Design and Qualification of a Novel Flex-Stretch-Flow Bioreactor for Engineering Heart Valve Tissues

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Statement of Purpose: Previous bioreactor studies using single deformation modes have shown that cyclic flexure [1, 2], stretch [3], and flow [4] (FSF) can independently stimulate engineered heart valve tissue formation. In the current study, a novel bioreactor system was developed for investigating both the independent and coupled effects of FSF on engineered heart valve tissue formation. The FSF bioreactor accommodates 24 rectangular tissue specimens (~ 25 x 7.5 x 1 mm), with flexure and stretch applied by a linear actuator. Flow is generated via a magnetically-coupled paddlewheel.

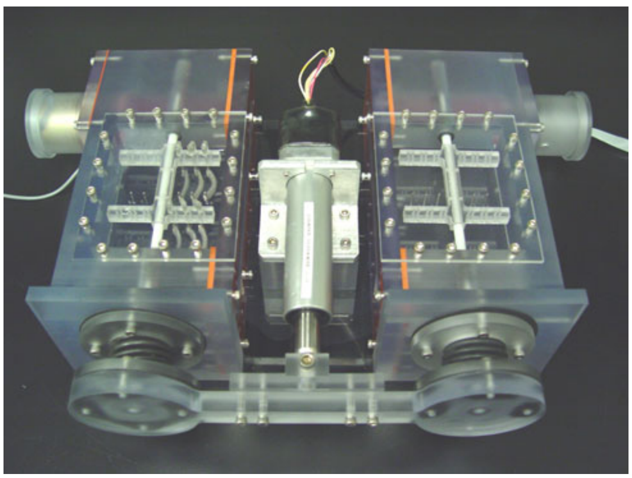

Figure 1 – The Flexure/Stretch/Flow (FSF) Bioreactor.

Methods: The FSF bioreactor (**Fig. 1**) was designed in a similar manner to our previous cyclic flexure bioreactor [1, 2]. The structural components of the FSF bioreactor were designed using Solidworks 3D CAD software (Solidworks, Corp., Concord, MA). Machined parts were fabricated from polycarbonate. The paddlewheel was fabricated by stereolithography (FineLine Prototyping, Inc., Raleigh, NC) using a high strength, water resistant resin (ProtoTherm 12120™; DSM Somos®, Newcastle, DE). The paddlewheel was magnetically coupled to a modified immersible stirrer (IM75; Corning Life Sciences, Acton, MA) by two cylindrical (1/4 x 3/4 in.) nickel-coated, grade N38 neodymium (NdFeB) magnets (K&J Magnetics, Inc., Jamison, PA). Synthetic sapphire ring jewel bearings (Bird Precision, Waltham, MA) provided low starting torque for effective magnetic torque transmission. All metallic components were made from 316 stainless steel. Cyclic flexure and/or stretch were applied by an environmentally-sealed linear actuator (UltraMotion, Mattitick, NY) controlled by Windows-based Si Programmer software (Applied Motion Products, Watsonville, CA).

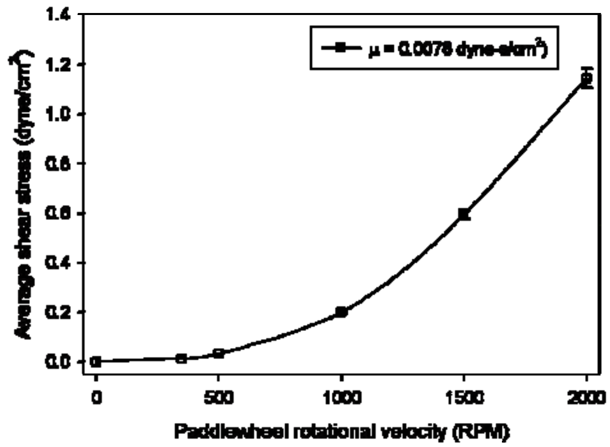

Figure 2 - Average fluid shear stress experienced by tissue specimens predicted as a function of paddlewheel rotational velocity for standard culture medium viscosity.

A computational fluid dynamics (CFD) model was developed using GAMBIT® and FLUENT® (v6.2) software (Fluent, Inc., Lebanon, NH). The effect of paddlewheel rotational velocity on flow rate was simulated using a 2-D dynamic mesh of 50,000 triangular fluid elements. The unsteady-state simulation (0.0001s time step) was solved for 350-2000 RPM rotational velocities and a viscosity of 0.0076 dyne-cm/s. 2-D velocity profiles were applied upstream of the specimens in a 3-D simulation to predict shear stresses. The model was validated by particle image velocimetry [5].

Results / Discussion: Velocity profiles predicted by the 2-D CFD model compared well with PIV measurements (data not shown). The maximum average fluid shear stress generated in the FSF bioreactor was found to be 1.145 dyne/cm^2 (**Fig. 2**). Inter and Intra-specimen variations in fluid shear stress were not significant.

Conclusions: The FSF bioreactor is suitable for applying independent and coupled cyclic flexure, stretch, and flow stimuli to engineered heart valve tissues at a range of sub and near physiologic levels.

Acknowledgments: NIH HL-68816 (MSS) and AHA fellowship 0415406U (GCE; PA-DE affiliate).

References:

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