Hemodynamics of the String Phenomenon in the Internal Thoracic Artery Grafted to the Left Anterior Descending Artery with Moderate Stenosis

Zhao, Hemodynamics of String Phenomenon

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Conflict of Interest

None

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Glossary of Abbreviations

<i>ITA:</i>	<i>Internal Thoracic Artery</i>
<i>3D:</i>	<i>3-Dimensional</i>
<i>0D:</i>	<i>0-Dimensional</i>
<i>LAD:</i>	<i>Left Anterior Descending Artery</i>
<i>LPM:</i>	<i>Lumped Parameter Model</i>
<i>WSS:</i>	<i>Wall Shear Stress</i>
<i>OSI:</i>	<i>Oscillatory Shear Index</i>
<i>CABG:</i>	<i>Coronary Artery Bypass Grafting</i>
<i>CFD:</i>	<i>Computational Fluid Dynamics</i>
<i>CT:</i>	<i>Computed Tomography</i>
<i>SVG:</i>	<i>Saphenous Vein Graft</i>

Abstract:

Purpose: The internal thoracic artery is the choice of graft for coronary artery bypass grafting due to the excellent long-term patency. However internal thoracic artery graft failures still occur due to diffuse narrowing, known as the string phenomenon. Studies suggest that the string phenomenon is caused by competitive flow when the coronary stenosis is not serious, but the hemodynamics of the string phenomenon are still unclear. The purpose of this study is to clarify the hemodynamic characteristics of the string phenomenon.

Materials: A patient-specific 3-dimensional model of the aortic arch and coronary arteries was reconstructed. A moderate stenosis was applied to the left anterior descending artery. The internal thoracic artery was used to bypass the stenosis. Two further 3D models were built to study the hemodynamics of the string phenomenon.

Methods: A numerical study was performed by coupling the 3D artery model with 0-dimensional lumped parameter model of the cardiovascular system.

Results: The graft flow, native coronary flow, wall shear stress and oscillatory shear index were calculated and illustrated. Inverse flow and high oscillatory shear index appeared on the internal thoracic artery graft when the stenosis was moderate.

Conclusion: High oscillatory shear index might be the major hemodynamic characteristic of the string phenomenon in internal thoracic artery graft. The inverse graft flow and the difference in graft flow caused by clamping the stenosis can be used to evaluate the probability of observing the string phenomenon.

Keywords: Internal Thoracic Artery Graft; 0D/3D Coupling Simulation; Hemodynamics; Coronary Artery Bypass Grafting (CABG); Computational Fluid Dynamics (CFD)

1. Background

The internal thoracic artery (ITA) is the choice of graft for coronary artery bypass grafting due to the excellent long-term patency of left ITA when grafted to the left anterior descending coronary artery. The 5, 10 and 15 year patencies of ITA graft has been reported as 98%, 95% and 88% respectively.(Tatoulis et al., 2004) However, many reports of ITA graft failure exist due to the so-called string phenomenon. The string phenomenon, or string sign, was first reported by Barner et al. in 1974.(Barner, 1974) Seki et al.(Seki et al., 1992) described it as the long-term postoperative luminal narrowing resulting in the diameter less than 1mm, while Nakajima et al (Nakajima et al., 2004) defined it as suffused stenosis in the arterial graft with a stenosis degree of more than 50%. Thus the string phenomenon in ITA is an intermediate process between shrinking and loss of function or occlusion.(Kitamura et al., 1992)

Most researchers hold the view that the string phenomenon is caused by the competitive flow when the stenosis in the native coronary artery is not serious.(Geha and Baue, 1979; Hashimoto et al., 1996; Kolozsvari et al., 2012; Manabe et al., 2010; Siebenmann et al., 1993) According to Berger et al. (Berger et al., 2004) the degree of stenosis is the most important factor affecting the incidence of ITA graft occlusion; the incidence of ITA graft occlusion is up to 79%, when the native coronary stenosis degree is less than 50%. A study by Shimizu et al. indicated that the string phenomenon appeared in all patients with moderate or mild stenosis (stenosis degree < 42%) at four weeks after surgery, and after one year, all ITA grafts were occluded when stenosis degree was less than 33%.(Shimizu et al., 2004) Moreover, it was reported that 4/5 of the ITA grafts applied on patients with moderate stenosis (stenosis degree < 50%) were occluded one or two years after surgery.(Seki et al., 1992) Siebenmann reported that the branch of a Y-type ITA graft used to bypass the moderate stenosis (stenosis degree < 50%) became occluded, while the branch used to bypass the serious stenosis (stenosis degree > 70%) was still patent in the same patient.(Siebenmann et al., 1993)

Many researchers have focused on the relationship between the stenosis rate and the string phenomenon of ITA grafts since the surgical results may be affected by the adaptive response to hemodynamic factors.(Butany et al., 1998; Leask et al., 2005) However few researchers have studied the hemodynamic details of the string phenomenon in ITA grafts. Interestingly, while saphenous vein graft (SVG) thrombosis is the major cause of morbidity and mortality following surgery, (Motwani and Topol, 1998; Peykar et al., 2004) some studies have indicated that the native coronary stenosis degree does not affect the patency of SVG.(Desai et al., 2004; Urschel et al., 1990) This may suggest that the hemodynamics of SVG and ITA grafts differ, but any differences are not clearly understood.

Usually, CABG was only applied on patients with stenosis in LAD, LCX and RCA at the same time. But if the degree of stenosis in one of the three branches is moderate, the surgeon will face a big problem – Whether the moderate stenosis should be bypassed or not? This problem is frequently exists in clinical. In this study, in order to simplify the study and highlight the purpose of this study, only the moderate stenosis in LAD was taken into consideration.

The 0D/3D coupling method was used in this study to perform a numerical simulation by coupling the lumped parameter model (LPM; 0D sub-model) and 3D vascular sub-models. This is an advanced method which has already been used in some related hemodynamic research.(Sankaran et al., 2012; Taylor et al., 2013) The interaction between two different

dimensional sub-models in a numerical simulation reproduces relatively more realistic conditions than a classical computational fluid dynamics (CFD) simulation, and it is possible to simulate the hemodynamics of both the 3D artery and the 0D cardiovascular system within one frame at the same time.

This work studies the hemodynamics of the string phenomenon by comparing the hemodynamics of an ITA in a high level of competitive flow (left anterior descending artery (LAD) stenosis degree $\approx 50\%$), with both the ITA at zero competitive flow (LAD occluded) and an SVG in a high level of competitive flow. The purpose was to elucidate the hemodynamic characteristics of the string phenomenon in ITA grafts.

2. Materials and Methods

2.1. Three-dimensional Reconstruction and Computational Models

Patient data from a 55-year-old male were provided by Anzhen Hospital. The patient's personal information was anonymized prior to analysis of the data. The cardiac output of the patient was measured to be 4.6 L/min by Doppler ultrasound. Computed tomography (CT) imaging using 460 slices, each of 512×512 pixels, was used for 3D reconstruction. The distance between each adjacent slice was 1 mm. The 3D anatomic geometry was reconstructed by using MimicsTM through both threshold segmentation and manual segmentation. Gaussian filtering was adopted to smooth the reconstructed surface. A moderate stenosis (stenosis degree $\approx 50\%$) was applied to the LAD by using 'PHANTOM DESKTOP' (a kind of force feedback device) and 'Freeform' (software of the 3D modeling system), both developed by GeomagicTM. Virtual surgery comprising either an ITA graft (Model 1) or SVG (Model 2) were implemented on the 3D model with moderate stenosis. The diameter of the ITA and the diameter of the SVG were 3 mm and 5 mm, respectively. In order to compare the hemodynamics of the ITA graft in a high and a low degree of competitive flow, a third 3D model (Model 3) with an ITA graft, in which the LAD was blocked entirely. The three 3D models are illustrated in Fig.1.

The 3D sub-models were meshed to generate the computational models. A hexahedral mesh was generated mainly by using the size control method with the assistance of the commercial software ANSYS-CFX (ANSYSTM). The mesh was refined in the areas of interest to make the simulation results more precise as the resolution was improved. The node and element numbers for the models are listed in Tab.1.

The number of nodes and elements in the three models are within the same order of magnitude. A steady state grid sensitivity analysis was carried out to ensure that the numbers of nodes and elements are large enough to ensure that the simulation results were stable and credible. During the grid sensitivity analysis, both the inlet pressure and area-averaged wall shear stress (WSS) were measured. The difference of inlet pressure and WSS are all within 0.5% for the last mesh that used in this study, as listed in Tab.2. Finally, based on these mesh, it cost about 30 hours for each case of simulation.

In the 3D simulation, it was assumed that the vessel walls were rigid. The blood flow was treated as an incompressible viscous Newtonian fluid. The density of the blood flow was 1050 kg/m^3 and the dynamic viscosity was $0.0035 \text{ Pa} \cdot \text{s}$.

2.2. The 0D/3D Coupled Model

The lumped parameter models (LPM / 0D part) used in this study were as described by Taylor

et al.(Taylor et al., 2013) On the basis of both the 3D vascular models and the LPMs, 0D/3D coupled models were constructed, as illustrated in Fig.2 for Model 1. The boundary conditions of the 3D part were supplied by the 0D calculation and the forcing terms of the 0D part were calculated by the 3D simulation. All the 3D models shared the same 0D part since the patient's peripheral vascular structure did not change with surgery. Therefore the difference in the simulation results can be considered to be caused only by the difference in the 3D models.

As shown in Fig.2, the inlet of the 3D model was coupled with a LPM of the heart, while all the systemic outlets were coupled with a LPM of the systemic block. Moreover, the coronary outlets were coupled with a LPM of the coronary microcirculation block. In each block, the resistance (R), capacitance (C) and inductance (L) were used to simulate the flow resistance, the compliance of the vessel and the inertia of the blood flow, respectively. In the heart block, a diode was used to simulate the valve in the heart, while the variable capacitors Cl_v were used to simulate the left ventricles. In coronary microcirculation block, the pressure of left ventricle was added at the cathode of capacitance C_{im} which accounts for the intramyocardial pump.(Taylor et al., 2013)

In the compartment of the ventricle, the function of pressure-volume relationship (1) was applied to demonstrate the cardiac cycle of the left ventricle.

$$E(t) = \frac{P(t)}{V(t) - V_0} \quad (1)$$

where $E(t)$ is the time-varying elastance ($mmHg / ml$), $V(t)$ and $P(t)$ are the ventricle volume (ml) and pressure ($mmHg$) respectively, and V_0 (ml) is the reference volume. Mathematically, the function can be approximated as:

$$E(t) = (E_{\max} - E_{\min}) \cdot E_n(t_n) + E_{\min} \quad (2)$$

where $E_n(t_n)$ (Stergiopoulos et al., 1996) is the normalized time varying elastance.

$$E_n(t_n) = 1.55 \left[\frac{\left(\frac{t_n}{0.7} \right)^{1.9}}{1 + \left(\frac{t_n}{0.7} \right)^{1.9}} \right] \left[\frac{1}{1 + \left(\frac{t_n}{1.17} \right)^{21.9}} \right] \quad (3)$$

Where $t_n = \frac{t}{T_{\max}}$, $T_{\max} = 0.2 + 0.15tc$, and tc is one cardiac cycle interval (s). In this

paper, we set $E_{\max} = 2.0$, $E_{\min} = 0.002458$ and $tc = 0.8s$.

The values of the parameters in the 0D network of coupled models were based on data from research into the modeling of coronary arteries.(Kim et al., 2010) By using the genetic algorithm, these values were adjusted to make sure that the cardiac output, the systolic and diastolic pressures matched the patient's data, and that the flow distribution in the 3D model was consistent with the diameter of each branch of the 3D model. The list of model predictions compared with the clinical data is shown in Tab.3. Note that the relationship between the flow distribution and the diameter of an artery has previously been published by Taylor et al.(Taylor et al., 2013) All the values of the parameters in the 0D network are listed in Tab.4.

2.3. Coupling Method

The 0D/3D coupled model was simulated by applying interface conditions and a coupling algorithm at defined time intervals (see Appendix for further details). The ANSYS-CFX was used for the 3D simulation, while the 0D part was calculated by FORTRAN routines based on CFX Junction Box. The data transmission between the 0D and 3D parts was implemented with CFX User CEL Function. The algorithm of coupling used in this study has been used in previous studies.(Ma et al., 2014; Zhao et al., 2015a; Zhao et al., 2015b)

3. Results

3.1. Graft Flow and Graft Pressure Drop

The graft flow is one of the most important indicators for evaluating the surgical results. It is also one of the few parameters that can be measured during a procedure. In other words, it is the key indicator used by surgeons to assess the effectiveness of a graft. Furthermore, it allows surgeons to decide whether or not a stenosis requires a further bypass. In order to elucidate the graft flow characteristics of the string phenomenon, graft flows for the three models are illustrated in Fig.3 and the time-averaged graft flows for the three models are listed in Tab.5. It can be seen that the graft flow of Model 1 is much lower than that of the other two models, whereas the graft flow rates of Models 2 and 3 are almost the same. Moreover, reverse flow exists in Model 1 during the systole period. In order to clarify the reason of the reverse flow the graft pressure drop of each model was also illustrated in Fig.3. The pressure drop of Model 1 during systole is negative.

3.2. Coronary Artery Flow

Because the competitive flow between the graft flow and the native coronary flow rate is closely related to the string phenomenon in the ITA graft, the flow through the stenosis in the native coronary artery is depicted in Fig.4. Moreover, the total LAD flow rates, as shown in Fig.4, were calculated from the sum of all the flow rates of the LAD outlets (outlets a, b and c). The time-averaged coronary flow rates are also listed in Tab.5. The stenosis flow of Model 1 is much higher than that of Model 2. The absolute values of maximum and minimum values of stenosis flow rates in Model 2 are both much larger than the average value, while, the average value of stenosis flow in Model 2 is close to 0. In contrast, the total LAD flows of these models are almost the same. That means that the effective perfusion of Model 2 is provided almost entirely by the SVG, but for Model 1 it is provided by both the ITA graft and the native stenosed coronary artery. In other words, serious competitive flow exists in Model 1.

3.3. Wall Shear Stress

Low WSS (<0.4 Pa) affects the long-term effectiveness of surgery.(Davies and Civelek, 2011) The waveforms of area-averaged WSS on the grafts are illustrated in Fig.5. The time-averaged values of these waveforms for Models 1, 2 and 3 are 0.926, 0.443 and 1.791 Pa, respectively. Moreover, the WSS distributions of these models at the moment of maximum graft flow are shown in Fig.6. It can be seen from the figure that the WSS in Model 1 and 3 is a high level throughout the graft (>0.4 Pa), while, in Model 2, low WSS values appear in some parts of the graft.

3.4. Oscillatory Shear Index

The oscillatory shear index (OSI) was calculated according to the expression in Eqn.4. The OSI distributions on the grafts of the three models are illustrated in Fig.7. It can be seen that

the OSI of the graft in Model 1 is high throughout, while, in Model 2 and Model 3, high OSI values only appear in a few localized areas. Moreover, the area-averaged OSI for the grafts in the three models are listed in Tab.6 and confirm that the OSI in Model 1 is significantly higher (by up to an order of magnitude) than that in the other models.

$$OSI = \frac{1}{2} \left(1 - \frac{\left| \int_0^T \overline{\tau_w} dt \right|}{\int_0^T |\overline{\tau_w}| dt} \right) \quad (4)$$

4. Discussion

4.1. Hemodynamic characters of string phenomenon

4.1.1. Inverse flow in the graft

A previous study by Pagni et al. indicated that a moderate stenosis will decrease the graft flow during the diastole, and lead to an inverse graft flow during the systole. This phenomenon may lead to the string phenomenon or occlusion of the ITA graft.(Pagni et al., 1997) This behavior is also shown in the results of this study: the inverse graft flow appears in Model 1 during the systole, but no inverse flow appears in the other two models. Moreover, the graft flow during the diastole of Model 1 is lower than that of the other two models.

4.1.2. Competitive flow

Some studies have indicated that the native coronary stenosis degree does not affect the patency of SVG.(Desai et al., 2004; Urschel et al., 1990) Our results (Fig.4 and Tab.5) show that the competitive flow degree of an SVG is lower than that of an ITA graft when each were used to bypass the same moderate stenosis in our models. In Model 1, the flow rate through the stenosis is comparable to the graft flow, whereas in Model 2, the graft flow is much higher than the flow through the stenosis. The low degree of competitive flow in the SVG might be the reason for the SVG results previously reported.(Desai et al., 2004; Urschel et al., 1990)

4.1.3. Low WSS & high OSI

Some researches declared that low WSS may decrease the long-term patency of the graft.(Corban et al., 2012; Davies and Civelek, 2011; Fan et al., 2014; Puri et al., 2015; Timmins et al., 2013) However, Fig.5 and Fig.6 indicate that the WSS on the graft in Model 1 is higher than that in Model 2. In Model 2, the area-averaged graft WSS is less than 0.4 Pa in most periods of the cardiac cycle. Moreover, even at the moment of maximum graft flow, there are low WSS areas in some parts of the SVG. Furthermore, this study indicates that the string phenomenon almost never appears in the SVG (Model 2), which suggests that the low WSS might not be the cause of the string phenomenon. In other words, the low WSS might be the cause of SVG failure through a mechanism distinct from the string phenomenon. In fact, some studies indicated that after the creation of SVG, the vein must undergo a series of dynamic structural changes to stabilize the arterial hemodynamic forces (high pressure, large flow speed and large circumferential stress) known as the remodeling of the vein.(Momin et al., 2015; Owens et al., 2015) The vein remodeling may lead to the proliferation of smooth muscle cells and restenosis finally.(Owens et al., 2015)

A study by Zhang et al. indicated that a lower OSI would decrease the opportunity of vascular intimal hyperplasia.(Zhang et al., 2012) It can be seen from Tab.6 and Fig.7 that the OSI on the graft in Model 1 is much higher than that of the other models. In Models 2 and 3, high OSI areas only appear in some localized positions, but in Model 1, the OSI is high throughout the

graft. Interestingly, the string phenomenon, when it occurs, also appears throughout the graft. This may suggest that the string phenomenon of an ITA graft maybe the adaptation caused by high OSI.

4.2. Difference between the SVG and the ITA graft

The inlet locations and the diameters of the grafts are the major geometrical differences between SVGs and ITA grafts. The study by Pagni et al. indicated that high competitive flow is caused by a pressure delay.(Pagni et al., 1997) The inlet of an SVG is closer to the aortic root than that of an ITA graft and therefore the pressure delay is less for an SVG than for an ITA graft. The pressure delay leads to a negative graft pressure drop during the systole period. The negative pressure drop of Model 1 can also be found in Fig.3. This might be the major reason for the inverse flow during the systole period in an ITA graft. The diameter of an SVG is usually larger than that of an ITA graft. It can be found that the flow rate through the stenosis and the graft flow in Model 1 are comparable, which means that the flow resistance of the ITA is similar to that of the native coronary artery with moderate stenosis. In contrast, the flow resistance of an SVG is lower than that of an ITA graft which might be the reason for the large graft flow through an SVG.

4.3. Clinical significance

4.3.1. Surgical decision on moderate stenosis

As previously mentioned, surgeons have been facing the problem – Whether a moderate stenosis should be bypassed or not? This problem may still not be completely resolved. But if a moderate stenosis was really need to be bypassed, the SVG is much better than ITA graft. Of course, the long-term patency of ITA is generally much better than SVG.(Tatoulis et al., 2004; Zacho et al., 2012) But SVG is a better choice for a moderate stenosis. Kawasuji et al. also give a similar conclusion based on clinical study.(Kawasuji et al., 1996)

4.3.2. Evaluation of the string phenomenon occurrence probability

Usually, the flow rate through the stenosis in native coronary artery is hard to measure. Only the graft flow can be measured and is the most common index used to evaluate surgical results. The results of this paper may suggest a method to evaluate the degree of competitive flow and the probability of the string phenomenon occurrence qualitatively based on the graft flow. Two important approaches should be taken into consideration. First, check the inverse flow in graft flow curve. If inverse flow exists in the graft, the competitive flow may be in a high level. The probability of string phenomenon occurrence may also be higher. Second, clamp the native coronary artery, and then compare the graft flow rate difference before and after clamping. If the difference is large, the degree of competitive flow is known to be high. The probability of string phenomenon may also be in a high level.

4.4. Future work

4.4.1. The relationship between stenosis degree and competitive flow

It can be found from this study that moderate stenosis might lead to high competitive flow and occurrence of string phenomenon. But the relationship between the stenosis degree and the level of competitive flow still need to be studied in our future work. In our research plan, a set of 3D models with different stenosis degree will be constructed to discuss the relationship between stenosis degree and competitive flow. It can also be found that the inverse flow in the graft is an important character of the ITA graft applied on a moderate stenosis. Thus, in our future work, the critical stenosis degree result in inverse flow in graft may be found.

4.4.2. The relationship between Fractional Flow Reserve (FFR) and string phenomenon

In clinical, FFR was a fractional index to evaluate the degree of myocardial ischemia. In general, the value of FFR decrease with the stenosis degree. But different patient may have different critical stenosis degree result in myocardial ischemia and low FFR. So the relationship among stenosis degree, FFR and string phenomenon is also an interesting research point, which may be studied in the future.

5. Limitation

Our model considered only the left ITA grafted to the LAD, since the left ITA is frequently used to bypass a stenosis in the LAD. The results and conclusions might be different for other surgical procedures, such as a right ITA grafted to the right coronary artery (RCA).

6. Conclusion

The high OSI might be the major hemodynamic characteristic leading to the string phenomenon in an ITA graft. A low WSS may not be a major actor in the string phenomenon. Moreover, the inverse graft flow and the difference of graft flow between a clamped and an unclamped native coronary artery can be used to evaluate the degree of competitive flow following a graft and thus the probability of occurrence of the string phenomenon.

Conflict of Interest Statement

No conflict of interest exist.

Appendix: 0D/3D coupling method

The 0D/3D coupled model was simulated by applying interface conditions and a coupling algorithm at given time intervals. The ANSYS-CFX was used for the 3D simulation, while the 0D part was calculated by FORTRAN routines based on CFX Junction Box. The data transmission between the 0D and 3D parts was implemented with CFX User CEL Function. The volume flow rate at the inlet and average normal pressure at the outlets of the 3D model were set up as the boundary conditions of the 3D simulation based on the 0D simulation. At the interfaces, equations (5) and (6) are considered as the forcing terms for 0D computation after calculation at each time interval.

$$\bar{P}_{3D,in} = \frac{1}{A_{3D,in}} \int_{\Gamma_{in}} P d\gamma = P_{0D,in} \quad (1)$$

$$Q_{3D,out} = \rho \int_{\Gamma_{out}} \mathbf{u} \cdot \mathbf{n}_i d\gamma = Q_{0D,out} \quad (2)$$

where $\bar{P}_{3D,in}$ is the average inlet pressure calculated by the 3D simulation, $Q_{3D,out}$ is the outlet flow rate calculated by the 3D simulation, $A_{3D,in}$ is the inlet area of the 3D sub-model, ρ is the density of the blood flow, Γ_{in} is the integration region of the inlet plane, Γ_{out} is the integration region of the outlet plane, P is the node pressure at the inlet area, $\mathbf{u}$ is the node velocity at the outlet area, $\mathbf{n}_i$ is the normal unit vector at the outlet, $d\gamma$ is the differential area, $P_{0D,in}$ is the forcing term inlet pressure set on the LPM, and $Q_{0D,out}$ is the forcing term outlet flow rate set on the LPM.

The coupling process was defined as illustrated in Fig.8. In this study, we tested the outlet pressure (P_{out}) and the inlet flow rate (Q_{in}) in different cardiac cycles; if the errors of these two values were within the standard residuals (ϵ), set to 0.0001, the simulation passed the convergence test, and the calculation stopped.

It is important to note that the value of the 3D simulation time interval and the value of the 0D calculation time interval differ. The 3D simulation time interval is 0.0025s, while the 0D calculation time interval is 0.000025s. To unify the time in the coupling simulation, for each time step simulated in the 3D sub-model, 100 time steps were calculated in the 0D sub-model. In the 0D calculation, the forcing terms, supplied by the 3D simulation, were interpolated using a linear method.

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Figure Legends

Fig.1 The reconstructed 3D models. In Model 1, ITAG was used to bypass a moderate stenosis; In Model 2, SVG was used to bypass the same stenosis; In Model 3, ITAG was used to bypass a clamped LAD

Fig.2 The structure of a 0D/3D coupled model. A lumped parameter model based on a variable capacitance was used to simulate the left heart and coupled with the 3D inlet; the 3D systemic outlets was coupled with lumped parameter model with three elements; the coronary outlets was coupled with lumped parameter model with a left ventricle pressure source.

Fig.3 The graft flow and pressure drop of each model. Reverse flow exists during the systole in Model 1; moreover, the graft pressure drop during the systole in Model 1 is also negative

Fig.4 The native coronary flow rate of each model. The flow rate through the stenosis in Model 1 is much higher than that in Model 2. But the total LAD flow rate of three models are almost the same.

Fig.5 Area-averaged WSS of each graft. The graft WSS in Model 2 is lower than the others; the graft WSS of Model 1 is not in a low level.

Fig.6 The WSS contours at the moment of maximum graft flow. The graft WSS in Model 2 is low, but that in Model 1 is much higher. This may suggest that string phenomenon is not caused by the low WSS.

Fig.7 The OSI contours of the grafts. The graft OSI of Model 1 is much higher than others throughout the graft, which may suggest that the string phenomenon is closely related to the high OSI.

Fig.8 Flow chart of the 0D/3D coupling algorithm. The coupling method is based on each time step. The 3D simulation is finalized by ANSYS-CFX, while the 0D part is calculated by FORTRAN routines based on CFX Junction Box.

Tab.1 The nodes and elements numbers of the 3D models

<i>Model</i>	<i>Nodes</i>	<i>Elements</i>
<i>1</i>	1025067	1313895
<i>2</i>	1019067	1305731
<i>3</i>	1109466	1450211

Tab.2 The area-averaged inlet pressure and wall shear stress among different meshes

Max Size (m)		0.015	0.003		0.0015		0.0003		0.00015	
		Value	Value	ε	Value	ε	Value	ε	Value	ε
Model 1	Pressure(mmHg)	78.165	85.896	9.9%	81.034	5.7%	83.520	3.1%	83.103	0.5%
	WSS(Pa)	0.619	0.590	4.7%	0.614	4.1%	0.608	1.0%	0.606	0.3%
Model 2	Pressure(mmHg)	80.067	85.970	7.4%	81.412	5.3%	83.519	2.6%	83.103	0.5%
	WSS(Pa)	0.615	0.601	2.3%	0.610	1.5%	0.607	0.5%	0.606	0.16%
Model 3	Pressure(mmHg)	79.173	85.893	8.5%	80.971	5.7%	83.517	3.1%	83.103	0.49%
	WSS(Pa)	0.618	0.593	4.0%	0.615	3.7%	0.608	1.1%	0.606	0.3%

Tab.3 The list of model predictions compared against clinical data

	<i>Model Predictions</i>	<i>Clinical Data</i>
<i>Systolic Pressure</i>	147.69 mmHg	147 mmHg
<i>Diastolic Pressure</i>	103.48 mmHg	103 mmHg
<i>Cardiac Output</i>	4.58 L/min	4.6 L/min

Tab.4 Values of the parameters in the 0D part of the coupled modelUnits: Resistance (mmHg s/ml), Inductance (mmHg s²/ml), Compliance (ml/mmHg)

<i>Heart Block</i>		<i>Rla</i>	<i>Rlv</i>	<i>Lla</i>	<i>Laa</i>	<i>Caa</i>
		0.00375	0.0075	0.00285	0.0037	0.95
		<i>Rp</i>	<i>Rd</i>	<i>C</i>		
<i>Systemic Block</i>	<i>RSA</i>	1.11759	9.32593	0.09233		
	<i>RCA</i>	1.05959	9.72588	0.09239		
	<i>LSA</i>	1.31011	9.56511	0.15900		
	<i>LCA</i>	1.31261	9.20108	0.15880		
	<i>DAO</i>	0.17026	1.51764	2.2653		
		<i>R</i>	<i>Rm</i>	<i>Rv</i>	<i>C</i>	<i>Cim</i>
<i>Coronary Microcirculation Block</i>	<i>a</i>	14.25808	129.51320	45.25413	0.00124	0.01269
	<i>b</i>	20.25463	135.50555	44.00247	0.00137	0.00909
	<i>c</i>	20.25463	135.50555	44.00247	0.00137	0.00909
	<i>d</i>	46.75302	110.00493	18.75154	0.00101	0.03540
	<i>e</i>	46.75302	110.00493	18.75154	0.00101	0.03540
	<i>f</i>	46.75302	110.00493	18.75154	0.00101	0.03540
	<i>g</i>	127.51049	207.76709	65.25537	0.00049	0.00956
	<i>h</i>	46.00987	156.76610	48.50506	0.00064	0.01941
	<i>i</i>	150.01332	264.77177	83.25685	0.00010	0.00927
	<i>j</i>	120.61332	211.27177	66.45685	0.00021	0.01427
	<i>k</i>	150.01332	264.77177	83.25685	0.00010	0.00927
	<i>l</i>	13.60104	155.51690	44.50530	0.00109	0.00920
	<i>m</i>	18.60104	145.51690	44.50530	0.00109	0.00920
	<i>n</i>	16.51641	136.27683	42.00839	0.00110	0.01365

Tab.5 Time-averaged graft flow and coronary flow

Unit: ml/min

<i>Model</i>	<i>Graft Flow</i>	<i>Stenosis Flow</i>	<i>LAD Flow</i>
<i>1</i>	38.5414	41.7074	80.8160
<i>2</i>	81.4267	0.6162	82.0429
<i>3</i>	79.5998	0.0	79.5998

Tab.6 Area-averaged OSI on the graft

<i>Model</i>	<i>1</i>	<i>2</i>	<i>3</i>
<i>Graft OSI</i>	0.0299	0.0047	0.0021

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