Computational modelling of multi-folded balloon delivery systems for coronary artery stenting: Insights into patient-specific stent malapposition

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Abstract

Despite the clinical effectiveness of coronary artery stenting, percutaneous coronary intervention (PCI) or "stenting" is not free of complications. Stent malapposition (SM) is a common feature of "stenting" particularly in challenging anatomy, such as that characterized by long, tortuous and bifurcated segments. SM is an important risk factor for stent thrombosis (ST) and recently it has been associated with longitudinal stent deformation. SM is the result of many factors including reference diameter, vessel tapering, the deployment pressure and the eccentric anatomy of the vessel. For the purpose of the present paper, virtual multi-folded balloon models have been developed for simulated deployment in both constant and varying diameter vessels under uniform pressure. The virtual balloons have been compared to available compliance charts to ensure realistic inflation response at nominal pressures. Thereafter, patient-specific simulations of stenting have been conducted aiming to reduce SM. Different scalar indicators, which allow a more global quantitative judgement of the mechanical performance of each delivery system, have been implemented. The results indicate that at constant pressure, the proposed balloon models can increase the minimum stent lumen area and thereby significantly decrease SM.

Keywords: Coronary stents, Balloon delivery systems, patient-specific model, stent malapposition, Finite Element Analysis

Abbreviations

PCI Percutaneous coronary intervention

SM Stent Malapposition

ST Stent thrombosis

DES Drug eluting stent

FEA Finite element analysis

RCA Right coronary artery

LAD Left anterior descenting

Cx Circumflex

LM Left main

TAC Total average curvature

TAT Total average torsion

VAS Volume average stress

AASM Area average stent malapposition

MLA Minimum lumen area

VG Volume gain

1 Introduction

One of the commonly occurring procedural factors that contributes to complications of percutaneous coronary intervention (PCI) is stent malapposition (SM), defined as the lack of contact between stent struts and the underlying vessel wall. Malapposed struts are associated with delayed neointimal healing, incomplete endothelialisation[15] and higher levels of thrombus deposition[36], especially after drug eluting stent (DES) implantation. The exact mechanisms by which SM contribute to stent thrombosis (ST) remain unclear[43]. However, it is speculated that stent material exposed in the lumen may trigger fibrin and platelet deposition[44]. More recently, SM has been identified as the key procedural cause of longitudinal stent deformation[16].

To reach the current stage of iterative stent development, different engineering tools have been used to investigate the mechanical stented environment. Among these techniques, computational modelling now provides very reliable and accurate information for PCI. In "virtual" studies, qualitative and quantitative information can be easily accessed in full model dimensionality that would be hardly detectable in *in vitro* and *in vivo* studies. Recently, novel stent designs and stenting techniques (especially for bifurcated vessels) have been investigated and proposed through very elegant virtual bench testing studies[9,31,35].

Finite element analysis (FEA) is one of the dominant tools for numerical studies, shedding light on the structural response of the arterial walls during/after stent implantation. To date, several FEA studies have been conducted providing scientific evidence for PCI procedures[29]. Although the majority of FEA studies have focused on the stent platform, there has been a paucity of research on the design of the delivery system. The modelling of balloon expansion has always been a challenging task due to its complex shape configuration and the complicated contact interaction with the stent. The first analytical balloon model was presented by Laroche et al.[22] in which the balloon was numerically folded by mapping its nodes in the unfolded configuration to a folded configuration. This methodology was successfully adopted by Mortier and co-workers to simulate patient-specific coronary bifurcation stenting[33]. In Gervaso et al.[12], a three folded balloon was modelled for free stent expansion. The balloon was folded by running a pre-expansion simulation, in which it was deflated by a negative pressure and, after assigning specific boundary condition, the balloon configured by three folds. At the same time, the work by De Beule et al.[6] introduced a more sophisticated way of generating virtual folded balloons. Based on micro-CT scans of a three folded balloon, an idealised virtual model was designed. However, as the folded models did not have tapered ends boundary conditions were implemented to the balloon ends to the catheter shaft during inflation. More recently, Zahedmanesh et al.[47] presented a dual step numerical methodology to fold the virtual balloon to the catheter shaft by deflating a balloon to three unfolded wings and then wrapping the wings around the catheter shaft. However, this approach has some limitations. The numerical folding can be carried out easily only for non-curved and planar expansions and it is computationally expensive. Additionally, the idealised models lack realistic characteristics which may affect the final result. As for the material model to describe the inflation behaviour of a balloon, different models have been used in the literature during the last decade. In particular, a two parameter Mooney-Rivlin model was used by Chua et al.[3]. Liang et al.[24] adopted a hyperelastic model to describe the transient expansion of the balloon. Laroche et al.[22] implemented an Ogden hyperelastic model. Later, Kiousis et al.[21] used a cylindrically orthotropic constitutive model to simulate balloon-stent expansions. In De Beule et al.[6], a method for mimicking the actual compliance of a specific size balloon was introduced. The constitutive model was assumed to be linear isotropic and the Young's modulus is extracted by the actual compliance charts provided by the manufacturers. This method has been implemented broadly during recent years in many state-of-the-art numerical studies[4,9,13,14,27,32–35,38]. Interestingly, there are also many other studies using isotropic, linear-elastic models to characterise the balloon inflation[11,12,25,30,31,47]. Although the actual inflation of an angioplasty balloon is characterised by anisotropic and hyperelastic behaviour, a linear isotropic model can adequately approximate the response of the balloon especially for nominal pressures. Beyond nominal pressures, and depending on balloon material and geometric characteristics, the balloon stiffening is more rapid and demonstrates a higher non-linear behaviour. Thus, to simulate the full transient response of an angioplasty balloon under a large range of pressures, a linear elastic model cannot be representative.

In this article, multi-folded balloon models have been developed to mitigate the risk of SM. All virtual balloon models have been calibrated and compared to manufacturer compliance charts to mimic actual compliance behaviour especially at target diameters. The virtual delivery systems are then applied to patient-specific simulations of stent deployment. For the purposes of this work, two patient specific models were constructed based on actual clinical cases. In particular, the major challenge in these cases was to cover dissections running from larger diameters into smaller diameters with only a single procedural approach so as to avoid prolonged and technically challenging procedures that may result in further complications. The main objective of this study was to compare different balloon delivery systems particularly with respect to increasing the minimum lumen area and complete strut apposition on the vessel walls under uniform balloon pressure. The authors believe that the investigated clinical problem of SM is highly correlated with the balloon mechanical performance. Specifically, it is dependent on the diameter and the pressure of the balloon.

2 Materials and methods

2.1 Geometry meshes and constitutive models

2.1.1 Multi-folded balloon models

Geometry The virtual balloon generation was based on a trigonometric function which controls different geometric characteristics of the dilation catheters. All the balloon models were generated in Rhinoceros 5.0, (Robert McNeel & Associates, USA), a commercially available NURBS package. Thus, the models are designed as NURBS surfaces and they are automated using python scripts. A more detailed description of the CAD generation can be found in S1.

Constitutive model The semi-compliant, high-pressure balloon material is assumed to be manufactured from polyethylene terephthalate which has high tensile strength and the ability to be moulded into ultra thin walls (5 to 50 μm) and very precise shapes. Thus, due to its thin walls, this material can provide extremely low profile balloons[42] enabling balloon catheter accessibility to very small coronary vessels. The balloon's elastic modulus is derived from compliance data as described by De Beule[5]. The balloon material is assumed linear elastic, isotropic and homogeneous and is in a state of plane stress. Since the relationship between the pressure and the diameter is not linear (i.e balloon inflation in large diameters, the presence of a stent and friction during the transient unfolding of the balloon), different values of the initial diameter D_{b0} were tested to obtain the best fit (between the actual and the virtual compliance charts). Then, based on these data and by means of dimensional analysis an empirical relationship was derived to predict the unpressurised diameter of balloons for desired target diameter under a certain pressure and Young's modulus. Fig. 1 depicts a compliance chart for a 3.5 mm balloon model (with/without mounted stent) with 0.02 mm wall thickness and 3.383 mm initial (predicted) diameter. By way of calibration, the virtual balloon is pressurised at a range of pressures and shown to closely follow the expansion behaviour of the actual interventional balloon especially at nominal pressures ($0.8 - 1.2$ MPa). A Young's modulus $E = 888.52$ MPa and a Poisson ratio $\nu = 0.4$ were used to model all the virtual balloons.

Delivery models for patient-specific simulations In the simulations that were conducted, the uniform balloons along with the tapered model were generated with six folds. As shown by Mortier et al.[32], six folded balloons can demonstrate more uniform and symmetric stent expansions, especially in cases where the deployment diameter is not constant along the length of the stent system (tapered balloon). The stepped balloon was designed with 12 folds since the diameter discrepancy between the proximal and the distal initial profile was ~ 1.3 *mm*. The material of the balloon is significantly increased for a 4.5 mm balloon, therefore, a twelve folded balloon can result in lower delivery system profile than a six fold. As a result, especially for computational purposes, the semi-crimped stent can be mounted on the balloon more easily. The mesh discretisation was carried out in ABAQUS CAE. In particular, the folded balloon models were discretised by four node quadrilateral membrane elements of type M3D4R. The number of elements varies depending on the balloon length and the folding configuration. The catheter shaft has been meshed by four node linear quadrilateral shell elements of type S4R. The catheter tips have been modelled by three-dimensional 8-node brick "reduced-integration" elements of type C3D8R.

2.1.2 Patient-specific vessels & stent model

Two patient-specific vessels were reconstructed for the purposes of this work: (a) a 52 *mm* long tortuous RCA with a severe stenosis (70% of percentage area stenosis) in the middle of its length and (b) a LM bifurcation with a 30% of area stenosis in the proximal part of the LAD after balloon pre-dilation. Intravascular ultrasound (IVUS) frames and bi-plane conventional angiography images were fused to generate three dimensional models of the vessels. Cross-sectional contours representing the borders of the lumen and the media were extracted in IVUS-Angio Tool, a free source software[7]. The final reconstructed vessels were then generated in Rhinoceros 5.0 as was the virtual stent model, which is based on the Xience device (Abbott Lab., IL, USA). All simulations were conducted in ABAQUS/Explicit v.6-12 (SIMULIA, Corporation, USA), a commercially available FEA solver ensuring quasi-staticity. Detailed information regarding the vessel reconstruction process, the construction of the virtual models, material properties, the simulation design and the stability of the numerical solutions can be found in previous work[41]. The mesh resolution of each instance modelled in this study differs according its length. However, for each instance, the seed size on the edges was selected according to the mesh independence tests. The procedure of the mesh-independence test is as follows: i) mesh-independence test of stent instance through free stent expansions by a deformable surface; a baseline size-mesh (based on previous work) was tested against a finer mesh and differences less than 2% was recorded, ii) mesh-independence test for the virtual balloons by simulating free stent balloon expansions; a baseline size-mesh (based on previous study of this group) was tested against a finer mesh and differences between expansion diameter remained less than 2% throughout the transient analysis, and iii) mesh-independence tests for small ideal vessels by simulating balloon stent expansions; a baseline size-mesh (based on previous study) was compared against a finer mesh and differences less than 0.5% were recorded. Also, period sensitivity tests were carried out to ensure the period independence of the simulation steps. As for the vessels, the walls comprise the intima-media layer extracted from the IVUS images along with the adventitia which was generated by assuming a scaling factor of 1.6 to non-diseased lumen areas[20,33]. The bifurcation model was extended to 5 *mm* along its edges for computational purposes (the IVUS frames for the bifurcation were obtained only along the stented region. Thus, the model has been extended to host the whole delivery system). The intima-media was modelled by using a hyperelastic, neo-Hookean strain energy function. The assumption was based on the fact that the average material of the vessel walls is plaque and the difficulty to extract the plaque composition from IVUS images; therefore, constitutive parameters for a soft plaque were selected as in the work by Pant et al.[39]. The adventitia was modelled as isotropic hyperelastic described by a sixth-order reduced polynomial strain energy function. The material parameters were defined by Holzapfel et al.[20] and they have been used within our group previously[38]. Fig. 2a and 2b illustrate the virtual CAD assembly for the reconstructed RCA and the LM bifurcation, respectively. To discretise the volume of the vessel walls with solid hexahedral structured elements, a partitioning approach has been implemented in this study. Specifically, each vessel was partitioned along its length by the Frenet planes defined on the central line of each lumen (see section 2.1.3). By this method, uniform small segments have been created along the entire length of each model enabling fast and accurate mesh discretisation. The mesh resolution for the RCA is depicted in Fig. 2c.

2.1.3 Geometric characterisation of vessels

Frenet frame and centreline calculation As the vessel is reconstructed, the IVUS pull-back line is used as a reference to geometrically characterise the vessel. The reconstructed IVUS pull-back is a line in space which can be geometrically characterised using classical differential geometry of curves. Let $\mathbf{C}(t) \in [0,L] \rightarrow \mathbb{R}^3$ and $\mathbf{C}(t) = [x(t), y(t), z(t)]$ be the pull-back path of the IVUS transducer as a function of an arbitrary parameter t. The local behaviour of the curve C can be described by the *moving frame* or *Frenet frame*, a right handed trihedron of three orthonormal vectors **T**, **N**, and **B** representing the tangential, the normal and the bi-normal unit vector, respectively, at each location on the curve[28]. Along with the orthonormal Frenet unit vectors, two scalar quantities, the curvature and the torsion are used to characterise the local behaviour of a 3D curve. Curvature, $k(t)$, measures the deviation of the curve from a straight line and it is always positive whereas torsion, $\tau(t)$, measures how much the curve deviates from being planar[28]. The Frenet equations are outlined in Table 1. The *Frenet frame* of the IVUS parametrised curve has been used to segment the vessel according to the *normal moving plane* which is defined as $(\mathbf{x}(t) - \mathbf{C}(t)) \cdot \mathbf{T}(t) = 0$, with $\mathbf{x}(t)$ a point x on the normal plane. At each location point $\mathbf{C}(t)$ a planar closed curve (cross section) $\mathbf{R}(t)$ is defined as the intersection of the normal plane $\mathbf{P}(t)$ with the volume of the lumen, $V(Q)$ (c.f Fig. 3). Alternatively, the cross section $\mathbf{R}(t)$ of $V(Q)$ at a point t on curve C is the region lying in $\mathbf{P}(t)$, or $\mathbf{R}(t) = r\mathbf{N}(\mathbf{t}) + p\mathbf{B}(\mathbf{t})$, with r and p real numbers lying in a region D(t) of the r-p plane[8]. Then, providing that, for any set of points $\mathbf{C}(t)$ and $\mathbf{C}(t+dt)$, the cross sections $\mathbf{R}(t)$ and $\mathbf{R}(t+dt)$ do not intersect, the centre of area of each cross section , $\mathbf{cp}(t)$, is calculated. A smooth curve at least $\mathscr{C}^2$ differentiable has been interpolated through all the calculated $\mathbf{cp}(t)$ points, see Fig. 3.

2.1.4 Indicators of stenting

To quantify the performance of stenting in the patient-specific cases, a number of metrics are defined. Some of the metrics are based on the geometric properties of the vessels and others on the structural response of the vessel walls. The metrics that are dependent on the geometrical characteristics of the deformed vessels have been calculated by using the vessel centre curve, cp, which is defined in section 2.1.3.

Total Average Curvature (TAC) A scalar metric is proposed to quantify the global curvature of the central curve, cp, pre and post-stenting. Since the curve has been sampled and parametrised along its length, TAC can be calculated using

$$TAC = \frac{\sum_{i=1}^{i=n_t} k_{cp_i} \delta cp'_i}{\sum_{i=1}^{i=n_t} \delta cp'_i} \tag{1}$$

where n_t is the total number of curve sampling points, k_{cp_i} is the local curvature of the central curve at the ith sampling point and $\delta cp'_i$ is the magnitude of the $\mathbf{cp}'$ at the ith sampling point.

Total Average Torsion (TAT) Similarly to TAC, TAT, is a global metric for the pre and post-stenting central curve torsion and is defined as

$$TAT = \frac{\sum_{i=1}^{i=n_t} \tau_{cp_i} \delta cp'_i}{\sum_{i=1}^{i=n_t} \delta cp'_i} \tag{2}$$

where τ_{cp_i} is the local torsion of the central curve at the ith sampling point.

Volume Average Stress (VAS) VAS represents the average change in the stress environment induced by the stent implantation. It was firstly proposed by Holzapfel et al. [19] and later adopted by Pant et al. [39]. Since the volume has been discretised by finite elements, the VAS formula is

$$VAS = \frac{\sum_{i=1}^{i=n_v} \sigma_i \delta V_i}{\sum_{i=1}^{i=n_v} \delta V_i} \tag{3}$$

where n_v is the total number of elements within the intima-media volume, σ_i represents the circumferential stress in the ith element of the volume, and δV_i is the volume of the ith element.

Spatial Quantification of SM To quantify the spatial variation of SM the outer surface of each stent is extracted and represented by a triangulated mesh. The SM along the outer surface of each stent is calculated as the Euclidean distance between each vertex point of the triangulated mesh and their projections to the lumen surface.

Area Average Stent Malapposition (AASM) Similarly to VAS, a metric for calculating the average malapposition is used post operatively. Since the surface is meshed by triangulated elements, the AASM can be expressed as

$$AASM = \frac{\sum_{i=1}^{i=n_s} SM_i \delta A_i}{\sum_{i=1}^{i=n_s} \delta A_i} \tag{4}$$

where n_s is the total number of the triangulated elements, SM_i is the malapposition in the ith element given by the euclidean distance between the centre point of the ith element and its projection to the lumen surface, and δA_i is the area of the ith element expressed as $\delta A_i = 0.5\|(\mathbf{v}_3 - \mathbf{v}_1) \times (\mathbf{v}_2 - \mathbf{v}_1)\|$, where $\mathbf{v}_j$ $(j = 1,3)$ denote the position vectors of the vertices of each element.

Minimum Lumen Area (MLA) & Volume Gain (VG) The area is calculated for each cross section, $\mathbf{R}_{cp}(t)$. The MLA is identified as the minimum area, $A(t)_{min}$, of a cross section $\mathbf{R}_{cp}(t)$ lying on the normal plane $\mathbf{P}_{cp}(t)$ for all t. Moreover, the lumen volume $V(Q)$ has been calculated as[8]

$$V(Q) = \int_t A(t)\|\mathbf{C}'(t)\|dt \tag{5}$$

where $A(t)$ is the area of each cross section $\mathbf{R}_{cp}(t)$. Then, the VG is calculated as $VG = (V - V_0)/V_0$, with V and V_0 the volume of the investigated vessel segment before and after stenting, respectively.

3 Results

3.1 Multi-folded balloon simulations

Tapered balloon free expansion The transient expansion of the tapered balloon model is depicted in fig 4a. The six-folded balloon is characterised by a uniform stent expansion with its proximal and distal segment expanded to 4.25 *mm* and 3.5 *mm*, respectively. In Fig. 5a, the virtual balloon compliance is illustrated. As can be observed, the balloon transient diameter variation has been recorded with or without mounted stent and there was no significant expansion diameter discrepancy ($< 2\%$). The pressure has been applied uniformly by a smooth curve up to 0.842 *MPa* along the entire inner surface of the balloon. The balloon was designed with a proximal length profile of 3.33 *mm* gradually increased to 4.04 *mm* distally along the length of the balloon.

Stepped balloon free expansion Frames at certain times in the stepped balloon expansion have been captured in Fig. 4b. On the left panel, the full stepped stent-catheter system is depicted whereas on the right, cross sections centrally to the model are illustrated demonstrating the transient unfolding of a twelve-folded balloon. The virtual stepped balloon was then designed with proximal and distal reference diameters of 4.1 *mm* and 2.80 *mm*, respectively, and target diameters 4.45 *mm* and 3.0 *mm*. Fig. 5b depicts how these are obtained by applying a uniform pressure of 1.012 *MPa*. Similarly to the tapered model, the virtual compliance was extracted for the stepped balloon with or without stent and discrepancies below 2% were recorded for the expansion diameter.

3.2 Patient-specific simulations

RCA "stenting" On the left panel of Fig. 6, the expansion simulations using a uniform balloon and the tapered balloon (section 3.1) are illustrated. Frames have been captured at specific times to demonstrate critical steps of the expansion simulations. The steps demonstrate (i) & (ii) the duration of the dog-boning phase, (iii) the maximum inflation of each balloon up to 0.842 *MPa* and (iv) the final configuration of the model after the deflation of the balloon. On the right panel, cross sections in the proximal portion of the vessel are illustrated to show the transient unfolding of the balloon model within the artery. Moreover, in the cross section images, regions with SM can be clearly observed. To quantify the better apposition produced by the tapered balloon evidenced in Figs. 6 and 7a, a more analytical quantification is given by the CDF (cumulative distribution function) as shown in Fig. 9a. In particular, the CDF plots demonstrate the possibility of a range of SM within the vessel (spatial quantification of SM calculated on the vertices of the upper triangulated stent surface). For instance, strut malapposition within a range of $0.00 - 0.025$ *mm* is approximately 66% and 74% for the uniform and the tapered balloon, respectively. Moreover, values of SM within a range of $0.00 - 0.05$ *mm* occur for 75% and 83% of stent outer surface for the uniform and tapered models, respectively. The greatest value of SM occurs in the proximal part of the uniform model and is calculated to be 0.715 *mm*, a gap which approximately equals the difference between the balloon and the vessel diameter. Importantly, high values of SM can be observed in both segments close to the middle of the vessel length. However, this is due to some aneurysmatic regions of the diseased reconstructed segment. In Table 2, the scalar "stenting" indicators for the RCA case are reported. The values show that the tapered model has significantly decreased the overall SM. At the same time, the MLA and the volume of the lumen have been significantly increased. The MLA relative to the reference model (pre-stenting) has been increased by 130% and 132% for the uniform and the tapered model, respectively. Correspondingly, the volume has increased by 4% and 12.8%. The TAC index indicates that the tapered balloon has been shown not to affect the curvature of the vessel. However, the tapered model does have an considerable impact on the planarity of the segment, as indicated by the TAT index. As far as the average stresses are concerned, the VAS index indicates that the tapered model has resulted in relatively higher stresses. The latter could be explained by the fact that the stent interacts with more volumetric mesh (comprising the arterial walls), especially in the proximal portion of the vessel. As a result more stresses contribute to the calculation of the VAS index (higher VAS numerator).

LM bifurcation "stenting" Fig. 8 illustrates different frames of the transient stent expansion simulation by an under-sized, an over-sized and a stepped balloon model (from left to right) presented in section 3.1. As for the RCA case, the frames have been captured at specific times of the deployment simulations demonstrating clearly transient model deformations throughout the entire period of the expansion simulations. In particular, the steps demonstrate (i) & (ii) the duration of the dog-boning phase, (iii) the maximum inflation of each balloon up to 1.012 MPa and (iv) the final configuration of the model after the balloon deflation. On the right panel of Fig. 8, cross sections in the middle of the stented region have been extracted. As can be observed, the stepped balloon provides very similar strut apposition with an oversized balloon based on the AASM index whereas the undersized balloon result in significant malapposition. The highest value of malapposition has been identified in the LM of the under-expanded model (~ 1.5 mm). As can be observed, high SM values are identified in the ostium of the Cx for all models due to the fact that the struts facing the Cx ostium are "wall-free" (Fig. 7b and 8). A more analytical description of SM can be given by the CDF shown in Fig. 9b. The percentage of strut malapposition within a range of $0.00-0.025$ mm is approximately 43%, 52% and 57% for the under-sized, stepped-sized and over-sized models, respectively. High values of SM for all the models is due to the Cx ostium. The percentage of exposed struts to a range of $0.00-0.1$ mm SM is $\sim 63\%$, $\sim 75\%$ and $\sim 83\%$ for the under-sized, the stepped-sized and the over-sized model, respectively. The stenting indicators for the LM bifurcation case are reported in Table 3. The MLA relative to the reference vessel is 1.6%, 3.6% and 2.3% higher for the under, over and stepped-sized approach, respectively. The volume gain relative to to the reference model is 2.1%, 19.8% and 3.5%. However, it can be observed that the stepped model provides a better approach compared to the undersized and the oversized delivery systems. In particular, the average malapposition has been decreased by half relative to the undersized approach and VAS is 65% less than that produced by the oversized balloon. Also, TAC and TAT indicate that the stepped approach is closer to the geometrical properties of the reference vessel especially relative to the over-sized balloon model.

4 Discussion

In Mortier et al.[32], the transient expansion of a stent was investigated by changing the balloon length, the folding pattern and the relative position of stent on the catheter. It was shown that changing these parameters can significantly affect the symmetry and uniformity of the transient expansion especially when the expansion target diameter is inconsistent. Thus, in the present study, the delivery system modelling strategy has been based on the parametric design of virtual balloons following comparison to commercially available compliance charts. It is assumed that for large diameter transitions, the number of the folds has to be increased for ensuring expansion uniformity[32]. The latter has been demonstrated clearly by the expansion of a twelve-folded balloon in the bifurcation case where the proximal and distal diameters differ by approximately 1.5 *mm* (c.f. Fig. 4b and 8). On the other hand, for a diameter difference of 0.7 *mm*, the deployment of a six-folded balloon resulted in relatively uniform expansion (c.f. Fig. 4a and 6).

Furthermore, this work has introduced several numerical indices quantifying and identifying local and global values of the investigated problem along with geometric characterisation of the vessels pre and post-stenting. These indices can provide a general idea of the procedural outcomes and, hopefully, in the future, could help to inform coronary interventions. The results demonstrate clearly that non uniform delivery systems can significantly increase the MLA and in parallel decrease the overall SM, especially, proximally to the stented segment, a region which is highly correlated with further unwanted events[16,46]. This is illustrated in Figs. 7a and 7b where the proximal stent segments are completely apposed to the vessel walls for the tapered and the stepped balloons. Also, the cross section images Figs. 6 and 8 indicate clearly the superior outcomes of the proposed deployments which could avoid the need for post-operative procedures such as post-balloon deployment. Especially for the bifurcation, it is well established that single stent procedures are preferable[2,17,37]. The suboptimal apposition of the stent struts to the proximal part of the main vessel could be solved by a provisional optimisation technique[23]. This would require an additional procedural step. Therefore, the proposed virtual balloons could potentially limit the procedure to a single step and, under a specific folding configuration, these models can be optimised for vessel accessibility. In addition, the wall stresses induced by non uniform balloons are kept within acceptable ranges (c.f. Tables 2 and 3) as for the standard models. This has also been numerically demonstrated in Morlacchi et al.[30], in which a tapered balloon resulted in reduced circumferential stresses after kissing balloon dilation in a bifurcated vessel. This is significant since high stress values have been shown to result in cellular proliferation[45].

When the PCI operator is aware that the proximal part of the stent is malapposed, the recommended action is to post-dilate the malapposed struts with a non compliant balloon. However, SM is frequently not detected using angiography alone. Given the low overall rate of use of IVUS/OCT imaging in most units, it is likely that the incidence of SM in lesions other than those of short length is relatively high. Our results indicate that a dedicated delivery system chosen by patient-specific criteria could help to avoid this procedural limitation by improving stent deployment in a single step. Importantly, it has been shown that under a specific pressure, non-uniform virtual balloon expansions can result in lumen gain by increasing the overall area along the entire length of the vessel. In contrast, by post-dilating only proximally malapposed struts, the MLA and the overall volume of the vessel are not likely to be significantly increased (always relatively to a non-uniform deployment) along the entire length of the stented segment.

The reconstructed vessels represent two real cases that include challenges frequently seen in clinical practice. Both segments are characterised by significant diameter discrepancy (> 0.5 *mm*) along their lengths. It has been shown that analytical geometrical quantification of the vessels can drive PCI with very good outcomes especially in improving the investigated complications. In particular, after calculating cross sectional areas along the intervened region, multi-folded balloons can be designed according to the desired inflation pressure and the diameter variation. This is very important for adequate stent expansion as has been shown in Tables 2 and 3. Specifically, the stepped balloon which has been designed for the bifurcated vessel provided superior performance compared to both the under-sized and the over-sized balloons as indicated by the indices. For almost the same average complete stent apposition with the over-sized balloon, it resulted in considerably less average stress, whereas the indices of TAC and TAT indicate that the stepped balloon has not changed the global geometrical properties of the intervened segment. Recently, a dedicated stent platform mounted on a semi-compliant stepped balloon has been developed[26] demonstrating invaluable clinical outcomes[10,40]. As for the tapered expansion, both MLA and the VG were increased and at the same time the AASM was decreased. Interestingly, the TAC index indicates clearly that the tapered model does not have any additional influence in the curvature of the vessel when compared with the standard model. However, it does have an impact on the planarity of the vessel. This could be explained by the fact that the tapered model attaches the stent to more volumetric elements (constituting the walls), especially in the proximal region of the vessel. The latter might be the reason for experiencing higher VAS in the RCA vessel expanded by the tapered balloon model.

To conclude, we have demonstrated the potential clinical utility for patient-specific delivery systems. In this work, the balloons have been designed after quantitative geometrical characterisation of the target vessel and result in deployment outcomes which are likely to limit potential post procedural complications. Moreover, in future, the development of a clinical tool which will integrate similar methods used in this work could help to conduct PCI planning through analytical virtual testing.

Limitations The major limitation of our work is the constitutive laws characterising the material behaviour of the vessel walls. More advanced constitutive models have been used in the literature with the most representative being the one implemented in Mortier et al.[33] and Conway et al.[4]. In this hyperelastic anisotropic model introduced in Holzapfel et al.[20], the fibre orientation and dispersion are taken into account with respect to a reference orthonormal coordinate system defined in each element of the mesh. For each layer, different scalar parameters are defined, derived by experimental testing. However, in order to implement advanced constitutive models, the calibration of the parameters is essential. Moreover, the fibre orientation and dispersion in a severely diseased vessel and in a bifurcation would be really difficult to obtain, especially by using available clinical data. In addition, the vessel description lacks an analytical model for the plaque composition. This is due to the fact that our reconstruction method is based on IVUS and conventional angiography from which the plaque composition is difficult to accurately define and orientate. A multilayer model would definitely have some influence on the stress values and the overall deformations of the walls. However, due to the comparative nature of this study, simpler models can still provide valuable results especially for indicating the non-physiological stress state in regions interacting with the stent system. For this reason, other aspects regarding the arterial wall conditions have also been neglected such as tissue pre-stretch and arterial blood pressure. An additional limitation of this work is that the balloon material behaviour is characterised by an isotropic and linear elastic model with the thickness of the balloon being constant. In reality, modern balloon models are dual layer composites. Therefore, balloons can be characterised by different anisotropic and hyperelastic models[18]. However, since the balloon models have been compared to real compliance charts, the virtual expansion behaviour should closely match that which occurs in clinical practice, especially at nominal pressures.

5 Conclusions

Numerical modelling by means of FEA can provide comprehensive and useful results for analytical investigation of stent deployment in PCI and thereby the avoidance of complications. In this study, a framework has been developed in which virtual balloon models have been proposed to mitigate the risk of SM in two patient-specific reconstructed vessels. Where a single step approach is to be followed, such delivery systems could potentially ensure complete strut apposition to the walls of the vessel in clinical practice. Scalar metrics based on the geometrical properties and the induced mechanical environment have been implemented to demonstrate numerically the pre- and the post-stenting vessel state. These metrics can direct more analytic optimisation studies and guide procedural planning. This study is, to the best of our knowledge, the first computational investigation of patient-specific "stenting" purely focused on the delivery system. The outcomes indicate that under constant pressure, non-uniform balloon models can result in better strut apposition and simultaneously increase the MLA and the vessel volume. Also, it has been shown that the geometrical properties of the stented segment do not alter significantly and the vessel is not exposed to higher stresses. At the end, the authors would like to emphasise that the comparisons are very specific to the investigated vessels. Population based studies could potentially result in more general findings and delivery systems according the vessel profile could be devised. Thus, further investigation is now required.

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Table 1: Frenet equations for an arbitrary parametrised curve C

Vectors	Frenet equations
Tangent	$\mathbf{T}(t) = \frac{\mathbf{C}'(t)}{\|\mathbf{C}'(t)\|}$
Normal	$\mathbf{N}(t) = \frac{(\mathbf{C}'(t)\times\mathbf{C}''(t))\times\mathbf{C}'(t)}{\|\mathbf{C}'(t)\times\mathbf{C}''(t)\|\cdot\|\mathbf{C}'(t)\|}$
Binormal	$\mathbf{B}(t) = \frac{\mathbf{C}'(t)\times\mathbf{C}''(t)}{\|(\mathbf{C}'(t)\times\mathbf{C}''(t)\|}$
Scalar quantities	
Curvature	$k(t) = \frac{\|\mathbf{C}'(t)\times\mathbf{C}''(t)\|}{\|\mathbf{C}'(t)\|^3}$
Torsion	$\tau(t) = \frac{<\mathbf{C}'(t)\times\mathbf{C}''(t),\mathbf{C}'''(t)>}{\|\mathbf{C}'(t)\times\mathbf{C}''(t)\|^2}$

Table 2: “Stenting indicators” for the RCA segment

Model	VAS	TAC	TAT	AASM	MLA (mm^2)	VG
RCA reference	-	0.139	0.224	-	3.714	-
RCA stented by uniform model	0.019	0.110	0.224	0.053	8.557	0.040
RCA stented by tapered model	0.025	0.110	0.144	0.031	8.601	0.128

Table 3: "Stenting indicators" for the LM bifurcation

Model	VAS	TAC	TAT	AASM	MLA (mm^2)	VG
LM bifurcation reference	-	0.061	0.217	-	4.929	-
LM bifurcation stented by under-sized model	0.004	0.059	0.175	0.445	5.010	0.021
LM bifurcation stented by over-sized model	0.020	0.050	0.059	0.228	5.108	0.198
LM bifurcation stented by stepped-sized model	0.007	0.058	0.216	0.230	5.044	0.035

Figure 1: Calibration of the virtual behaviour of a 3.5 *mm* balloon model: Simulation balloon compliance charts for a 6-folded balloon configuration superimposed on the manufacturer's data

[1].

Figure 2: Virtual reconstructed models back-projected to the CA images and numerical mesh discretisation for the RCA case. (a) Virtual RCA model. (b) Virtual LM bifurcation model. (c) Structured hex mesh generated in ABAQUS.

Figure 3: Lumen and normal plane intersection along a point t in the parametrised IVUS pull-back curve: **T**, **N**, and **B** is the tangential, the normal and the bi-normal vector at any $\mathbf{C}(t)$ point of the arbitrary parametrised curve C, respectively. $\mathbf{cp}(t)$ is the centre of area of each $\mathbf{R}(t)$ created by the intersection of the normal plane $\mathbf{P}(t)$ and the volume Q. cp is the interpolated curve passing through all the $\mathbf{cp}(t)$ points.

Figure 4: Transient inflation of varying diameter virtual balloon models. (a) Transient free stent expansion with a tapered balloon. On the right, cross sections centrally to the model (dashed line) are extracted to illustrate the transient unfolding of the six-folded balloon. (b) Transient free stent expansion with a stepped balloon.

Figure 5: Virtual compliance charts for varying diameter delivery systems without/with mounted stents. (a) Virtual compliance for a tapered balloon: proximal and distal target diameters of 3.5 *mm* and 4.25 *mm*, respectively. (b) Virtual compliance for a stepped balloon: proximal and distal target diameters of 3.02 *mm* and 4.46 *mm*, respectively.

Figure 6: Transient patient-specific RCA stent expansion with a non-tapered and a tapered balloon

Figure 7: Patient-specific spatial stent malapposition after stent deployment. (a) Actual stent malapposition after stent deployment in the RCA case: areas of stent with the red colour are incomplete apposed to the lumen walls. The higher the intensity of red, the higher the amount of malapposition. (b) Actual stent malapposition after stent deployment: areas of stent with the red colour are incomplete apposed to the lumen walls. The higher the intensity of red, the higher the amount of malapposition.

Figure 8: Transient patient-specific bifurcation stent expansion with undersized, oversized and a stepped tapered balloon model

Figure 9: Cumulative distribution functions for patient-specific spatial SM after each expansion step. (a) CDF graphs of virtual stent malapposition within the RCA segment. (b) CDF graphs of virtual stent malapposition within the LM bifurcation segment.