

A computational model of the human eye: a step towards defining cell spraying parameters to treat retinal diseases

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INTRODUCTION: Millions of people suffer from retinal degenerative diseases. Despite recent progress in developing stem cell therapies for retinal diseases, methods for delivery are still subject of intense research. Aerosol technology is a promising technique that can spray cells evenly¹ across the retinal surface, promoting cell attachment and survival². Optimizing cell spraying parameters (such as volume flow rate, air pressure and surface area covered) is costly to perform experimentally, thus creating the need for an alternative rapid and cost-effective technique. We use computational modelling as a tool to simulate stem cells delivery onto the inner retinal surface, hence define spraying parameters for aerosol systems.

METHODS: the experimental protocol consists of spraying a cellular scaffold (fibrin-derived hydrogel plus cells) onto the retina and stabilise the intraocular pressure as during vitrectomy. Hence, the computational setup consists of the geometry of the human eye (mimicked using a hemisphere with a diameter of 25 mm) and an injector with a diameter of 0.6 mm (setup summarised in Fig. 1).

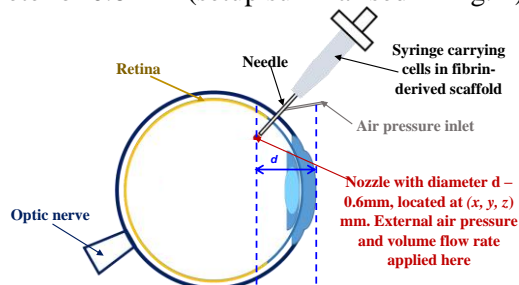


Fig.1: Schematic geometry of the eye, showing injector nozzle position, optic nerve and retina locations.

A mesh with an edge size of 0.2 mm is applied to the geometry using the finite element solver STAR-CCM+®. The material properties of the fibrin-derived hydrogel are determined using the rheometer DHR-3 (TA Instruments), and then imported into STAR-CCM+. We explore volume flow rates between 100 and 400 μLs^{-1} , with air pressures varying between 10 to 100 kPa. The spatial and temporal distribution of droplets are predicted.

RESULTS: The results demonstrate a strong dependence of spraying outputs on volume flow rate and pressure. The surface area covered by the spray system is dependent on the cone angle used for

spraying as shown in Fig. 2. The outer cone angle used to spray the cell suspension can be used to control the surface area of the retina that is covered.

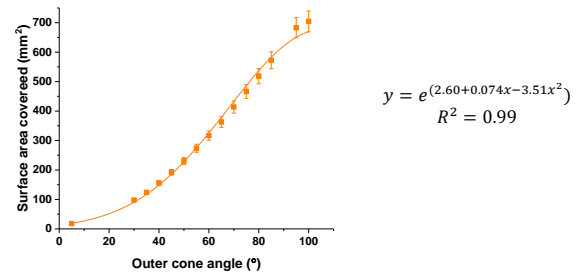


Fig.2: We present the surface area covering the inner retina for each spraying event as a function of the specified outer cone angle of sprayed cellular suspension ($R^2=0.99$).

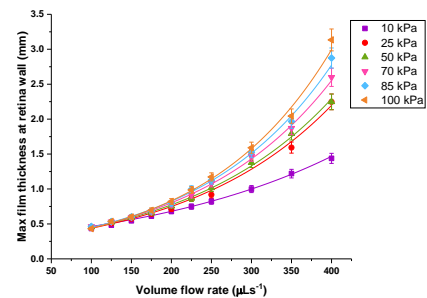


Fig.3: We present the maximum film thickness values for each spraying event as a function of volume flow rate and injector pressure ($R^2=0.99$).

These parameters could be used to predict operating parameters that enable a desired thickness on the retina to be achieved (see Fig 3). For example, the exponential relationship between maximum film thickness/mm (y) and volume flow rate/ μLs^{-1} (x) at 10 kPa is:

$$y = 0.30e^{0.004x}$$

DISCUSSION & CONCLUSIONS: This work indicates that simulation protocols may provide a platform to derive specific spraying parameters and could predict the required number of cells needed for each spraying event. Validation of these methods will require experimental testing *ex-vivo* and *in vivo* before they can be translated into the clinic and merits further investigations.

REFERENCES: ¹RE Maclaren et al (2006) Retinal Repair by Transplantation of Photoreceptor Precursors. *Nature*. 444:203-7. ² A Roberts et al (2005) Aerosol delivery of mammalian cells for tissue engineering. *Biotechnol Bioeng* 91 (7)801-7.