

## **Unveiling LDL Dynamics Post-Stent Intervention: A Deep Dive into Transport and Accumulation**

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**Submitted: 25<sup>th</sup> October 2024**

**Accepted: 15<sup>th</sup> January 2025**

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## Abstract

The endovascular stent implantation is a significant and efficacious cardiovascular interventional treatment. However, the underlying mechanisms behind in-stent neoarteriosclerosis and restenosis following the intervention remain unclear. Our hypothesis posits that stent implantation may impact the transportation of low-density lipoproteins (LDL) within the host artery, thereby disrupting its concentration distribution and leading to adverse clinical events. To validate this hypothesis, we conducted a numerical investigation to examine the influence of stenting on LDL distribution, utilizing a lumen-wall model based on the coronary artery. The findings of the study suggest that the introduction of an implanted stent can disrupt blood flow and result in an abnormal accumulation of lipids on the inner surface of the arterial wall, particularly in the vicinity of the strut protrusion. Additionally, improper stent implantation, characterized by thick struts, reduced spacing between struts, and non-streamlined struts, can exacerbate the local mechanical conditions of the host artery and contribute to a relatively high concentration of low-density lipoprotein (LDL) near the stent strut. In summary, the presence of a stent in the artery leads to an elevated LDL concentration both within the stented segment and downstream, potentially leading to adverse consequences.

**Keywords:** Low-Density Lipoproteins; Hemodynamics; Stents; Restenosis; Thrombosis

## 1 Introduction

Stenting intervention is a widely accessible and efficacious approach for the treatment of stenotic atherosclerosis, particularly in cases of coronary stenosis. Nonetheless, this intervention may give rise to clinical cardiac events in the course of post-stenting follow-up. The compromised advantages of this strategy serve as clinical evidence of the comparatively elevated risks associated with recurrent stenosis, neoarteriosclerosis, and thrombosis [9],[10]. According to clinical data, the restenosis rates of stent implantation ranged from 16% to 44% [35], and late stent thrombosis accounted for approximately 1% but caused more than 90% of the disability or death [30].

The incidence of adverse events following stent implantation is intricately linked to the altered mechanical conditions within the host artery. These alterations, induced by stenting, result in significant damage to the arterial wall, particularly affecting the vascular endothelial cells, as a consequence of the compressive forces exerted by the stent struts. This process subsequently triggers vascular remodeling, inflammation, and healing[15]. Furthermore, the presence of protruding stent struts can disrupt the flow within the lumen, leading to stagnation and separation of the fluid around these struts [17]-[29]. This unfavorable fluid behavior primarily contributes to vascular injury and the development of recurrent stenosis and thrombosis. The initial occurrence of in-stent restenosis can be attributed to damage to the vascular wall and loss of endothelial cells, particularly in the vicinity of the stented segment. This endothelial denudation and dysfunction serve as significant factors in the occurrence of injury events and subsequent adverse outcomes [24].

The destruction of endothelial cells and the glycocalyx layer has the potential to expedite the infiltration and buildup of detrimental macromolecules, including LDL, within the arterial wall [15],[33]. Experimental evidence has shown that the heightened water conductivity and permeability of endothelial cells result in swift macromolecule accumulation in the intima following their destruction[36],[37]. Furthermore, the restoration of endothelial function subsequent to percutaneous coronary interventions is inadequate, as evidenced by compromised intercellular junctions, heightened permeability, and increased hydraulic conductivity [24]. These studies have demonstrated that endothelial incompetence and/or dysfunction at the stented segment can significantly augment LDL transport, resulting in heightened deposition and accumulation of LDL within the arterial wall. The accumulation of lipids within the arterial wall has been established as a crucial factor in the initiation and progression of atherosclerosis. Consequently, the elevated presence of LDL in the intima may be associated with an increased burden of plaque, ultimately contributing to the accelerated development of in-stent neoatherosclerosis [11]. In contrast to atherosclerosis occurring in native arteries, the accelerated development of neoatherosclerosis in the stented segment is characterized by the presence of lipid-rich and atherosclerotic yellow neointima. This neointima serves as a crucial factor contributing to stenting failure. Postmortem investigations have consistently observed the frequent occurrence of lipid-laden intima in lesions that have undergone sirolimus-eluting or bare-metal stent placement, particularly in the later stages[22].

Additionally, the presence of external factors, such as significant impairment to vascular endothelial cells and the specific design of the stent, can exacerbate and expedite the development of neoatherosclerosis lesions. As previously stated, the size of the stent's struts, the spacing between them, and the overall shape of the struts have been found to be correlated with the formation of vortices or the extent of disrupted blood

flow subsequent to the intervention[1]. Furthermore, research indicates that an optimized stent design can result in improved blood flow patterns, thereby enhancing the efficacy of the intervention while minimizing the occurrence of in-stent thrombosis and restenosis [2]-[28].

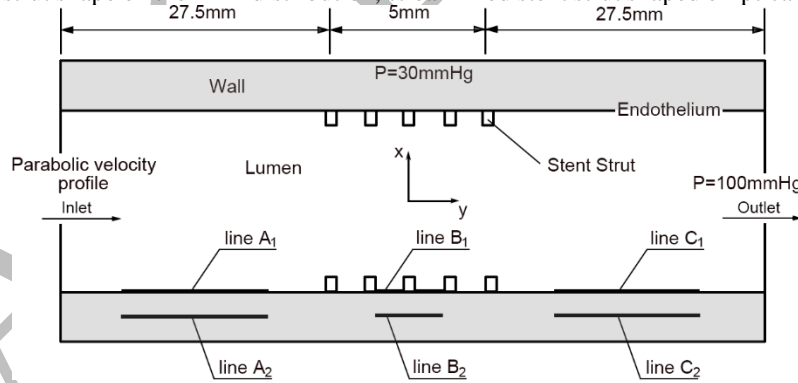
Since the in-stent atherosclerosis after the intervention is similar to that in the native artery, accelerated neoatherosclerosis in the stented segment has been associated with the mass transport and distribution of atherogenic lipids[8]. Elevated hydraulic conductivity and water filtration rate across the arterial wall in the stented segment, and higher residence time of atherogenic lipids at a high level are proposed to account for accelerated atherosclerosis after the intervention. Current work numerically simulated LDL mass transport in models after interventions and compared the impact of different damage degrees on host arterial wall on LDL distribution to verify our hypothesis. The change in LDL concentration due to different stenting scenarios was also discussed.

The occurrence of in-stent atherosclerosis following the intervention bears resemblance to that observed in the native artery, and it has been linked to the transportation and dispersion of atherogenic lipids. The accelerated development of neoatherosclerosis in the stented segment is hypothesized to be influenced by increased hydraulic conductivity and water filtration rate across the arterial wall within this segment, as well as prolonged exposure of atherogenic lipids at elevated concentrations. The present study employed numerical simulations to investigate the transport of LDL mass in models following interventions, and to assess the influence of varying degrees of damage to the host arterial wall on LDL distribution, thereby validating our hypothesis. Additionally, the alteration in LDL concentration resulting from different stenting scenarios was also examined and discussed.

## 2 Methods

### 2.1 Geometry of computational model

Fig. 1 displays the computational models to investigate LDL concentration in stented coronary. The ideal artery was simplified as a cylinder (two dimension) with a length of 60 mm, and thickness of arterial wall and the outer diameter of artery were set to be 0.34 and 3.7 mm, which were in accordance with size of the human left coronary artery[7]. Implanted stent was emplaced in the middle of artery and was simplified as a ten independent rectangle struts ( $0.162\text{mm} \times 0.081\text{mm}$ , named N in Table 1) without connection, the distance between struts was 1 mm[16]. To study the effect of stent thickness, stent strut thicknesses were  $162.0\ \mu\text{m}$  (named N),  $145.8\ \mu\text{m}$  (named T1) and  $121.5\ \mu\text{m}$  (named T2). To study the impact of strut spacing, the distance between struts is  $1000\ \mu\text{m}$  (named N),  $2000\ \mu\text{m}$  (named S2) and  $4000\ \mu\text{m}$  (named S2). To study the influence of strut shape on the LDL distribution, streamlined stent strut shaped elliptical was constructed.



**Fig.1.** Schematic illustration of computational model after the stent intervention. Representative lines for the numerical data postprocessing. Line A, B and C lie at the upstream, middle, and downstream of the stented segment. Here subscript 1 indicates on luminal surface wall artery wall, while 2 indicates in the arterial wall.

**Table1** Stent struts parameter ( $\mu\text{m}$ )

Strut Name	Thickness	Spacing	Strut Shape
N	162.0	1000	Rectangles
T1	145.8	1000	Rectangles
T2	121.5	1000	Rectangles
S1	162.0	2000	Rectangles

S2	162.0	4000	Rectangles
S3	162.0	2000	elliptical

## 2.2 Numerical approaches

### 2.2.1 Fluid dynamics

#### (a) Lumen

Numerical simulations for blood flow in arterial lumen was performed based on the two-dimensional (2D), incompressible Navier–Stokes equation and continuity equation [39].

$$\rho_l \left( \frac{\partial \mathbf{u}_l}{\partial t} + \mathbf{u}_l \cdot \nabla \mathbf{u}_l \right) = -\nabla p_l + \nabla \cdot \boldsymbol{\tau} \quad (1)$$

$$\nabla \cdot \mathbf{u}_l = 0 \quad (2)$$

where  $\rho_l$  ( $\rho_l=1050 \text{ kg/m}^3$ ) and  $\boldsymbol{\tau}$  stand respectively for the density and the stress tensor [21]. The two-dimensional velocity vector and pressure in the arterial lumen are represented by  $\mathbf{u}_l$  and  $p_l$ , respectively.

$$\boldsymbol{\tau} = 2\mu(\dot{\gamma})\mathbf{S} \quad (3)$$

where  $\dot{\gamma}$  and  $\mathbf{S}$  stand respectively the shear rate and for the rate of deformation tensor. The viscosity of blood flow was described by Carreau model[32].

$$\mu(\dot{\gamma}) = \mu_\infty + (\mu_0 - \mu_\infty) [1 + (\lambda\dot{\gamma})^2]^{\frac{n-1}{2}} \quad (4)$$

where  $\mu_\infty$  and  $\mu_0$  represent respectively the viscosity at infinite shear rate ( $\mu_\infty=0.00345 \text{ kg/(ms)}$ ) and at zero shear rate ( $\mu_0=0.056 \text{ kg/(ms)}$ ),  $\lambda$  stands for the time constant ( $\lambda=3.31 \text{ s}$ ) and  $n$  stands for the power law index ( $n=0.36$ ).

#### (b) Endothelium

The solution of Kedeme-Katchalsky equation was applied for the simulation of the transmural fluid flow across the endothelium ( $J_v$ ) [31].

$$J_v = L_p(\Delta p - \sigma\Delta\pi) \quad (5)$$

where  $L_p$  stands for the hydraulic conductivity of endothelium,  $J_v$  is the volume flux,  $\sigma$  is the endothelium osmotic reflection coefficient. [Since the influence of osmotic pressure on fluid flow is negligible compared to the hydrostatic pressure difference across the endothelial layer.  \$\Delta\pi\$  in this study stand for the oncotic pressure difference neglected in the present simulation, the pressure drop is  \$\Delta p\$ .](#)

#### (c) Arterial wall

Darcy's Law coupled with continuity equations was applied for the transmural fluid flow across the host arterial wall.

$$\frac{\mu_w}{K_w} \mathbf{u}_w = -\nabla(p_w) \quad (6)$$

$$\nabla \cdot \mathbf{u}_w = 0 \quad (7)$$

where  $p_w$  and  $\mathbf{u}_w$  for pressure and velocity vector on the arterial wall,  $K_w$  represents the hydraulic permeability ( $1.34 \times 10^{-18} \text{ m}^3$ ), and  $\mu_w$  is viscosity of blood flow ( $7.2 \times 10^{-4} \text{ kg/(ms)}$ ).

### 2.2.2 Solute dynamics

#### (a) Lumen

LDL transport in blood was modeled by the convection-diffusion equations[19].

$$\mathbf{u}_l \cdot \nabla c_l - D_l \Delta c_l = 0 \quad (8)$$

where  $c_l$  stands for LDL concentration in the arterial lumen,  $D_l$  is the LDL diffusion coefficient in blood flow ( $5.898 \times 10^{-12} \text{ m}^2/\text{s}$ ) [20].

#### (b) Endothelium

The Kedeme-Katchalsky equation was be used to describe LDL flux across the endothelium( $J_s$ ) [19].

$$J_s = P_{end} \Delta c_l + (1 - \sigma_f) J_v c_m \quad (9)$$

where  $\Delta c_l$  stands for LDL concentration difference after cross endothelium,  $P_{end}$  stands for the LDL permeability,  $\sigma_f$  represents LDL reflection coefficient,  $c_m$  stands for the mean concentration on both sides of the endothelium ( $c_m=0.997$ ).

#### (c) Arterial wall

The transport of LDL in the host artery wall was given by the convection-diffusion-reaction equation [31].

$$\nabla \cdot (-D_w \nabla c_w + K_{lag} c_w \mathbf{u}_w) = r_w c_w \quad (10)$$

where  $D_w$  stands for the LDL effective diffusivity in arterial wall ( $D_w=1.42 \times 10^{-12} \text{ m}^2/\text{s}$ ),  $K_{lag}$  represents LDL lag coefficient ( $K_{lag}=0.1486$ ), and  $r_w$  is the LDL chemical reaction rate ( $r_w = -6.05 \times 10^{-4} \text{ s}^{-1}$ ).

### 2.2.3 Boundary conditions

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### *blood flow*

A parabolic velocity waveform with an average value of 0.24 m/s was applied at the computational model inlet for the pulsating flow [13]. 100 mmHg was set at the computational model outlet, and a constant 30 mmHg was applied to the outer arterial wall, which are from the healthy intravascular pressure [36]. The endothelium boundary on one side of the lumen (the wall to lumen transmembrane velocity of fluid) was set to be  $J_v$ , and the other side of the wall was set to be  $-J_v$  [37].

### *LDL*

Concentration of LDL ( $c_0$ ) was chosen to be  $2.86 \times 10^2 \text{ mol/m}^3$  at the inlet of arterial lumen [37]. The endothelium boundary on one side of the lumen (the wall to lumen flux of LDL) was set to be  $J_s$ , the other side of the wall was set to be  $-J_s$ .

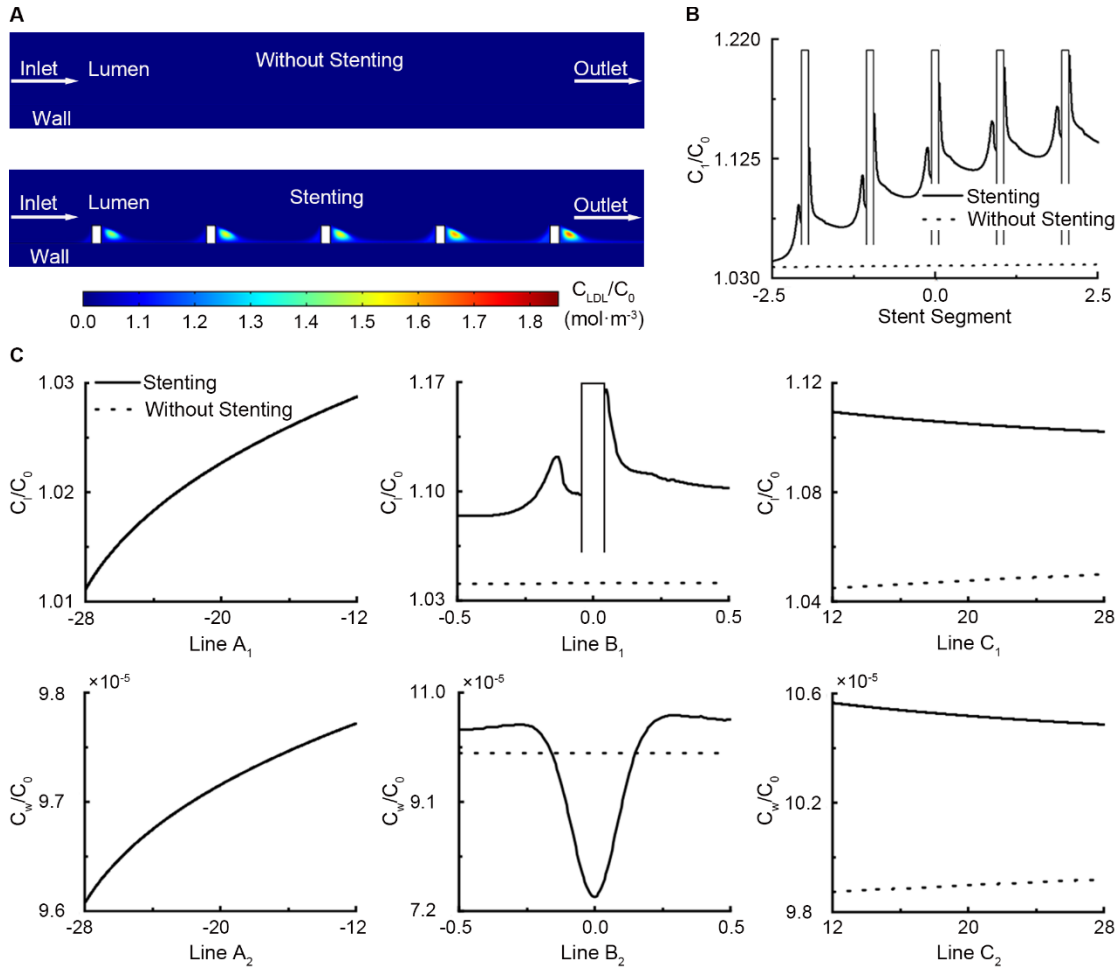
### 2.2.4 Computation procedures

These numerical simulations were finished in COMSOL Multiphysics by a validated finite element algorithm. The flow simulation was firstly carried out for velocity and pressure fields, which then served for the simulation of LDL transport. The triangular mesh is applied for the computational study, the element size of the lumen is 0.2 mm, and the vessel wall is 0.08 mm, the elements near the stent are refined, and the boundary layer of the fluid domain is set to 15 layers. MUMPS solver is used in for all cases in this work. The density of the mesh is a critical factor influencing the accuracy of numerical calculations. Accordingly, this study develops five models with progressively increasing mesh densities, ranging from 50,000 to 500,000 cells. The results indicate that the relative error between two cases drops below 5% when the number of mesh cells exceeds 300,000, thereby confirming the grid independence. Consequently, the results obtained with this mesh density are used for subsequent analysis.

## 3 Results

### 3.1 Effect of the stenting

Fig. 2(A) shows the axial distribution of LDL in the coronary artery. Compared to the model without intervention, implanted stent would significantly increase the concentration of LDL near stent strut, especially for the stent strut downstream edge, where the strut would lead to flow disruption, causing flow stagnation and recirculation. LDL concentration near stent strut would further increase at the downstream struts, and the last strut is suffering from the highest LDL concentration. As shown in the Fig. 2(B), the protruded stent struts cause LDL concentration to rise sharply near the strut. The downstream stent struts are obviously impacted by the downstream LDL concentration, and LDL concentration near struts would display a clear increase with the distance between the strut relative to the start one. LDL concentration would be relatively low in the start stent strut and be significantly elevated at the last one. The maximum value of LDL concentration near the end strut is 1.3 times higher than the start one.



**Fig. 2.** Effect of stent implantation on the transport of LDL. **A** Distribution of LDL in the coronary artery. **B** The profile of LDL concentration on the luminal surface the model near the implanted stent. The solid black line is the artery after stenting, while the dashed line is the control case without stenting. **C** The profile of LDL concentration at the representative lines.

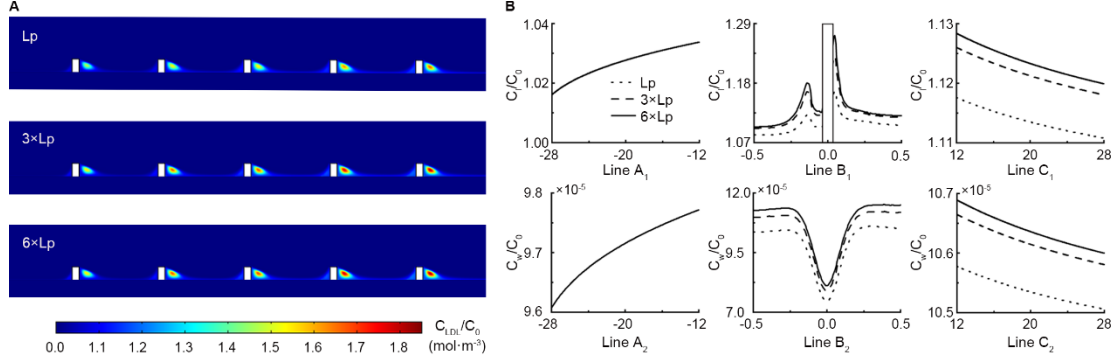
To facilitate present the effect of stenting on the host artery, the representative lines on the luminal surface and in artery wall were selected shown in Fig. 2C. It has been observed that the LDL concentration is almost the same both on the luminal surface and within arterial wall, for the upstream region of the stented segment, while there is a large difference between models in the region of stented segment and downstream of that region. There is the largest fluctuation and high level of LDL concentration along the line B<sub>1</sub>, which was about 12% higher than the model without stenting. LDL concentration on the line B<sub>2</sub> would slightly increase both at the upstream and downstream of the strut edge, while this curve shows a sharp decrease under the implanted strut in artery wall. Although LDL concentration tends to slowly decrease at downstream of stented segment, the significant difference between the cases with and without stent can still be observed, and this value in the case with stent is at least 7% higher than the one without on luminal surface and in the arterial wall.

### 3.2 Effect of the conductivity hydraulic near the strut

Fig.3A shows the distribution of LDL for the host artery with different the hydraulic conductivities at the stented segment. It is evident that when compared with the healthy artery wall, the models with high hydraulic conductivity could gradually lead to high level of LDL concentration at the stented segment and downstream of that region. Nevertheless, these changes of LDL concentration due to high hydraulic conductivities is not noticeable in the most region of host arteries. The highest concentration for each model is located at the last strut downstream edge, and which are the 1.67, 1.81 and 1.83, respectively. The curves shown in Fig.3B further present effect of the conductivity hydraulic on the distribution of LDL. As shown this figure, the upstream of stented segment shows no difference both on the luminal surface of arterial wall (Line A<sub>1</sub>) and in the wall (Line A<sub>2</sub>), while LDL concentration changes greatly at stented segment. Along the Line B<sub>1</sub>, the

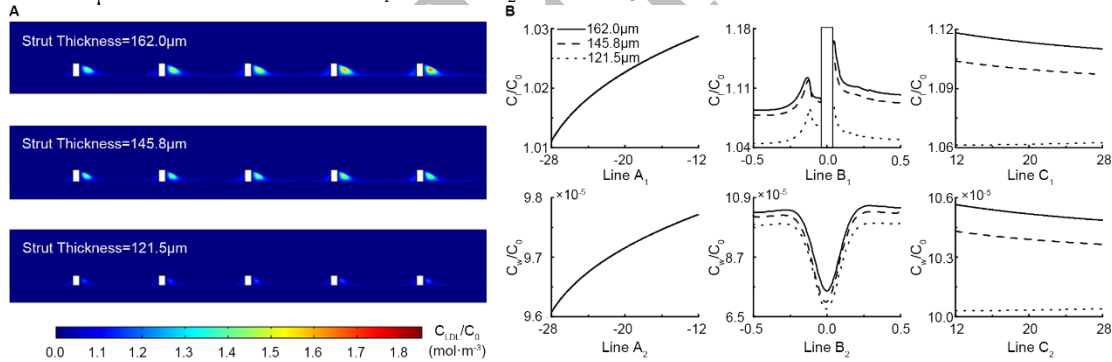
maximum concentration is increased by approximate 6% and 10% for the models with 3- and 6-times hydraulic conductivity, respectively, compared to the healthy artery wall. And the maximum values are respectively increased by 6% and 10% along the Line B<sub>2</sub>. Moreover, high hydraulic conductivity would slightly increase the LDL concentration at the downstream of stented segment, but it would slowly decrease with the distance relate to the starting stented segment.

### 3.3 Effect of the strut thickness



**Fig. 3.** Effect of the conductivity hydraulic on the transport of LDL. **A** Distribution of LDL in the coronary artery. **B** The profile of LDL concentration at the representative lines.  $L_p$ ,  $3 \times L_p$  and  $6 \times L_p$  are one, three and six times larger than the conductivity hydraulic in the health artery.

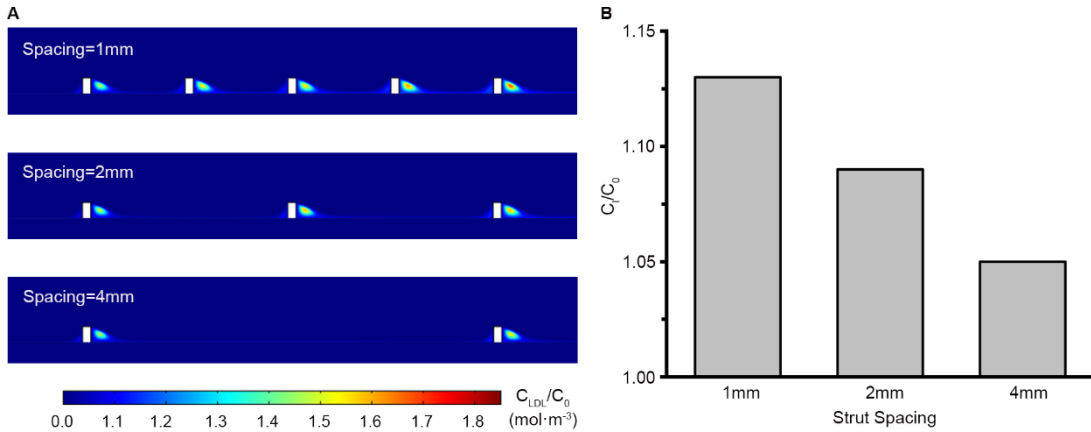
Fig.4 illustrates the impact of strut thickness on the distribution of LDL in coronary. As shown in the Fig.4A, the thick strut would obviously increase the magnitude of LDL concentration at the stented segment and downstream of that region. The maximum LDL concentration in 122- $\mu\text{m}$  strut case is approximately 22% for 146- $\mu\text{m}$  strut and 30% for 162- $\mu\text{m}$  strut. As evident from Fig.4B, compared to the other cases, the change of LDL in 122- $\mu\text{m}$  strut is more obviously near the strut than others, and the maximum values would decrease approximately 6% for the thin strut on the line B<sub>1</sub> and 10% on the line B<sub>2</sub>. The maximum LDL concentration for 122- $\mu\text{m}$  strut both on the line C<sub>1</sub> and line C<sub>2</sub> are about 5% smaller than thicker cases.



**Fig. 4.** Effect of strut thickness on the LDL distribution. **A** Distribution of LDL in the coronary artery. **B** The profile of LDL concentration along the representative lines.

### 3.4 Effect of strut spacing

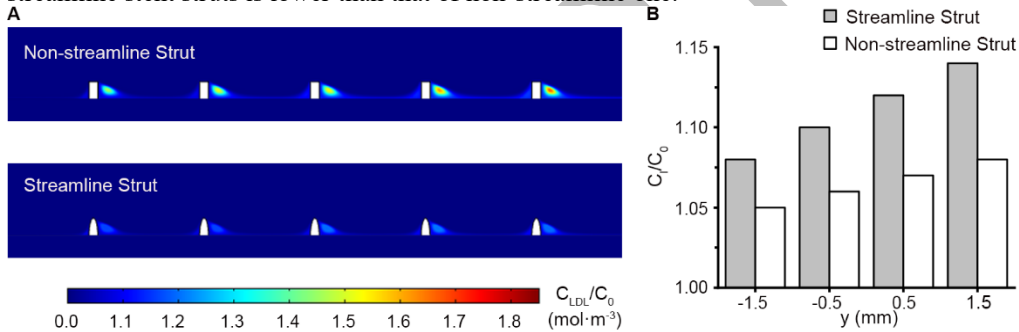
Fig.5A illustrates the impact of strut spacing on the distribution of LDL in coronary artery. The high LDL induced by strut protrusion would clearly decrease with the large strut spacing, showing the lowest level at the last strut. Compared with small spacing (spacing=1 mm), the maximum concentration of LDL for doubled spacing (spacing=2 mm) is reduced from 1.67 to 1.60, and this value reduces to 1.55 when the strut spacing has quadrupled (spacing=4 mm). The LDL concentration decreases less than 5% both on the luminal surface and in artery wall when the strut spacing increased from 1 mm to 2 mm, while the maximum concentration would reduce more than 10% on the line B<sub>1</sub> for the quadrupled strut. Moreover, as evident from Fig. 5B, the average concentration in the stented segment drops from 1.14 to 1.05 when the strut spacing increase from 1mm to 4 mm.



**Fig. 5.** Effect of strut spacing on the distribution of LDL. **A** Distribution of LDL in the coronary artery. **B** The profile of LDL concentration at the representative lines.

### 3.5 Effect of the shape of strut

Fig.6 illustrates the impact of streamline-strut on the LDL distribution in the coronary artery. As evident from figure, the streamline-strut would greatly suppress high LDL concentration both at the stented segment and the downstream, the maximum concentration near the last strut would decrease approximately 30% for the strut with streamline one, and the average concentration in the stented segment would drop to 1.05, as shown in Fig 6. In addition, we can clearly see from Fig. 6B that the average concentration between each streamline stent struts is lower than that of non-streamline one.



**Fig. 6.** Effect of strut shape on the distribution of LDL.

## 4 Discussion

The clinical significance of percutaneous coronary interventions has been diminished due to the occurrence of late failures characterized by neoarteriosclerosis, stent restenosis, and stent thrombosis. It is widely acknowledged that these events are closely linked to the adverse hemodynamics resulting from stent struts [23],[27]. Nevertheless, initial studies did not adequately elucidate the accelerated development of neoarteriosclerosis following stenting compared to atherosclerosis in native arteries, which is typically initiated and established by the excessive infiltration and accumulation of atherogenic lipoproteins in the arterial wall [4],[25]. The excessive infiltration and accumulation of atherogenic lipoproteins in the arterial wall are believed to be the initiators and drivers of atherosclerosis. This study proposes that the transport of low-density lipids after stenting may play a crucial role in the occurrence and progression of neoatherosclerosis.

The findings of this study demonstrate that the presence of a stent in the artery leads to elevated levels of LDL, particularly in the stented segment, with the distal edge of the last strut experiencing the highest concentration of LDL. This study demonstrated that the presence of a stent in the host artery resulted in elevated levels of LDL, particularly in the stented segment and the distal edge of the last strut. The excessive accumulation of LDL in these areas may contribute to the development of in-stent neoarteriosclerosis, a critical factor in the formation of lesions leading to late stent failure. This condition is characterized by an abundance of macrophages containing lipid droplets within the arterial wall. Atherosclerosis of the native coronary arteries is a common chronic condition that typically requires several decades to manifest clinically symptomatic symptoms. Conversely, neoarteriosclerosis tends to develop within months to years after the



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implantation of a stent, as supported by pathological and clinical imaging data [14]. The etiology of in-stent neoarteriosclerosis involves multiple factors.

The occurrence and development of in-stent events have been linked to the hemodynamic changes caused by stenting. Flow separation and stagnation flow around stent struts disrupt the local flow in the host artery, leading to vascular damage and adverse events [17],[23]. Previous research has identified a noteworthy inverse relationship between wall shear stress (WSS) and the concentration of low-density lipoprotein (LDL) on the luminal surface. Additionally, regions with low WSS may experience accelerated accumulation of LDL[18]. The present numerical study confirms that the LDL concentration at the distal edge of the strut surpasses that at the proximal edge. We have observed a significant increase in LDL concentration downstream of the segment-treated stent, with the highest concentration found at the distal side of the stent. It is worth noting that there could be additional factors contributing to the occurrence of frequent clinical events following stenting, apart from elevated nonphysiological stress levels. Seo et al[29] revealed that WSS exhibits a higher magnitude at the proximal region of the stent, while it decreases significantly towards the distal end. This finding confirms the accuracy and dependability of our numerical simulation.

Previous research has established a strong correlation between the distribution of LDL distribution and the hydraulic conductivity of the arterial walls, indicating their role in mass transport[3],[34]. The application of stenting introduces abnormal tension stress, squeezing pressure, and flow shear stress, which can potentially inflict substantial harm to the arterial wall, thereby initiating adverse clinical symptoms. The augmentation of hydraulic conductivity and the partial impairment of the endothelial glycocalyx layer have been found to promote the infiltration and accumulation of atherogenic lipids, specifically LDL, within the arterial wall of the host. Experimental evidence has demonstrated that the compromised arterial wall exhibits heightened permeability and hydraulic conductivity, resulting in an increased buildup of macromolecules within the intima layer[12],[36]. Furthermore, the findings of the current study indicate that as hydraulic conductivity rises, there is a concurrent increase in the accumulation of LDL on the luminal surface and within the arterial wall. Furthermore, the arterial wall may experience significant damage, resulting in an elevation of LDL levels both on the surface of the lumen and within the vascular wall. It should be noted that although high LDL levels are not typically observed in the majority of the host artery due to its six times hydraulic conductivity, the accumulation of LDL caused by this increased conductivity can further expedite the development of in-stent events.

Additionally, the findings of this study indicate that the design of the stent is linked to the distribution and accumulation of LDL. The reduction in strut spacing and increase in strut size, along with the adoption of a non-streamline shape and longer stent length, would result in heightened adverse local hemodynamics within the host artery and significant damage to the arterial wall. Beier et al. found that a smaller strut spacing would enlarge the area within the host arterial wall under low wall shear stress, and improved clinical outcomes have been reported following stenting with fewer struts or wider strut spacing [2]. Kolandaivelu and Kastrati demonstrated that thicker struts could exacerbate blood flow disturbances within the arterial lumen, increase the degree of separation, and expand the reflux area. The incidence of restenosis and late thrombosis was found to be higher in arteries treated with thick stents compared to those treated with thin stents[16],[26]. Poon et al. and Hisao et al. have suggested that the use of streamlined and thin stents can effectively mitigate flow disturbances, characterized by short distances of blood flow separation [28],[29]. The adverse hemodynamic conditions created by the stent design around the strut may alter the transport of LDL in the artery, resulting in elevated local LDL concentrations following stent placement. Furthermore, the occurrence of significant vascular endothelial damage caused by inadequate design or improper implantation leads to elevated hydraulic conductivity. This, in turn, facilitates the transportation of LDL from the lumen to the arterial wall, thereby amplifying the likelihood of adverse clinical events subsequent to stenting. **The results underscore the critical importance of stent design. While ensuring sufficient structural support of vascular stents, it is essential to minimize the protrusion height within the lumen and increase the spacing between stent struts to achieve a more uniform and lower LDL concentration distribution. However, certain geometric configurations are sometimes unavoidable. For instance, large biodegradable stents, constrained by material properties, inherently require larger dimensions, which can increase the risks associated with implantation. In such cases, it becomes imperative to optimize both the implantation method and the overall stent structure to mitigate these risks effectively[6],[38].**

Firstly, the numerical models were simplified to an idealized straight configuration, which does not account for the complex geometries observed in clinical scenarios. Furthermore, in addition to coronary arteries, other host vessels such as carotid and femoral arteries should also be investigated to derive more generalizable conclusions. Additionally, the potential impact of tissue prolapse between stent struts on LDL

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distribution was overlooked. Moreover, the conductivity hydraulic after different stent implantations were assumed as multiplied without measurement.

## **5 Conclusion**

The process of intracoronary stenting has the potential to exert a synergistic effect on both the concentration and distribution of LDL in the host artery. Factors such as increased severity of damage resulting from the intervention, narrower spacing between stents, thicker stent struts, and shorter stent length can exacerbate local infiltration and accumulation of LDL, thereby accelerating the development of neoarteriosclerosis, in-stent restenosis, and late thrombosis.

## **Acknowledgements**

This work is supported by National Natural Science Research Foundation of China (No. 12372305, 12272153, 12202274, 11902126), Social Development Science and Technology Support Project of Changzhou (CE20235044), Changzhou Science and Technology Support Program (CJ20241077), Outstanding young backbone teacher of Jiangsu Qinglan Project, Zhongwu young innovative talents projection from Jiangsu Institute of Technology, and the Interdisciplinary Program of Shanghai Jiao Tong University (project number YG2022QN049).

## **Conflict of interest**

The authors declare no competing interests.

## **Authors' contributions**

Zhenmin Fan and Xiao Liu conceived the idea. Zhenmin Fan, Jialiang Yao and Kailei Liu conducted the analyses. Zhenmin Fan, Jialiang Yao, and Mingyuan Liu provided the data. Zhenmin Fan, Xia Ye and Xiaoyan Deng wrote the paper. All authors contributed to the writing and revisions.

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## **Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## **Consent for publication**

We consent for the publication of this work.

## **Ethics approval and consent to participate**

Not applicable.

## **Reference**

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