IN SILICO MODELLING OF ENDOVASCULAR DRUG DELIVERY FROM DRUG-COATED BALLOONS

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Introduction

The treatment of ischaemic artery disease has improved substantially in recent decades since the inclusion of local delivery of antirestenotic drug [1]. Drug-coated balloons (DCBs) are a promising temporary modality of drug delivery, serving as an alternative or complement to the implantation of permanent stents. The principle relies on the endovascular inflation of a balloon transferring part of its drug coating to the vessel on contact during a short time window. A greater understanding of the underlying mechanisms of DCB delivery and how the combination of procedural parameters, such as inflation time, inflation pressure, and drug loading, affect its performance is required. To this end, in silico modelling is explored.

Methods

We present a multiphysics computational model of endovascular drug delivery from a DCB. A finite element method framework is developed to represent 2D-axisymmetric idealised geometries of the device and multi-layered arterial wall, with the interdependent processes of balloon inflation, contact, artery deformation, transmural filtration, drug transport and retention simulated. To emphasize the early events of DCB delivery, all processes are simulated in a space and time-dependent fashion while accounting for the spatial frame deformation. Long-term retention of drug within the artery (up to 28 days) is observed.

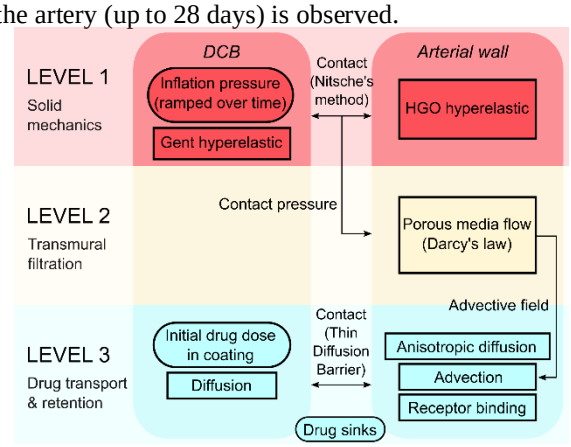

Figure 1: Diagram summarizing the model architecture.

The hyperelastic structural mechanics of the DCB and arterial wall are described respectively by a phenomenological Gent material model, and a Holzapfel-Gasser-Ogden (HGO) material model accounting for anisotropic fibre orientation, as proposed in [2] and implemented in [3].

Drug transport is governed by diffusion and advection, and drug retention follows two phases of non-linear, reversible, and saturable binding reactions.

Results

The main outputs of the simulation are the drug release profile from the DCB and the drug distribution across the arterial wall, in free and bound states. Drug content (DC) and specific receptor saturation (sRS) are common measures of safety and efficacy, respectively, and may be assessed while attempting variations in balloon inflation pressure, contact time, drug dose and delivery rate.

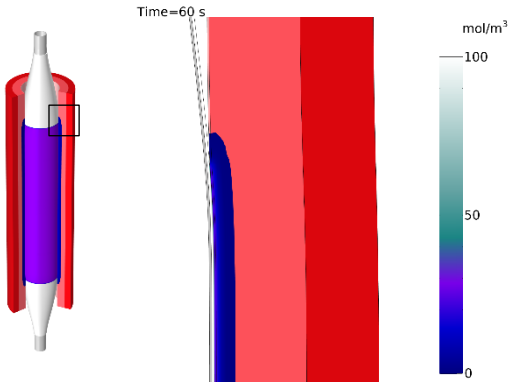

Figure 2: Simulation overview during drug delivery, highlighting the spatial distribution of total drug concentration.

Discussion

The present work demonstrates the potential of in silico modelling as an assisting experimental tool alongside the traditional ways of preclinical and clinical testing. Medical device development greatly benefits of the reproduction and analysis of complex events, such as the endovascular delivery of drug, from the convenience of a computer. We suggest that sophisticated DCB delivery models accounting for time-dependent multiphysics phenomena may be more representative of clinically observed conditions. Moreover, beyond useful insights, they could provide a platform for hypothesis testing and optimization — tasks that may be impractical if restricted to in vivo and in vitro settings.

References

1. McGinty, Math Biosci, 257:80-90, 2014.
2. Gasser et al, J R Soc Interface, 3(6):15-35, 2006.
3. Escuer et al, J Mech Behav Biomed Mater, 104:103610, 2020.