Structural Optimization for Transport Efficiency in Porous Tissue Scaffolds

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The failing of tissue scaffolding is commonly attributed to insufficient nutrient supply and ill cell distribution (Malda et al. 2004). The non-uniform increase in cell number across scaffold can subsequently lead to a self-imposed transport barrier, which further intensifies cell distribution deviation, forming an adverse feedback cycle (Koch et al. 2010). Past studies have attempted to resolve such nutrient transportation issue by means of structural optimization on a microscopic scale. Although direct manipulation of structural variables may yield optimal physical properties (Chen et al. 2010), biological factors can complicate the structural transition process and influence the final outcome (Chen et al. 2011). Hence, to ensure the effectiveness of the design process, biological modeling must be integrated into the optimization procedure with appropriate design criteria to address the relationships and non-linearity among nutrient transport, cell growth, change in physical properties and the ability to secure long term nutrient supply.

The goal of this study was to determine the optimal porous scaffold structure that allows maximum cell survival at steady state under perfusion. The simulation was performed on one-dimensional models using porosity as the primary variable; dependent variables including oxygen concentration profile, cell volume, and permeability at steady state were computed through an iterative algorithm. The objective was to maximize the overall scaffold permeability to fluid flow; the total cell settlement was the indicator of design performance. The structural profile evolved based on the flow resistance criterion, which is a sensitivity function derived from a given permeability-to-porosity relationship. The initial designs were of uniform porosity across the entire scaffold with a volume constraint.

The results show clear structural evolution along with improvement in total steady-state cell volume. The porosity profiles of tissue scaffold changed from the initially uniform shapes to some profiles similar to the steady-state oxygen concentration, as to create buffering space and accommodate volumetric changes. The porosity pattern of the total scaffold-cell constitute evolved from the initial dense front, porous back, with curved transition in between, to a globally uniform form. The total flow resistance was minimized under such a uniform condition as anticipated in simple 1D simulation. Introducing diffusion criterion resulted in a non-linear profile that affected porosity particularly near the scaffold-fluid interfaces. The non-uniform cell distribution was found inevitable and would intensify with decreasing flow rate. However, the results showed an increasing effectiveness in performing design optimization on more ill-conditioned models.

This study has demonstrated the capability of resolving the adverse interplay between cell deposition and the resultant transport efficiency through a structural optimization procedure. The incorporation of nonlinear transient modeling into an optimization procedure made possible to directly relate the change in the final mass transport output to the change in initial structural porosity using appropriate design criteria. The optimal designs showed improved long-term cell viability in tissue scaffold construct.

References

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