European Cells and Materials Vol. 32. Suppl. 4, 2016 (page 126) ISSN 1473-2262

Mathematical modelling as a tool to inform the design of spray systems for cell-based therapies

M Nweze[1, 3], T Baker[1], GA Limb[2], RJ Shipley[1]

[1] *Department of Mechanical Engineering, University College London, London, UK* [2] *Institute of Ophthalmology, University College London, London, UK and* [3]*Institute of Medical Physics and Biomedical Engineering, University College London, London, UK*

INTRODUCTION: Chronic degenerative disease such as cancer, Parkinson's disease and cardiovascular diseases are the leading cause of mortality worldwide[1]. According to the World Health Organisation, chronic diseases constitute 85%[2] of deaths in the United Kingdom; they also cause permanent loss of cells and organ dysfunction. Cell-based therapies provide a diverse range of treatment options, and spraying of cells directly to the affected area is one delivery mechanism that has been shown to promote cell proliferation and cell viability, as cells are delivered on a layer-by-layer basis in a fast and controlled manner, thus accelerating the healing process[3,4]. The requirements of cell spraying are specific to the tissue being treated, especially due to geometric variability between tissues. It is essential to understand the link between cell spraying output (e.g. volume of cells delivered, surface area and the spatial distribution of delivery), and input (air pressure, nozzle dimensions, volume flow rate of cell suspension); we aim to use computational modelling as a tool to inform these relationships, enabling organ-specific application of spray systems for cell delivery. Here we present a case study based on spraying cells to the back a human eye, a therapeutic option for treating blindness.

METHODS: We use the CFD solver, STAR-CCM+®, to enable spatial simulations of spraying in realistic clinical geometries. The human eye is represented by a three dimensional hemisphere with a diameter of 25 mm, where an injector with a nozzle diameter of 0.6 mm, positioned using cylindrical coordinate system at (3,7,0) from the centre of the geometry provides the location at which cells are sprayed into the eye. Typically a cell suspension (cells plus supporting matrix components) is injected at a rate of 2ml/s at a spraying angle of 120° for 2s, with an air pressure of 2 bars applied at the injector (these are realistic parameters used for commercially available cell-delivery spraying systems[3]). A continuum mechanics approach was used with the cellular suspension drops described using a multiphase model, and the spatial distribution of drops tracked in time. Boundary conditions on the hemisphere and nozzle input were chosen to represent the input parameters described above

RESULTS: For given output parameters, we are able to predict the thickness of the cellular suspension (see Fig 1), which varied over 1.3-2mm over the time course of one spraying event. The thickness and variability of this layer thickness is determined by the flow rate of delivery and spraying pressure. The section of the eye that is covered is determined by the spraying direction and nozzle geometry, and the model enables these parameters to be varied to inform spray operation.

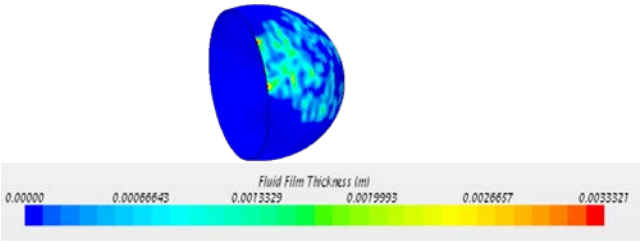

Fig. 1: Image of the hemisphere showing fluid film thickness distribution over the surface area.

DISCUSSION & CONCLUSIONS: The computational models developed provide insight into the link between spraying pressure and flow rate, and the spatial distribution of delivered cells. These simulations provide a starting point for building standardised computational models relevant to more complex geometries and spraying scenarios, with a view to informing cell delivery parameters in a way that minimises costly and time consuming experimentation.

REFERENCES: [1]WHO (2016) *Chronic diseases and health promotion*. [online] Available at http://www.who.int/chp/en/ [Accessed 5 May 2016]. [2] WHO (2016) *The impact of chronic disease in the United Kingdom*.[online]Available at http://www.who.int/chp/chronic_disease_report/media/uk.pdf?ua=1[Accessed 5 May 2016]. [3]A.L Thiebes, S. Albers, C. Klopsch et al (2015) *BioResearch Open Access* **4**:278-287. [4]A Roberts, B.E. Wyslouzil and L. Bonassar (2005) *Biotechnology & Bioengineering* **91**(7):801-807.

ACKNOWLEDGEMENTS: This work is supported by the EPSRC and the NIHR.