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A Novel Biochamberfor modeling of atherosclerotic arteries: In-vitro Capabilities and Applications

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A Novel Biochamber for modeling of atherosclerotic arteries: In-vitro Capabilities and Applications

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Background

Atherosclerosis is a chronic disease that involves the lipid accumulation and inflammation of the arterial wall [1,2]. Despite great efforts, its pathophysiology has not been fully elucidated. Existent drugs can reduce its progression but there are no available drugs to prevent from its complications [3,4]. Atherosclerosis remains the leading global cause of death [5].

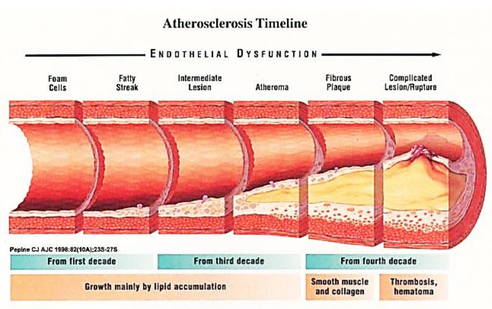

Fig. 1. Atherosclerosis Timeline [6]

Objective

The purpose of this work is to design and build a customized biochamber which can be used for the following studies:

- Study the pathophysiology of atherosclerosis in vitro & ex vivo
- Investigate the mechanisms of atherosclerotic plaque disruption
- Examine the direct effect of different anti-atherosclerotic drugs on lesions
- Use as a stenting simulation device for both research and educational purposes

Materials and Methods

The biochamber is made of FDA-compliant optically clear and cast acrylic (Figure 2,3). The dimensions after assembly are $13\frac{1}{2}in$ height, $10\frac{3}{4}in$ width and $5in$ depth. There are two cutouts on two sides which enable the researchers to easily access the inside for mounting the artery or measuring certain parameters. Each cutout is covered by an acrylic lid that is fastened by wing head thumb screws and sealed by a silicon rubber O-ring underneath. The chamber then filled with medium. The chamber has six main adjustable sealed ports primarily used as the input and output of the fluid flow. There are also two extra ports at the bottom for draining the fluid out or circulation of medium inside the chamber.

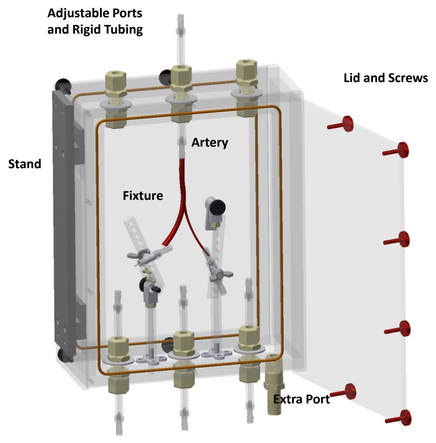

Fig. 2. Chamber CAD design

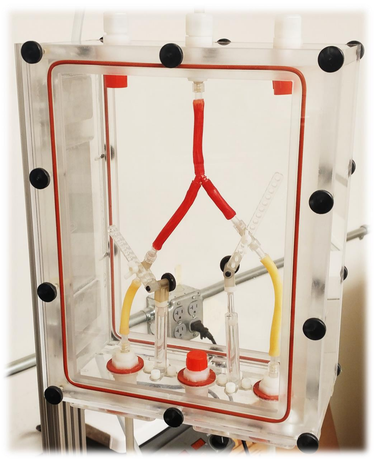

Fig. 3. Built Chamber

To flow the fluid into the artery at least two of the six ports should be used. Each port is holding a 5-10in long rigid tube with female luer lock at each end. The tube slides vertically in the port to meet the artery with specific length. Using this feature arteries form several vascular beds with different shapes and sizes can be mounted (e.g. coronary, carotid, femoral).

Figure 4 shows that, the unique feature of two 5 DOF fixtures that were designed to accommodate arterial bifurcations with different branch lengths and bifurcation angle. Furthermore, all of the connections and fittings are perfectly designed to accommodate pressure and flow wires, intravascular imaging catheters (OCT, IVUS), stents and microcatheters for local drug delivery. Another unique feature of this biochamber is that all of the parts are made of non-metal material which make the device CT- and MRI-compatible.

Fig. 4. Bifurcation Holder

To provide a similar in vivo condition, the medium temperature around the artery is maintained 37°C by a circulation which pumps 37°C medium in the chamber with adjustable volume rate (Figure 5).

Finally, all parts are capable to be sterilized by Ethylene Oxide (EtO) process to be used for multiple tests and studies.

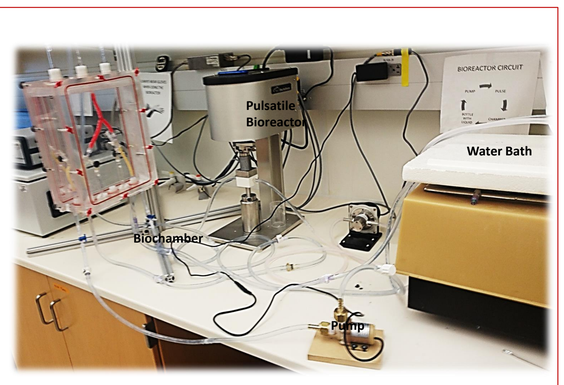

Fig. 5. Bioreactor System (Experiment setup)

To prove the desired functionality, several experiments are carried (Figure 6). A femoral artery from a human cadaver was mounted in the Biochamber (Figure #). The Biochamber was connected to the commercially available bioreactor and Dulbecco's Modified Eagle's Medium (DMEM) + 10% Fetal Calf Serum (FCS) were used as the circulatory fluid in a close loop system. To maintain the vitality of the artery the Biochamber was filled with DMEM + 10% FCS. The circulating fluid temperature was maintained $37°C\ (98.6°F)$ and the flow rate of 40-1000 mL/min and pulse rate of 50-300 beats/min were applied to simulate the human body condition. A multipurpose 6f catheter was advanced through an external port into the mounted artery to prove the compatibility of chamber with other medical devices. These tests were being carried out on the chamber with different hemodynamic conditions for 4 weeks nonstop.

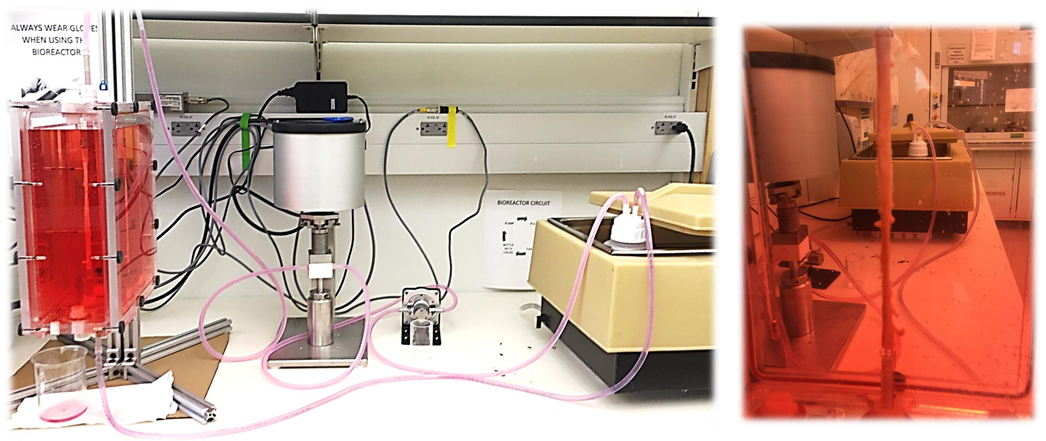

Fig. 6. Reliability experiment

Results

- No leakage was seen in the Biochamber and connection fittings under any flow and pulse rate.
- Successful accommodation of the intravascular imaging catheters, stent catheters and microcatheters for local drug delivery.
- Successful accommodation of arteries with different sizes and shapes using 5 DOF fixture, rigid tubes and connection fittings.

Conclusion

A highly flexible fully customized biochamber was successfully designed, built and tested. This biochamber has the potential to allow state-of-the-art research in atherosclerosis serving as bridge to in-vivo animal studies. It will enable the development of new imaging modalities, better understanding of the pathobiology of atherosclerosis, investigation of new drugs and testing of new stent designs and techniques

Future Works

Temperature measurement in the artery.

Improvement of catheter accommodation.

X-ray detectible marks for length measurement of the artery in imaging.

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