A NEW EX VIVO SETUP FOR DETERMINING MECHANICAL CHARACTERISTICS OF ARTERIAL SEGMENTS

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INTRODUCTION

Atherosclerosis of the coronary arteries, characterised by a narrowed lumen or stenosis, is the major cause of death in the western society. Stenosis can be treated by catheter-based interventions like percutanous transluminal coronary angioplasty (PTCA). During this procedure relatively high mechanical loads are induced locally on the vascular cells (VCs) resulting in injury of the wall. A possible response to this injury is the chronic renarrowing of the dilated vessel, or restenosis. Intraluminal coronary radiation therapy (ICRT) has shown good results in the prevention of restenosis. Another response to high mechanical loads might be remodelling of the vascular wall that can result in changes in the mechanical characteristics of the arterial segment. By optimising both PTCA and ICRT procedures restenosis rates may be reduced even more. To obtain knowledge an *ex vivo* vascular model may be helpful. The aim of this study is to develop an experimental set-up in which coronary arterial segments can be conditioned and perfused under physiological conditions such that PTCA, ICRT or any other catheter-based intraluminal intervention can be applied. The physiological loads on the coronary vascular wall, wall shear stress (τ_w), circumferential ($\varepsilon_{\theta\theta}$), and axial ($\varepsilon_{zz}$) strain, result from pulsating blood flow and the contracting heart. These mechanical factors seem to be important for the functional maintenance of VCs. Arterial culture systems described in literature [1,2] only apply flow and pressure. Axial strain is not considered. Because coronary arteries are situated on the heart the axial elongation can reach levels up to 20% and therefore ε_{zz} cannot be neglected. In the new experimental set-up the important characteristics of these periodic loads can be reconstructed and applied to arterial specimens. Furthermore, force-elongation and pressure-diameter relations can be determined.

METHODS

In the new experimental setup, shown in figure 1, the important characteristics of the periodic axial strain and internal pressure can be reconstructed and applied to the coronary arterial samples. Lowercase bold letters refer to figure 1.

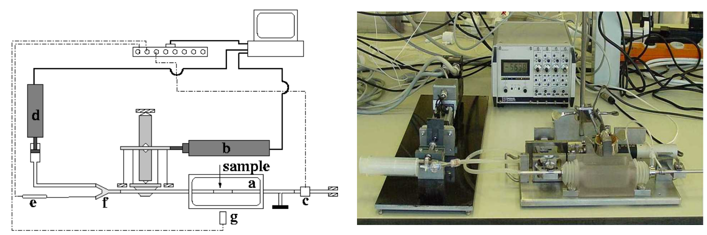

Figure 1. Schematic drawing (l) and overview of setup

Apparatus description

On both sides the arterial segment was tied to a vessel cannula (30005, Medtronic, The Netherlands). The cannulae were connected to stainless steel tubes, one of which maybe moved axially. Together with the tubes, the segment was immersed in cell culture medium inside a polycarbonate (PC) organ bath (**a**). The sinusoidal axial elongation of the vessel was generated with a freely programmable linear actuator (**b**, PI 235.5 DG, Physik Instrumente, Germany) and controller (C842, Physik Instrumente, Germany) that was attached to the movable stainless steel tube. The resulting axial force was measured with a force transducer (**c**, XFTC101-M%M-20, J&M instruments, The Netherlands) that was situated at the end of the fixed stainless steel tube. Silicon tubes were connected to both stainless steel tubes. By filling the tubes with cell culture medium the arterial segment was completely surrounded by medium. The transmural pressure was applied by a piston-pump (**d**, Parker Hannifin, The Netherlands) that was connected to one of the silicon tubes. The other silicon tube was closed. The sinusoidal movement of the piston was synchronised with the axial extension and the transmural pressure was measured with a pressure sensor (**e**, PressureWire IV, RADI Medical Systems, Sweden) that was inserted in to the arterial segment through an Y-connector (**f**). Using an ultrasound based wall tracking system (**g**, Biophysics, Maastricht University, The Netherlands) situated above the arterial segment the external diameter of the specimen was determined.

All signals were monitored with a multi I/O data acquisition system (National Instruments, USA) at a sampling frequency of 50 Hz.

Arterial preparation and nutrition

The epicardial part of the left anterior descending coronary artery (LAD) was excised from a porcine heart. Under sterile conditions the pericard was opened and the LAD located. Its side branches were closed with sutured wire. The LAD was opened on the cranial side and a vessel cannula was inserted in downstream direction. A suture wire was used to tie the artery to the cannula. The same procedure was repeated at the caudal side of the LAD but now the cannula was inserted in upstream direction. After measuring the *in vivo* length the LAD was completely excised. The LAD was placed in the setup very easily with LUER lock connectors. After clamping and filling the bath and silicon tubes with cell culture medium (DMEM complemented with FBS and 1% 100 IU penicillin/streptomycin), the LAD was stretched until the measured *in vivo* length was regained. The time between dissection of the heart from the animal and the placing of the segment in to the setup was less than 90 minutes.

Applied loads

First the arterial segments were pressurised sinusoidally at a 1 Hz frequency between 0 and 16 kPa without axial elongation. After that the segments were stretched sinusoidally up to 5 % of its *in vivo* length with the same frequency. Finally both periodic loads were applied synchronously. For the pressure–diameter relationship the outer diameter of the arterial segments is used.

RESULTS

Figure 2 shows the pressure–diameter curve obtained from a LAD on which only pressure was applied. Two force–elongation curves obtained from a LAD that was stretched periodically are shown in figure 3. Both the force–elongation and the pressure diameter curves of a LAD that was synchronously pressurized and stretched are shown in figure 4.

DISCUSSION

The outer diameter of the LAD remained somewhat constant up to 10 kPa. At higher transmural pressure the outer diameter increased. During the experiment it was difficult to keep the LAD pressurized because of medium leakage at the side branches. The presence of the side branches made it also difficult to obtain good diameter measurements. The nonlinearity in the force–elongation curves was reproducible. By increasing the elongation, even up to 20 %, the complete mechanical trajectory can be monitored. Data obtained from the synchronously loaded LAD shows a force–elongation curve with the same characteristics as in the test before. So applied pressure does not significantly influence the axial behaviour. But the pressure–diameter curve is highly moderated by diameter changes as a result of the axial elongation of the arterial segment. Here the periodic loads are applied synchronously with only one phase. A phase-shift between the applied pressure and elongation may influence the pressure-diameter curve.

CONCLUSIONS

The newly developed experimental setup enables mechanical characterization of arterial segments. Furthermore, the setup can be used for long term *ex vivo* culturing of arterial segments while monitoring mechanical characteristics and for monitoring vascular wall changes after applying catheter-based interventions to the cultured segments.

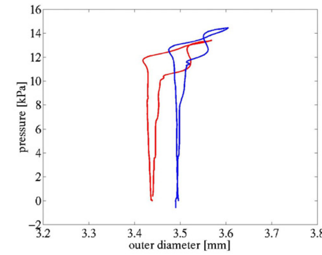

Figure 2. Pressure – diameter curve of pressurized LAD

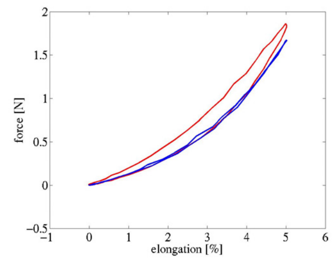

Figure 3. Force - strain curve of elongated LAD

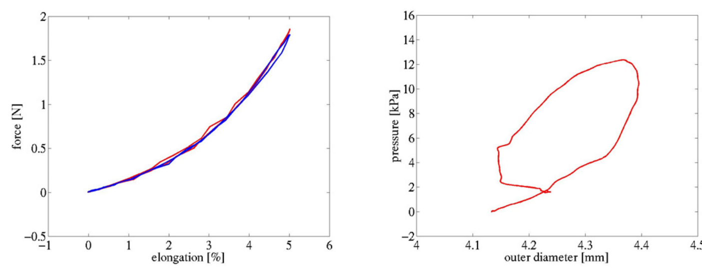

Figure 4. Force - strain and pressure – diameter curve of synchronically loaded LAD

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