pin caused the expansion of the seal over the length of the pin’s penetration depth. When the pin sealed the gap, the fluid was forced to enter the ceramic, to finally exit through the outlet surface.
As a result, the pin position was the influential factor for the flow and determined the ratio between passage through either the gap or the ceramic.

With this principle, flow-rates ranged from 150 to 4000 nL per minute. In contrast to concept A, concept B offers the advantage of a continuous flow modulation.

2.4 Experiments

To calculate the intrinsic permeability of the ceramics, each ceramic was measured for standardized flow. For the evaluation, it was necessary to determine both, in- and out-flow area as well as the length of the pathway through the ceramic in direction of the fluid flow.

The zirconia specimens were tested in a glass capillary without bore holes, measuring solely the flow through the ceramic. Accordingly, for the alumina tubes both endings were sealed with caps. The fluid was injected to the inside of the tube, flowing through the ceramic and leaving the specimen through the outer surface.

The experimental setup for the permeability evaluation is shown in Figure 3. A pressure source connected to the pressure container filled with the test fluid was modulated using a pressure regulator. A ceramic bacterial filter with pore sizes of 0.22 µm was interposed between the fluid source and the flow sensor. The resistance of the bacterial filter was found to be negligibly small compared to the ceramic throttles.

Based on the pressure difference of 2.5 bar produced by the infusion device, the flow in the experiments was measured between 1 and 4 bar to investigate the behavior of the permeability in relation to the pressure.

2.5 Simulations with GeoDict

For the application of the software, a validation in terms of consistency of the experimental and virtual results was carried out. The convergence of the structures was investigated to estimate further containment of the solver parameters such as the termination accuracy. Information about the deviation due to mesh resolution and corresponding computational times were obtained, which was used for simulations of variations in the throttle geometry.

3 Results

Based on the results of the permeability evaluation, the physics parameters were implemented in the simulations.

3.1 Laboratory Experiments

Following equation 1, the permeability constants were calculated according to Darcy’s law from the flow measurement results. The flow-pressure curves for the zirconia in Figure 4, shows sections of linear and non linear behavior.

The flow was measured with sensors using a thermal propagation principle in the ranges of 70 to 1500 nL and 30 to 1000 µL. A differential pressure sensor installed right after the flow sensor denoted the internal pressure within the system just before the ceramic specimen.

For the determination of the fluid viscosity, the ambient temperature was measured with an external sensor. As testing fluid, aqua ad injectabilia (aqua ad.) was chosen. The viscous behavior, as well as the actual viscosity values, were comparable to the original drug mixture with isotonic (0.9%) saline solution in the infusion device. First, the system was completely filled and all remaining air bubbles removed. The ceramic testing assemblies were prefilled under vacuum in order to prevent time dependent changes in the measurements due to remaining air in the ceramic pores [8].

Based on the pressure difference of 2.5 bar produced by the infusion device, the flow in the experiments was measured between 1 and 4 bar to investigate the behavior of the permeability in relation to the pressure.
pressure dependency. At small pressure differences, electro-molecular forces between the solid and fluid phase in the porous media influence the flow. At high pressures in turn, restrictive friction effects may result in non-linearity [9]. Subsequent flow measurements will need to incorporate applying pressures less than 1 bar to further investigate the linearity of the behavior.

As shown in Figure 6, a significant deviation from flow, yielded with the standard area, is achieved by maximization of this area at decreasing penetration depth of the pin. In conclusion, an extension of the outflow area may enlarge the throttle’s drug flow modulation range having to accept merely a small increase of the lower flow rate limit.

4 Conclusion

The permeability constants of the zirconia and alumina samples were calculated from flow measurements and verified by a second set of reference measurements, which will have to be followed by a quantitative evaluation. A validation of the initial simulations with the implemented physics parameters collected from the measurements was successful in terms of convergence and consistency. The virtual investigation on geometric throttle variations showed that alterations in the positions of the bore holes and the size of the outflow area may have beneficial effects on the possible flow range modulation.

5 Acknowledgements

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6 References