Delivery of an Injectable Biomaterial to the Striatum- a Computational Analysis

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***Abstract*— The delivery of a cell-embedded hydrogel to the striatum is a promising strategy for Parkinson's disease. In this study, a computational model of the intrastriatal injection was used to analyze the delivery process.**

I. Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disorder. In PD, the dopaminergic neurons in substantia nigra degenerate, resulting in less dopamine being available for neurotransmission in the corpus striatum. Recently, cell therapy has emerged as a promising therapeutic strategy. To increase cell viability, biomaterials are used to facilitate cell deposition through intrastriatal injection. However, the existing cell 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.

II. Methods

The delivery of collagen via intrastriatal injection was modelled computationally in the two-dimensional space. The striatum was modelled as a circular space, with an area of 3.98 cm^2 corresponding to the mean volume of putamen in Parkinson's disease patients [2]. Within the finite volume method framework, the Volume of Fluid (VOF) method was used, assuming two isothermal and immiscible fluids. The flow of collagen was considered incompressible, with non-Newtonian fluid behavior characterized experimentally, and constant inlet velocity corresponding to a maximum delivery volume.

III. Results

The interaction between the collagen and the brain tissue phases was analyzed first, using two types of needle tips, a blunt needle tip and bevel needle tip (Fig. 1A, 1B). The effects of collagen injection on the pressure fields within the striatum were also examined (Fig. 1C, 1D). A difference in the pressure between the two needle tips was observed, with the bevel tip showing a higher pressure on the site of the delivery.

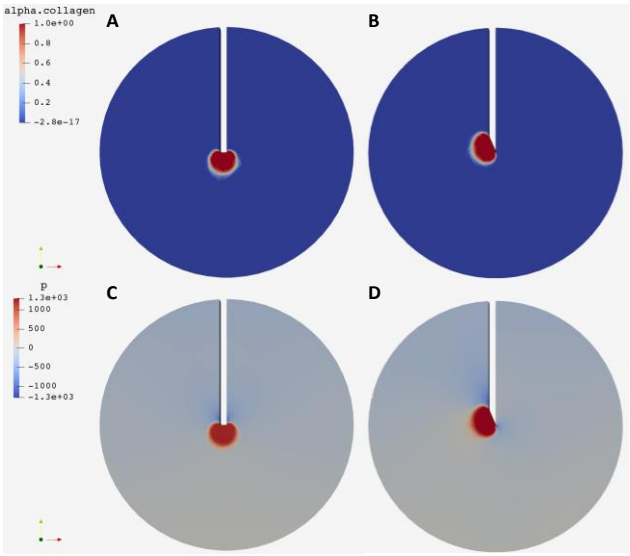

Figure 1: Two-dimensional model of collagen delivery to the striatum. A) Injection with a blunt tip. Collagen (red) and brain tissue (blue) phases, a=1 indicates collagen, a=0 indicates brain tissue, and 0<a<1 indicates the interface. B) Injection with a bevel tip (same colouring as in A). C) Pressure distribution for collagen injected with a blunt tip. D) Pressure distribution for collagen injected with a bevel tip.

IV. Conclusions

Intrastriatal injection of a cell-embedded hydrogel is a complex process which is not yet well characterized. Computational analysis of the delivery can help identify the obstacles facing clinical translation. Further analysis is required including 3D reconstruction from MRI images and computational modelling in the three-dimensional space. Future work will also examine new designs for the needle tip and their affect on the pressure distribution at the delivery site.

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