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In-vitro Study of Effect of the Design of the Stent on the Arterial Waveforms

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Abstract

Peripheral arterial disease (PAD) occurs as a result of atherosclerosis, which involves plaque formation on the inner walls of the arteries. This reduces the size of the vessel's lumen and restricts blood flow to the leg muscles, leading to pain, the death of tissue and even the amputation of the lower leg. One treatment method for PAD is the placement of a stent, which acts as a scaffold holding open the artery, increasing blood flow to the lower extremities. However, the stents for PAD are known to fail more regularly due to the complicated biomechanical conditions such as heavy calcified and long atherosclerotic lesions. Stenting in the peripheral arteries still fail in 25% of vessels after 2 years. One of the major influences on the rate of restenosis is the rate at which the platelets become activated. This activation is controlled by changes of wall shear stress, which is in turn influenced by the flow rate, and pressure. This study hypothesizes that stents in the arteries can cause the reflection of the waveform, which would alter the flow rate and pressure waveforms, causing increase in the rate of restenosis. This is potentially why various in-vivo studies have found that stents with thicker struts cause increased levels of restenosis.
In this study, the effect of stent design on haemodynamic flow will be investigated, with the intention of optimising the designs currently in use in medicine. By setting up an in-vitro experiment, with an artificial artery, it is possible to record the flow rate, change in diameter and pressure caused to the blood flow by the stent. In this experiment, it is intended to use a series of 3D printed stents of two designs (Palmaz and Zigzag), with differing, strut thickness to determine which causes the most reflection, in an attempt to optimise the stent design.

Keywords: Stent; reflection; peripheral arteries; flowrate; pressure; diameter;

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1. Introduction

Peripheral arterial disease is the build-up of fatty deposits known as plaques, traditionally through atherosclerosis, along the peripheral arteries, which cause restriction to the blood flow. This deprives certain muscle groups and tissues in the lower limbs of oxygen and can cause a build-up of carbon dioxide, which in extreme cases can lead to tissue death (gangrene), requiring amputation. To prevent this from occurring one treatment method is angioplasty with the placement of a stent at the plaque location. A stent acts as a vascular scaffold holding open the vessel allowing blood flow to resume. Stenting involves minimally invasive surgery, lowering the risk of infection compared to other surgical procedures, and can be combined with medication to apply the drugs directly at the plaque location. However, as the plaques in the peripheral arteries are typically longer and more heavily calcified, stents in the peripheral arteries are exposed to more biomechanical forces than in other regions. Therefore, stents that work well in other parts of the body are not suitable for this region. It was reported that 50% of stents in peripheral arteries fail due to restenosis within 2 years (null et al., 2008).

Restenosis occurs due to activated platelets binding to the stented area, which in turn induces smooth muscle cell proliferation, this build up causing restriction to the blood flow. Platelets are continuously experiencing stretching, compression, causing them to be sheared by local gradients within the flow. When exposed to above average shear stress, they react with chemical and enzymatic responses, i.e. become activated. It has been found that it is not just an elevated shear stress that causes the activation but changes from high to low causes platelets to activate 20 times faster than only exposure to elevated stress (Koskinas et al., 2012).

A reflective wave will be generated within a vessel if there is a change in the vessels material properties or a change in the geometry. When a stent is placed within the vessel, there are dramatic changes within the material and geometrical properties within the vessel. For example, the stent would traditionally make the vessel stiffer due to the metal not having the same level of flexibility as the vessel wall. Due to the nature of the struts, there would also be an increase in surface area perpendicular to the flow rate, again producing a change in the reflection. As different stent designs have different material and geometrical properties, by changing the stent design and material properties, the stents can produce different reflective waves (Parker and Jones, 1990).

A change in the level of reflection will induce a change in the flow rate, the pressure and the vessel diameter. An increase in reflection will cause an increase in the pressure and the vessel diameter, due to superimposition, whilst due to the vector nature of velocity an increase in reflection will cause the velocity to decrease. The wall shear stress (WSS) is the drag force produced as the fluid moves across the surface of the vessel. The WSS is proportional to the velocity gradient; therefore, any change in the reflective wave caused by the discontinuity of material and geometry by the stenting in the peripheral artery could cause the alteration of the WSS, hence, possible resulting in the restenosis at the edge of the stent (Alemu and Bluestein, 2007).

In this study, two types of the design of peripheral artery stent (Palmaz design and Zigzag design), manufactured by using additive manufacturing techniques, are implemented into in-vitro arterial system to assess how the design of the stent will affect the hemodynamic performance. The pulsatile arterial waveforms in term of the velocity, pressure, and arterial vessel wall movement were measured simultaneously at three sites proximal to the stents. The measured arterial waveforms for two types of the stents were compared with those in the healthy arterial system (no stent). It was found that both stent designs showed an increase in reflection compared to the healthy waveform, while the Palmaz stent produced less reflection than the Zigzag stent, implying that it is the better design in terms of haemodynamic flow.

2. Experiment Set-up

An in-vitro experiment was set up, as shown in Fig 1, to simulate the superficial femoral artery, where the change in the flowrate, pressure and diameter waveforms were measured. This was repeated twice with two different stent designs being placed within the artificial artery, allowing the impact each stent had on the various waveforms to be observed.

2.1 Experimental Set-up

The experimental setup, consists of a latex tube (Bard Medical, USA) to simulate the blood vessel, a pulsatile pump (Harvard Apparatus, USA) to represent the heart, a reservoir to represent the blood supply, a tank to represent the surrounding tissue pressure, and a series of 3D printed stents (Birmingham University, UK), using water simulate the blood. Water is often used to simulate the blood flow in in-vitro studies (Li et al., 2016), due to their similar densities (water, 1000kg/m^3 blood, 1060kg/m^3). The latex tube was 45cm long with an internal diameter of 6.35mm. The latex tube was used to simulate an artery as in various other studies (Walker et al., 1999). The latex tube was placed within the tank connected to the inlet and outlet, and submerged under water, where the water level was kept at 2cm above the tube to maintain pressure on the liquid within the vessel. The stent was placed in the tube 10 cm from the outlet.

The inlet of the latex tube was connected to the pulsatile pump via a PVC pipe. The pulsatile pump represented the left ventricle of the heart within the system, to generate the signature pulsatile flow found in the peripheral arteries. The settings of the pump was adjusted until the desired waveform taken from the literature, was achieved. The pulse setting was set to 70rpm, with an output phase ratio % systole / % diastole of 35/65, and a stroke volume of 25cc. The pump was connected to the reservoir tank, drawing water from the reservoir tank to pump it through the latex tube.

The outlet of the latex tube was connected to a reservoir via a PVC pipe. The reservoir tank was placed so that the water level was 32cm above the latex tube, so that the pressure in the vessel would be close to that of the human body. This reservoir provides the backward wave that is required to generate the healthy waveform.

The stents were manually inserted within the latex tube. The stents were made out of nitinol, produced through selective laser melting. Two designs were examined in this study as shown in Fig. 2, one a balloon expandable design known as a Palmaz stent, the other was a self-expanding design known as Zigzag. Both stents were 2cm long with an external diameter of 8 mm. the Palmaz design had a strut thickness of 550µm, and the Zigzag had a strut thickness of 250 µm.

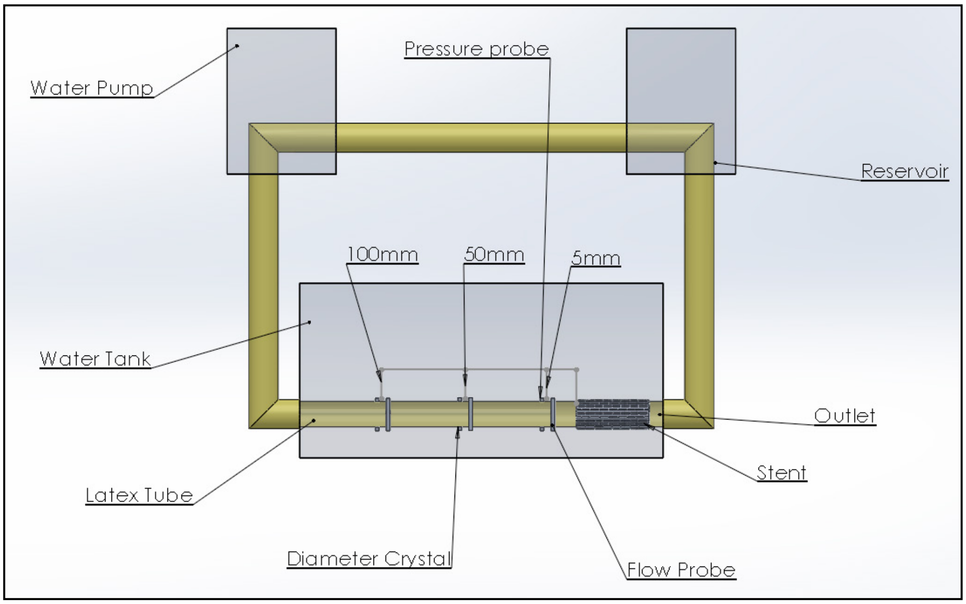

Fig. 1. Experimental set-up.

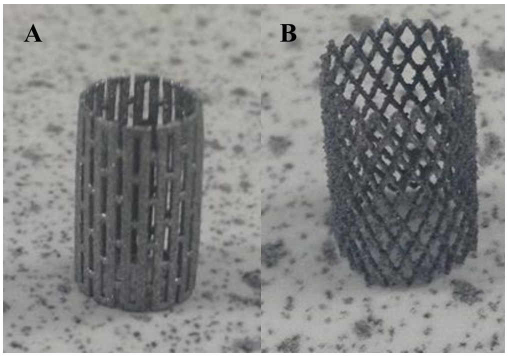

Fig. 2. Stent manufactured with additive manufacturing technology: (A): Palmaz; (B) Zigzag.

2.2 Measurement

Simultaneous, flow, pressure and diameter readings, were measured at various axial locations, along the latex tube. They were recorded at 5mm, 50mm and 100mm, from the inlet end of the stent. The diameter was measured using two 1mm diameter crystals(Sonometrics Corporation, Canada), which were attached to the surface of the latex tube, using silicone gel, directly opposite each other, recording the distance between. The flow rate was recorded using an 8mm transonic COnfidence flow probe (Transonic, USA), placed 5mm from the diameter crystals, which clips around the latex tube, and uses ultrasonic transmission to track the flowrate within the latex tube. The pressure sensor (Sonometrics Corporation, Canada), was inserted via the inlet and placed 5mm from the flow rate probe. All the sensors are connected to the SonoSOFT (Sonometrics Corporation, Canada), which allows the storage and displaying of the recorded data.

3. Results

3.1 Diameter

In terms of diameter near the inlet, the change in diameter is very similar for all three waveforms, with the Zigzag wave having a slightly higher peak than the Palmaz and healthy waveforms, as shown in Fig 3. As the waveform neared the stent area, the change in diameter increased in both the Palmaz and the Zigzag waveforms, however there was little or no change in the healthy waveform as it moved from the inlet towards the outlet. The healthy waveform had an amplitude of 0.422mm at 5mm, 0.432mm at 50mm, and 0.437mm at 100mm. At all distances the Zigzag waveform made the largest change in diameter. Whilst the Palmaz design did cause a large change in the diameter at 5mm from the stent location, this change is reduced at a more significant rate than the Palmaz. The Palmaz waveform's peak dropped 0.06 mm within the first 5cm, whilst the Zigzag only dropped 0.03mm. Despite this drop in the peak between 5mm and 50mm, the overall amplitude of the diameter waveform increased for the Palmaz and the Zigzag between 5mm and 50mm. The Palmaz diameter waveform had an amplitude of 0.498mm at 5mm, 0.546mm at 50mm, and 0.484mm at 100mm. This is due to the stiffness of the stent resisting the closing force of the vessel; this resistive force is not existent at 50 and 100mm.

3.2 Pressure

In terms of pressure near the inlet, the change in pressure is very similar for all three waveforms, with the healthy having a slightly higher peak than the other waveforms, as shown in Fig 4. As the waveforms approach the stent area there is a slight separation of the waveforms at 5mm from the stent area. At 5mm, the peak pressure is higher for the Zigzag design, and the Palmaz deign compared to the healthy waveform, with the Palmaz having the highest pressure.

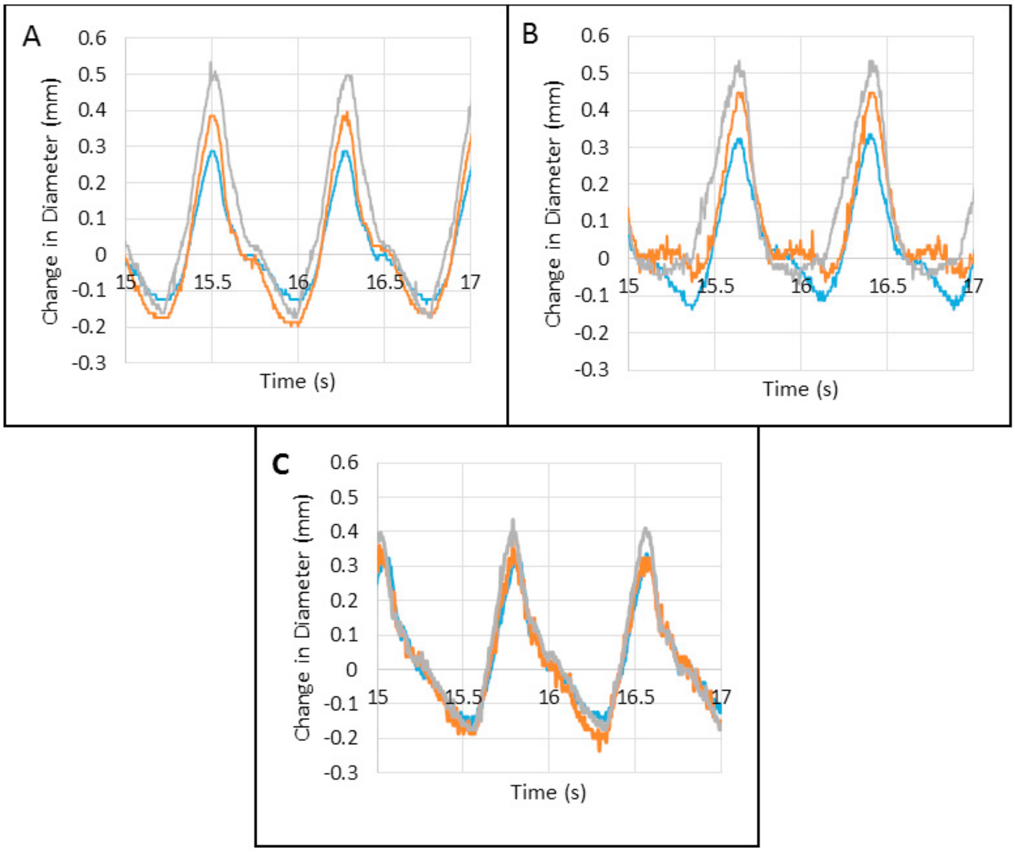

Fig. 3. Change in diameter at A) 5mm, B) 50mm, and C) 100mm (Blue=Healthy, Red=Palmaz, Green=Zigzag).

At 5mm the peak of the healthy waveform was 70mmhg, the Palmaz was 73.28mmhg, and the Zigzag's peak was 82.96mmhg. Meanwhile at 100mm the peak of the healthy waveform was 74.05mmhg, the Palmaz was 70.09mmhg, and the Zigzag was 69.23mmhg.

3.3 Flowrate

Towards the inlet, the three-flowrate waveforms are all very similar, with the healthy waveform slightly larger than that of the other two, as shown in Fig 5. However, as the wave approaches the stent area the waves start to differ, with the healthy wave changing a little if at all, and the Palmaz and Zigzag stents lowering the flow rate. At 5mm from the stent area, the Zigzag stent waveform had the lowest max flow rate of the three waveforms, with the Palmaz in second. At 5mm the healthy peak was 1.17L/min, the Palmaz was 0.87L/min, and the Zigzag was 0.57L/min. whilst at 100mm the healthy peak was 1.15L/min, the Palmaz was 0.99L/min, and the Zigzag was 0.94L/min. At 5mm the healthy amplitude was 1.24L/min, the Palmaz was 0.92L/min, and the Zigzag was 0.58L/min. whilst at 100mm the healthy amplitude was 1.36L/min, the Palmaz was 1.19L/min, and the Zigzag was 1.16L/min.

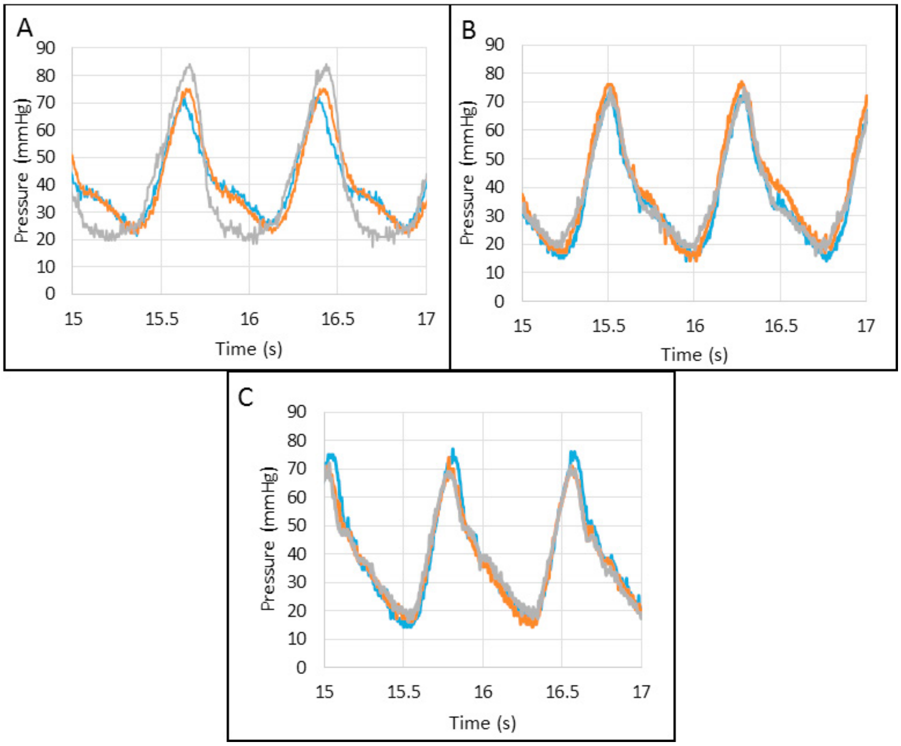

Fig. 4. Change in pressure at A) 5mm, B) 50mm, and C) 100mm (Blue=Healthy, Red=Palmaz, Green=Zigzag).

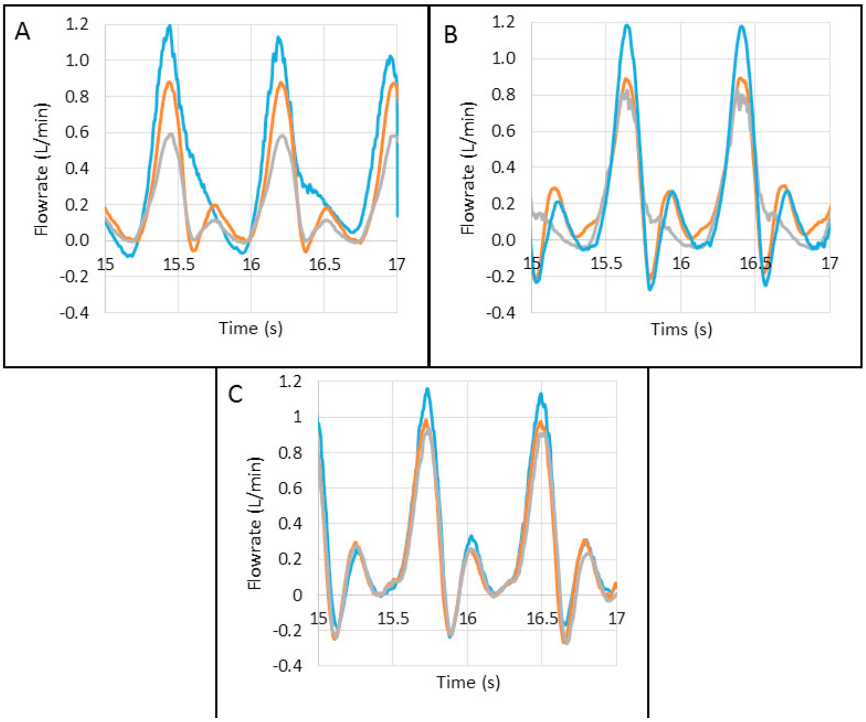

Fig. 5. Change in flowrate at A) 5mm, B) 50mm and C) 100mm (Blue=Healthy, Red=Palmaz, Green=Zigzag)

4. Discussion

4.1 Diameter

The increase in diameter found in the Palmaz and Zigzag waveforms could be due to an increased level of reflection. An increased level of reflection would cause an increased amount of water travelling back down the vessel; the diameter of the vessel is dependent on the amount of water flowing through that point. Therefore, an increased level of reflection would cause an increase in the diameter. This effect will lessen further from the reflective site, towards the inlet, as the reflective wave would dissipate due to the oncoming flow. These results would imply that there was an increase in reflection with the Palmaz and the Zigzag stent, with the Zigzag stent causing the greater reflection.

4.2 Pressure

As with diameter, due to an increase in the volume of water at one location due to an increase in reflection, would cause an increase in pressure prior to the point of reflection. This effect dissipated much faster for the pressure than for the diameter. This could in part be due to the change in diameter, as when the diameter of a vessel increases the pressure decreases. However, this would not cancel out the change in pressure totally as the elastic forces of the vessel would continue to apply pressure to the water. These results would also imply that there was an increase in reflection with the Palmaz and the Zigzag stent, with the Zigzag stent causing the greater reflection

4.3 Flowrate

Due to the flowrate being directional, any reflection would traditionally cause a decrease in the overall flowrate. As a larger negative flowrate would cause a larger drop in the flow rate, a large drop in flow rate can be attributed to an increase in reflection. Again, this effect dissipates as the reflective wave moves away from the site of reflection, so the waveform returns to that similar to the healthy. These results would imply that there was an increase in reflection with the Palmaz and the Zigzag stent, with the Zigzag stent causing the greater reflection.

4.4 Summary

These results also showed that in all cases the Zigzag stent design caused more reflection than the Palmaz design. This is believed to be due to a larger number of surfaces interfering with the flow. When the Zigzag stent is looked at closely, it is clear that there would be reflection caused by each of the diamond shapes, as though they would not be perpendicular to the flow they would be in a position to interfere and cause reflection. The Palmaz stent design has fewer struts that would act as reflective surfaces with most struts running in the same direction as the flow. This is very important as most self-expanding stents are created with a similar open Zigzag design. As this design is causing an increase in reflection, they may require optimization.

Though this study found that in terms of haemodynamic flow the Palmaz is the better design, in practice this may not be the most suitable. Due to its high radial strength and stiffness if a Palmaz stent was applied to an area of PAD it would likely fail and fracture due to surrounding forces within the leg. However, it is clear that the effect the stent causes on the haemodynamic flow is a factor that should be considered in stent development and optimisation. It is clear from the results that the effect of design changes on the haemodynamic flow and its influence on restenosis requires more research.

5. Conclusion

Analysis results imply that wave intensity analysis could be used to assess the design and properties of the stent, leading to the optimization of current designs and development of new ones. Both stent designs showed an increase in reflection compared to the healthy waveform, showing that they are interfering with the haemodynamic flow. It was observed that the Palmaz stent produced less reflection than the Zigzag stent, implying that it is the better design in terms of haemodynamic flow.

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