Computational replication of the patient-specific stenting procedure for coronary artery bifurcations: from OCT and CT imaging to structural and hemodynamics analyses

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42 **ABSTRACT**

43 The optimal stenting technique for coronary artery bifurcations is still debated. With additional
44 advances computational simulations can soon be used to compare stent designs or strategies based
45 on verified structural and hemodynamics results in order to identify the optimal solution for each
46 individual's anatomy. In this study, patient-specific simulations of stent deployment were
47 performed for 2 cases to replicate the complete procedure conducted by interventional cardiologists.
48 Subsequent computational fluid dynamics (CFD) analyses were conducted to quantify
49 hemodynamics quantities linked to restenosis.

50 Patient-specific pre-operative models of coronary bifurcations were reconstructed from CT
51 angiography and optical coherence tomography (OCT). Plaque location and composition were
52 estimated from OCT and assigned to models, and structural simulations were performed in Abaqus.
53 Artery geometries after virtual stent expansion of Xience Prime or Nobori stents created in
54 SolidWorks were compared to post-operative geometry from OCT and CT before being extracted
55 and used for CFD simulations in SimVascular. Inflow boundary conditions based on body surface
56 area, and downstream vascular resistances and capacitances were applied at branches to mimic
57 physiology.

58 Artery geometries obtained after virtual expansion were in good agreement with those
59 reconstructed from patient images. Quantitative comparison of the distance between reconstructed
60 and post-stent geometries revealed a maximum difference in area of 20.4%. Adverse indices of wall
61 shear stress were more pronounced for thicker Nobori stents in both patients. These findings verify
62 structural analyses of stent expansion, introduce a workflow to combine software packages for solid
63 and fluid mechanics analysis, and underscore important stent design features from prior idealized
64 studies. The proposed approach may ultimately be useful in determining an optimal choice of stent
65 and position for each patient.

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73 **Keywords:** mathematical model, finite element analysis, computational fluid dynamics, coronary
74 bifurcation, stent

1. INTRODUCTION

The treatment of complex coronary lesions such as bifurcation lesions remains a challenge in interventional cardiology because of lower success rates and higher restenosis rates as compared to non-complex lesions (Lassen et al., 2014). Since the introduction of drug eluting stents in 2004, restenosis rate after stent implantation have fallen below 10% in several randomized clinical trials (Dangas et al., 2010). However, this rate increases when coronary bifurcation lesions are treated (Lemos et al., 2004; Mauri et al., 2008; Zahn et al., 2005).

The optimal stenting technique for treating diseased coronary bifurcations is still debated without a consensus among interventional cardiologists (Lassen et al., 2014). Indeed, the post-operative follow-up is influenced by different factors such as stent design (Morton et al., 2004; Timmins et al., 2011, 2008), the use of one or two stents (Katritsis et al., 2009; Zhang et al., 2009), plaque morphology and composition (Timmins et al., 2008), arterial injury caused by stent deployment (Kornowski et al., 1998; Schwartz et al., 1992), and adverse hemodynamics induced by the stent struts protruding inside the lumen (Foin et al., 2014). A number of studies proved that neointima thickening (NT), which can lead to in-stent restenosis, is related to increased wall stress post-stenting (Timmins et al., 2011) and to altered local fluid dynamics (e.g. low and oscillating wall shear stress; WSS) provoked by the stent presence within the coronary artery (LaDisa Jr. et al., 2005; Malek et al., 1999).

In this context, virtual simulations of patient-specific coronary bifurcation stenting can be used to compare the effect of different stent designs or stenting strategies on structural and fluid dynamics results in order to identify the optimal solution for each individual's anatomy (Migliavacca et al., 2015). In several previous studies (Chiastra et al., 2013; Ellwein et al., 2011; Gundert et al., 2011; Morlacchi et al., 2013; Mortier et al., 2015) patient-specific structural and fluid dynamic simulations were conducted. However, the post-operative geometry obtained after virtual stent deployment was rarely compared with the *in vivo* post-operative images (Morlacchi et al., 2013). Moreover, when performed, this comparison is often qualitative and based only on computed tomography (CT) and angiography data. The use of optical coherence tomography (OCT) images allows better model verification, because of its high spatial resolution compared to CT and angiography (Farooq et al., 2009; Ferrante et al., 2013).

In this study patient-specific simulations of stent deployment are performed to replicate the complete procedure followed by clinicians to treat coronary bifurcations. OCT and CT images are used to reconstruct the 3D models of the coronary bifurcations. The reliability of structural finite-element analyses (FEA) in predicting post-operative geometric outcomes is evaluated. Subsequent computational fluid dynamics (CFD) analyses are conducted to quantify the influence of local

hemodynamics variables (e.g. indices of WSS). Different stent designs and stent positioning within the patient-specific models are studied to explore potential post-operative scenarios.

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112 2. MATERIALS AND METHODS

113 2.1 Imaging and reconstruction of artery morphology and composition

114 Accurate reconstruction of artery geometry is critical to the patient-specific modeling process,
115 and depends on imaging resolution. This study used a hybrid approach of CT angiography and OCT
116 to reconstruct artery geometry within the stented region by mathematically determining the location
117 of the OCT imaging wire during image acquisition (Ellwein et al., 2011). These method combines
118 conventional and invasive high-resolution imaging modalities (**Fig.1A**). We refer to the use of CT
119 and OCT data with this approach as *Hybrid OC-CT* (see details below).

120 This investigation was approved by the ethics committees of all participating institutions.
121 Informed consent was obtained for the use of data in this study. Coronary angiography, CT and
122 OCT imaging were performed before (i.e. pre-PCI) and immediately after stenting (i.e. post-stent)
123 as previously reported (Otake et al., 2009). OCT images were acquired and quantified as discussed
124 elsewhere (Ellwein et al., 2011; Nakazato et al., 2015).

125 Separate pre-PCI and post-stenting lumen models were created for two patients (namely, Cases
126 1 and 2). Case 1 consisted of a left anterior descending/first diagonal (LAD/D1) bifurcation of a 70-
127 year-old female while Case 2 is a left circumflex artery (LCX) with two branches of a 73-year-old
128 male. Pre-PCI lumen models were used to simulate local deformations caused by stenting from
129 FEA (see details below). The post-stenting models were created to validate the accuracy of
130 deformations from FEA. For both lumen models (i.e. pre-PCI and post-stenting), high resolution
131 OCT segments were registered within the region of interest using *Hybrid OC-CT* (Ellwein et al.,
132 2011). Briefly, OCT images were processed to isolate lumen contours in Matlab (MathWorks Inc.,
133 Natick, MA, USA). The wire pullback pathway (**Fig.1A**) was determined by minimizing total
134 bending energy within the lumen volume delineated by CT. Lumen segments from OCT were then
135 registered on the wire pathway using landmarks where possible. Remaining lumen segments were
136 then positioned longitudinally according to OCT image spacing. All lumen segments were then
137 oriented orthogonal to the wire pathway and rotated such that their centroids aligned with the artery
138 centerline. The aligned and oriented lumen segments were loaded into SimVascular (simtk.org) for
139 lofting and blending, thus obtaining lumen geometries (**Fig.1A**).

140 OCT data did not allow for measurement of wall thickness because of its reduced tissue
141 penetration (Waksman et al., 2013). To create external arterial wall surfaces (**Fig.1B**),
142 circumferential cross-sections orthogonal to lumen centerlines were smoothly connected using a

143 lofting operation. These cross-sections were defined only in the regions where no plaques or
144 symmetric atherosclerotic plaques were recognized by imaging in order to obtain a smooth external
145 wall and locate potential asymmetric plaques (Morlacchi et al., 2013). A ratio between the arterial
146 wall thickness and the healthy lumen as presented elsewhere (Holzapfel et al., 2005) was used to
147 calculate the cross-sectional diameters. The arterial wall was meshed with ~100,000 eight-node
148 cubic elements with reduced integration using ICEM CFD (ANSYS Inc., Canonsburg, PA, USA)
149 (**Fig.2A**). The mesh density is comparable to that used in a previous work (Capelli et al., 2009) in
150 which similar coronary artery models were implemented and numerically verified. An isotropic
151 hyperplastic constitutive model based on a reduced polynomial strain energy density function of
152 sixth order (Morlacchi et al., 2011) was implemented to describe the arterial wall material
153 properties. The coefficients of the hyperelastic model (**Table 1**) were identified from the
154 experimental results obtained on media layer specimens of human coronary arteries in the
155 circumferential direction (Holzapfel et al., 2005).

156 Since the exact radial plaque position within the arterial wall could not be deduced by the
157 patient images, a previously developed method for plaque identification (Morlacchi et al., 2013)
158 was applied and extended (**Fig.2A**). First, a centerline was identified from the external wall surface.
159 Second, the distance between this centerline and each element of the arterial wall was calculated in
160 the radial direction. Lastly, a healthy radius was assumed based on angiography inspection of non-
161 atherosclerotic locations. All elements with a distance less than the healthy radius (**Fig.2A**, black
162 arrows) were considered as plaque. Both investigated cases resulted in a local maximum area
163 stenosis of ~70%.

164 A different composition was then assigned to each region of plaque. To achieve this, a trained
165 interventional cardiologist manually delineated different plaque regions by looking at each OCT
166 slice and then delineating the plaque regions on the longitudinal view to convey where the different
167 components were located (**Fig.2B-C**). In Case 1 the majority of the plaque was classified as soft
168 (**Fig.2B**). In Case 2 the plaque was mainly stiff (i.e. fibrous plaque) with a small region of soft
169 material (i.e. fibrous and lipid plaque) close to the proximal side branch (**Fig.2C**). Soft and stiff
170 plaques were modeled using an isotropic hyperelastic law based on experimental data (Loree et al.,
171 1994) with ideal plasticity to simulate rupture at the experimental tensile stress values (~400kPa).
172 The material parameters are listed in **Table 1**. A density value of 1120 kg/m³ was used for both
173 arterial wall and plaques (Morlacchi et al., 2011).

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175 2.2 Stent and balloon models

176 The commercially available Xience Prime (Abbott Laboratories, Abbott Park, IL, USA) and
177 Nobori (Terumo, Somerset, NJ, USA) DES were considered in this study. The two stents are
178 characterized by a different strut thickness (**Table 2**). Geometries were created using SolidWorks
179 (Dassault Systèmes SolidWorks Corp., Waltham, MA, USA). Both stents are fabricated from a
180 cobalt-chromium alloy that can be described by a von Mises-Hill plasticity model with isotropic
181 hardening. The following material properties were assigned to the stent models during FEA: Young
182 modulus (233 GPa), Poisson coefficient (0.35), yield stress (414 MPa), ultimate stress (933 MPa),
183 deformation at break (44.5%), and material density (8000 kg/m³). The geometries were discretized
184 with a highly regular hexahedral mesh of ~120,000 reduced integration cubic elements using
185 HyperMesh software package (Altair Engineering, Troy, MI, USA).

186 Geometric models of angioplasty and stent delivery balloons were created in their crimped
187 configuration using SolidWorks. The balloon thickness was 0.025 mm. The polymeric material of
188 the balloons was described using a linear elastic isotropic model with a Young modulus of 1.45 GPa
189 and a Poisson coefficient of 0.3. The balloon models were discretized with ~25,000 reduced
190 integration membrane elements.

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192 **2.3 Structural simulations of stent deployment**

193 The following virtual stent expansion simulations were performed in the coronary bifurcation
194 models to replicate the real stenting procedure performed by the interventional cardiologists who
195 treated the cases featured (**Fig.3**):

- 196 1) Angioplasty: a balloon was inserted at the site of the atherosclerotic lesion and then inflated to
197 open the narrowed coronary artery. 2.5x18 mm and 3.5x18 mm balloons were used for Cases 1
198 and 2, respectively.
- 199 2) Provisional side branch stenting technique (PSB): first, a stent in its crimped state was
200 positioned in the main branch at the narrowing. Second, the stent was expanded by balloon
201 inflation. Last, the balloon was deflated and the stent remained in place, holding the artery open.
202 2.5x18 mm Xience Prime and 3.5x18 mm Nobori stents were implanted in Cases 1 and 2,
203 respectively.

204 Stent expansions were conducted in Abaqus/Explicit (Dassault Systèmes Simulia Corp.,
205 Providence, RI, USA) as a quasi-static process as discussed in detail elsewhere (Morlacchi et al.,
206 2013, 2011).

207 To investigate the biomechanical influence of different stent designs and position, additional
208 scenarios were also examined. Cases 1 and 2 were used to evaluate hemodynamic performance by
209 comparing CFD results from Xience Prime and the Nobori stents. Case 2 was also used to evaluate

the importance of stent positioning on the post-operative geometry obtained after virtual stent deployment relative to that from post-stent patient images via *Hybrid OC-CT*. Specifically, the Nobori stent was virtually implanted in three different positions by moving the stent distally relative to the first diagonal branch.

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2.4 CFD simulations

Lumen and arterial wall deformations from FEA were extracted for CFD. Briefly, a NASTRAN file exported from ICEM CFD was loaded into ParaView (Kitware Inc., Clifton Park, NY, USA) where the surface was extracted and saved as a VTK multiblock file. A discrete solid model was then created from this surface file using SimVascular. Faces were renamed to delineate between those of the stent and artery wall for use in assigning edge sizes to mesh elements. Meshing parameters were iteratively adjusted until the meshing procedure was successful at writing out a mesh of sufficient density to resolve local flow features, while working within the computational limits of the local CPU (HP Z420 E5-1620 3.6 GHz workstations with 16GB RAM). Meshing parameters included a default global max edge size of 1.0 mm, 0.15 mm edge size for wall faces, and 0.04 mm edge size for stent faces. The wall and stent face minimum edge sizes were then adjusted on a case-by-case basis until a successful mesh was achieved. Any meshing errors could typically be mitigated for faces on the wall by reducing the size of elements to 0.1-0.08 mm. Errors on stent faces could similarly be mitigated by reducing local edges sizes to 0.02-0.008 mm.

Boundary conditions for CFD were determined from patient-specific anthropometric data as discussed elsewhere (Ellwein et al., 2011). Briefly, using cardiac output, blood flow through the artery undergoing stenting was determined assuming the coronary arteries receive 5% of the cardiac output, and the right and left coronary arteries receive 16% and 84%, respectively (Ellwein et al., 2011; Leaman et al., 1981). A typical coronary inflow waveform (**Fig. 4**) (LaDisa Jr. et al., 2002) was then scaled to match the mean blood flow, and introduced as a time-varying Womersley velocity profile. Blood was assumed to be a Newtonian fluid with a viscosity and constant density of 4 cP and 1,060 kg/m³, respectively. WSS was assumed to be equal in the main vessel and side branches (Ellwein et al., 2011; Williams et al., 2010). A three-element Windkessel representation was applied at each outlet (**Table 3**) to replicate the physiological influence of the arterial tree distal to the arteries in the computational model after stent implantation (Ellwein et al., 2011; Williams et al., 2010).

CFD simulations were run using an in house stabilized finite element solver with commercial linear solver component LESLIB (Altair Engineering) to solve the time-dependent Navier-Stokes

equations. Standard convergence criteria were employed and simulations were run until the outlet pressure and flow were periodic.

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2.5 Analysis of results

The open-source software PyFormex (www.nongnu.org/pyformex/) was used to quantify the distance between lumen surfaces of the post-stent geometry obtained after virtual stent deployment and *Hybrid OC-CT*. The two geometries were manually registered using the position of the side branches as a reference. The area of the geometry obtained after virtual stent deployment with a distance greater than 0.25 mm (i.e. twice the strut thickness of the Nobori stent) was then calculated.

Malapposed struts (defined as struts not in contact or within 0.1 mm of the lumen surface) were identified (Iannaccone et al., 2014). The percent area of malapposed struts with respect to the total area of the abluminal stent surface was calculated. Although the relation between incomplete stent apposition and adverse cardiovascular events is still under debate, it has been shown that malapposed struts can alter shear stress distribution, potentially leading to stent thrombosis (Attizzani et al., 2014).

Indices of WSS previously linked to NT were also determined. Time-averaged WSS (TAWSS) and oscillatory shear index (OSI) were computed over the last cardiac cycle as in previous studies (He and Ku, 1996; Tang et al., 2006) and visualized using ParaView. It has been shown that low TAWSS (<0.4 Pa) and high temporal oscillations quantified by OSI (>0.1) are associated with NT (LaDisa Jr. et al., 2005; Malek et al., 1999; Wentzel et al., 2008), therefore the artery surface exposed to values outside these limits was used to quantify the impact of the implanted stent.

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3. RESULTS

The reliability of FEA for virtual stent deployment was first verified. FEA took ~24 hours on one node of a cluster (two quad-core Intel Xeon E5620 2.40 GHz with 3 GB RAM and INFINIBAND Mellanox interconnections). **Figure 5** shows superimposition of the post-operative lumen geometry obtained after virtual stent expansion and that from *Hybrid OC-CT*. A good qualitative agreement between the two geometries can be observed for both cases. Regions of the post-operative geometries obtained after virtual stent expansion with a distance >0.25 mm relative to those reconstructed from *Hybrid OC-CT* are highlighted in red. Percent differences in area were 14.8% and 20.4% for Cases 1 and 2, respectively.

Malapposed struts are highlighted in red in **Figs.6-7** for both cases, and the percent area of malapposed struts is reported in **Table 4** for both Xience Prime and Nobori stents. For Case 1,

malapposed struts are only present in the bifurcation ostium (**Fig.6**). For Case 2, malapposed struts are localized at the bifurcation ostia and also at the proximal part of the stent (**Fig.7**). The percent area of malapposed struts was reduced from ~4.9% to ~1.3% by moving the Nobori stent distally to the first branch from Position A to Position C (**Table 4, Fig.7**). The Xience Prime showed a lower percentage of malapposition than Nobori implanted in the implanted position (i.e. Position B), likely due to its different stent design impacting interaction with components of the arterial wall.

CFD analysis was subsequently performed to quantify post-stenting results between different stent designs. After optimizing the local mesh edge size for 2-6 hours depending on the model being studied, CFD run times averaged ~15 hours per simulation (range 8-26 hours) using 56 cores of an Intel Nehalem cluster with 3 GB/core of RAM.

Distributions of TAWSS for Case 1 are shown in **Fig.8**. The patient for this case was implanted with a 2.5x18 mm Xience Prime stent (**Fig.8A**). Virtual implantation of a 2.5x18 mm Nobori stent is also shown for comparison (**Fig.8B**). Portions of the artery lumen exposed to adverse TAWSS previously implicated in NT (i.e. < 0.4 Pa) are also shown in the figure. The area of low TAWSS was more pronounced for the Nobori stent as compared to the Xience Prime stent that was actually implanted (6.80% vs 4.07%, **Table 5**). Straightening of the artery caused skewing of the velocity profile toward the surface nearest the bifurcation, and resulted in a pronounced area of low TAWSS on the opposite surface within the proximal portion of the stent. A second focal region of low TAWSS was found directly opposite the bifurcation. The degree to which this region extended circumferentially was influenced by the stent implanted, and the orientation of struts within this region. Sites of low TAWSS were more pronounced around struts of the Nobori stent due to their greater thickness. This prevented re-establishing of local near-wall velocity patterns as was observed distal to the bifurcation for the Xience Prime stent. Distributions of OSI are shown in **Fig.9**. Overall artery morphology in the proximal stented region and the bifurcation also contributed to elevated OSI in these regions, but differences in the area exposed to $OSI > 0.1$ were more modest than for TAWSS (3.55% vs 3.70% for the Xience Prime and Nobori stents, respectively, **Table 5**).

Distributions of TAWSS for Case 2 are shown in **Fig.10**. The patient for this case was implanted with a 3.5x18 mm Nobori stent (**Fig.10A**) and virtual implantation of a 3.5x18 mm Xience Prime stent is also shown for comparison (**Fig.10B**). Areas of low TAWSS were localized to the entrance region of both stents where there was a sudden expansion in diameter, as well as downstream from an adjacent region of residual plaque and malapposition in the Nobori stent. The area of low TAWSS in Case 2 was also more pronounced for the Nobori stent as compared to the Xience Prime stent (27.1% vs 22.5%, **Table 5**). The regions of sudden expansion and downstream of the residual plaque within the stent also contributed to elevated OSI in these regions (**Fig.11**), and differences in

the area exposed to $OSI > 0.1$ were more pronounced than for Case 1 (8.15% vs 6.02% for the Nobori and Xience Prime, respectively, **Table 5**).

4. DISCUSSION

The use of computer models for predicting and interpreting outcomes related to the treatment of coronary artery bifurcation stenting is gaining popularity, and gaining an increasing level of interest (Migliavacca et al., 2015; Mortier et al., 2015, 2010). This is likely due in large part to a number of papers in recent years showing how patient-specific data can be used to precisely reproduce the anatomy of a coronary bifurcation, which can then be subjected to virtual bench testing of stents. These computational studies have generated striking agreement with experimental results suggesting they can be useful and powerful tools that shed additional light on aspects of interest to interventional cardiologists (Chiastra et al., 2015). This approach is particularly useful for the quantification of stent malapposition or indices of WSS in stented regions that are not immediately measurable during a procedure. With this in mind, the current investigation underscores the use of patient-specific FEA with subsequent CFD modeling as a means of predicting post-operative scenarios without necessarily having to physical deploy a stent. The main findings of this work are related to verifying FEA of stent expansion, successful integration of a workflow combining multiple software packages for solid and fluid mechanics analysis, and an alignment of patient-specific CFD results generated from this workflow with stent design features that have been shown to be important in idealized studies to date.

In completing the objective above, the current work achieves several notable ‘firsts’. In contrast to using an idealized artery or single imaging modality for reconstruction before FEA, the pre-PCI and post-stenting artery geometries here were created using *Hybrid OC-CT*, which allows for reconstruction at 15 μm resolution. The pre-PCI reconstruction was used as the starting point for FEA, and the post-stenting reconstruction was used to scrutinize the accuracy of its subsequent local deformations, which represents another unique aspect of the current investigation. The use of a sequential approach (i.e. from FEA to CFD analyses) allowed us to take also into account the local deformation of the artery lumen due to stent expansion. As previously demonstrated (Martin et al., 2014; Morlacchi et al., 2011), local hemodynamics are very sensitive to the stented geometry and a sequential approach can provide a more accurate replication of the local hemodynamic environment.

The arterial geometries obtained after virtual expansion were qualitatively in good agreement with those from patient images. Quantitative comparison between the post-stent geometries resulted in a maximum difference in area of 20.4% (Case 2). We believe this is a very promising result. The

345 manual registration process followed in this study is believed to have resulted in overestimation of
346 differences in geometry obtained after virtual stent deployment relative to the geometry
347 reconstructed from patient images. An optimization process could be implented for registration of
348 the post-stent geometries in order to minimize the areas with distance higher than 0.25 mm.

349 We also presented a workflow that, while accounting for all the steps conducted by an
350 interventional cardiologist, can systematically be used to quantify the relative contributions of
351 geometrical factors (e.g. strut malapposition) and biomechanical stimuli. The consideration of
352 factors from a solid mechanics (e.g. local deformation) and fluid mechanics (e.g. WSS) perspective
353 is unique, but also very important since both have been implicated in restenosis and markers of late
354 stent thrombosis. The approach presented here blends some of the most common and well
355 documented software packages from both the commercial and open source domains. Although
356 atypical, this approach allows us to leveage the best features from mutiple software packages and
357 provides a starting point for other researcher to do the same.

358 The current work also paves the way for the use of simulations in larger trials to predictively
359 evaluate the optimal stent for a given patient and/or assess their risk for suboptimal clinical
360 outcomes rooted in biomechanics after coronary artery DES implantation. For example, the notion
361 of being able to select the optimal stent for a given patient was investigated for both cases by
362 comparing the Xience Prime and Nobori stents in terms of malapposition, TAWSS, and OSI results.
363 The best stent position was evaluted virtually by implanting the Nobori stent in three different
364 positions. The percentage of malapposed struts was reduced by moving the stent distally to the first
365 branch. The case with the stent in its implanted position (Position B) showed results bounded by the
366 two extreme positions. The patient-specific cases presented here also confirm conclusions from
367 prior idealized studies regarding stent design characteristics and their effect on adverse WSS
368 distributions. Stent geometry has been shown to affect the distribution of WSS, and, in turn, affect
369 NT (LaDisa Jr. et al., 2005). Gundert et al. (Gundert et al., 2013) reviewed a hierarchy of factors
370 that can result in adverse WSS distributions by virtually implanting various stents into idealized
371 coronary arteries. The hierarchy includes strut thickness that was drastically different between the
372 two stents used in the current investigation, stent-to-lumen area ratio, angle of struts relative to the
373 primary direction of blood flow, and the arrangement of connector elements (Gundert et al., 2012).
374 However, it is conceivable that not all patient-specific CFD simulations conduted from FEA will
375 adhere to this hierarchy of design features elucidated by theoretical stented CFD models. Exclusions
376 may include stents with similar strut thicknesses, or patients with a more complex plaque
377 distribution creating a heterogeneity in material properties within the stented region.

378 The advancements shown in this work are perfectly timed as ~150 key opinion leaders from
379 academia, industry and cardiology recently expressed their willingness to adopt a new way of
380 thinking that includes the possibility of simulating interventions using patient-specific data
381 (Stankovic et al., 2013). Unfortunately enthusiasm is tempered by the fact that translation of virtual
382 patient-specific computational modeling to the clinic is dependent on the time needed to obtain the
383 results, as well as to their reliability. To complete the full procedure applied here (artery
384 reconstruction and its discretization, setting of FEA and CFD models, and solving, excluding the
385 time for image acquiring and creation of stent and balloon models), ~3 days are required with the
386 available computational resources. Further advancements to speed up and automate the procedure
387 are therefore required.

388 Although this study shows promising results, some limitations are present. The arterial wall
389 thickness and the external wall geometry could not be deduced from available imaging data. The
390 plaque identification process might be improved with more tissue testing and expedited by
391 implementing a semi-automatic algorithm for delineating the location and composition of plaque
392 from OCT data (Celi and Berti, 2014; Celi et al., 2013). Limitations of the CFD simulations are
393 related to the boundary conditions imposed, use of a Newtonian fluid, and neglecting movement of
394 the arterial wall after stent implantation. Closed-loop, lumped-parameter networks, initially
395 developed to model single ventricle physiology, were recently applied to the coronary arteries
396 (Sankaran et al., 2012). Implementation of these tools would better replicate relationships between
397 local flow and global circulatory dynamics (Bove et al., 2007; Corsini et al., 2011; Kim et al.,
398 2010). The rigid-wall assumption implemented here appears adequate when the aim of the study is
399 the analysis of near-wall hemodynamic quantities (Chiastra et al., 2014) within the stent since
400 implantation typically renders most of the artery rigid (LaDisa Jr. et al., 2002).

401

402 **5. CONCLUSIONS**

403 The methodology described here to virtually simulate stent implantation is reliable by taking
404 into account intrinsic errors and assumptions due to image reconstruction and numerical modeling.
405 Furthermore, the proposed workflow (from FEA to CFD analyses) may provide useful information
406 for pre-interventional planning by choosing the optimal stent type and position for each individual's
407 anatomy.

408

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415 *CT* approach.

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417 **7. CONFLICT OF INTEREST**

418 The authors have no conflicts of interest to declare.

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420 **8. REFERENCES**

- 421 Attizzani, G.F., Capodanno, D., Ohno, Y., Tamburino, C., 2014. Mechanisms, pathophysiology,
422 and clinical aspects of incomplete stent apposition. *J. Am. Coll. Cardiol.* 63, 1355–67.
- 423 Bove, E.L., de Leval, M.R., Migliavacca, F., Balossino, R., Dubini, G., 2007. Toward optimal
424 hemodynamics: computer modeling of the Fontan circuit. *Pediatr. Cardiol.* 28, 477–81.
- 425 Capelli, C., Gervaso, F., Petrini, L., Dubini, G., Migliavacca, F., 2009. Assessment of tissue
426 prolapse after balloon-expandable stenting: influence of stent cell geometry. *Med. Eng. Phys.*
427 31, 441–7.
- 428 Celi, S., Berti, S., 2014. In-vivo segmentation and quantification of coronary lesions by optical
429 coherence tomography images for a lesion type definition and stenosis grading. *Med. Image*
430 *Anal.* 18, 1157–1168.
- 431 Celi, S., Vaghetti, M., Palmieri, C., Berti, S., 2013. Superficial coronary calcium analysis by OCT:
432 Looking forward an imaging algorithm for an automatic 3D quantification. *Int. J. Cardiol.* 168,
433 2958–2960.
- 434 Chiastra, C., Grundeken, M.J., Wu, W., Serruys, P.W., de Winter, R.J., Dubini, G., Wykrzykowska,
435 J.J., Migliavacca, F., 2015. First report on free expansion simulations of a dedicated
436 bifurcation stent mounted on a stepped balloon. *EuroIntervention* 10, e1–3.
- 437 Chiastra, C., Migliavacca, F., Martinez, M.A., Malve, M., 2014. On the necessity of modelling
438 fluid-structure interaction for stented coronary arteries. *J. Mech. Behav. Biomed. Mater.* 34,
439 217–230.
- 440 Chiastra, C., Morlacchi, S., Gallo, D., Morbiducci, U., Cárdenes, R., Larrabide, I., Migliavacca, F.,
441 2013. Computational fluid dynamic simulations of image-based stented coronary bifurcation
442 models. *J. R. Soc. Interface* 10, 20130193.
- 443 Corsini, C., Cosentino, D., Pennati, G., Dubini, G., Hsia, T.Y., Migliavacca, F., 2011. Multiscale
444 models of the hybrid palliation for hypoplastic left heart syndrome. *J. Biomech.* 44, 767–770.
- 445 Dangas, G.D., Claessen, B.E., Caixeta, A., Sanidas, E. a., Mintz, G.S., Mehran, R., 2010. In-stent
446 restenosis in the drug-eluting stent era. *J. Am. Coll. Cardiol.* 56, 1897–1907.

447 Ellwein, L.M., Otake, H., Gundert, T.J., Koo, B.-K., Shinke, T., Honda, Y., Shite, J., LaDisa, J.F.,
448 2011. Optical Coherence Tomography for Patient-specific 3D Artery Reconstruction and
449 Evaluation of Wall Shear Stress in a Left Circumflex Coronary Artery. *Cardiovasc. Eng.*
450 *Technol.* 2, 212–227.

451 Farooq, M.U., Khasnis, A., Majid, A., Kassab, M.Y., 2009. The role of optical coherence
452 tomography in vascular medicine. *Vasc. Med.* 14, 63–71.

453 Ferrante, G., Presbitero, P., Whitbourn, R., Barlis, P., 2013. Current applications of optical
454 coherence tomography for coronary intervention. *Int. J. Cardiol.* 165, 7–16.

455 Foin, N., Gutiérrez-Chico, J.L., Nakatani, S., Torii, R., Bourantas, C. V., Sen, S., Nijjer, S., Petraco,
456 R., Kousera, C., Ghione, M., Onuma, Y., Garcia-Garcia, H.M., Francis, D.P., Wong, P., Di
457 Mario, C., Davies, J.E., Serruys, P.W., 2014. Incomplete stent apposition causes high shear
458 flow disturbances and delay in neointimal coverage as a function of strut to wall detachment
459 distance implications for the management of incomplete stent apposition. *Circ. Cardiovasc.*
460 *Interv.* 7, 180–189.

461 Gundert, T.J., Dholakia, R.J., McMahon, D., LaDisa, J.F., 2013. Computational fluid dynamics
462 evaluation of equivalency in hemodynamic alterations between Driver, Integrity, and similar
463 stents implanted into an idealized coronary artery. *J. Med. Device.* 7, 11004.

464 Gundert, T.J., Marsden, A.L., Yang, W., Marks, D.S., LaDisa Jr., J.F., 2012. Identification of
465 hemodynamically optimal coronary stent designs based on vessel caliber. *IEEE Trans Biomed*
466 *Eng* 59, 1992–2002.

467 Gundert, T.J., Shadden, S.C., Williams, A.R., Koo, B.K., Feinstein, J. a., Ladisa, J.F., 2011. A rapid
468 and computationally inexpensive method to virtually implant current and next-generation
469 stents into subject-specific computational fluid dynamics models. *Ann. Biomed. Eng.* 39,
470 1423–1437.

471 He, X., Ku, D.N., 1996. Pulsatile flow in the human left coronary artery bifurcation: average
472 conditions. *J. Biomech. Eng* 118.

473 Holzapfel, G.A., Sommer, G., Gasser, C.T., Regitnig, P., 2005. Determination of layer-specific
474 mechanical properties of human coronary arteries with nonatherosclerotic intimal thickening
475 and related constitutive modeling. *Am J Physiol Hear. Circ Physiol* 289, H2048–58.

476 Iannaccone, F., De Bock, S., De Beule, M., Vermassen, F., Van Herzeele, I., Verdonck, P., Segers,
477 P., Verhegghe, B., 2014. Feasibility of a priori numerical assessment of plaque scaffolding
478 after carotid artery stenting in clinical routine: proof of concept. *Int. J. Artif. Organs* 37, 928–
479 939.

480 Katritsis, G.D., Siontis, G.C.M., Ioannidis, J.P. a, 2009. Double versus single stenting for coronary
481 bifurcation lesions a meta-analysis. *Circ. Cardiovasc. Interv.* 2, 409–415.

482 Kim, H.J., Vignon-Clementel, I.E., Figueroa, C. a., Jansen, K.E., Taylor, C. a., 2010. Developing
483 computational methods for three-dimensional finite element simulations of coronary blood
484 flow. *Finite Elem. Anal. Des.* 46, 514–525.

485 Kornowski, R., Hong, M.K., Tio, F.O., Bramwell, O., Wu, H., Leon, M.B., 1998. In-stent
486 restenosis: Contributions of inflammatory responses and arterial injury to neointimal
487 hyperplasia. *J. Am. Coll. Cardiol.* 31, 224–230.

488 LaDisa Jr., J.F., Hettrick, D.A., Olson, L.E., Guler, I., Gross, E.R., Kress, T.T., Kersten, J.R.,
489 Warltier, D.C., Pagel, P.S., 2002. Stent implantation alters coronary artery hemodynamics and
490 wall shear stress during maximal vasodilation. *J Appl Physiol* 93, 1939–1946.

491 LaDisa Jr., J.F., Olson, L.E., Molthen, R.C., Hettrick, D.A., Pratt, P.F., Hardel, M.D., Kersten, J.R.,
492 Warltier, D.C., Pagel, P.S., 2005. Alterations in wall shear stress predict sites of neointimal
493 hyperplasia after stent implantation in rabbit iliac arteries. *Am J Physiol Hear. Circ Physiol*
494 288, H2465–75.

495 Lassen, J.F., Holm, N.R., Stankovic, G., Lefèvre, T., Chieffo, A., Hildick-Smith, D., Pan, M.,
496 Darremont, O., Albiero, R., Ferenc, M., Louvard, Y., 2014. Percutaneous coronary
497 intervention for coronary bifurcation disease: consensus from the first 10 years of the
498 European Bifurcation Club meetings. *EuroIntervention* 10, 545–60.

499 Leaman, D.M., Brower, R.W., Meester, G.T., Serruys, P., van den Brand, M., 1981. Coronary
500 artery atherosclerosis: severity of the disease, severity of angina pectoris and compromised left
501 ventricular function. *Circulation* 63, 285–299.

502 Lemos, P.A., Serruys, P.W., van Domburg, R.T., Saia, F., Arampatzis, C.A., Hoyer, A., Degertekin,
503 M., Tanabe, K., Daemen, J., Liu, T.K.K., McFadden, E., Sianos, G., Hofma, S.H., Smits, P.C.,
504 van der Giessen, W.J., de Feyter, P.J., 2004. Unrestricted utilization of sirolimus-eluting stents
505 compared with conventional bare stent implantation in the “real world”: the Rapamycin-
506 Eluting Stent Evaluated At Rotterdam Cardiology Hospital (RESEARCH) registry. *Circulation*
507 109, 190–5.

508 Loree, H.M., Grodzinsky, A.J., Park, S.Y., Gibson, L.J., Lee, R.T., 1994. Static circumferential
509 tangential modulus of human atherosclerotic tissue. *J Biomech* 27, 195–204.

510 Malek, a M., Alper, S.L., Izumo, S., 1999. Hemodynamic shear stress and its role in atherosclerosis.
511 *JAMA* 282, 2035–2042.

512 Martin, D.M., Murphy, E. a., Boyle, F.J., 2014. Computational fluid dynamics analysis of balloon-
513 expandable coronary stents: Influence of stent and vessel deformation. *Med. Eng. Phys.* 36,
514 1047–1056.

515 Mauri, L., Silbaugh, T.S., Wolf, R.E., Zelevinsky, K., Lovett, A., Zhou, Z., Resnic, F.S., Normand,
516 S.-L.T., 2008. Long-term clinical outcomes after drug-eluting and bare-metal stenting in
517 Massachusetts. *Circulation* 118, 1817–27.

518 Migliavacca, F., Chiastra, C., Chatzizisis, Y.S., Dubini, G., 2015. Virtual bench testing to study
519 coronary bifurcation stenting. *EuroIntervention* 11 Suppl V, V31–V34.

520 Morlacchi, S., Chiastra, C., Gastaldi, D., Giancarlo, P., Dubini, G., Migliavacca, F., 2011.
521 Sequential structural and fluid Dynamic numerical simulations of a stented bifurcated coronary
522 artery. *J. Biomech. Eng.* 133, 121010.

523 Morlacchi, S., Colleoni, S.G., Cárdenes, R., Chiastra, C., Diez, J.L., Larrabide, I., Migliavacca, F.,
524 2013. Patient-specific simulations of stenting procedures in coronary bifurcations: two clinical
525 cases. *Med. Eng. Phys.* 35, 1272–81.

526 Mortier, P., De Beule, M., Dubini, G., Hikichi, Y., Murasato, Y., Ormiston, J.A., 2010. Coronary
527 bifurcation stenting: insights from in vitro and virtual bench testing. *EuroIntervention* 6 Suppl
528 J, J53–60.

529 Mortier, P., De Beule, M., Segers, P., Verdonck, P., Verhegghe, B., 2011. Virtual bench testing of
530 new generation coronary stents. *EuroIntervention* 7, 369–376.

531 Mortier, P., Wentzel, J.J., De Santis, G., Chiastra, C., Migliavacca, F., De Beule, M., Louvard, Y.,
532 Dubini, G., 2015. Patient-specific computer modelling of coronary bifurcation stenting: the
533 John Doe programme. *EuroIntervention* 11 Suppl V, V35–V39.

534 Morton, A.C., Crossman, D., Gunn, J., 2004. The influence of physical stent parameters upon
535 restenosis. *Pathol. Biol.* 52, 196–205.

536 Nakazato, R., Otake, H., Konishi, A., Iwasaki, M., Koo, B.-K., Fukuya, H., Shinke, T., Hirata, K.-I.,
537 Leipsic, J., Berman, D.S., Min, J.K., 2015. Atherosclerotic plaque characterization by CT
538 angiography for identification of high-risk coronary artery lesions: a comparison to optical
539 coherence tomography. *Eur. Heart J. Cardiovasc. Imaging* 16, 373–9.

540 Otake, H., Shite, J., Ako, J., Shinke, T., Tanino, Y., Ogasawara, D., Sawada, T., Miyoshi, N., Kato,
541 H., Koo, B.K., Honda, Y., Fitzgerald, P.J., Hirata, K., 2009. Local determinants of thrombus
542 formation following sirolimus-eluting stent implantation assessed by optical coherence
543 tomography. *JACC Cardiovasc Interv* 2, 459–466.

544 Sankaran, S., Esmaily Moghadam, M., Kahn, A.M., Tseng, E.E., Guccione, J.M., Marsden, A.L.,
545 2012. Patient-specific multiscale modeling of blood flow for coronary artery bypass graft
546 surgery. *Ann Biomed Eng* 40, 2228–2242.

547 Schwartz, R.S., Huber, K.C., Murphy, J.G., Edwards, W.D., Camrud, a R., Vlietstra, R.E., Holmes,
548 D.R., 1992. Restenosis and the proportional neointimal response to coronary artery injury:
549 results in a porcine model. *J. Am. Coll. Cardiol.* 19, 267–274.

550 Stankovic, G., Lefevre, T., Chieffo, A., Hildick-Smith, D., Lassen, J.F., Pan, M., Darremont, O.,
551 Albiero, R., Ferenc, M., Finet, G., Adriaenssens, T., Koo, B.K., Burzotta, F., Louvard, Y.,
552 2013. Consensus from the 7th European Bifurcation Club meeting. *EuroIntervention* 9, 36–45.

553 Tang, B.T., Cheng, C.P., Draney, M.T., Wilson, N.M., Tsao, P.S., Herfkens, R.J., Taylor, C.A.,
554 2006. Abdominal aortic hemodynamics in young healthy adults at rest and during lower limb
555 exercise: quantification using image-based computer modeling. *Am J Physiol Hear. Circ*
556 *Physiol* 291, H668–76.

557 Timmins, L.H., Meyer, C. a, Moreno, M.R., Moore, J.E., 2008. Effects of stent design and
558 atherosclerotic plaque composition on arterial wall biomechanics. *J. Endovasc. Ther.* 15, 643–
559 654.

560 Timmins, L.H., Miller, M.W., Clubb, F.J., Moore, J.E., 2011. Increased artery wall stress post-
561 stenting leads to greater intimal thickening. *Lab. Invest.* 91, 955–967.

562 Waksman, R., Kitabata, H., Prati, F., Albertucci, M., Mintz, G.S., 2013. Intravascular ultrasound
563 versus optical coherence tomography guidance. *J. Am. Coll. Cardiol.* 62, S32–S40.

564 Wentzel, J.J., Gijssen, F.J.H., Schuurbiers, J.C.H., van der Steen, A.F.W., Serruys, P.W., 2008. The
565 influence of shear stress on in-stent restenosis and thrombosis. *EuroIntervention* 4 Suppl C,
566 C27–C32.

567 Williams, A.R., Koo, B.-K., Gundert, T.J., Fitzgerald, P.J., LaDisa, J.F., 2010. Local hemodynamic
568 changes caused by main branch stent implantation and subsequent virtual side branch balloon
569 angioplasty in a representative coronary bifurcation. *J. Appl. Physiol.* 109, 532–40.

570 Zahn, R., Hamm, C.W., Schneider, S., Zeymer, U., Nienaber, C.A., Richardt, G., Kelm, M.,
571 Levenson, B., Bonzel, T., Tebbe, U., Sabin, G., Senges, J., 2005. Incidence and predictors of
572 target vessel revascularization and clinical event rates of the sirolimus-eluting coronary stent
573 (results from the prospective multicenter German Cypher Stent Registry). *Am. J. Cardiol.* 95,
574 1302–8.

575 Zhang, F., Dong, L., Ge, J., 2009. Simple versus complex stenting strategy for coronary artery
576 bifurcation lesions in the drug-eluting stent era: a meta-analysis of randomised trials. *Heart* 95,
577 1676–81.

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579 **TABLE CAPTIONS**

580

581 **Table 1** – Coefficients of strain energy density function for the arterial wall and the atherosclerotic
582 plaques.

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584 **Table 2** – Geometric characteristics of the stent models

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586 **Table 3** – Parameters of the three-element Windkessel model applied at each outlet for the two
587 cases studied.

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589 **Table 4** – Malapposition for all investigated cases.

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591 **Table 5** – Indices of wall shear stress (WSS) including time-averaged wall shear stress (TAWSS)
592 and oscillatory shear index (OSI). These indices were compared between the implanted stent for
593 Cases 1 and 2 (Xience Prime and Nobori, respectively) and virtual implantation of the second stent.

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FIGURE CAPTIONS

Figure 1 – Creation of a patient-specific coronary artery bifurcation model using Case 1 as an example. A) *Hybrid OC-CT* method to obtain the 3D lumen geometry (Ellwein et al., 2011): (top) detection of lumen contours, (center) registration of the detected contours orthogonal to the imaging wire pathway, (bottom) final 3D lumen geometry, which was obtained by lofting lumen contours after registration. The center panel also shows differences between the imaging wire pathway (black) and the lumen centerline (grey). B) 3D solid model of the lumen and vessel wall.

Figure 2 – Plaque modeling. A) Plaque identification process (Morlacchi et al., 2013) using Case 2 as an example. The distance between each grid node and the centerline of the external wall is computed. The elements are characterized by assuming a distance less than the physiological lumen radius represents regions of plaque. B-C) Assignment of plaque composition, which is based on the information given by optical coherence tomography (OCT) images, for Cases 1 and 2, respectively.

Figure 3 – Main steps of the stenting procedure that was followed for Cases 1 (left) and 2 (right): A) insertion of the angioplasty balloon; B) expansion of the angioplasty balloon; C) insertion of the stent crimped on a balloon; D) stent expansion; E) final geometric configuration after stent recoil.

Figure 4 – Coronary waveforms used as inlet boundary conditions for CFD simulations. The mean inflow for each case was estimated from patient-specific anthropometric data assuming a normal cardiac index, that the coronary arteries receive 5% of the cardiac output, and that the right and left coronary arteries receive 16% and 84%, respectively. The coronary inflow waveform in the figure was then scaled to match the calculated mean blood flow, and introduced as a time-varying Womersley velocity profile.

Figure 5 – Comparison between the post-stenting geometry reconstructed from patient images (grey) and the geometry obtained after virtual stent deployment (blue) for Cases 1 (left) and 2 (right). Regions of the geometry obtained after virtual stent deployment that are greater than 0.25 mm from the geometry reconstructed from patient images are shown in red. Comparison was only performed in the stented region. Two views are shown for clarity as indicated by differences in the flow direction in the top vs bottom images.

628 **Figure 6** – Quantification of stent malapposition for Case 1: A) Xience Prime stent; B) Nobori
629 stent. Malapposed struts are shown in red.

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631 **Figure 7** – Quantification of stent malapposition for Case 2. A-C) Nobori stent in the three
632 positions investigated; D) Xience Prime stent. Malapposed struts are shown in red.

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634 **Figure 8** – Time-averaged wall shear stress (TAWSS) distributions for Case 1. Differences in
635 TAWSS previously linked to neointimal thickness are shown in the figure and quantified in Table 5
636 by comparing CFD results from the implanted Xience Prime stent (A) vs the virtually-implanted
637 Nobori stent (B). Two views are shown for clarity as indicated by differences in the flow direction
638 in the left vs right images. The full range of TAWSS values is shown for both stents in each view.
639 The lumen area exposed to the TAWSS < 0.4 Pa (see legend) is also isolated for both stents in each
640 view.

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642 **Figure 9** – Oscillatory shear index (OSI) distributions for Case 1. Differences in OSI are shown in
643 the figure and quantified in Table 5 by comparing CFD results from the implanted Xience Prime
644 stent (A) vs the virtually-implanted Nobori stent (B). Two views are shown for clarity as indicated
645 by differences in the flow direction in the left vs right images.

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647 **Figure 10** – Time-Averaged Wall Shear Stress (TAWSS) distributions for Case 2. Differences in
648 TAWSS previously linked to neointimal thickness are shown in the figure and quantified in Table 5
649 by comparing CFD results from the implanted Nobori stent (A) vs the virtually-implanted Xience
650 Prime stent (B). Two views are shown for clarity as indicated by differences in the flow direction in
651 the left vs right images. The full range of TAWSS values is shown for both stents in each view. The
652 lumen area exposed to the TAWSS < 0.4 Pa (see legend) is also isolated for both stents in each
653 view.

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655 **Figure 11** – Oscillatory Shear Index (OSI) distributions for Case 2. Differences in OSI are shown in
656 the figure and quantified in Table 5 by comparing CFD results from the implanted Nobori stent (A)
657 vs the virtually-implanted Xience Prime stent (B). Two views are shown for clarity as indicated by
658 differences in the flow direction in the left vs right images.

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664 **TABLES**

665

666 **Table 1** – Coefficients of strain energy density function for the arterial wall and the atherosclerotic
667 plaques

	C10 [MPa]	C20 [MPa]	C30 [MPa]	C40 [MPa]	C50 [MPa]	C60 [MPa]
Arterial wall (media layer)	6.52E-03	4.90E-02	9.26E-03	7.60E-01	-4.30E-01	8.70E-02
Soft plaque	2.38E-03	1.90E-01	-3.90E-01	3.37E+00	-2.54E+00	5.70E-01
Stiff plaque	1.21E-02	1.54E+00	2.19E+00	2.14E+02	-3.35E+03	1.34E+05

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671 **Table 2** – Geometric characteristics of the stent models

Stent model	External diameter (expanded configuration) [mm]	Length [mm]	Strut thickness [μm]
Xience Prime	2.5 (<i>Case 1</i>)	18	81
	3.5 (<i>Case 2</i>)		
Nobori	2.5 (<i>Case 1</i>)	18	125
	3.5 (<i>Case 2</i>)		

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675 **Table 3** – Parameters of the three-element Windkessel model applied at each outlet for the two
676 cases studied.

Case	Branch	Characteristic impedance [dyn·s·cm ⁻⁵]	Capacitance [cm ⁵ /dyn]	Distal resistance [dyn·s·cm ⁻⁵]
1	Side Branch	4.66E+04	5.50E-07	2.92E+05
	Outlet	1.64E+04	9.00E-07	4.36E+04
2	Proximal Side Branch	7.83E+04	4.60E-08	1.95E+06
	Distal Side Branch	8.45E+04	4.00E-08	2.16E+06
	Outlet	8.70E+03	1.50E-06	6.64E+04

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Table 4 – Malapposition for all investigated cases.

Case	Stent	Malapposition
		[perc. area with distance > 0.1 mm]
1	Xience Prime (<i>Implanted</i>)	0.90 %
1	Nobori	1.53 %
2	Nobori (pos. A)	4.92 %
2	Nobori (pos. B - <i>Implanted</i>)	2.35 %
2	Nobori (pos. C)	1.32 %
2	Xience Prime (pos. B)	0.95 %

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Table 5 – Indices of wall shear stress (WSS) including time-averaged wall shear stress (TAWSS) and oscillatory shear index (OSI). These indices were compared between the implanted stent for Cases 1 and 2 (Xience Prime and Nobori, respectively) and virtual implantation of the second stent.

Case	Stent	TAWSS	OSI
		[perc. area TAWSS < 0.4 Pa]	[perc. area with OSI > 0.1]
1	Xience Prime (<i>Implanted</i>)	4.07 %	3.55%
1	Nobori	6.80 %	3.70 %
2	Nobori (<i>Implanted</i>)	27.1 %	8.15 %
2	Xience Prime	22.5 %	6.02 %

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Figure 1

A)

B)

Figure 2

Figure 3

Figure 4

Figure 5

Case 1

Case 2

Figure 6

A) Xience Prime

■ Malapposed
■ Well-apposed

B) Nobori

Figure 7

Figure 8

Figure 9

Figure 10

A) Nobori

Flow
→

Flow
←

B) Xience Prime

Flow
→

Flow
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Figure 11