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Numerical Analysis of Collagen Injection to the Striatum

I.M. Syntouka[1,2], P.E. Riches[1], A. Kazakidi[1]

[1] Biomedical Elngineering Department, University of Strathclyde, Glasgow, G1 1XQ. [2]Collagen Solutions Plc, Glasgow, G33 1AP.

Introduction

Parkinson's disease (PD) is a degenerative disorder that affects dopaminergic neurons in the *substantia nigra*. In PD, the dopaminergic neurons degenerate, resulting in less dopamine being available for neurotransmission. Cell therapy, along with the use of biomaterials, has emerged as a promising therapeutic strategy. However, the existing delivery approaches have shown limited success in clinical translation[1]. This study aims to develop a device for the delivery of a cell-embedded *in situ* forming collagen hydrogel. Here, computational approaches on the delivery of collagen to the striatum are presented, to gain insight into different parameters affecting the delivery.

Methods

The delivery of collagen to the striatum was modelled computationally in the two-dimensional and three-dimensional spaces. In 2D, the striatum was modelled as a circular space, with an area of 3.98 cm^2 corresponding to the mean volume of putamen in PD patients[2]. The 3D model was reconstructed from MRI images of rodents provided by MIRCen (CEA, France). Within the finite volume method framework, the Volume of Fluid (VOF) method was used, assuming two isothermal and immiscible fluids, representing the collagen hydrogel and the striatum. The collagen flow was considered incompressible, with non-Newtonian fluid behavior characterized experimentally, and constant inlet velocity corresponding to a maximum delivery volume.

Results & Discussion

Two different designs of needle tips were used for the delivery, a blunt and a bevel tip. The interaction between collagen and the striatal tissue phases was analyzed in both the simplified 2D geometry and the anatomically-realistic 3D model. The fluid phase distribution was computed, with a=1 indicating collagen, a=0, brain tissue and 0<a<1 indicating the interface. The effects of collagen injection on the pressure fields within the striatum were also examined. A difference in the pressure between the two needle tips was observed, with the bevel tip showing higher pressure values on the delivery site. The fluid phase distribution of the collagen hydrogel within the anatomically-correct 3D model was similar, being in good qualitative agreement with experimental observations.

Conclusion

The intrastriatal injection of a hydrogel is a complex process and computational analysis of the delivery can help identify the obstacles facing clinical translation. Further analysis is required including the development of a hyper elastic model for the brain tissue.

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