A Numerical Investigation of Stresses, Printing Efficiency, Printability, and Cell Viability in Nozzle Printheads for 3D Extrusion Bioprinting

(Osaka. U.)○(Stu) Zhang C. · (Stu) Hidaka M. · (Reg) Kojima M. · (Reg) Sakai S. · (Reg) Okano Y.*

1. Introduction

3D (three-dimensional) extrusion bioprinting is a rapidly developing field in tissue engineering. Recent advances have ushered in a new stage of producing customized and bioengineered structures serving in regenerative medicine, pharmacokinetics, and basic cell biology studies.[1] 3D extrusion bioprinters extrude bioinks (hydrogels that contain living cells) to form filaments and scaffolds that can later be cross-linked and used to construct desired biostructures.

Controlling stresses inside the needle during the extrusion is crucial to balancing printing resolution and cell viability.[2] As experimentally observing stresses is complex, the need to utilize numerical simulation to understand and optimize needle geometries, printing efficiency, printability, and cell viability becomes an urgent task for 3D extrusion bioprinting devices. This investigation considers alginate-based bioinks; they are the most used commercial bioinks due to their low cost, biocompatibility, and facile gelation.[3]

2. Numerical Method

This research numerically investigates three types of needles (90º cylindrical needle, 45º cylindrical needle, and tapered 6.36º needle (Fig. 1)) and their stresses/cell viability distributions.

The numerical simulation was executed by OpenFOAM. The following assumptions are made when concerning the analytical solution and simulation inside the needle: (I) the bioink acts as an incompressible power-law fluid; (II) there is no slip between the bioink and the smooth needle wall; (III) gravity influence is negligible due to fine needle size; (IV) the flow inside the needle is fully developed and laminar. The governing equations include continuity equation, Navier–Stokes equations, and Poisson equation for pressure.

In addition, to assess the printability of the printed strand, the Herschel–Bulkley fluid model is used to recover the effect of yield stress at the low shear rate states.

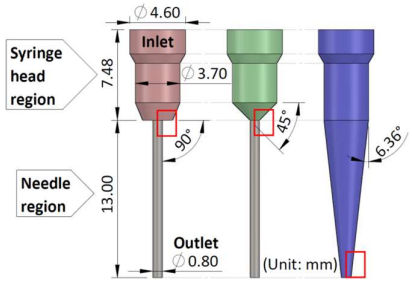

Fig. 1. Dimensions of needles in the simulation.

3. Results and Discussion

The stress profiles (around boxed regions in Fig. 1) of the 90º cylindrical needle are shown in Fig. 2. The magnitude of stresses decreases as temperature increases and increases as concentration increases (typical allowable shear stress to achieve 80% cell viability for fibroblasts is 5 kPa in 30 ms[1]).

The Herschel–Bulkley fluid model accurately estimates (81.1%) printed strand diameter. Further investigation of stresses inside the printed strand and cell viability is required.

With the existing cell viability model[2] and a constant flow rate, cylindrical needles exhibit low cell viability (~84%) in central needle inlet regions. The tapered needle manifests high cell viability (~94%) within most of its volume.

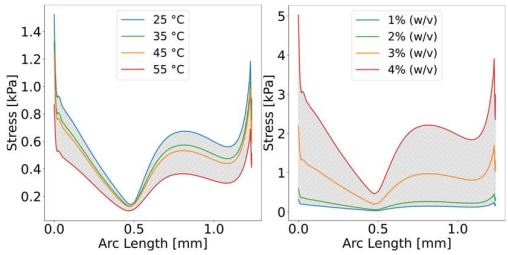

Fig. 2. Effects on the exerted stresses with temperature changes (left) and concentration changes (right).

4. Conclusion

The study of stress profiles inside three types of needles is conducted. The printability of the printed strand is validated. Cell viability distributions are obtained with an existing model.

When the volumetric flow rate remains constant, altering the bioink's temperature or concentration results in nonlinear changes in stresses and apparent viscosity profiles. Furthermore, the low-stress regions manifest dull responses to such changes; the high-stress regions' responses are much brisker. A combination of temperature and concentration change could lead to cell viability optimization.

References

1) Zhang, Y. *et al*., 3D Extrusion Bioprinting, Nat. Rev. Methods Primers, **1**(1), 1-20 (2021).
2) Blaeser, A. *et al*., Controlling Shear Stress in 3D Bioprinting is a Key Factor to Balance Printing Resolution and Stem Cell Integrity, Adv. Healthcare Mater., **5**(3), 326-333 (2016).
3) Piras, C. *et al*., Multicomponent Polysaccharide Alginate-based Bioinks, J. Mater. Chem. B, **8**(36), 8171-8188 (2020).

*okano.yasunori.es@osaka-u.ac.jp