Design Exploration and Optimization of Intravascular Stent using Surrogate Model

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Nowadays, the intravascular stent has been popularly used to treat patients with intravascular disorders such as stenosis. With the main objective is to re-open the narrowed lumen area due to stenosis, stent has been broadly used during the last couple of decades. During its deployment process, stent, which works as a solid scaffold to the blood vessel, interacts with the blood flow and blood vessel surface both along the re-opening of the stenotic lumen and the stent landing zone area. This scaffolding functions will resulting the contact phenomena where stent pushes the vessel wall and change the vessel geometry shape which may lead to some cases of vessel wall’s injury due to an excessive pressure on the vessel wall. Moreover, the presence of the stent’s strut inside the blood vessel will disturb the intravascular blood flow and also change the blood vessel hemodynamic environment. Therefore, due to the complication of these stent-vessel wall and flow interaction, post-stenting problem is usually exists in the form of post-stenting lumen re-blockage which causing the re-narrowing vessel’s lumen area on the stented site.

Post-stenting lumen re-blockage is one of the most examples of the adverse effect of stent implantation which a result from both hemodynamics and mechanical interaction between stent struts and blood vessel wall’s tissue. The factor of flow alignment around the strut vicinity, vessel deformation, also stent geometrical design (e.g., inter-strut gap, length, and strut cross-section) are believed to be responsible for changes in the blood flow and its hemodynamic conditions which promotes this re-blockage problem. From the hemodynamic point of view, the change of intravascular lumen shape will introduce the flow alignment. Besides, as stent struts exists on the blood vessel surface, the main blood flow will instantly disturbed and causing further flow separation phenomenon. Longer recirculation zone, change of the position of re-attachment point, and fluctuation wall shear stress (WSS) are several factors which believed to be existed behind this re-blockage problem. Moreover, the mechanical stress exerted to the blood vessel surface is believed to promote thrombus formation due to the cell’s injury. Therefore, further investigations on the
stent-vessel interaction and how stent's design influence the intravascular physical behavior in both hemodynamics and mechanical is needed.

Coping with all of the problems and design challenges concerning the mentioned factors, further research and investigations are included in the present thesis:

1. Investigation on how the wall deformation caused by the stent-vessel contact during the deployment procedure will affect the blood flow environment in the stented blood vessel segment (Chapter 3).
2. Select the best stent design configuration and explore the design criteria to minimize the area with the presence of low wall shear stress (WSS) along the stent deployment area (Chapter 4).
3. Observe and compare how the different stent design affect the post-stented intravascular condition to minimize both of low WSS area and exerted mechanical stress (Chapter 5).
4. Apply the computational surrogate-based design exploration to a realistic cellular flow chamber design to predict the behavior of endothelial cells (ECs) under the flow exposure with the placement of two stent struts (Chapter 6).

This thesis presents the computational numerical simulation works based on finite element method (FEM) in two-dimensional (Chapter 3 and 4) and three-dimensional (Chapters 5 and 6) geometry models in a step-by-step fashion. Structure contact simulation between stent and vessel wall is carried out to obtain the 0.14 mm vessel expansion (Chapter 3). With this geometry changes, further effects of how blood flow and hemodynamics condition will altered around the stent deployment area is investigated in this chapter. In Chapters 3-5, Strut gap (G) within the range from 1 mm to 3 mm and the strut size length (SL) from 0.05 mm to 0.45 mm are considered as the design variables for study case. Meanwhile, similar range of gap factor (G) and strut orientation angle (α) within range of 70°-90° relative to the inflow direction is used in the cases of Chapter 6. With various configuration setup combining each design variables, G·SL or G·α, computational simulations have been carried out to obtain the pattern of system behavior under the change of design variables' configurations. Focusing to the effects of stent geometry design towards the treatment performances, application of single optimization method to minimize the appearance of low WSS area (ω) along the deployment area has been conducted in the Chapter 4. Additionally, more investigation on the strut cross sectional effects to the hemodynamics performance has been performed in Chapter 5. Hypothetically, the better hemodynamic performance can be obtained by the stent with streamlined cross-sectional shape. Therefore, in the Chapter 5, two different strut's shape configurations: rectangular and triangular, are adopted as the cross-section of a stent strut and compared to see the effects of the
cross-section towards two objective functions; minimizing $\omega$ and average stress on the vessel surface along the deployment area. These works have been performed with surrogate model constructions which were obtained based on the Kriging estimation method, and optimization works obtained based on expected improvement (EI) in Chapter 4 and expected hypervolume improvement (EHVI) in Chapter 5. After all trials of computational based optimization and design exploration works have been successfully done consecutively in Chapter 4 and 5, application of surrogate model construction towards a real system is proposed. New computational model based on the parallel flow chamber system for cellular mechanics experiment study has been constructed in Chapter 6. In this experimental apparatus, observation of how endothelial cells (ECs) behave under certain flow conditions can be carried on in order to understand more about the relation between flow and blood vessel cellular conditions. Moreover, the relation between hemodynamics factors i.e. WSS and WSS gradient and the cell migration has still not yet well understood. In particular for the case of stented flow conditions, in which the flow conditions may changes due to the presence of the stent struts. Afterwards, the surrogate model map is constructed to predict the ECs migration under the flow exposure system with the placement of two stent struts. With the constructed surrogate model, specific G$\alpha$ configuration is suggested to be put in to the experimental trial. All specific materials and methods applied to obtain all results were respectively reported in Chapters 3, 4, 5 and 6 were explained in Chapter 2.

Results of the present thesis show several new finding and understanding, which have been listed and discussed in detail in each chapter’s Discussion and Conclusion part, and also in Chapter 7. However, it would be remiss to not to mention here about several general conclusions as follow:

• The analysis of the post-deployment state of the stent with wall deformation shows that significant differences are observed primarily on the flow pattern and low WSS ratio ($\omega$) appearance along the blood vessel, therefore this study suggest that the wall deformation is necessary for the post-stenting simulation (Chapter 3).

• The SL factor has been observed to be very strong for influencing the size of recirculation zone (RCZ), while G factor influence more for the flow stagnation in the inter-strut area. However, when both parameters come together, unique flow effect will emerge (Chapter 3).

• In consideration of the parametric sensitivity, the Surrogate model constructed with the objective of $\omega$ shows that the SL factor is more influencing than G to the behavior of the stent deployment systems. (Chapter 4).
From the surrogate model map, several design recommendations can be obtained (Chapter 4):

a. Strut’s size more than 300 μm is better to avoid, since it produces very high ω value.

b. Combinations of small struts and a narrow gap are not recommended, due to the sudden increment of ω on this area.

c. Longer inter-strut gap is necessary for smaller strut size in order to keep the ω percentage low.

d. Narrow ω increment area is noticeable on the SL range 0.25 – 0.30 mm and above for the larger G configuration, therefore careful selection process is needed concerning this particular area.

e. The optimized designed point to minimizing ω has been found under the configuration of G=2.99 mm and SL=0.1 mm.

From surrogate model map obtained for the average stress minimization case, the SL factor remains as the dominated factor on influencing the system behavior. Decrement of SL gives a dramatic increment on average shear stress value. Therefore, in consideration of previous results from single objective work, trade-off condition is appear on each suggested design: hemodynamically, smaller SL is desirable in contrary, average stress is better in the bigger SL. So that, multiobjective analysis is considered to be necessary to find the balance between both objectives.

Multiobjective optimization with EHVI can find the proper balance between two objectives. Three non-dominated points are obtained for the rectangular strut case with G-SL configurations of 2.81 mm – 0.39 mm, 1.96 mm – 0.08 mm and 2.13 mm – 0.06 mm. For triangular shape, one non-dominated point has been acquired with G-SL configuration of 2.00 mm – 0.43 mm (Chapter 5).

Based the comparison of performance between different strut shape, the triangular strut is predicted to produce better intravascular hemodynamics. This is proved by a wider area of low ω is generated by triangular strut shape. Meanwhile, for the average stress, both strut types show no significant differences (Chapter 5).

Surrogate model map has been constructed on minimizing the appearance of WSS gradient (WSSG) on the bottom part of parallel flow experiment's chamber (Chapter 6).

Observations of extreme maxima and minima for objectives average WSSG and ω have been obtained from the surrogate model map and suggested to be put into a test in the experimental
system to predict ECs migration under flow exposure experiment (Chapter 6).

- From the experiment trial based on the suggested configuration for smallest average WSSG, high density of ECs are observed on the inter-strut area. This result suggests that the tendency of WSS magnitude effect is indicated to be the reason behind ECs migration and its high concentration in the inter-strut area instead of WSSG.

Several limitations are still being addressed on this thesis since many assumptions have been applied throughout this work. Geometry simplifications of stent design and assumptions of physical model both on flow and solid mechanical properties are utilized on this research. Blood flow is modeled as incompressible and Newtonian flow, and solid properties of blood vessel is considered as linear elastic material. Blood flow phenomenon is simplified as a constant inlet flow with laminar parabolic profiles. All computational processes have been performed based on finite element method (FEM) with a limited element numbers. Therefore, further works with higher computational capability to handle higher mesh elements is necessary to improve the model. Solver capability to cope with nonlinearity solid mechanical model is also encourage to enhance the solid mechanics deformation of the vessel wall.

Regardless of the limitation of this work and alongside with the aforementioned key findings, this thesis may allegedly benefit further stent design process since the surrogate model can be used as an effective tools to observe the stent behaviors and the physical behavior change around its deployment area. Apart from any other direct optimization process, this method also beneficial for design exploration process which is useful to make a broader selections of design recommendations. Moreover, surrogate model based optimization is known as an efficient way to perform a high computational cost of FEM-based computational optimization. With reasonable number of simulation iteration, the surrogate model map is constructed to capture the general tendency of the system behavior towards design variable. With this surrogate model map, more design selection can be used as alternative to reach the similar optimization goals and overcome the limitation of experimental resources. Furthermore, as shown by the work in the Chapter 6, surrogate model can be used as an effective way to make a better plan for experimental trials, additionally it provides more information to understand the physical reason behind the experiment data.