MODELING IMPLICATIONS IN SIMULATION-BASED DESIGN OF STENTS

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ABSTRACT
Variations associated with stenting systems, artery properties, and doctor skills necessitate a better understanding of coronary artery stents so as to facilitate the design of stents that are customized to individual patients. This paper presents the development of an integrated computer simulation-based design approach using engineering finite element analysis (FEA) models for capturing stent knowledge, utility theory-based decision models for representing the design preferences, and statistics-based surrogate models for improving process efficiency. Two focuses of the paper are: 1) understanding the significance of engineering analysis and surrogate models in the simulation-based design of medical devices; 2) investigating the modeling implications in the context of stent design. The study reveals that the advanced nonlinear FEA software with analysis capacities on large deformation and contact interaction has offered a platform to execute high fidelity simulations, yet the selection of appropriate analysis models is still subject to the tradeoff between cost of analysis and accuracy of solution; the cost-prohibitive simulations necessitate the employment of surrogate models in subsequent multi-objective design optimization. A detailed comparison between regression models and Kriging models suggests the importance of sampling schemes in successfully implementing Kriging methods.

Keywords: Simulation-Based Design, Decision-Based Design, Multi-Objective Design Optimization, Finite Element Analysis, Tradeoff, Surrogate model, Kriging, Coronary Artery Stent.

INTRODUCTION
Stent is a medical device that is widely used in the treatment of coronary artery disease (CAD). CAD occurs when plaque – the fatty deposits builds up inside the walls of a coronary artery. Over time, this buildup of plaque hardens arterial walls, narrows arterial lumen and restricts the blood flows to the heart muscles, a process termed atherosclerosis.

The resultant reduction in the oxygen supply causes angina, namely, chest pain or discomfort triggered from heart muscles starving for oxygen. In its worst scenario, the artery can get completely blocked, cutting off the flow of blood to an area of the heart and resulting in a heart attack. As an alternative to coronary bypass surgery, stenting technique is a minimally invasive medical procedure used to dilate the opening of a narrowed coronary artery for ensuring blood supply to heart muscles [1,2,3,4,5].

From an engineering viewpoint, stents can be studied as medical implants with a tubular mesh structure made of noninterference material, such as sterile metal, that, if successfully implanted, can facilitate the opening of the narrowed arteries [4,5,6]. During the implanting procedure, the stent is wrapped tightly around the balloon-tipped catheter, which is then inserted through a blood vessel in the groin or arm into the narrowed artery. Once in place, the balloon is inflated which expands the mesh; once being expanded, the permanent mesh acts like a scaffold that supports the artery walls and keeps them open [4,5,6]. Since the U.S. Food and Drug Administration (FDA) approved the first coronary stent in 1994 [7,8], various kinds of stent have been implanted for treating CAD patients. Among them the diamond shaped Palmaz-Schatz balloon-expandable stent, the first FDA approved stent [7,8], is the most fundamental type. Figure 1 shows the principle of stenting procedure of a typical coronary stent in which the collapsed stent is expanded into its expected size inside a narrowed blood vessel [9].

![Figure 1: Principles of stenting procedure](image-url)
Despite the wide usage of stents, nuances in stent design and construction have shown significant impact on the immediate and long-term clinical outcomes of stenting technique [10,11,12,13,14]. A primary concern is that the stent may take undesired shape due to inhomogeneous expansion, increasing the chance and magnitude of stent irritation to the artery; this situation is worsen when intrinsic variations associated with stenting systems, artery properties, and doctor skills are not within the control. Correspondingly, a better understanding of stent behavior is essential to a better design of stents that are customized to individual patients.

**Engineering Design of Stents**

A recent review on implications of stent design for restenosis based on nine independent clinical reports shows that the stent geometry designed to optimize expansion and later recoil is a prerequisite for favorable clinical outcomes [12]. From an engineering viewpoint, the optimal expansion and later recoil of a stent can be characterized by three physical attributes, namely, radial recoil, dogboning, and foreshortening [15,16]. The critical attribute is the radial recoil which is the percentage reduction in profile diameter of an expanded stent due to the release of elastic energy in stent structure when its expanding pressure is unloaded. Dogboning is the measure of non-uniformness in stent expansion which takes the shape of a dogbone. And foreshortening refers to the maximum percentage reduction in stent length in the process of expanding stent. Mathematically they can be expressed as follows:

\[
\text{Radial recoil} = \frac{R_{\text{load}}^{\text{outer}} - R_{\text{unload}}^{\text{outer}}}{R_{\text{load}}^{\text{outer}}} \quad (1)
\]

\[
\text{Dogboning} = \frac{R_{\text{load}}^{\text{distal}} - R_{\text{load}}^{\text{central}}}{R_{\text{load}}^{\text{distal}}} \quad (2)
\]

\[
\text{Foreshortening} = \frac{L - L_{\text{load}}^{\text{unload}}}{L} \quad (3)
\]

Referring to Figure 2, \( R \) is the stent outer radius; \( L \) is the stent length; \( i \) is any site along stent axis where the maximum radial displacement occurs. The “load” and “unload” superscripts denote the loading status associated with the measured physical value; the “distal” and “central” subscripts refer to the sites where the attribute values are measured.

A modified definition of dogboning is employed in this study that effectively measures the uniformity of stent expansion, taking into consideration that the minimum expansion is not necessarily at the central portion. Accordingly, dogboning is defined as follows:

\[
\text{Dogboning} = \frac{R_{\text{Max}}^{\text{load}} - R_{\text{Min}}^{\text{load}}}{R_{\text{Max}}^{\text{load}}} \quad (4)
\]

Here, the subscripts “Max” and “Min” refer to the maximum and the minimum radial displacements respectively during the stent expanding process.

Radial recoil, dogboning, and foreshortening are indicators of the quality of the stent expansion defining the effectiveness of the stenting procedure [15,16]. Therefore, they can be interpreted as the safety attributes in the design of stents. Other than these safety attributes, additional design requirements may include the following: 1) Stent should be doctor-friendly and easy to expand, which requires that the expanding pressure should not be too high; in addition, high pressure demands special design for expanding balloon, adding in more cost. 2) Since stent resides in the coronary artery, it should be light, which translates to the smallest volume requirement. Finally, any design of stent has to conform to its material properties, which then means that the stresses in the stent cannot exceed ultimate strength (\( \sigma_{\text{UTS}} \)) of stent material. From these design requirements, the engineering design of stents can be stated as a minimization problem as follows:

**Minimize:**

1) Radial recoil (RR) \( (5) \)
2) Dogboning (DB) \( (6) \)
3) Foreshortening (FS) \( (7) \)
4) Volume (V) \( (8) \)
5) Pressure (P) \( (9) \)

**Subject to:**

1) \( \sigma_{\text{max}} < \sigma_{\text{UTS}} = 530 \text{MPa} \) \( (10) \)
2) Design variables \( \in \) feasible design space \( (11) \)
3) The minimum \( \Phi_{\text{outer}}^{\text{unload}} = 3 \text{mm} \) \( (12) \)

Here, \( \Phi_{\text{outer}}^{\text{unload}} \) is the outer diameter of expanded stent. Since there is dogboning at stent expansion, the minimum outer diameter of an expanded stent is selected to be the datum value.

Figure 3a shows a diamond shaped stent structure with a fixed pattern of repeating basic constitutive structure; figure 3c is the illustration of ideal stent expansion. For this stent structure, the geometry can be defined by the stent wall thickness (\( t \)), stent wire thickness (\( w \)), and the open slot length (\( l_{\text{slot}} \)) [Figure 3b]. Preliminary results from finite element analysis indicate that the infeasible regions in the design space...
Figure 3: A diamond shaped stent with repeating basic constitutive units in the original and expanded statuses

can be avoided by setting the wire thickness (w) to be comparable in size to the wall thickness (t). Accordingly, the width is set to a pre-assigned value of w=0.8t, and the 2nd constraint becomes: \( t: 0.02\text{mm} \leq t \leq 0.3\text{mm} \cap \{ \text{slot}: 2\text{mm} \leq \text{slot} \leq 3\text{mm} \}. \) The particular bounds in the 2nd constraint are obtained through rational guessing which is beyond the scope of this paper. In this setup, the volume of the stent, which is the remains after the cuboids have been cut away from hollow cylinder wall, can be reduced to the following closed-form expression:

\[
V = (t - t^2)(1.6\pi + 60w \times \text{slot})
= 5.027t - 5.027t^2 + 48\text{slot} \times t^2 - 48\text{slot} \times t^3
\]

Conversely, there are no closed-form expressions for Radial recoil (RR), Dogboning (DB), Foreshortening (FS), Pressure (P), and maximum stress \( \sigma_{\text{max}} \). Take note that the 3rd constraint implies that the required pressure P is an unknown value at which the expanded stent has a minimum outer diameter 3mm. Furthermore, it is unknown about where these minimum diameters take place upon and after pressure loading and how much the minimum outer diameter of the stent remains (may be at different stent cross-section) after pressure is released. It is challenging to solve this highly nonlinear and open-ended multi-objective design problem. For example, the relationship between the expanded profiles and the initial geometry is unknown, which makes it hard to define the profile of an expanded stent, given its initial geometry, not to mention RR, DB, FS, P, and \( \sigma_{\text{max}} \). In fact, forming a stent into the desired expansion is a complex process in which appropriate plastic deformation at different portion of the stent must take place so that the desired stent deformation field can be obtained collectively. This process requires a proper distribution of energy to different portions of the stent, which is difficult to be quantified. Mathematically, there are no closed-form expressions to map the deformation field to the initial stent structure, since the process of expanding stent is of large nonlinear deformation, specifically the final profile shrinks when the expanding pressure is unloaded. So far there is no analytical method available to solve this problem other than physical experiment on the expansion process or using expensive finite element analysis to simulate the results [15,16]. Figure 4 shows the typical nonlinear time histories of the length of stent the radial displacement at the node associated with \( R_{\text{load}} \) during stent dilating process. This result is obtained from using a complex simulation FEA model of stent [Detailed in next section].

Figure 4: Deformation histories in radial and longitudinal directions, the negative means reduction

Computer Simulation-Based Engineering Design

Computer simulation-based engineering design approach, when constructed appropriately to reflect the system information, can greatly help in reducing the cost involved in the search of optimal design sets and shortening the design cycle and subsequent time to market[17]. Figure 5 illustrates
general procedures involved in a simulation-based engineering design approach. Computer simulation models such as FEA models have been widely used for supporting engineering decision making in many engineering domains. Statistics-based surrogate models, which are built through response surface methods (RSM), Kriging, etc., are increasingly employed for accelerating the finding of optimal design in high fidelity simulations. Decision models, which represent design preference quantitatively, have facilitated the optimal trade-off engineering decision in constrained multi-objective pursuit. With the advancements in cyber infrastructure and information technology, engineering design through modeling and simulations in computers is rapidly emerging as an indispensable cost-effective method and time saving tool in product design process.

Accordingly, a better understanding of stent behaviors can be achieved through a methodical simulation-based engineering modeling and analysis study. If successful, such an approach can provide the basis for not only an optimized stent structure conform to its engineering properties, but also one that is tailor-made to individual patients. However, the study of the fidelity of such simulation-based computer models, especially in the context of overall design decisions, is still at an infancy stage. It is then the goal of this paper to study the simulation-based design of coronary stents, focusing on the effects of simulation-based computer models used in the analysis and design optimization.

SIMULATION MODELS IN STENT DESIGN

The various stages of the integrated computer simulation-based design approach include the development of engineering analysis models (FEA models), the formulation of decision models based on well-established decision-based design methods, the construction of accurate yet cost-effective surrogate models in lieu of actual highly time-consuming numerical analysis models, and a search process (generic algorithm (GA)) that enables the finding of optimal design sets. A schematic representation of the proposed design procedure is shown in Figure 6. These various stages are discussed in detail in the following sections.

Engineering Analysis Models

Engineering analysis models are designed to simulate the behavior of a physical system in terms of design variables and performance variables in order to produce performance forecast in what-if scenarios. With idealizations and simplifications being made during model construction, simulation-based computer models such as the FEA are abstractions of (approximations to) the reality. However, they offer a cost-efficient view into the behavior of the systems under consideration and offer a viable method of designing such artifacts. In such a scenario, the problem of finding the most-appropriate model can be studied as a tradeoff problem in cost and accuracy [18,19].

In this paper, for comparison purposes, various different FEA models with different levels of detail are considered in the engineering analysis of coronary stents. Figure 7 shows eight possible analysis models with initial and expanded profiles associated with each individual model. The pictures are screen snapshots of finite element analysis results in the initial and expanded stent states and the corresponding radial displacement contours. They are listed in their increasing order of complexity and computational efforts. Among them, the Beam model is the simplest which takes only one beam element of the stent mesh. The half-cell and the one-cell models take one half of and one basic cell structure of the stent respectively. The Branch model maps on to the one half of a single stent unit, corresponding to one longitudinal branch of the stent unit starting from its midsection to its end. The half-ring and full-ring models, as the name implies, views the stent profile as a ring structure. The quarter-tube and half-tube models treat the entire stent structure as a unit.
All the different stent models are built with the same stent geometry with a stent length of 16mm, stent wall thickness of 0.1mm, a stent wire width of 0.131mm, and a stent slot length of 2.88mm (Figure 3). However, the finite elements are similar as shown in Figure 8, which shows 3 alternative FEA models.

The different simplifications and idealizations done in model building are based on the axial symmetry assumption in geometry, loading and boundary conditions. In the comparison study, a pressure of 0.6MPa is applied to the stent gradually in 6 load steps, and then, unloaded in another 6 steps.

A detailed study of the results from the different models show that while the models may appear to be different for novice designers, experts in finite element analysis would have immediately recognized the symmetry property in the different models and would have expected only two distinct set of results (Table 1). The duplication in results is to be expected since the mesh pattern of finite elements applied to discretize the structure was the same for the models (1-3,5-6), and similarly, identical in models (4,6-8).

However, the simulation times of individual models are significantly different within each set of similar models. In this case, the Beam model among the first group of models producing the same simulation results takes the minimal simulation time of 260 seconds, while the Branch model among the second group producing the other set of results takes the minimal simulation time of 2,167 seconds [Table 1]. All the models are run on a Pentium 4 machine with 3GHz CPU, available physical memory 780MB, and cache memory 512KB.

Model 8, the half-tube model, is the most comprehensive of the models with an associated simulation time of more than 32 times longer than the time associated with model 4, the Branch model. Given that the analysis results are identical in these two cases for the load condition, it is apparent that model 4 is sufficiently accurate to analyze the critical properties of stents. Similarly, the simulation time is about 250 times less using model 1, the Beam model, when compared to model 8. However, the results from the Beam model show large errors, 5.3% for RR, 5.8% for $\sigma_{\text{Max}}$, 13.7% for FS, and 60.6% for DB, indicating that this model over simplifies the stent topology. On this basis, one can conclude that the most cost-effective, yet accurate, model is the Branch model (Model 4). While the results are trivial in this case, the process of evaluating the tradeoffs between cost of analysis and accuracy of results still provide a rational approach to appropriate analysis model selection. In earlier works, the authors have detailed the complexity in the selection of most appropriate analysis models based on cost and accuracy [19]. Furthermore, the results are based on a single point analysis, and as such, they do not automatically guarantee the model’s validity over the entire design space. Nevertheless, such a conclusion can be drawn in this case from the symmetry properties of the models, and accordingly, this study will investigate the Branch model in the subsequent engineering design of stents. It is to be noted that even this Branch model is computationally intensive. For example, a single analysis run at a sample point (0.286, 2.780) took nearly 5,460 minutes, i.e., 91 hours on the Pentium 4 machine with 3GHz CPU, necessitating the use of sampling based surrogate models that is detailed in the following section.

Figure 8: Finite elements in Stent FEA models - Beam, Branch, and Half-Tube (with different scale)

<table>
<thead>
<tr>
<th>No.</th>
<th>Models</th>
<th>Element</th>
<th>Node</th>
<th>Time Spent</th>
<th>RR</th>
<th>DB</th>
<th>FS</th>
<th>$\sigma_{\text{Max}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Model Generation</td>
<td>Solution</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>sec</td>
<td>sec</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>1</td>
<td>Beam</td>
<td>1,048</td>
<td>1,590</td>
<td>4</td>
<td>260</td>
<td>1.9</td>
<td>25.1</td>
<td>14.9</td>
</tr>
<tr>
<td>2</td>
<td>Half-Cell</td>
<td>2,096</td>
<td>3,140</td>
<td>4</td>
<td>597</td>
<td>1.9</td>
<td>25.1</td>
<td>14.9</td>
</tr>
<tr>
<td>3</td>
<td>One-Cell</td>
<td>4,192</td>
<td>6,190</td>
<td>8</td>
<td>1,428</td>
<td>1.9</td>
<td>25.1</td>
<td>14.9</td>
</tr>
<tr>
<td>4</td>
<td>Branch</td>
<td>5,240</td>
<td>7,770</td>
<td>16</td>
<td>2,167</td>
<td>2.0</td>
<td>40.3</td>
<td>13.1</td>
</tr>
<tr>
<td>5</td>
<td>Half-Ring</td>
<td>6,288</td>
<td>9,340</td>
<td>12</td>
<td>2,585</td>
<td>1.9</td>
<td>25.1</td>
<td>14.9</td>
</tr>
<tr>
<td>6</td>
<td>Full-Ring</td>
<td>12,576</td>
<td>18,600</td>
<td>34</td>
<td>3,754</td>
<td>1.9</td>
<td>25.1</td>
<td>14.9</td>
</tr>
<tr>
<td>7</td>
<td>1/4-Tube</td>
<td>31,440</td>
<td>45,670</td>
<td>168</td>
<td>16,035</td>
<td>2.0</td>
<td>40.3</td>
<td>13.1</td>
</tr>
<tr>
<td>8</td>
<td>Half-Tube</td>
<td>62,880</td>
<td>90,960</td>
<td>898</td>
<td>65,785</td>
<td>2.0</td>
<td>40.3</td>
<td>13.1</td>
</tr>
<tr>
<td>Max. Discrepancy (%) = (Max-Min)/Min × 100%</td>
<td>5,900</td>
<td>5,621</td>
<td>22,350</td>
<td>25,182</td>
<td>5.3</td>
<td>60.6</td>
<td>13.7</td>
<td>5.8</td>
</tr>
</tbody>
</table>
Surrogate Models in Engineering Design of Stents

Surrogate models have one more level of abstraction from the reality compared with analysis models, and their purpose is to provide a structure to the design problem and increase the speed and ease of computation during design optimization. In general, surrogate models are built using simpler approximations through low-order polynomial regressions or interpolation methods such as Kriging constructed from a few expensive runs of computer simulation models [20,21,22]. Besides personal preference, the selection of surrogate types is influenced by the level of uncertainty associated with collected data and the degree of nonlinearity with the studied system. If there is significant randomness associated with collected data such as in physical experiments and system attributes are of less nonlinearity, low-order polynomial regression is more appropriate; if there is no randomness in the collected data such as the case in deterministic computer experiments and the system attributes are of arbitrary nonlinearity, interpolation surrogate models are appropriate which can facilitate global scale fidelity and resume the values at observed points, even though the involved calculation burden in constructing a Kriging model is much higher [23]. Since in reality there is no a priori knowledge available that can guarantee smooth variation in system behavior, it is a reasonable and risk-averse decision to prefer Kriging model in approximating the computer models of complex medical devices such as artery stents.

As stated before, stent model 4, the Branch model shown in Figure 7, is used in the engineering analysis phase for obtaining simulation results on the mapping relationship between stent attributes and the design variables (Figure 3). The sample schemes for model building are built using Latin Hypercube Sampling (LHS) method [24,25] based on the principle of Design of Experiments (DOE) [21,22,24]. For comparative purposes, two different sample sizes are studied with 10 points and 5 points. Figure 9 shows the sampling points in the design space \( \{t \in [0.02, 0.3]; l_{\text{slot}} \in [2, 3.2]\} \). For comparison, both the least squares fit with 2nd-order polynomial models and the Kriging models are employed to create surrogate models for each stent attribute [26,27,28]. Subsequently, the results are transformed to corresponding single attribute utility models and the multi-attributes utility model is built from Eq. 23 and 24.

![Figure 9: 2 different sampling schemes in design space](image)

Decision Model for Stent Design

The goal in this particular stent design is to maximize the performance and safety, while keeping the cost and difficulty of its implementations to their lowest possible value. This requires the study of engineering design as an iterative decision-making procedure [29,30]. Fundamental to decision making is the concept of value, which measures what is preferred or desirable about a design [31]. Expected utility theory is a normative approach to decision making through a rational evaluation of design alternatives with three main components, namely, options, expectations, and value, where the decision rule is that the preferred decision is that option whose expectation has the highest value (utility) [31]. In the context of engineering design, the quintessence of this method can be stated as first modeling the decision scenario resulting in a mapping from the design option space to the performance attribute space, and constructing an overall utility function that reflects the designer’s preference information including tradeoffs among system attributes [32,33]. Here, the mechanism to get preference structure is based on the notion of the lottery, referred to as a von Neumann-Morgenstem lottery, and from employing the certainty equivalent which is the value at which the decision maker is indifferent to a lottery between the best and the worst. In this approach, lottery questions provide the basis for describing the logic between attribute bounds, where analytical function formulations are typically used to complete the preference structure description. Similarly, lottery questions form the basis for eliciting tradeoff information among attributes. On this basis, Krishnamurty and his associates have developed a Trade-off based Engineering Design (TRED) procedure [32]. TRED method enables the formulation of the preference-based design metrics for the stent design problem. Here, standard exponential based monotonic Single Attribute Functions (SAU) that indicate the decision maker’s preferences on the individual attribute values are generated for the five minimization attributes and a Boltzmann Sigmoidal function is used to represent the stress constraint attribute [32,33]. The different selection in model types between stress attribute and other five attributes is based on the fact that more improvement on objective attributes means higher utility of them, and that the utility of constraint attribute is one if the design is feasible and zero if infeasible. A Sigmoidal function improves upon step function in that it is closer to reality at the neighbor of constraint [32,33]. Specifically, SAUs of attributes are obtained by setting up von Neumann-Morgenstem lottery question for each attribute. Figure 10 shows the lottery question for finding the SAU of RR. Here, the designer is indifferent to the certain value 2% and an uncertain value of 0 (the best value for RR) with a probability of 80%, thus, the utility of 2% RR is 0.8. Similarly, lottery questions are generated for all the attributes. The utility evaluator [34] is then used to construct exponential formulation based mathematical expressions, resulting in attribute utility functions as follows:
Figure 10: Lottery question for RR (%)

\[ U_{RR} = 1.18 - 0.175e^{RR/2.628} \]  (14)

\[ U_{DB} = 1.02 - 0.023e^{DB/6.559} \]  (15)

\[ U_{FS} = 1.32 - 0.323e^{FS/9.862} \]  (16)

\[ U_y = 1.83 - 0.835e^{y/13.968} \]  (17)

\[ U_p = -0.02 + 0.939e^{P/1.848} \]  (18)

By using the Boltzmann Sigmoidal function, the SAU for the stress constraint attribute is constructed as:

\[ SAU_{\sigma_{\text{total}}} = \frac{1}{1 + e^{\frac{SAU_{\sigma_{\text{total}}}}{10}}} \]  (19)

Among the 5 minimization attributes, RR, DB, and FS are the performance indices related to the safety goal of stent design; V and P are related to the operational goal of stent design. To maximize the utilities of safety goal and operational goal, the multi-attribute utility (MAU) function is developed using a new set of lottery questions [32,35]. In its standard form, MAU is:

\[ MAU (\bar{x}) = \frac{1}{K} \left[ \prod_{i=1}^{n} (Kk_iU_i(x_i) + 1) - 1 \right] \]  (20)

\[ MAU(\bar{x}) = \sum k_i U_i(x_i) \]  for additive utility

(21)

where \(1 + K = \prod_{i=1}^{n} (1 + k_i)\) or \(\sum_{i=1}^{n} k_i = 1\) for additive utility

(22)

\(\bar{x}\) is the attribute vector, and \(x_i\) is the ith attribute.

Here, trade-off values are obtained through a new set of lottery questions in which the coefficients \(k_i\) of MAU are quantified as the individual probability value where designer is indifferent to the certainty of one single best attribute and the uncertain chance toward the best combinations of all attributes. For example, as shown in figure 11, the coefficient is 0.333 for attribute RR, when the designer is indifferent to the certain value (RR\(^*\), DB\(^0\), FS\(^0\)) and the 33.3% chance of best combination (RR\(^*\), DB\(^*\), FS\(^*\)), where RR\(^*\) stands for the best value of RR, and DB\(^0\), FS\(^0\) the worst values of DB and FS respectively.

Similarly, the coefficients for attributes DB, FS, V, and P are obtained through lottery questions and are listed in Table 2. The overall utility of stent design is then the result of trade-offs between safety utilities and operation utilities. This can be mathematically expressed as follows:

\[ MAU_{\text{total}} = (K_{\text{safety}} \times MAU_{\text{safety}} + K_{\text{oper}} \times MAU_{\text{oper}}) \times SAU_{\sigma_{\text{total}}} \]  (23)

For the preference set up in Table 2 which refers to the cases of additive utility:

\[ MAU_{\text{total}} = \frac{0.5(U_{RR} + U_{DB} + U_{FS}) + 0.01([U_y + 7U_y])}{1 + e^{-7[SAU_{\sigma_{\text{total}}}]/10}} \]  (24)

Table 2: Design preferences on attributes

<table>
<thead>
<tr>
<th>Decision Model</th>
<th>Safety</th>
<th>Operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAU_{\text{safety}}</td>
<td>MAU_{\text{oper}}</td>
<td></td>
</tr>
<tr>
<td>K_{RR}</td>
<td>K_{DB}</td>
<td>K_{FS}</td>
</tr>
<tr>
<td>1</td>
<td>1/3</td>
<td>1/3</td>
</tr>
</tbody>
</table>

RESULTS AND DISCUSSION

For surrogate modeling purposes, as stated before, the finite element simulation results using the Branch model are sampled with 10 and 5 LHS points (Tables 3-4). To investigate the effects of different modeling techniques, regression analysis based response surface methods and interpolation based Kriging methods are considered in the construction of single and multi-attribute decision models.

Table 3: Stent attribute responses at 10 LHS points

<table>
<thead>
<tr>
<th>#</th>
<th>Design Space</th>
<th>Attribute Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>#</td>
<td>( t )</td>
<td>bslot</td>
</tr>
<tr>
<td>mm</td>
<td>mm</td>
<td>%</td>
</tr>
<tr>
<td>1</td>
<td>0.034</td>
<td>2.30</td>
</tr>
<tr>
<td>2</td>
<td>0.062</td>
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</tr>
<tr>
<td>8</td>
<td>0.23</td>
<td>3.02</td>
</tr>
<tr>
<td>9</td>
<td>0.258</td>
<td>2.42</td>
</tr>
<tr>
<td>10</td>
<td>0.286</td>
<td>2.78</td>
</tr>
</tbody>
</table>
The 2nd-order polynomial based response surrogate models of the stent attributes RR, DB, FS, and P are shown in Figure 12. However, from 5 sample points, only pure quadratic polynomial models can be created. The graphical illustrations of the built models on 10 LHS sample scheme are shown in Figure 12.

Table 5: Surrogate models for attribute RR, DB, FS, and P and \( \sigma_{\text{max}} \); Analytical model for attribute V. (sample scheme: 10 LHS)

<table>
<thead>
<tr>
<th>Design Space</th>
<th>Attribute Responses</th>
<th>( \sigma_{\text{max}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( t )-Islot</td>
<td>RR, DB, FS, V, P</td>
<td>5.027x1 – 5.027 x1</td>
</tr>
<tr>
<td>mm</td>
<td></td>
<td>19.89</td>
</tr>
<tr>
<td>mm</td>
<td></td>
<td>11.70</td>
</tr>
<tr>
<td>mm</td>
<td></td>
<td>8.52</td>
</tr>
<tr>
<td>mm</td>
<td></td>
<td>5.500</td>
</tr>
</tbody>
</table>

Table 6: Surrogate models for attribute RR, DB, FS, and P and \( \sigma_{\text{max}} \); Analytical model for attribute V. (sample scheme: 5 LHS)

<table>
<thead>
<tr>
<th>Design Space</th>
<th>Attribute Responses</th>
<th>( \sigma_{\text{max}} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( t )-Islot</td>
<td>RR, DB, FS, V, P</td>
<td>9.21 + 66.73x1 – 8.75x2 – 29.21x1x2 + 112.48x1</td>
</tr>
<tr>
<td>mm</td>
<td></td>
<td>4.03</td>
</tr>
<tr>
<td>mm</td>
<td></td>
<td>71.46</td>
</tr>
<tr>
<td>mm</td>
<td></td>
<td>3.43x2</td>
</tr>
<tr>
<td>mm</td>
<td></td>
<td>1320.4x1</td>
</tr>
</tbody>
</table>

Note: \( x_1 \) stands for \( t \); \( x_2 \) stands for \( l_{\text{slot}} \).

In this study, three different Kriging models, the 0th-order, the 1st-order and the 2nd-order Kriging interpolation models are considered. Unlike the polynomial based response surface models with explicit mathematical forms, Kriging models are generally described in matrix form [36] as:

\[
\hat{y} = f^T(x)(F^T R^{-1} F)^{-1} F^T R^{-1} Y \\
+ r^T(x)(Y – F(F^T R^{-1} F)^{-1} F^T R^{-1} Y) \\
\]

Here, \( \hat{y} \) denotes the prediction of one of the stent attributes, i.e., RR, DB, FS, P and \( \sigma_{\text{max}} \); \( Y_{n×d} \) is the corresponding known attribute sample value vector, where \( n \) is the sample size. Depending on Kriging type, \( f(x) \) and \( F \) takes different polynomial form:

for 0th-order Kriging,

\[
f(x) = 1 \text{ and } F = ([1 \ 1 \ldots \ 1]')_{n×1};
\]

for 1st-order Kriging,

\[
f(x) = [1 \ t \ t^2] \text{ and } F = (f(S_i) \ f(S_j) \ldots \ f(S_n))_{n×1}';
\]

for second-order Kriging,

\[
\hat{y} = [1 \ t \ t^2 \ t^3 \ t^4 \ t^5] \text{ and } F = (f(S_i) \ f(S_j) \ldots \ f(S_n))_{n×6}';
\]

\[
\hat{y} = [R(S_1,x) \ R(S_2,x) \ldots \ R(S_n,x)]'
\]

With each element \( R(S_{i},x) = \exp\{\hat{\theta}(S_{i} – S_{i})^2 + (S_{i} – t_{i})^2\} \), where \( q, r = 1, 2, \ldots, n \). \( \hat{\theta} \) is the MLE that minimizes correlation function \( \varphi(\theta) = |R|^2 \sigma^2 \), where the variance \( \sigma^2 \) is:

\[
\sigma^2 = \frac{1}{n} \{Y – F(F^T R^{-1} F)^{-1} F^T R^{-1} Y\} R' \{Y – F(F^T R^{-1} F)^{-1} F^T R^{-1} Y\}'
\]

Obviously, Kriging methods involve a lot of calculations; fortunately, there are software tools [36] available for automatically handling the aforementioned calculations. To this end, accuracy, efficiency, and robustness of each resulting surrogate model are investigated and compared for the two different surrogate techniques and the two different sampling schemes.

Figure 12 shows a graphical comparison of the different surrogate models, i.e., 2nd-order RSM polynomial, 0th-order Kriging, 1st-order Kriging, and 2nd-order Kriging, for the five attributes, i.e., RR, DB, FS, P and \( \sigma_{\text{max}} \), which are listed at the left side of the corresponding graph. Since there is an analytical solution for stent attribute Volume, it does not need surrogate model.
The graphical comparisons appear to indicate that there are small discrepancies between different surrogate models for the attributes foreshortening (FS), pressure (P) and maximum allowable stress ($\sigma_{\text{max}}$). However, for radial recoil (RR) and dogboning (DB), there are significant differences in the surrogate models. The question of how to choose the most appropriate surrogate model can be perplexing, since there exists no a priori information about the functional behavior of these attributes. The situation is complicated by the fact that these two attributes (RR and DB) are critical in the optimum design of stents, and hence, the errors associated with the surrogate model will have a significant impact in the final design. Figure 13 highlights the importance of sampling size. While an optimal sampling size cannot be known a priori, it is clear that a larger sampling size will provide a better model than a small sample size. The following sections detail the errors from using these surrogate models in the optimal stent design process.
The purpose of surrogate models in engineering design of systems is to discriminate among competing design alternatives and predict the optimal design candidates accurately and efficiently. To study the modeling errors from using different surrogate models, the overall utility (MAU) based on simulation results and the particular design preference of the designer (Table 2) are constructed using each surrogate model. Figure 14 shows MAU plots from using the 0th- and 1st-order Kriging models. The figure confirms the utility method’s ability to map the design information onto a single scalar value in a multi-attribute design scenario. At this particular setting of designer’s preference, the utility method is shown to be robust against modeling errors.
preferences, the utility plot is sensitive in the high value zone, suggesting possibly that many designs can yield similar utility values. However, this is one hypothetical case, and the MAU plot will be different if the preferences are changed.

However, with different surrogate models, the predicted optimal designs may vary significantly. Figure 15 and table 7 demonstrate that, based on 10 LHS data, the prediction from 1st-order Kriging is significantly different from other 3 predictions; in fact, this prediction (t=0.02, lslot=3.2) is infeasible as the finite element analysis simulation based on this configuration never converged. The challenge then is how to choose the most appropriate model that will guarantee accurate and reliable design solution. However, the best solution may not be known without first identifying the best model for the design process. Therefore, in the absence of a priori knowledge or clairvoyance, the only mechanism to check the fidelity of the models is to validate them at the predicted optima. Model validation at the predicted optima can not only provide the most accurate assessment of the modeling errors, but can also enable guiding information about future subsequent model updating.

For the purpose of contrasting, the relative errors associated with each surrogate model of individual stent attributes, i.e. RR, DB, FS, V, P, and σ\text{max}, are plotted in Figures 16-21. The errors are estimated at the predicted optimal points listed in table 7, except for the infeasible point predicted from the first order Kriging model. The horizontal axes list stent attributes, and vertical axes show the error measurements using different surrogate models at their predicted optima. The errors are calculated by contrasting the surrogate model results to the FEA simulation results at the predicted optimal stent configurations. In the legends, if the errors of the models are estimated at their own predicted optimal points, the “@...”s are ignored. Figures 16-18 show the results for the 10 point sampling scheme, and Figures 19-21 illustrate the results from the 5 point sampling scheme.

Figure 16 indicates that the errors associated with RSM polynomial are significantly larger than those associated with the 0th-order Kriging surrogate model. Figure 17 shows that the errors associated with the RSM polynomial are comparable or slightly larger than those from using the 2nd-order Kriging surrogate model. From Figure 18, the results of 0th-order Kriging surrogate model can be inferred to be significantly better than the 2nd-order Kriging surrogate model in terms of fidelity at the predicted optima. All surrogate models tend to have high errors associated with the pressure (P) estimation indicating the great sensitivity of P over the design space. The zero errors associated with the volume (V) predictions are expected as they are deterministic analytical calculations, requiring no simplifications. The observations that errors fluctuate over zero indicate that, with the identical sampling design, the built surrogate models deviate from the original FEA models in a random manner: some predict more than the reality is; and others predict less. This result conforms to the fact that they are built through different modeling methods and each of them is actually a “statistic” derived from sampled data. In this specific problem and particular sampling scheme, Kriging methods are significantly better than RSM approaches. However, the conclusive statement about which method is better can’t be made until “sufficient” studies have been done that can reduce errors in statistical inference.

### Table 7: Predicted optimal design from different surrogate models (sample scheme: 10 LHS)

<table>
<thead>
<tr>
<th>Surrogate model</th>
<th>Predicted Optimal Design</th>
<th>t</th>
<th>lslot</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSM polynomial</td>
<td></td>
<td>0.136</td>
<td>2.906</td>
</tr>
<tr>
<td>0th-order Kriging</td>
<td></td>
<td>0.111</td>
<td>2.934</td>
</tr>
<tr>
<td>1st-order Kriging</td>
<td></td>
<td>0.020</td>
<td>3.200</td>
</tr>
<tr>
<td>2nd-order Kriging</td>
<td></td>
<td>0.136</td>
<td>2.961</td>
</tr>
</tbody>
</table>

![Figure 15: Comparison of multi-attribute models built from different surrogate techniques](image)

![Figure 16: Error comparison: 0th-order Kriging model vs. RSM polynomial (sample scheme: 10 LHS)](image)
A similar analysis of the surrogate models using the 5 point sample size shows that the number is insufficient for creating the 2nd-order full quadratic RSM polynomial model and the 2nd-order Kriging surrogate model. Alternatively, the 2nd-order pure quadratic RSM polynomial model, the 0th-order Kriging and the 1st-order Kriging surrogate models are compared. Table 8 lists the associated dissimilar predicted global optimal solutions.

Table 8: Predicted optimal design from different surrogate models (sample scheme: 5 LHS)

<table>
<thead>
<tr>
<th>Surrogate model</th>
<th>Predicted Optimal Design</th>
<th>t</th>
<th>Islot</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSM polynomial</td>
<td></td>
<td>0.127</td>
<td>2.898</td>
</tr>
<tr>
<td>0th-order Kriging</td>
<td></td>
<td>0.171</td>
<td>3.200</td>
</tr>
<tr>
<td>1st-order Kriging</td>
<td></td>
<td>0.175</td>
<td>2.758</td>
</tr>
</tbody>
</table>

In this setup, errors associated with the RSM polynomials are consistently smaller than both Kriging models, especially about the predictions of stent attribute FS and P (Figures 19-20). However, none of the optimal solutions correspond to the results from the 10 point sample scheme. In fact, with such a sample size, the estimated variances calculated from the scarce data can be very large, undermining the rationale behind the statistical methods. With the increase in sample size, the errors associated with the Kriging methods reduce considerably, indicating the sensitivity of Kriging methods to the sample scheme. It is also interesting that the 1st-order Kriging surrogate model shows smaller errors compared to the 0th-order Kriging model in terms of fidelity at the predicted optimal solution (Figure 21), though the 0th-order Kriging method came out on top in the 10 point sample scheme (Figure 18).
Error comparisons among different surrogate techniques suggest that there are significant variations in the predictions of global optimal design solutions; without a priori knowledge on the system behavior and the suitability of a particular surrogate technique, the predictions made from any one particular surrogate model cannot be accepted without validation at design points.

SUMMARY

This paper presents the development of a simulation models-based approach to the design of stents. The three main phases of the simulation-models based design approach are discussed in detail, namely, the development of appropriate engineering analysis models, the construction of preference-based decision models, and the statistics-based surrogate models using different sampling schemes and methods for optimization. The results suggest that the simulation-models based approach can provide the basis for systematic design of complex medical devices such as coronary stents. The results also show that the fidelity of the simulation-models based design approach are heavily influenced by not only the surrogate models, but also the sampling scheme which can be a decisive factor in the successful implementation of statistics based surrogate models. A general conclusion is that if there is no a priori knowledge about the studied system or modeling techniques, the resulting models have to be validated, irrespective of the surrogate approach used in the design process, before the results are considered for implementation. Such a validation process is critical to checking the fidelity of the analysis models, the consistency of the decision models, the appropriateness of the surrogate models, and most importantly, the accuracy, reliability and robustness of the resulting design solutions.

ACKNOWLEDGEMENT

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REFERENCES