Project description:

Development of an Intervertebral Disc Bioreactor

Master's Thesis project proposal

Mechanical stimulation during tissue growth, turnover or degeneration is known to trigger cellular responses. To provide this stimulation *in vitro*, a bioreactor is required. Not only does this device simulate *in vivo* conditions, but it also allows manipulation of specific parameters. Further, it is possible to exclude unwanted influences and develop a culture model with controlled environmental properties. Under these conditions, investigations of mechanobiological properties of tissues and organs are feasible. This information can then be applied to the development of grafts or research in tissue engineering.

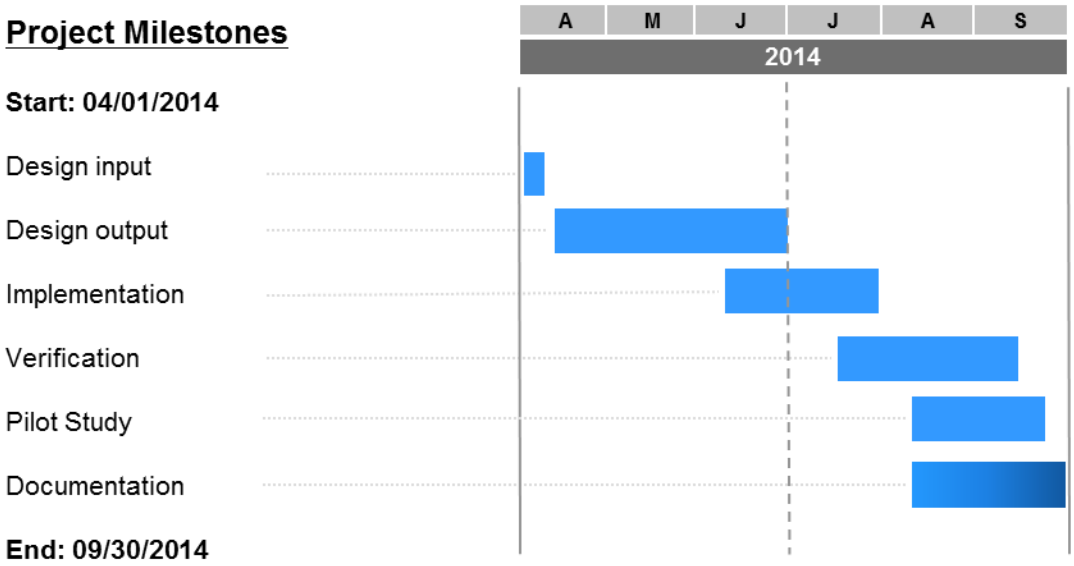
The goal of this project is to develop a bioreactor for intervertebral disc research. Similar to *in vivo* conditions, the intervertebral discs require static and dynamic compression loads exerted by the bioreactor to perform adequate investigations. To ensure cell survival, the discs must remain in culture at all times. This demands a regular exchange of nutrition fluid, preferably provided by the bioreactor. Environmental conditions, such as temperature, air composition and humidity, need to be regulated by incorporating the bioreactor within an incubator. Hence, the dimensions of the bioreactor may not exceed those of the incubator.

Recently, there has been growing interest to use using organ cultures to study disease progression and repair. Bioreactors can be used to maintain bone-disc-bone motion segments (i.e. disc organ culture) to study disc degeneration, herniation, and potential repair strategies. Dr. O'Connell's collaboration with Dr. James Cook's laboratory at the University of Missouri, Columbia, demonstrated the feasibility of maintaining cell viability, mechanical properties, and biochemical composition of rat lumbar discs in culture (3 weeks).[1] This study aims to expand on that research by developing a bioreactor that will be capable of applying physiological levels of load to disc cultures of various animal model species.

A representative animal model for human intervertebral discs has yet to be found. Based on geometric parameters, the mouse and rat lumbar, and mouse tail discs are the closest representation of the human lumbar intervertebral disc geometry.[2] However, no known study investigating the effect of mechanical loading of intervertebral discs from different species has been done. Therefore, it is beneficial to design a bioreactor compatible with a large range of disc geometries obtained from different species. In addition, this broadens the spectrum of tests with possible graft geometries for tissue engineering.

This project is bound to a time span of six months. Starting date is April 1st 2014. The development phase is divided into design output and implementation (Figure below). One important milestone is the design output after three months. Implementation and optimization are the next major steps. The project is brought to an end with the verification of the bioreactor. Submission of the report is on September 30th 2014.

Outcome of this project is a fully functioning bioreactor ready for mechanical loading of intervertebral discs for tissue engineering purposes. A pilot study will be performed to verify that the compressive bioreactor produces results comparable to published data on articular cartilage and engineered cartilage constructs.[3,4]



References:

1. *O'Connell GD, Vresilovic EJ, Elliott DM*. Comparison of Animals Used in Disc Research to Human Lumbar Disc Geometry. *Spine, 2007*
2. *Edamura K, Stannard JT, Stoker AM, O'Connell GD, Kuroki K, Hung CT, Choma TJ, Jeffries JT, Cook JL*. A Whole Organ Culture Model for Intervertebral Disc Using Rat Tail Explants in a Rotating Bioreactor. Abstract for poster presentation, 58th Annual Meeting of the Orthopaedic Research Society, San Francisco, CA USA, 2012
3. *Chahine NO, Albro MB, Lima EG, et al*. Effect of Dynamic Loading on the Transport of Solutes into Agarose Hydrogels, *Biophysical Journal, 2009*
4. *Mauck RL, Soltz MA, Wang CC, et al.* Functional Tissue Engineering of Articular Cartilage Through Dynamic Loading of Chondrocyte-Seeded Agarose Gels, *Journal of Biomedical Engineering, 2000*