Computational analysis of intrastriatal delivery of collagen

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INTRODUCTION: Parkinson's disease (PD) is a degenerative disorder that affects dopaminergic neurons in substantia nigra. Recently, cell therapy has emerged as a promising therapeutic strategy, with biomaterials being used to facilitate the cell deposition through intrastriatal injection. However, the existing delivery approaches have shown limited success in clinical translation. 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 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 PD patients. Within the finite volume method framework, the Volume of Fluid (VOF) method was used, assuming two isothermal and immiscible fluids. 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: The interaction between the collagen and the brain tissue phases was analyzed, using two types of needle tips, a blunt needle tip and bevel needle tip (Fig. 1A, 1B). Alpha indicates the phase distribution, 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 (Fig. 1C, 1D). A difference in the pressure between the two needle tips was observed, with the bevel tip showing higher pressure on the site of the delivery.

CONCLUSIONS: 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 3D reconstruction from MRI images and modelling in the three-dimensional space.

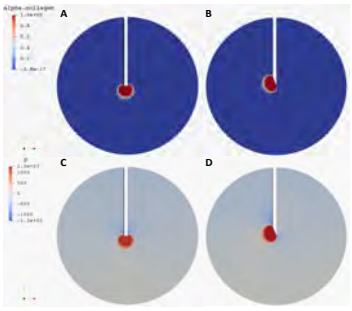

Figure 1: Two-dimensional model of collagen delivery to the striatum. (A) Interaction between collagen and brain tissue when injected with a blunt tip and (B) a bevel tip. (C) Pressure distribution for collagen injected with a blunt tip and (D) a bevel tip.

ACKNOWLEDGEMENTS: European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie Innovative Training Network grant agreement No 676408