

Towards an effective, needle-based delivery device for Parkinson's disease: a simulation study on the impact of needle diameter

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Introduction

Recently, several therapies have emerged for Parkinson's disease, a challenging neurodegenerative disorder. However, clinical translation is restricted, partially due to limitations in delivering therapeutics to the Central Nervous System (CNS) which cannot be reached by systemic administration. An alternative method, that bypasses the blood brain barrier and offers high-concentrated deposition in the diseased region, is intrastriatal delivery of a cell-loaded in situ forming collagen hydrogel. However, this strategy has disadvantages, including neuroimmune response and haemorrhage. To minimize these responses, an optimised medical device should be designed. Of main consideration is the volume dispensed and the needle dimensions. Current approaches use 18-20-Gauge diameter needles and multiple cranial penetrations [1]. Additionally, fluid forces acting on cells may lead to cell disruption and death [2]. This study aims to develop a novel device for the effective delivery of a cell-loaded in situ forming collagen hydrogel to the CNS. A simulation study on constricted channels representing the needle was performed to gain insight into the optimal needle diameter.

Methods

Experimental verification of the non-Newtonian properties of the collagen solution was performed using a rotational viscometer. Syringes with smaller needle diameters (22-26-Gauge) were tested to minimise possible haemorrhage during injection. Utilising a finite volume approach in OpenFOAM[3], straight needles, emanating co-axially from a common syringe, were computationally modelled as 2D sudden contractions (Fig.1). The flow was considered incompressible, with non-Newtonian fluid constitutive behaviour characterised experimentally, and with a constant inlet velocity corresponding to maximum delivery volume. The effects of needle diameter on velocity and shear stresses were examined.

Results

The collagen solution exhibited non-Newtonian, shear-thinning behaviour, fitted by the power-law, with a flow consistency index, k , of 26.95, and exponent, n , of 0.9608 giving a kinematic viscosity of 24-26 $\mu\text{m}^2/\text{s}$. Simulation results demonstrated a higher fluid velocity in the 26-Gauge needle (Fig.1), almost twice that of the 22-Gauge, and the accelerated fluid entered the needle from regions further away from the wall. Shear stresses indicated a greater influence of the higher-Gauge needle on the collagen solution.

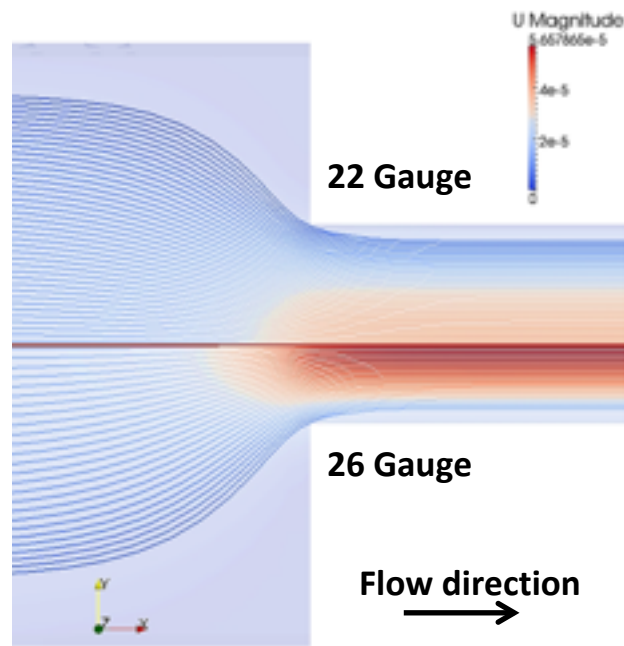


Fig.1: Velocity streamlines along simplified needles of 22-Gauge (top) and 26-Gauge (bottom) diameters.

Discussion

This study highlights the importance of needle diameter on the design of new delivery devices. As cells pass from the syringe barrel to the needle, the pressure drop and the increased velocity could damage them. This is more likely to occur using higher-Gauge needles, which are otherwise preferred for reducing haemorrhage risks. Further analysis is required including simulation of cells during injection and analysis of their deformation.

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References

1. Potts MB et al.,(2013)*Surgical Neurology International*.;4(Suppl 1):S22-S30.
2. Aguado BA et al.,(2012)*Tissue Eng. Part A* 18, 806–815.
3. www.openfoam.com