**The Impact of Imperfect Frame Deployment and Rotational Orientation on Stress within the Prosthetic Leaflets During Transcatheter Aortic Valve Implantation.**

Original Article.

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**Abstract**

TAVI devices are manufactured with cylindrical frames. However, the frames are rarely cylindrical post-deployment since deformation due to localised under expansion can be induced by calcified material on the native valve leaflets exerting irregular forces upon the frame. Consequently, the leaflets within a deformed TAVI device may undergo elevated stress during operation, which may lead to premature device failure.

Using computational analysis a complete TAVI device model was simulated undergoing deployment into an aortic root model derived from CT data for a patient with severe calcific aortic stenosis, followed by a pressure simulated cardiac cycle. The complete analysis was performed eight times, each with the device at a different rotational orientation relative to the native valve, with an increment spacing of 15 degrees.

The TAVI device frames consistently featured significant distortions associated with bulky calcified material at the base of the non-coronary sinus. It was found that the average von Mises stress in the prosthetic valves was only increased in one of the cases relative to an idealised device. However, the maximum von Mises stress in the prosthetic valves was elevated in the majority of the cases.

Furthermore, it was found that there were preferable orientations to deploy the prosthetic device, in this case, when the prosthetic leaflets were aligned with the native leaflets. As device orientation deviated from this orientation, the stresses in the valve increased because the distance between the commissures decreased. This potentially could represent a sufficient increase in stress to induce variation in device lifespan.

**Introduction**

Aortic stenosis (AS) is a condition in which calcification of the valve leaflets and distortion of the architecture progressively inhibit proper function. Approximately 2% of the Western population over the age of 65 have AS (Nkomo et al. 2006). Left untreated, AS is likely to result in mortality once it is associated with symptoms. Conventional treatment for AS is surgical valve replacement (SVR). Unfortunately, due to the extremely invasive nature of SVR, approximately 31% of patients are considered unsuitable for the procedure, most often in light of their advanced age and advanced comorbidities (Iung et al. 2003). As a result, an alternative minimally invasive treatment option was developed: transcatheter aortic valve implantation (TAVI).

Prosthetic TAVI devices incorporate a valve that is normally stitched to the interior of a stent-like frame. Many of these devices are crimped onto delivery catheters that are passed retrogradely along stiff wires from arterial access sites to the diseased aortic valve. Once the device position is deemed correct, the device is deployed, either through self-expansion or balloon-expansion. The metallic frame forces and retains the native valve open, while the prosthetic valve immediately undertakes the essential functions of antegrade blood flow from the left ventricle to the aorta whilst preventing significant regurgitation during diastole.

To date, limited data has been published on the life span of TAVI devices: the first human TAVI procedure was performed in 2002 and so long term durability data is not yet available. Furthermore, since the commonest devices have undergone several design iterations over the last few years to improve their deliverability and performance, medium/long term outcome data is not based on the latest versions. However, very recent data has confirmed that TAVI valve restenosis or regurgitation normally induced by degeneration, does occur in a significant proportion of patients. This represents an important target for further research (Dvir D. 2016).

As the aortic root is elliptical in many patients, and given that the bulky material associated with classical aortic stenosis is irregular, it is common for the devices to fail to achieve a cylindrical profile. This in turn could result in elevated operating stress within the valve resulting in reduced device lifespan due to fatigue (Thubrikar et al. 1981).

**Figure 1**

Frame distortion, as evidenced by asymmetrical expansion, cannot necessarily be deemed as a procedural failure, since apart from post dilatation there are no other therapeutic avenues for treatment, and many patients are therefore discharged from hospital despite the devices being visibly distorted (for example see Figure 1). There have been few studies describing the incidence of frame distortion. The most relevant study by *Schultz et al. (2009)* identified the average eccentricity in a sample of 158 patients was 87 – 92% dependent upon where the device was measured. However, due to the small sample size, and limited scope of the study, the overall incidence of distorted devices cannot be concluded.

In order to further the understanding of frame distortion, and the implications it may have for the life expectancy of prosthetic leaflets, computational simulation was employed to assess the operational stress of the leaflets following deployment in a heavily calcified aortic root. Furthermore, since frame distortion was found to vary depending on the orientation of the device relative to the aortic root, the effect on leaflet stresses was assessed by performing the deployment simulation at different angular orientations of the prosthesis.

Computational simulation of TAVI devices is an emerging area of research with several sophisticated simulations already described in the literature (Morganti, et al. 2014, Sturla et al. 2016, Wang et al. 2015) and the findings by *Gunning et al. (2014)* demonstrates that elliptical TAVI devices post deployment will increase the stress within the valve. However, the leaflets were mapped to the device post deployment which draws into question the reliability of the results. Furthermore, only two simulations were used to demonstrate the variation in stress, such that it is not possible to determine any trends associated with orientation of the TAVI device.

**Methods**

ScanIP (Simpleware 2014) was used to extract the features of the aortic root model (Figure 2) from a medical CT scan of a heart during diastole. The patient was 83 years old, with aortic stenosis and was being actively considered for TAVI. The leaflets and eight specific masses associated with degenerative aortic stenosis were identified and incorporated into the aortic root model by means of tie constraints.

Abaqus v6.13 Explicit (SIMULIA 2015) was used to simulate a TAVI device based on the SAPIEN XT (Edwards LifeSciences 2013) undergoing deployment into an aortic root, after which the device was simulated undergoing a cardiac cycle. The simulation was repeated eight times, each with the device in a different rotational orientation relative to the native valve. The device orientation was defined by the angle between the native leaflets and prosthetic leaflets (graphically shown in Figure 3). The angles simulated were θ = 0°, θ = 15°, θ = 30°, θ = 45°, θ = 60°, θ = 75°, θ = 90° and θ=105°. As the device has a rotational symmetry of order three, further simulations were not required. The native valve does not have rotational symmetry as the non-coronary leaflet is larger than the other two. As a result, the case of θ = 0° was constructed such that the prosthetic leaflets aligned as closely as possible to the native leaflets. The axial position of the device was determined to be suitable and representative of a real TAVI procedure.

**Figure 2**

**Figure 3**

The aortic root, aorta, left ventricular outflow tract (LVOT) and native leaflets were considered to have uniform density of 1.1 g/cm3 and consistent Rayleigh damping factor of α = 800 (β = 0). The calcified masses were assumed to have a density of 2 g/cm3 and remained undamped (Morganti et al. 2014). Nine different regions of the aortic root were defined, which were represented by eight different elastic models. The aorta and LVOT were assumed to be linearly elastic with an elastic modulus of 2 MPa and a Poisson’s ratio of 0.45. The calcified masses were also assumed to be linearly elastic, with an elastic modulus of 12.6 MPa and a Poisson’s ratio of 0.35 (Holzapfel, Sommer, and Regitnig 2004). The remaining six regions defining the sinuses and leaflets were assumed to be hyperelastic with a nearly incompressible reduced polynomial hyperelastic model, as defined by:

|  |  |  |
| --- | --- | --- |
|  |  | [1] |

where *U* is the strain energy potential, *N* is the polynomial order, *Cij* and *Di* are material parameters and is the first deviatoric strain invariant defined as:

|  |  |  |
| --- | --- | --- |
|  |  | [2] |

are the diviatoric stretches given by:

|  |  |  |
| --- | --- | --- |
|  |  | [3] |

*J* is the total volume ratio, *Jel* is the elastic volume ratio and *λi* are the principal stretches. The initial shear modulus (*µ0*) and bulk modulus (*K0*) are defined as:

|  |  |  |
| --- | --- | --- |
|  |  | [4] |
|  |  | [5] |

The tissue was assumed to be nearly incompressible, with a Poisson’s ratio of 0.475, as defined by:

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| --- | --- | --- |
|  |  | [6] |

For N = 6, the values of Ci0 are shown in Table 1 (SIMULIA 2014, Morganti et al. 2014).

**Table 1**

The TAVI device and delivery system were based on the SAPIEN XT and NovaFlex delivery system (Figure 4). The development of the model has been described elsewhere (Bailey, Curzen, and Bressloff 2015). In summary, the delivery apparatus comprised a balloon, cone and wire. The TAVI device featured a frame, cuff, leaflets and six clips that held the device together. The material properties for the frame and clips were based upon Cobalt Chromium MP35N, while the material properties for the balloon was based on polyethylene terephthalate. The leaflets were assumed to be hyperelastic and employed the Ogden hyperelastic model.

**Figure 4**

The simulation had two distinct steps: device deployment and a cardiac cycle. A detailed description of the simulation is given in the appendix. In brief, the delivery balloon and TAVI device were positioned in the transapical deployment orientation, such that the delivery system made no contact with the aortic root. The TAVI device was first crimped by means of a cylindrical surface, before being deployed through balloon inflation. Once the device had been deployed, the balloon was deflated and a representative pressure load was applied to the leaflets to simulate a cardiac cycle.

For comparative purposes, an idealised pre-crimped frame with a diameter of 26 mm was also simulated undergoing a cardiac cycle.

**Results**

Each simulation took 81 hours to compute, running across 16 cores on dual Xeon E5-4640 CPUs. The frames in all eight simulations were distorted due to a large calcified plaque protruding into the body of the leaflet as shown in Figure 5. The variation in the relative position of the prosthetic commissures, and the frame distortion results in different closed leaflet shapes and coaptation lines (Figure 5 (B, D, F and H)).

**Figure 5**

As the device was rotated, the stress within the leaflets also varied. The ensemble averaged von Mises stress () within the leaflets during a cardiac cycle is shown in Figure 6 (A) for the idealised frame, for the case of θ = 0 and θ = 30 degrees (the minimum and maximum observed, respectively). The idealised valve exhibited unusual characteristics: when the valve was open was extremely low, however, while the valve was closed was greater than the case of θ = 0° and very similar to the θ = 30° case.

Four time points were selected (highlighted in Figure 6 (A)) in which the valvular stresses for all the simulations were compared, and plotted in Figure 6 (B).

σ ̅ is not necessarily a good measure of valve failure, rather maximum stress should be considered. The maximum von Mises stress (σmax) was defined as the average von Mises stress, in the 1% of elements experiencing greatest stress in the prosthetic valve at t2 (the time point of greatest stress). The relationship between σmax and has a strong linear relationship (R2 = 0.94) as shown in Figure 6 (C).

The time averaged valvular von Mises stress over an entire cardiac cycle was calculated by the following

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| --- | --- | --- |
|  |  | [7] |

where N is the number of frames of data collected over a cardiac cycle. The amplitude of average von Mises stress over a cardiac cycle can be defined as

|  |  |  |
| --- | --- | --- |
|  |  | [8] |

where and are, respectively, the maximum and minimum average von Mises stress experienced by the valve over a cardiac cycle. and are plotted against each other in Figure 6 (D), both of which have a range of 17%.

Noting that greatest stresses were experienced at t2, the von Mises stress distribution within the prosthetic leaflets for the case of θ = 0°, θ = 30° and the idealised case are shown in Figure 7.

**Figure 6**

**Figure 7**

**Discussion**

Initial inspection of the results shown in Figure 6 (A), suggest a distorted frame may be beneficial for the TAVI device as is reduced in all cases other than the case of θ = 30° which, relative to the ideal case, has a higher stress of just 1.2% (measured at t2). However, a different picture emerges when considering the peak stress in the valves, σmax (shown in Figure 6 (C)). Although the idealised frame has a relatively large average stress, it has a lower σmax than all but one deployed device (θ = 0°). The range of variation between the simulated cases of and σmax was 16% and 37% respectively.

Due to the complex material properties, and variation between each valve, no fatigue failure criteria for the valves is known, therefore the number of cycles that each valve can undergo cannot be calculated. However, it is still possible to determine which valves are more susceptible to fatigue. Both and are measures of susceptibility to fatigue and, ideally, both should be as low as possible. Figure 6 (D) shows and plotted against each other, from which a linear is discernible (R2 = 0.78). It can therefore be determined that the deployment orientation can affect the life expectancy of a device from a fatigue perspective.

The stress distributions within the leaflets for the idealised, θ = 0° and θ = 30° cases are shown in Figure 7. The closed idealised valve had rotational symmetry of order three. As a result, the stress distribution across all three leaflets was identical. For the cases of θ = 0° and θ = 30°, this was not the case as the device frame no longer has rotational symmetry. It is visually apparent that the stress within the deployed valves is reduced in the body of the leaflets, but increases at the lower edges which are attached to both the cuff and the frame.

The valves were deployed to a diameter of 26 mm, from which the distortion reduced the diameter to an average of 23.25 mm (standard deviation of 0.075 mm). The reduction in diameter results in excess material within the leaflets to cover the orifice area resulting in the leaflets sagging in the closed position. This sagging increases the angle to which the base of the leaflet deforms during a cardiac cycle, resulting in increased stresses. However, no trend was found between device radius and stress within the valve (correlation between radius and at t2 resulted in an R2 value of 0.01).

An alternative measure of radius was found: the radius of a circle that passes through all three prosthetic commissures – rc. rc takes into account both the radius of the device, but also the dispersion of the commissures about the circle. r­c has an inverse linear relationship with at t2 (R2 = 0.82) as shown in Figure 8. The idealised valve, however, does not follow the same trend as the deployed devices. rc also has a strong quadratic relationship with θ and rc (R2 = 0.97).

**Figure 8**

Figures 6 C and D show an interesting trend, with the exception of the case θ = 30°. As the device deviates from θ = 0°, all measures of stress (, , and ) increase to a maximum (at approximately θ = 60°) before decreasing again. This trend was also found to correlate with *rc*. The large plaque responsible for the majority of the frame distortion (pictured in Figure 5) is centred in the base of the non-coronary leaflet. As the prosthetic valve orientation changes, the prosthetic commissure passes the plaque which decreases r­c. Furthermore, the location of the prosthetic leaflet relative to the plaque alters the degree of distortion damage to the commissarial region, which is thought to increase the stress in the valve.

The case of θ = 30° does not follow the trend, rather it experiences a significantly increased , , and . This is thought to be because the plaque that deforms the frame is non symmetrical, and has a large mass protruding from one side. When θ = 30°, the commissure of the prosthetic valve falls across this protrusion (Figure 5 (C and D)). Although this does not greatly affect rc­, it skews the valve by twisting the commissure. Unfortunately, no measure of skew could be found that accurately represented the data. If the data point at θ = 30° is removed from Figure 6 (C) and Figure 8 the correlation between the data and the trend line is improved to an R2 value of 0.96, and 0.91 (from 0.94 and 0.82) respectively. However, the data correlation between and (Figure 6 (D)) decreases from 0.78 to 0.75.

There are a number of limitations associated with this work, most notably with respect to the material properties assigned to the native tissue and prosthetic leaflets. The material properties were modelled as either hyperelastic or linearly elastic, isotropic and homogeneous. In reality, the material properties are hyperelastic anisotropic and inhomogeneous. However, because the material properties of interest are in plane with the tissue, and the tissue is nearly orthotropic, this is assumed to be a reasonable limitation. The areas that were linearly elastic do not directly affect the simulation (with the exception of the plaques). The plaques were modelled as linearly elastic, but since they function as near non-deformable masses, this is not an unrealistic assumption. However, the plaques can break up, yet no failure material properties were assigned due to the complexity of the problem.

The prosthetic TAVI device model was not derived from measurements, rather it was developed from limited data and visual inspection and therefore may not behave in an identical manner to the actual SAPIEN XT device. It will however suffice as demonstrating how this type of TAVI device is likely to behave.

The prosthetic leaflets do not retain any residual stress from the forming process. As a result, the idealised valve in the initial position has an average stress of zero. This is unlikely to be true as the valves are formed from planar sheets of material.

**Conclusion.**

The average von Mises stress within the modelled valve is not greatly increased by the presence of a distorted frame in comparison to an idealised frame and, in all but one case (θ = 30°), the average von Mises stress was, in fact, reduced. However, maximum von Mises stress within the idealised valve was less than the distorted counterparts in 87.5% of cases, which suggests that the distorted frames in some orientations may be more vulnerable to premature failure.

As the orientation of the device altered, as did the average von Mises stress, maximum von Mises stress, average von Mises stress amplitude over a cardiac cycle and the von Mises stress averaged over the entire cardiac cycle increased by 16%, 37%, 17% and 17%, respectively. There was an identifiable trend: as the device deviated from the most preferable orientation of θ = 0°, all measures of stress increased to a maximum at approximately θ = 60°, before decreasing again. This shows that the most preferable orientation of the device is at θ = 0°, while the least preferable orientations are at θ = 30° and θ = 60° in this particular aortic root model.

The variations of the stress metrics are attributed to asymmetric frame distortion and the associated variation in the effective aortic root area. As the commissures pass a large plaque in the base of the leaflets, the commissures are pushed together, which decreases rc - a measure of valve radius. As the degenerative material is not symmetrical, the case of θ = 30° had an elevated stress as the commissure lay across a protrusion of plaque.

It is therefore concluded that frame distortion can create significant variation of stress within the leaflets which is likely to accelerate the deterioration of the valve. Furthermore, optimal device orientations can be identified which may be a driving force for future devices to have rotational orientation control. These results could have clinical implications for the assessment of patients being considered for TAVI and, in particular, demand further research into the potential role for computer simulation as a routine component of the TAVI work-up algorithm for such patients in order to personalise their care.

**Appendix**

The simulations developed to analyse post-deployment leaflet operating stress had two phases: device deployment and a cardiac cycle. During the first phase, the SAPIEN XT computational model underwent deployment by means of the NovaFlex+ delivery system into a native aortic root. The delivery balloon was positioned in a transapical deployment orientation within the native aortic root model, such that the centre of the balloon passes through the centre of the valve, and no part of the delivery system was in contact with the aortic root model. The SAPIEN XT model was positioned concentrically with the balloon such that the device lined up with the native aortic root and the centre of the balloon. During the second phase, a pressure was applied to the device leaflets that followed a loading profile representative of the pressure experienced by the aortic valve during a cardiac cycle (Hole, J. W. 1996). The duration of the cardiac cycle (0.78 seconds) was accelerated (to 0.38 seconds) for the purposes of computational efficiency, since none of the material models used are time dependent, this is an acceptable measure to take. Furthermore, a linear increase of pressure was applied to the valve in order to achieve the initial pressure of the cardiac cycle, over a 0.01 second time period.

Two additional components are present in the simulation: a cylindrical surface and a bullet shaped surface. The cylindrical surface radially contracts in order to crimp the TAVI device. The bullet shaped surface is used to push the native leaflets open in order to avoid volumetric intersection between the leaflets and the prosthetic device.

Boundary conditions were applied to the upper and lower edges of the aortic root inhibiting motion in all degrees of freedom. Further boundary conditions were applied to the upper and lower edge of the balloon, the upper edge was constrained in all dimensions, while the lower edge was constrained such that it could only move along the axis of the balloon. The contact properties were defined as *hard* normal behaviour and frictionless tangential behaviour. The simulation constitutes four steps which are described below.

Step 1: In step first step, there was self-contact applied to the native tissue, prosthetic valve (with exception of the cuff) and the delivery system. Furthermore, contact definitions were defined between the bullet shaped surface and native tissue, prosthetic device (with exception of the cuff) and balloon, and the crimping surface and prosthetic device. During the step, the TAVI device was crimped by means of the cylindrical surface. Displacement boundary conditions reduced the diameter of the cylinder from 26 mm to 10 mm, thus reducing the diameter of the frame to 10 mm at its widest point. Simultaneously, a bullet shaped surface was displaced through the native leaflets forcing them open. This step was modelled over a 0.02 second time step.

Step 2: At the beginning of this step, two contact pairings were removed: the first was the pairing between the bullet shaped surface and the native valve, the second was between the crimping surface and the frame. This allowed the frame and native valve to elastically recoil. Contact pairings between the native tissue and the prosthetic device and its delivery system were instated. The boundary condition on the lower edge of the aortic root was removed at the beginning of this step also. Simultaneously, a pressure load of magnitude 0.45 MPa was applied to the internal surface of the balloon over a time period of 0.045 seconds.

Step 3: The pressure within the balloon was alleviated allowing the balloon to elastically recoil to an orientation similar to its original position. All contact pairings featuring the delivery apparatus were removed. This step was modelled over 0.01 seconds.

Step 4: During this step a boundary condition was applied to the TAVI device frame inhibiting motion in all degrees of freedom. A pressure load was applied to the aortic side of the prosthetic leaflets to simulate a cardiac cycle. This step time was determined by the loading profile: 0.039 seconds.

**Conflict of Interest Statement**

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