Simulation of Excimer Laser Microfabricated Tissue Engineering Scaffold Microstructural Deformations and Effective Stiffness

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Statement of Purpose: Excimer laser (e.g., 248 nm, 193 nm) microablation has been used to process polymers into geometrically well-defined microstructures on relatively small (i.e., < 50 microns) length scales. Using 248 nm excimer laser microablation, poly(glycerol sebacate) (PGS) tissue engineering scaffolds exhibiting an accordion-like honeycomb microstructure were recently reported (Fig.1A) [1]. In that study, the scaffold was empirically designed to match the anisotropic mechanical properties of native myocardium. While the previous empirical design approach was effective, allowing for matching of scaffold to tissue stiffness by varying polymer curing conditions and pore geometry, it involved a time-consuming sequence of iterative fabrication and characterization steps. Further, while the previous empirical design approach allowed for prediction of the macro-scale scaffold effective stiffnesses, it yielded no information regarding scaffold structural element deformations at the micro-scale. Thus, toward a more efficient and robust scaffold design approach, and to provide insight into the deformations of scaffold structural elements at length scales relevant to cells, here we used a periodic finite element approach to retrospectively predict the anisotropic effective stiffnesses of an accordion-like honeycomb PGS scaffold.

Methods: Experimental data for the scaffold microstructure dimensions under no external loading and for the mechanical properties of PGS and the accordion-like honeycomb scaffolds were previously published [1]. In brief, in [1] PGS polymer was synthesized by reacting glycerol and sebacic acid (1:1 molar ratio; Sigma) under heat (120°C) and vacuum (~ 15 mTorr) for 72 hours [2], cast into 250 micron-thick sheets by curing (7.5 hours at 160°C) on sucrose-coated silicon wafers in a vacuum oven [3], and microfabricated using a Rapid X 1000 system (Resonetics, Nashua, NH) with a 248 nm krypton fluoride LPX200 excimer laser (Coherent-Lambda Physik). Periodic finite element simulations on a periodic unit cell (Fig.1B) of the accordion-like honeycomb scaffold were carried out using Zset software [4]. Due to the square geometrical features of the scaffold and to facilitate obtaining a periodic boundary mesh, the mesh consisted of square elements with a quadratic interpolation. A mesh density of 20 square elements per edge was determined from a mesh independence study. Isotropic linear elasticity was assumed for both phases (PGS structural elements and void space). The scaffold effective stiffnesses in the two orthogonal directions were calculated by homogenization from the fourth-rank elasticity tensor of the infinite medium (including the infinite tessellation of the scaffold unit cell).

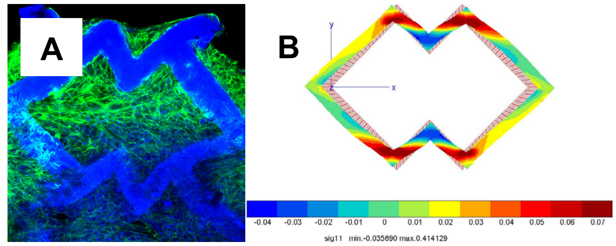

Figure 1. (**A**) Confocal micrograph of a heart cell seeded accordion-like honeycomb scaffold (F-actin in green; neonatal rat heart cell nuclei and PGS scaffold in blue; unpublished image from study [1]). (**B**) Periodic finite element simulation of the accordion-like honeycomb unit cell at 10% tensile strain (applied along the long-axis of the pore). Color scale indicates the stress component along the long axis direction (dark red = +70 kPa (tensile stress) and dark blue = -40 kPa (compressive stress)).

Results: The anisotropic effective stiffnesses of the accordion-like honeycomb PGS scaffold were previously reported to be 83±2 kPa (tested in uniaxial tension along long-axis of pores) and 31±1 kPa in the orthogonal direction (fabricated from PGS cured for 7.5 hours at 160C, with a PGS stiffness of 825±62 kPa) [1]. The periodic finite element stimulations predicted effective stiffness values of 81 kPa (simulated loading along the long-axis of pores) and 33 kPa in the orthogonal direction.

Conclusions: Here we demonstrated that a periodic finite element simulation on a unit cell of the accordion-like honeycomb microstructure could be utilized to yield a good approximation of the macro-scale scaffold effective stiffnesses. The periodic finite element simulation could thus be used to predict scaffold effective stiffness in the case of a different PGS stiffness (which has been precisely controlled previously by varying curing time at constant temperature [1]), or in the case of different microstructural element dimensions (e.g., changes in the width of the scaffold structural elements). In future studies this design approach will aid in developing scaffolds with mechanical properties better suited for heart cell-mediated contraction.

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References:
[1] (Engelmayr GC Jr. Nat Mater. 2008;7:1003-10.)
[2] (Wang Y. Nat Biotechnol. 2002;20:602-6.)
[3] (Fidkowski C. Tissue Eng. 2005;11:302-9.)
[4] (Zset, Mines ParisTech – ONERA – NW Numerics, http://zebulon.onera.fr/English/index.html)