FSF Bioreactor Design Improvement, Restoration, and Testing

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Introduction:

A bioreactor that is capable of cyclic flexure, stretch, and flow (FSF) has been previously designed and built by Engelmayr et al [1]. The bioreactor is used to implement mechanical stimuli on engineered heart valve tissue [2]. In this mechanical environment, enhanced tissue formation has been found [1]. The FSF bioreactor is shown in diagram A.

Twenty four strips of tissue can be placed in the bioreactor. These tissues undergo flexure and stretch provided by a linear actuator. Fluid Flow is driven by a magnetic coupling system in conjunction with a paddle wheel, which is very energy efficient because it uses magnetic power. As described by Engelmayr et al [1], the FSF bioreactor was used to successfully achieve the acceleration of heart valve tissue formation. After 3 weeks, the collagen content of the tissue was 75% higher than tissue without mechanical stimuli; the tissue stiffness was drastically increased as well.

In this project, we focus on this bioreactor design and proceed with relevant cell/tissue culture followed by engineered valvular tissue development.

Methods:

Stage I

This portion has been removed due to confidentiality issues.

Stage II: Cell Culture Process Experience

The purpose of the next stage is to gain experience doing cell culture. We will culture ovine bone marrow stem cells, which will expand in triple flasks. When confluence is reached, i.e. there is no more room for expansion in the flask, we will split the cells into more flasks. Some of the cells will be seeded into scaffolds, and be continued to be grown in culture. Eventually these scaffolds will be placed in the bioreactor.

Stage III: Testing and Experiment

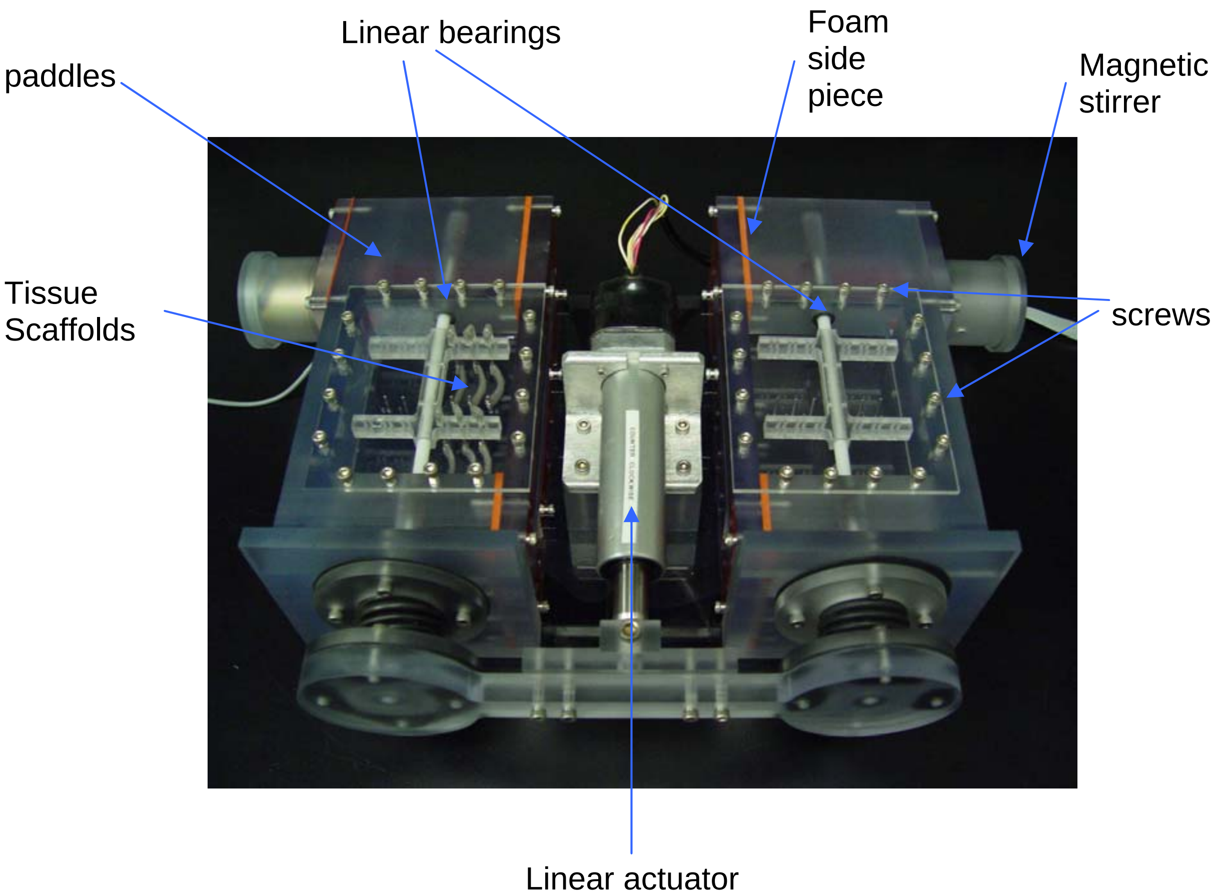
First, we will do a dry run on the FSF bioreactor, which means water for the liquid and acellular scaffolds. This is known as a dry run. Also, by this time, there will be enough cells to seed a scaffold, which provide a 3-D structure for the cells to develop into tissue. Without this 3-D matrix structure, the cells will keep dividing, but they will not grow into tissue. Also, we will perform a static 3D culture in a hybridization tube to ensure a uniform distribution of cells within the scaffold. Finally, we will perform an experiment with the bioreactor using the seeded scaffolds. The time period will be one week, with one group undergoing flex, stretch, and flow while the other group will serve as the control. After one week, a collagen assay will be used to determine the collagen content in both tissues. The higher collagen content may be indicative of more robust tissue formation. Also, a software that models the flow in the FSF bioreactor is commercially available, so time permitting, a simple computational simulation will be used to compare the results of the experiment.

Expected Results:

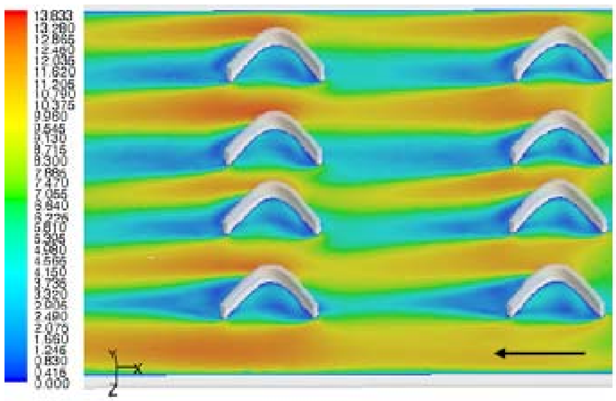
In stage 3, the effect of mechanical stimuli should accelerate the tissue growth, which will be seen in higher collagen content.

Diagrams:

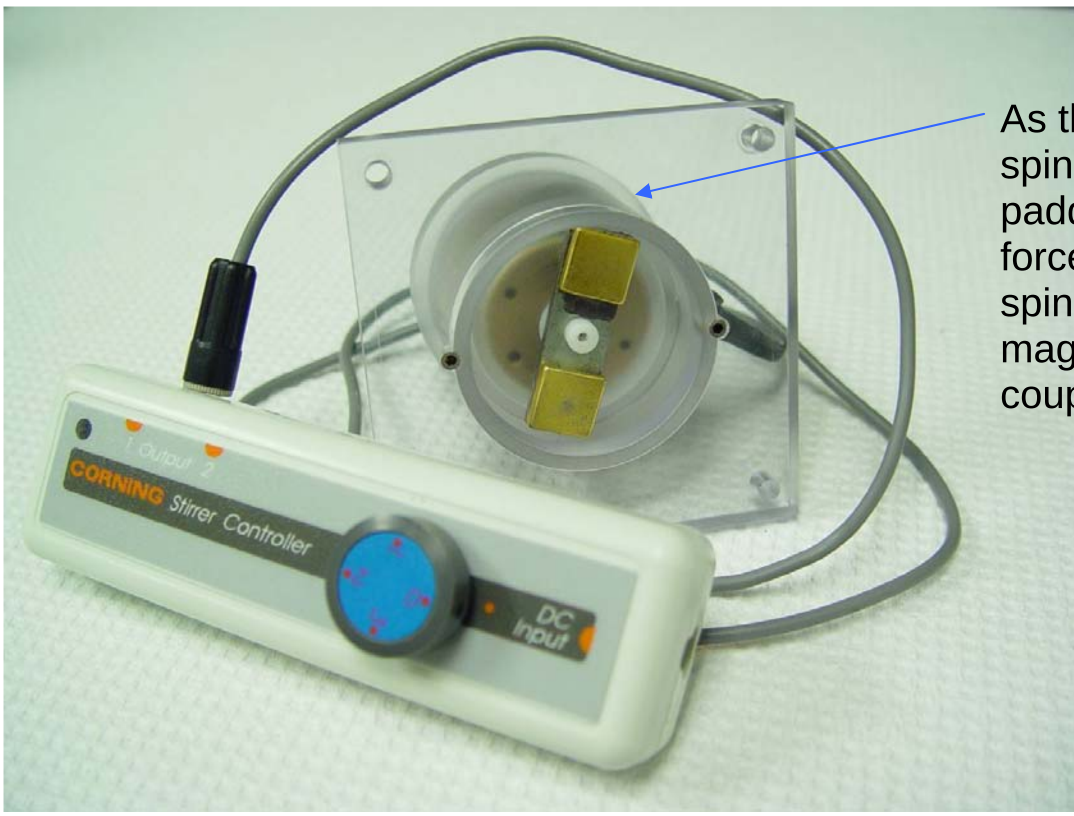
A: FSF bioreactor developed by George Engelmayr, Jr. , Ph.D [2]



B: Scaffolds Under Flexure [2]

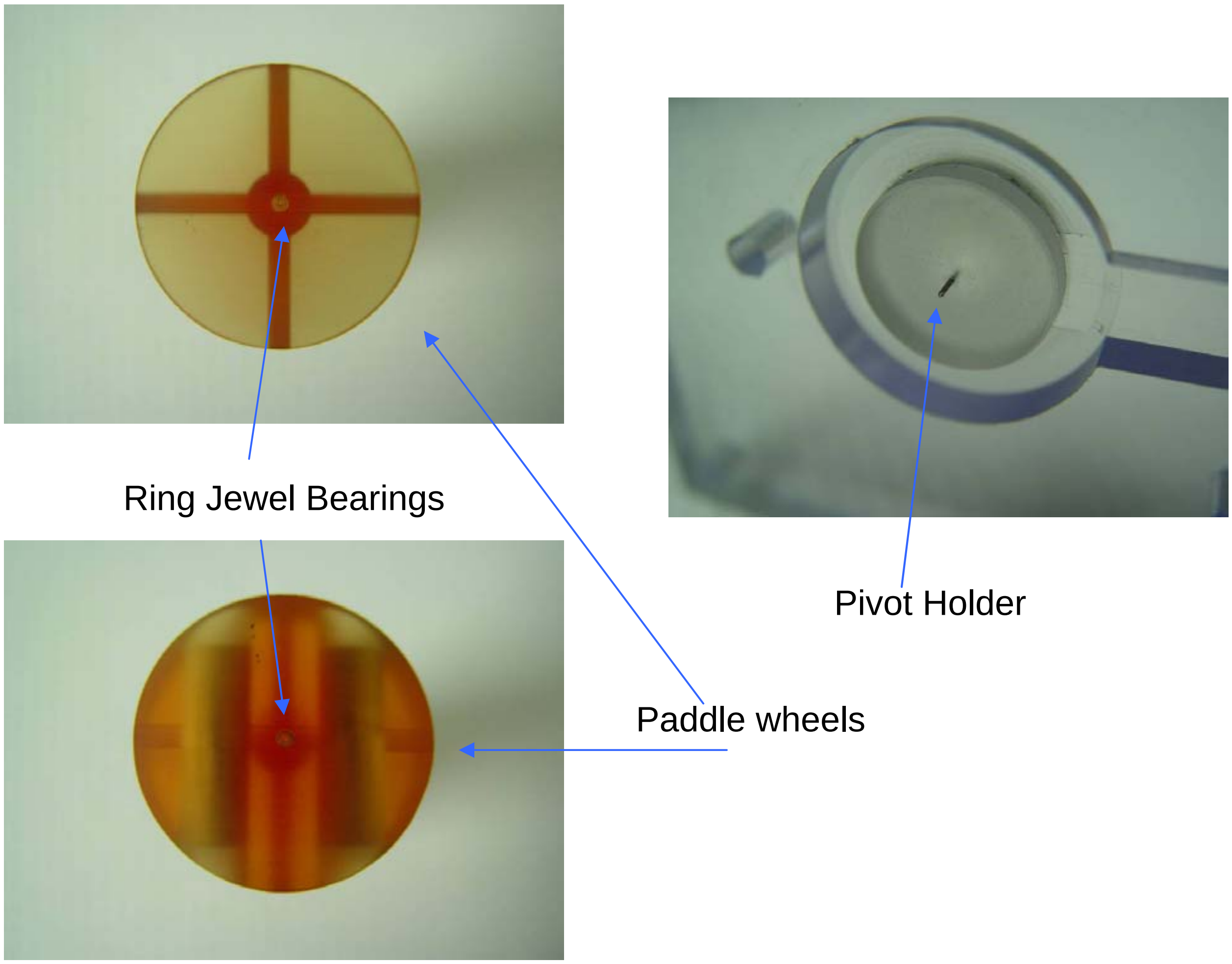


C: Magnetic Coupling System



As this wheel spins, the paddle is forced to spin by magnetic coupling.

D: Paddle Wheels and Parts



References:

[1] Engelmayr Jr George C., Sales Virna L., Mayer Jr John E., Sacks Michael S. Cyclic flexure and laminar flow synergistically accelerate mesenchymal stem cell-mediated engineered tissue formation: Implications for engineered heart valve tissues. Biomaterials 27 (2006): 6083–6095.

[2] Engelmayr Jr George C. , Soletti Lorenzo, Vigmostad Sarah, Budilarto Stephanus, Federspiel William, Chandran Krishnan, Vorp David, Sacks Michael. Design and Qualification of a Novel Flex-Stretch-Flow Bioreactor for Engineering Heart Valve Tissues, Society of Heart Valve Disease, 4^{th} Biennials meeting, June 15^{th}-18^{th}, New York, NY.