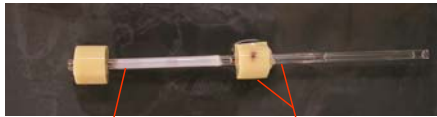


# Design of a Bioreactor for Vascular Tissue Engineering

Patrick Allen, advised by Dr. Andrew Rapoff (Union) and Dr. Jan Stegemann (RPI)

## Motivation

- Heart attacks strike 1.2 million Americans per year, and the most common treatment is coronary artery bypass grafting.
- Current bypass grafts call for donation of a vein from the patient or the use of a Dacron or Teflon synthetic vessel.
- In many cases, donation veins are already ruined by atherosclerosis, and synthetic implants suffer from thrombosis (blockage due to plaque).
- A fully engineered, implantable blood vessel created *in vitro* is the "Holy Grail of tissue engineering".



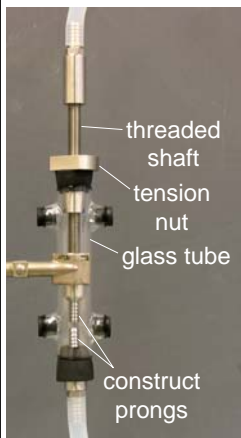
collagen construct glass mandrel and rubber stopper (from construct manufacture)

**Figure 1: A statically cultured, collagen based vascular construct.**

## Product Design Specifications

- The design process was driven by the tissue engineering needs of the Stegemann lab group.
- From a wide variety of possible design goals, a list of concrete, feasible requirements were formalized. The bioreactor must:
  1. have the ability to impart stresses to tubular or solid constructs with minimal modification.
  2. apply static longitudinal stress to solid or tubular constructs.
  3. apply dynamic circumferential stress to tube constructs.
  4. allow tube constructs to exist under either a low or high shear stress environment.
  5. be adaptable to a variety of construct dimensions.
  6. have a nutrient circulation system which minimizes the required volume of biochemicals.
  7. maintain the construct and all working fluids within the RPI BME department tissue culture core incubator.
  8. maintain the construct and working fluids in a sterile condition.

## Strain Assembly



**Figure 3: Strain assembly prototype.**

- The strain assembly combines the roles of the construct mold and mechanical stimulator.
- During construct formation, solubilized collagen with SMCs is poured into the glass tube.
- After 2-3 hours' incubation, collagen will solidify in a tubular (lumen) shape, adhering to ribbed construct prongs.
- Circumferential stress is applied by periodically cycling the intraluminal pressure, inflating and deflating the construct.
- Longitudinal stress is applied by rotating tension nut, retracting upper construct prong to slightly stretch the construct lengthwise.
- Fluid shear stress can be controlled with media flow rate.

## Acknowledgements

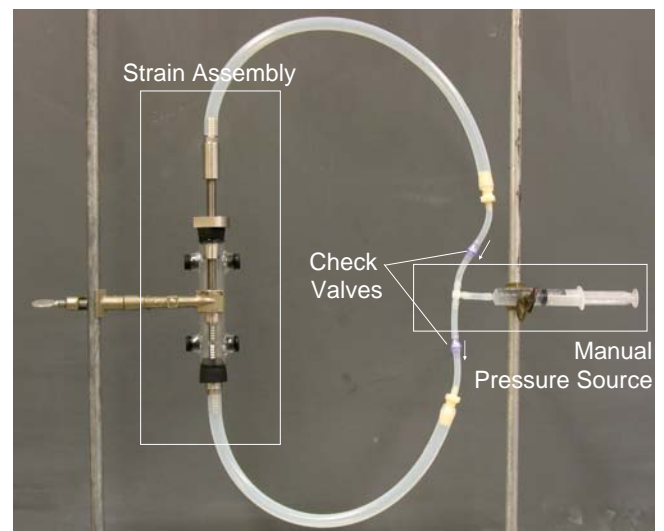
Dr. Andrew Rapoff, Dr. Jan Stegemann, Shaneen Rowe, Jim Howard (Union Machine Shop), Bill Jones (GE Glassblowing shop)

## Role of Mechanical Stimulation

- Collagen based, smooth muscle cell (SMC) seeded constructs with consistent mechanical properties can be molded in test tubes and statically cultured in Petri dishes.
- Statically cultured constructs are weak and look like a mess of spaghetti on the microscale, with SMC's randomly positioned like tomato chunks.



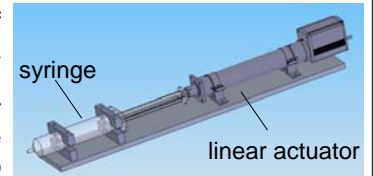
- Periodic mechanical stimulation causes seeded SMC's to remodel the protein matrix until it is stronger and more organized, arranged like uncooked spaghetti.
- Mechanical stimulation increases cell reproduction, protein synthesis and construct strength in resistance to applied stress.
- Fundamental stress forms for tubes: circumferential, longitudinal, torsion and surface shear.



**Figure 2: Bioreactor prototype**

## Pressure Source

- The pressure source consists of a disposable syringe driven by a programmable linear actuator.
- Using a programmable linear actuator will allow for pressure waveform to be precisely tuned to optimize construct response.



**Figure 4: Pressure source.**

- Actuator can be programmed with respect to:
  - speed => fluid flow rate OR force => fluid pressure
- Concept manually proven with syringe, actuator not set up.

## Conclusions

- A bioreactor to apply circumferential, longitudinal and fluid shear stress to collagen based vascular constructs was prototyped.
- Future work will call for incorporation of the linear actuator and size reduction of strain assembly for lab testing to begin.
- Study of stress parameters' impact on construct viability.