

1 Investigation of the haemodynamic environment of bifurcation plaques within the left  
2 coronary artery in realistic patient models based on CT images

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20 **Abstract**

21 The aim of this study was to investigate the plaques at the left coronary artery and their  
22 effect on the haemodynamic and wall shear stress (WSS) in realistic patient models.  
23 Three sample patients with left coronary disease were selected based on CT data. The  
24 plaques were present at the left anterior descending and left circumflex branches with  
25 more than 50% lumen narrowing. Computational fluid dynamics (CFD) analysis was  
26 used to perform simulation of patient-specific models with realistic physiological  
27 conditions that demonstrate *in vivo* cardiac flow. WSS and blood flow in the left coronary  
28 artery were measured during cardiac cycles. Our results showed that WSS was found to  
29 increase at the stenotic locations and decrease at pre- and post-plaque locations, whilst  
30 the recirculation location was found at post-plaque regions. There is a strong correlation  
31 between coronary bifurcation plaques and hemodynamic and WSS changes, based on the  
32 realistic coronary disease models.

33 **Key words:** Atherosclerosis, hemodynamic, computational fluid dynamics, coronary  
34 artery disease, plaques

35 **1. Introduction**

36 Computed tomography (CT), a non-invasive medical imaging modality, is increasingly  
37 used to diagnose coronary artery disease (CAD), in particular, the evaluation of coronary  
38 plaques with regard to their effect on a patient's prognosis [1, 2]. The emergence of  
39 multislice coronary computed tomography angiography (CCTA) and the latest CT  
40 scanners, has enabled CAD, and coronary plaque detection with high diagnostic accuracy  
41 [1, 2]. However, it is limited to the anatomical details and is unable to provide the  
42 haemodynamic changes in the coronary artery due to the presence of plaques. The CCTA  
43 has been used to characterise the different compositions of coronary plaques, with similar  
44 diagnostic value when compared to intravascular ultrasound [3]. Computational fluid  
45 dynamics (CFD) has overcome the limitations of CT imaging, and previous studies have  
46 used CFD to analyse the haemodynamic parameters in reconstructed coronary arteries, to  
47 indicate a plaque's progression [4, 5].

48 Haemodynamic variation is an important factor which influences the change of  
49 static pressure and wall shear stress (WSS) in the artery, thus enabling the investigation  
50 of the development of atherosclerotic plaques [6-8]. Coronary plaques are generally  
51 formed at bifurcation locations, as confirmed by previous studies [6-11]. The plaques  
52 commonly form at the left anterior descending (LAD) and left circumflex (LCX) [9, 12]  
53 and lead to the lumen narrowing with at least 50% stenosis, inducing myocardial  
54 ischemic changes [7, 13]. Therefore, the study of the local blood flow changes due to  
55 plaques at left coronary bifurcation in realistic vascular geometry can provide an  
56 improved understanding of their effect. The purpose of this study was to investigate the

57 corresponding influence of plaques on hemodynamic variations at coronary bifurcations,  
58 with specific patients in CAD.

## 59 **2. Materials and Methods**

### 60 **2.1 Patient data selection**

61 Three patients with suspected CAD underwent multi-slice coronary CT  
62 angiography and were selected for this study, based on CT findings. CT data was  
63 processed to reconstruct the 3D left coronary artery models. All patients had clinical  
64 symptoms of typical chest pain and a history of hypertension. Coronary CT angiography  
65 showed significant lumen stenosis caused by plaques in the left coronary artery and its  
66 branches. The patient demographics are shown Table 1. At least 60% lumen stenosis was  
67 noticed at the LAD and LCX, since more than 50% lumen narrowing leads to significant  
68 blood flow variations within the coronary artery disease [7]. The original sample patient's  
69 volume CT data was collected in "DICOM format". The calcified plaque-locations were  
70 analysed with use of a 3D visualisation tool, virtual intravascular endoscopy (VIE), to  
71 visualise the stenosis lumen in the sample specific-patients as shown in Fig. 1. The  
72 commercial biomedical imaging software Analyze 7.0 (Analyze Direct, Inc., Lexana, KS,  
73 USA) was used to identify plaque locations at the bifurcations, and segment the left  
74 coronary artery (LCA) and its branches. These medical imaging techniques were applied  
75 to generate 3D LCA models with object-map creations, manual hand editing, and  
76 segmented post-processing techniques, with details having been described in previous  
77 studies [14, 15]. The 3D LCA surfaces were created, consisting of left main stem (LMS),  
78 LAD, LCX and its side-branches. The 3D LCA surfaces were saved in "Binary STL  
79 format" for generation of the computational models.

80 In summary, four plaques were simulated in these 3 selected patients, with two  
81 plaques simulated in the LAD and LCX in patient 1, one plaque in the LAD in patient 2,  
82 and another plaque in the left bifurcation in the remaining patient.

### 83 **2.2 Computational left coronary and plaques modelling**

84 Patient's binary STL files were transferred to computer workstation, and Blender  
85 version 2.48 (Blender Institute, Amsterdam, Netherlands) was used for reconstruction  
86 purposes. The LCA surfaces were gently smoothed to reduce any non-physical artefacts  
87 caused by sharp edges. Patient's surface models were kept to the original rough surface  
88 geometry, however unwanted anatomical structures (such as bones, soft tissues) and  
89 digital artefacts were removed. The computational LCA models that were used in this  
90 study are shown in Fig. 2. LCA models were saved into "STL format" for mesh  
91 generation. ANSYS ICEM CFD version 12 (ANSYS, Inc., Canonsburg, PA, USA) was  
92 used to generate the computational elements of the study models (details having been  
93 described in previous studies [6, 16, 17]). The LCA models were configured with a  
94 hexahedral mesh of approximately  $1 \times 10^6$  nodes and  $9 \times 10^5$  elements, while the plaque-  
95 sections were configured with a tetrahedral mesh of around  $1.5 \times 10^4$  nodes and  $7.8 \times 10^4$   
96 elements. Meshing models were saved in 'GTM format' for computation of  
97 haemodynamic analysis.

### 98 **2.3 Computational hemodynamic analysis**

99 A time dependent simulation was computed, using realistic physiological  
100 boundary conditions to model the actual *in vivo* conditions. The accurate boundary  
101 conditions of pulsatile flow velocity and pressure were calculated based on Fourier series  
102 equations, reconstructed from pulsatile graphs taken from McDonald's Blood Flow in

103 Arteries [18] using Matlab (MathWorks, Inc. Natick, MA, USA). The velocity and  
104 pressure profiles were applied at the main inlet (left main stem) and outlets (left anterior  
105 descending and left circumflex), respectively, for all study LCA models [6]. Rheological  
106 properties were applied with a blood density of  $1060 \text{ kg/m}^3$ , blood viscosity of  $0.0035 \text{ Pa}$   
107  $\text{s}$  [19, 20] and plaque was assumed to be a rigid body [21]. No-slip conditions were  
108 applied at the coronary walls, and blood was assumed to be Newtonian. Blood flow was  
109 assumed to be laminar and incompressible [22]. ANSYS CFX version 12 (ANSYS, Inc.,  
110 Canonsburg, PA, USA) was used to solve the Navier-Stokes equations by  
111 approximately 100 iterations per time-step within 1.0 second of pulsatile flow and  
112 pressure (1 time-step is representing 0.0125 seconds). A converged solution was obtained  
113 for a residual target of less than  $0.1 \times 10^{-3}$ , and the computational time consumption was  
114 roughly 2 hours for each study case. The hemodynamic profiles and wall shear stress  
115 were calculated and visualised using ANSYS CFD-Post version 12 (ANSYS, Inc.).

### 116 **3. Results**

#### 117 **3.1 Effect of plaques on blood flow at the left coronary bifurcation**

118 The current study was performed based on *in vivo* physiological conditions during  
119 cardiac cycles. The peak systolic and mid diastolic phases were indicated at the time of  
120 0.4 sec and 0.7 sec, respectively. The results of this simulation show the influence of  
121 bifurcation plaques located at the LAD and LCX branches on hemodynamic changes.  
122 Fig. 3 demonstrates the plaque's effect on flow velocity patterns at the left bifurcation.  
123 The 10 coloured levels were used to show the velocity values which ranged from 0 mm/s  
124 to 30.5 mm/s. The LCA model with patient's diseased bifurcation plaques demonstrated a  
125 significant increase of flow velocity at the plaque locations, which ranged from 27.11

126 mm/s to 30.5 mm/s (peak systolic) and 23.72 mm/s to 27.11 mm/s (mid diastolic, not  
127 shown). Highest velocity was reached at LAD and LCX branches where coronary  
128 plaques resulted in significant lumen narrowing. The recirculating regions were found at  
129 post-plaque locations in the LAD and LCX (Fig. 3).

### 130 **3.2 Effect of plaques on wall shear stress at the left coronary bifurcation**

131 Calculated WSS was visualised at the velocity peak of the systolic and diastolic  
132 phases, as shown in Fig. 4. The contour of 10 coloured scales was used to show the WSS  
133 values, which ranged from 0 Pa to 3.50 Pa (Fig. 4). WSS distributions in all three patients  
134 were similar, with high WSS values ranging from 3.15 Pa to 3.50 Pa at the plaque  
135 locations (Fig. 4). Low WSS was found at pre- and post-plaque locations (values ranged  
136 from 0 Pa to 0.70 Pa).

## 137 **4. Discussion**

138 This study shows that bifurcation plaques can produce significant haemodynamic  
139 effects on blood flow and WSS changes in realistic patient-specific models of the left  
140 coronary artery. The results of this study provide a clinical understanding of coronary  
141 plaques with regard to their subsequent effect on blood flow, which could lead to the  
142 worsening of atherosclerosis. Plaques are usually located at the bifurcated regions, and  
143 early studies have shown that plaques form at the coronary bifurcation [6-12]. The  
144 current medical imaging modality of CT is limited to anatomical details, but fails to  
145 analyse the haemodynamic and WSS changes [1-3, 9]. Computational analysis of  
146 reconstructed coronary vessels is available to detect blood flow and WSS changes in the  
147 restricted conditions of modern imaging diagnosis [6, 16, 17].

148           This study investigated two main areas: flow velocity and wall shear stress, and  
149 quantified the effects of bifurcation plaques on haemodynamic factors in patient-specific  
150 left coronary artery models. Selected patient's artery geometry was reconstructed to  
151 generate the LCA models with significant lumen stenosis. High WSS regions (Fig. 4)  
152 were found at the stenotic locations and this seems to indicate that the potential plaques  
153 may rupture at high WSS locations [23]. Low WSS locations (Fig. 4) were found at pre-  
154 and post- plaque locations, these causes may lead to the progression of plaques [6-8].  
155 Flow velocity was increased at stenotic locations, and recirculating flow was displayed at  
156 post-plaque locations (as shown in Fig. 3). According to the haemodynamic analysis, the  
157 plaques tend to develop at post-plaque locations, in low flow velocity, recirculating  
158 regions [6-8]. Our investigation provides an insight into the effect of bifurcation plaques  
159 at LAD and LCX branches on the haemodynamic parameters and demonstrates the  
160 subsequent haemodynamics surrounding plaque locations.

161           Recent studies have presented the clinical data regarding the distribution of high-  
162 risk plaques in human coronary arteries [24, 25] and focal development of atherosclerosis  
163 was related to the plaque configuration in the bifurcation regions. It has been shown that  
164 the stenoses in left coronary bifurcations may cause haemodynamic and WSS variations  
165 to the main coronary arteries and their side-branches [26, 27]. The role of WSS  
166 distribution is associated with the plaque progression and a region of high WSS has been  
167 considered contributing to the rupture and thrombosis in atherosclerotic plaques, while  
168 the location of low WSS may lead to developed progression of plaque area [28]. Our  
169 results are in line with these reports as we noticed the high WSS at the stenotic positions  
170 and low WSS at the pre- and post-plaque conditions. These findings are valuable for



171 improving understanding of the effects of plaques, consequently the mechanisms of  
172 development of atherosclerosis.

173 Patient-specific LCA models of CFD analysis have some limitations that should  
174 be addressed. The simulation did not consider the elasticity of the coronary wall. The  
175 surface of the stenoses was assumed to be smooth and this assumption has been shown to  
176 be reasonable in this case [26]. Furthermore, the assumption of a non-Newtonian  
177 viscosity can be important in low flow areas. However, assumption of a rigid coronary  
178 wall is reasonable in this configuration [22]. Furthermore, patient-specific LCA models  
179 were limited as only three patients were included in this study. It is possible that plaques  
180 only occur at one side of the coronary artery, resulting in stenosis. Future studies with  
181 inclusion of more coronary models with different configurations based on a more realistic  
182 idealized geometry should be performed.

183 In conclusion, we performed a computational analysis of bifurcation plaques in  
184 the realistic left coronary artery with coronary disease, at bifurcation locations between  
185 LAD and LCX. There is a direct influence of bifurcation plaques in the left coronary  
186 artery on haemodynamic and WSS changes, such as recirculating flow, low flow velocity  
187 regions, and high WSS, indicating the potential risk for plaques to rupture. Further  
188 studies focusing on the larger populations of patient-specific left coronary disease should  
189 be performed to verify our results.

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191 **References**

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282 remodeling in patients with coronary artery disease. *Circulation* 124:779-788

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291 **Figure legends**

292 Fig. 1. CT virtual intravascular endoscopy imaging was generated to identify the  
293 calcified plaque locations at the bifurcation in the left coronary artery (top left  
294 image). Extensive calcified plaque is demonstrated at the left anterior  
295 descending on 2D axial (top right image), and coronal and sagittal views (top  
296 left and right images).

297 Fig. 2. The reconstructed patient-specific left coronary models have been used in this  
298 analysis and these models correspond to the patients in Table 1.

299 Fig. 3. Visualisation of velocity streamlines of Patient ‘A’ with presence of coronary  
300 plaques (A) and without plaques (B) during the systolic peak of 0.4 s. Arrows  
301 indicate the regions of low flow velocity which occurred at pre- and post-  
302 plaque positions. Double arrows reveal the regions of high flow velocity.

303 Fig. 4. Visualisation of wall shear stress of the three patients with the coronary plaques  
304 condition during the systolic peak of 0.4 s. Arrows indicate the regions of low  
305 wall shear stress which occurred at pre- and post-plaque positions.

Fig. 1

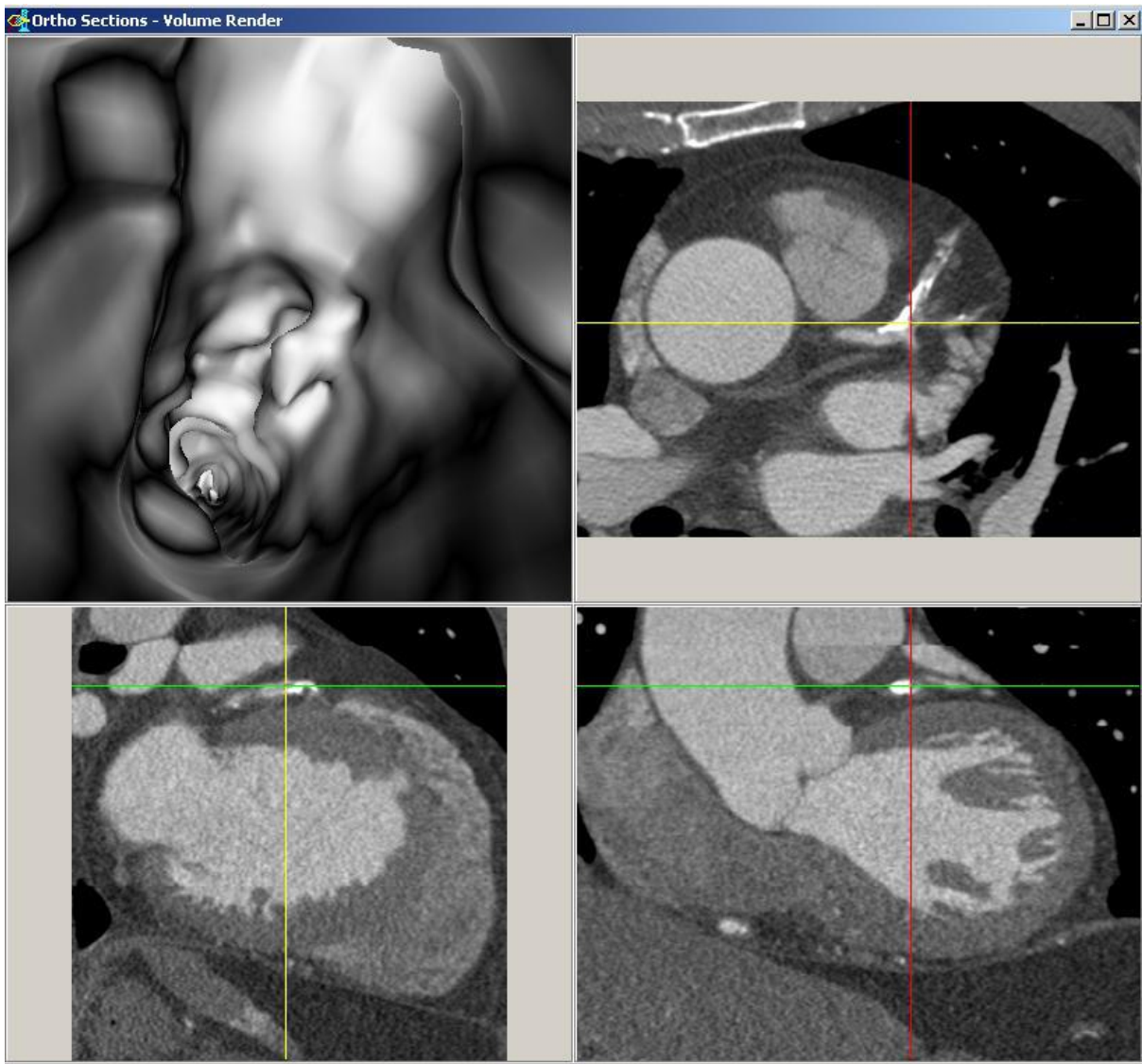




Fig. 2

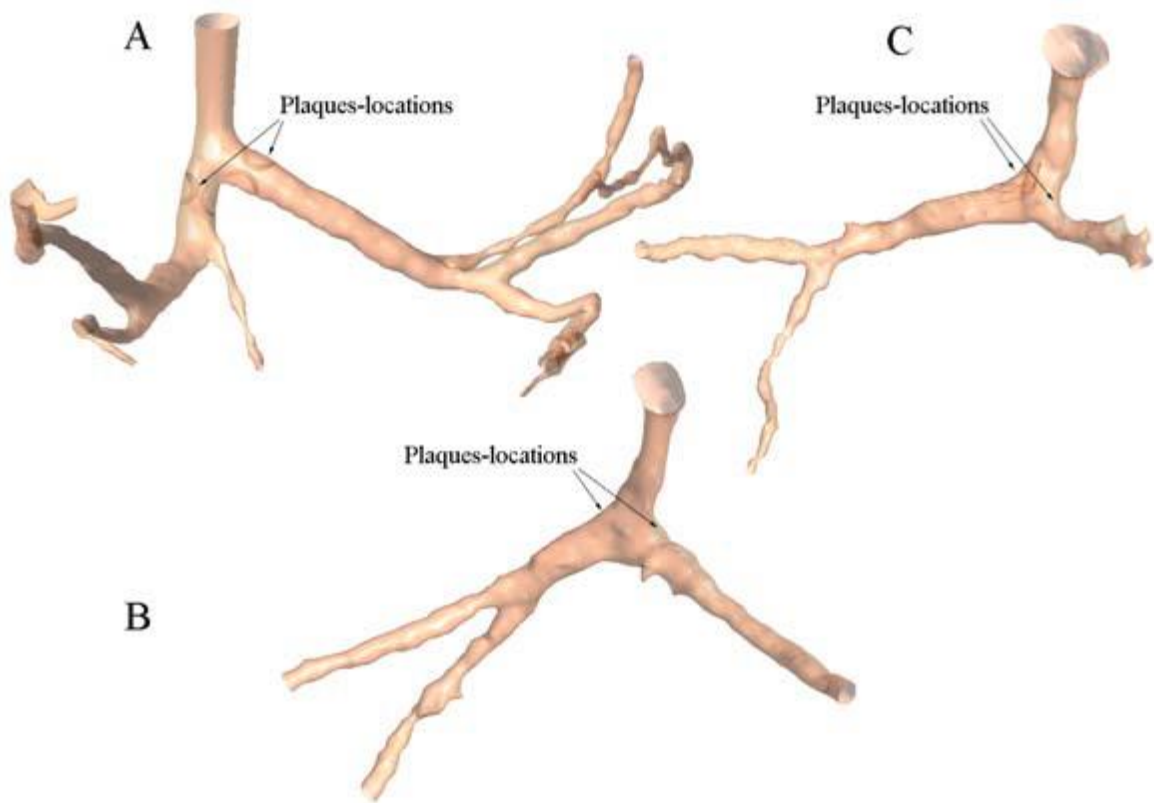


Fig. 3

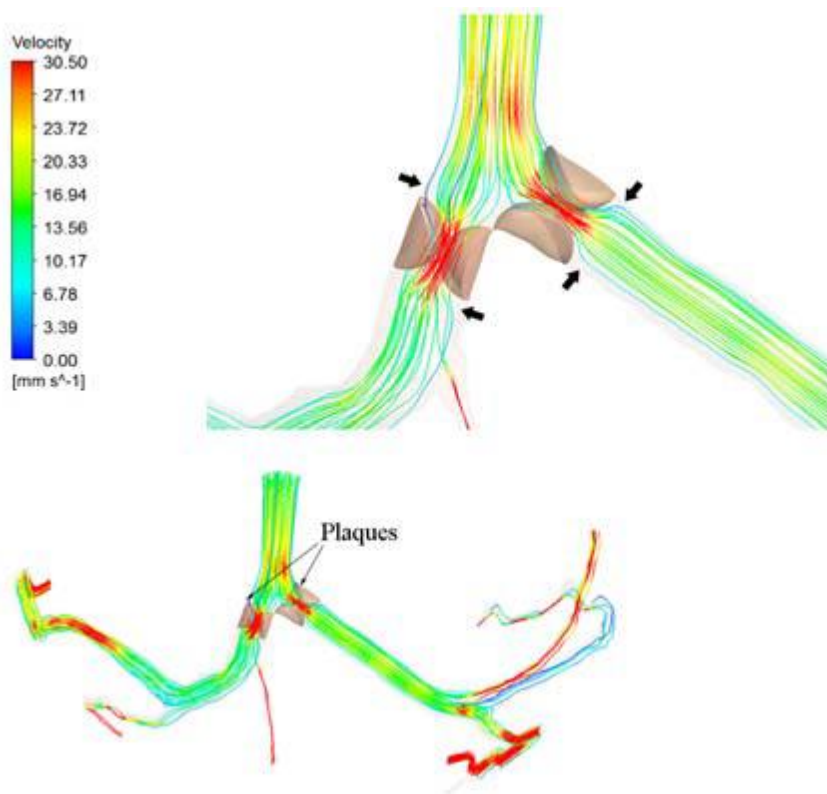


Fig. 4

