Evaluate Medical Device Design Robustness by Combining Statistical and Probabilistic Tools with Finite Element Analysis

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Abstract: Finite Element Analysis (FEA) has been widely used to analyze the in vivo structural response of implantable medical devices and assess device performance, reliability and durability. Take stents for example. Several characteristics like radial force, peak stresses and strains and fatigue safety factors can be determined using these modeling techniques. As all physical phenomena are stochastic, all design parameters have built-in variability. On the other hand, stents are typically modeled with nominal dimensions and material properties. Minimum and maximum dimensions are used in certain instances, while other dimensional variances are often not considered. In addition, the in vivo boundary conditions also vary widely across patient population. Therefore, in order to obtain a robust design, parameter variations and their influence on device performance need to be understood. Probabilistic analysis techniques like Monte Carlo sampling combined with FEA are helpful in understanding these stochastic processes and in determining probability of failure and design reliability. In this study, FEA using Abaqus is combined with statistical and probabilistic analysis using Isight to demonstrate how these techniques work together to evaluate the robustness of medical device designs.

Keywords: Implantable Medical Device, Probabilistic Modeling, Stent

1. Introduction

Endovascular Stent-Grafts are used to prevent rupture of vessel wall due to Aneurysm (Figure 1), a disease which causes weakening of walls and abnormal swelling of Aorta. The stent grafts consist of stent rings attached to membrane-like graft material. Long-term performance of a stent graft depends on radial strength and fatigue resistance of stent rings as well as other factors.

Finite Element Analysis (FEA) has been widely used to understand the in vivo structural response of implantable medical devices like stent-grafts. Upon careful verification and validation, FEA models can provide device designers and regulatory agencies with critical characteristics for the device including performance, reliability and durability. Take stents for example, several characteristics like radial force, peak stresses and strains and fatigue safety factors can be determined using these modeling techniques. Frequently, these device characteristics are competing with each other. In terms of stents, in order to satisfy the targets of better performance and higher packing density for lower profile delivery catheters, the stents need to be optimized further, which in many cases results in reduction of safety margins. It is important to understand how design parameters affect these competing characteristics to achieve optimal design. FEA models combined with statistical tools such as DOE and response surface could be helpful in understanding the design space.

As all physical phenomena are stochastic, all design parameters have built-in variability. On the other hand, stents are typically modeled with nominal dimensions and material properties. Although, minimum and maximum dimensions are used in certain instances (e.g. stent strut width, thickness etc.), other dimensional variance due to manufacturing (Figure 1) are often not taken into consideration. In addition, the in vivo boundary conditions like radial distension of the vessel also vary widely across patient population. Therefore, in order to obtain a robust design, the variation of such parameters and their influence on the device performance outcome need to be understood in depth. Probabilistic analysis techniques like Monte Carlo sampling combined with FEA could be helpful in understanding these stochastic processes and could also help in determining probability of success and design reliability. With advances in high performance computing, large number of analyses can now be performed in a reasonable amount of time, which allows device designers and analysts to combine statistic and probabilistic techniques with FEA to evaluate medical device robustness and further optimize designs.

In this study, building upon a stent-graft design example, FEA using Abaqus is combined with statistic and probabilistic analysis using Isight to demonstrate how these techniques could work together to evaluate the robustness of medical device designs.

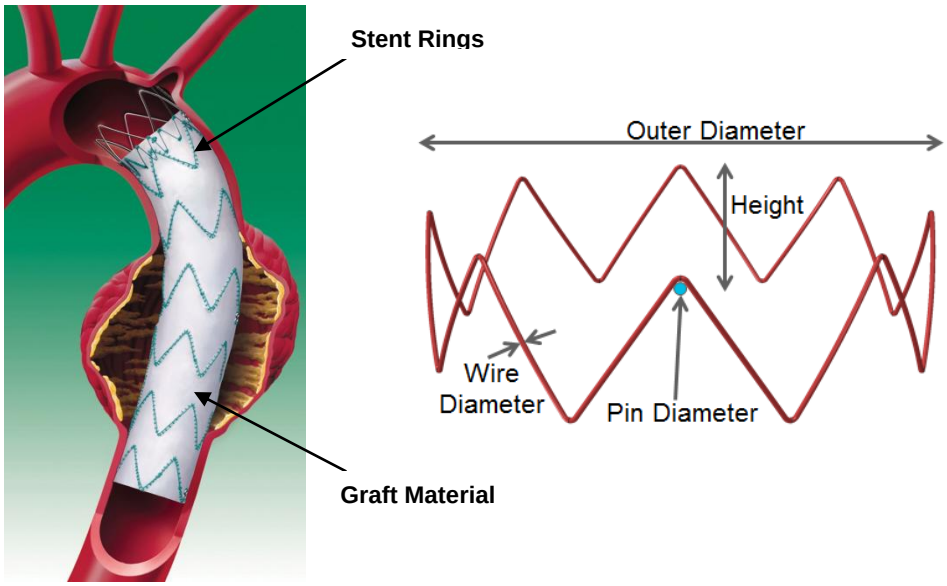

Figure 1: Thoracic Aneurysm with Talent™ Thoracic stent graft (left) and stent design parameters which could affect its performance (right).

2. Methods

A parametric model of a stent ring was developed within Abaqus/CAE with a rigid representation of vessel to mimic in vivo environment. The expected manufacturing variability such as stent height, outer diameter, crown radius, wire diameter, material properties and vessel diameter were incorporated in the model for this study. The stent geometry consisted of a single half-crown due to symmetric design with symmetry boundary conditions at open ends and 6x6 mesh with C3D8R element across its circular cross-section. Nitinol superelastic material properties were assigned to the stent with parameters determined from experimental data. The stent was subjected to a sequence of quasi-static loading steps in Abaqus/Standard to capture different stages of deformation i.e. crimping to delivery catheter, deployment to vessel and pulsatile loading due to vessel dilatation. The safety factors were calculated based on the strains in the stent during pulsatile loading and the endurance limit of Nitinol. The output parameters of interest were 1) crimp strains to ensure that stent does not undergo any permanent plastic deformation, 2) radial force at deployment to ensure proper stent-graft apposition to vessel wall and 3) safety factor under fatigue loading.

A Design of Experiment (DOE) was run with 200 virtual experiments using Abaqus as the FEA solver and the Latin Hypercube technique[1] as the DOE generator in Isight (Figure 2). The Latin Hypercube technique allows for more combinations for each input parameter therefore it is more efficient compared to full factorial methods for the same level of accuracy. The input parameters for this DOE were varied based on literature data and manufacturing tolerances as follows:

- Stent Height: ±10%
- Wire Diameter: ±10%
- Crown Radius: ±25%
- Outer Diameter: -1% to +2%
- Vessel Diameter: ±2.5%
- Material plateaus: ±10%

The outputs from the DOE were used to create a response surface approximation within Isight which was further used for probabilistic analysis (Figure 2). Sufficiently large number of points for DOE (200 points) ensured that approximation errors were less than 1% for all the outputs based on the error analysis. This approximation was combined with expected manufacturing variability in stent height, outer diameter, crown radius, wire diameter, material properties and vessel dilation (Figure 3) to generate a probabilistic distribution of crimp strains, radial force and fatigue safety factors. Several probabilistic sampling point distribution techniques are available in Isight ranging from a complete random sampling to targeted sampling around the failure point. Users choose the technique based on the purpose of the probabilistic analysis and the desired number of sampling points. To demonstrate differences between these techniques, a few of the sampling techniques were applied in this study to compare the advantages and disadvantages of each approach. Specifically, the traditional Monte Carlo sampling method,[2] an analytical method based on Taylor's series expansion,[3] a Most Probable Point (MPP) search method,[4] and a hybrid (MPP search + sampling) method called importance sampling[5] were used to measure performance variation and determine the probability of success and the confidence interval. The lower and

upper bounds of the performance measurements were obtained and compared with stent performance specifications.

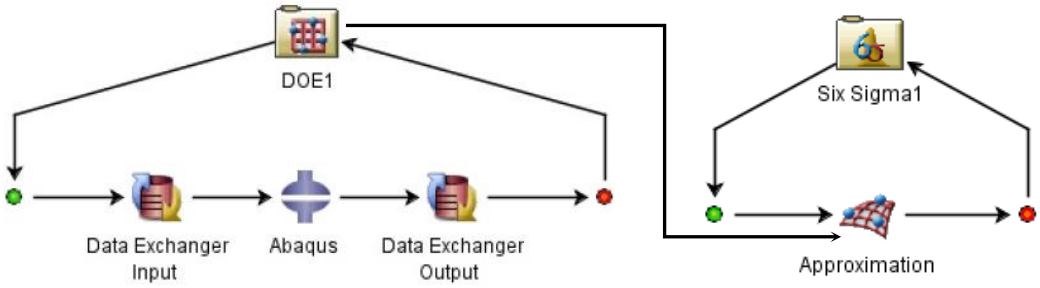

Figure 2: Isight workflow for DOE (left) and probabilistic evaluation (right).

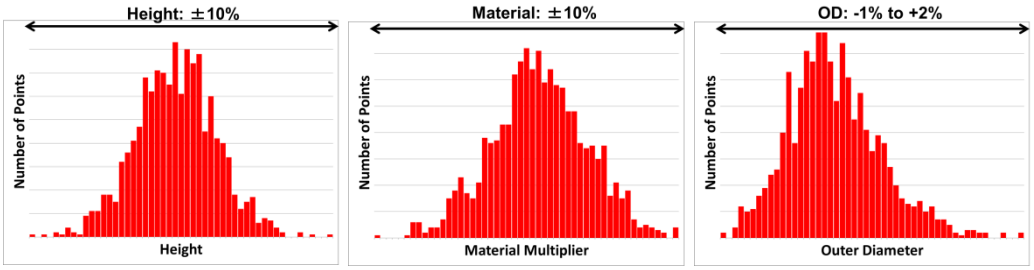

Figure 3: Statistical Distribution of Inputs used for probabilistic analysis.

3. Results

A probabilistic approach was developed and successfully implemented to understand the variation in the radial and fatigue performance of a stent ring with different manufacturing tolerances and boundary conditions (Figure 4). Further insight into sensitivity of design parameters on performance characteristics like radial force and crimp strains was developed using sensitivity plots (Figure 5). In this example, wire diameter and stent height were determined to be the most critical design parameters to achieve target crimp strains. In addition, crimp strains had the lowest probability of success based on superelastic strain limit of 8% (Figure 6). Limited radial force data was also collected from bench test under deployed configuration. The data ranged from 3.2 to 3.8N. Radial force data from the Monte Carlo simulation varied from 2.4 to 5.7N with 45% of data lying within the range of 3.2 to 3.8N (Figure 7). A comparison of radial force data from bench test and simulation provided sufficient evidence that these probabilistic simulations were able to accurately capture the inherent variability in stent performance.

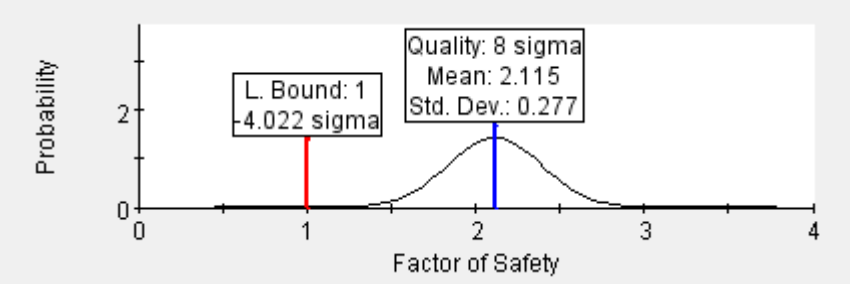

Figure 4: Probabilistic distribution of factor of safety from the Monte Carlo simulation.

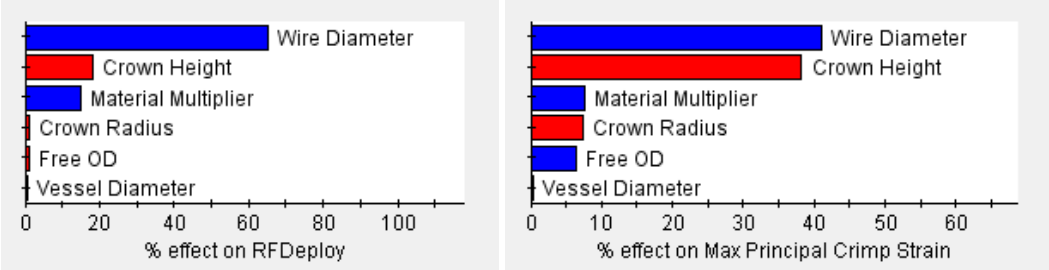

Figure 5: Sensitivity plots (Pareto distribution) for radial force (left) and crimp strains (right). Blue bars indicate positive correlation and red bars indicate negative correlation.

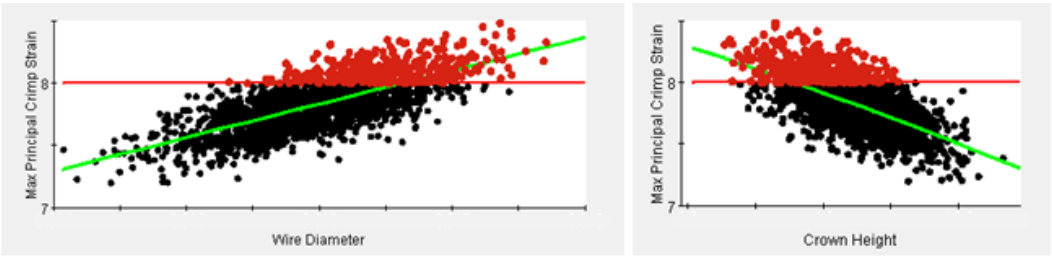

Figure 6: Scatter plot of crimp strain with change in stent wire diameter (left) and crown height (right). Red data points indicate points which failed the criteria of crimp strain less than 8%. Green line represents the trend line indicating positive correlation with wire diameter and negative correlation with stent crown height.

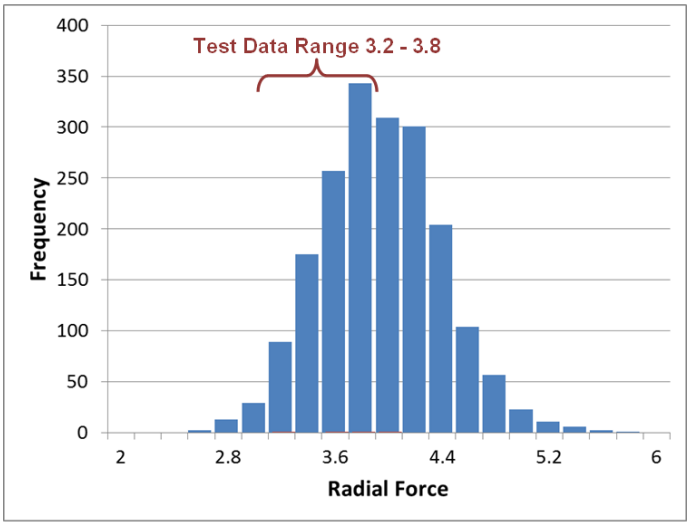

Figure 7: Radial force frequency distribution obtained from Monte Carlo simulation. Test data ranged from 3.2 – 3.8N for four samples which lies well within the values predicted from simulation.

Comparison of various probabilistic (Six Sigma) techniques (Table 1) reveled that Monte Carlo simulations require largest number of sampling points (1526) to provide converged results. Lower number of samples for Monte Carlo sampling method resulted in deviation from most accurate values for both probability of success and confidence interval. On the other hand, importance sampling with 505 samples predicted a tighter confidence interval. Other techniques like mean value and first order reliability methods were also able to predict similar probability of success as the other two methods with much smaller sample size.

Table 1: Stent probabilistic analysis results

Technique (samples)	**Probability of Success with 97.5% one sided confidence**
Monte Carlo (1526)	0.807 – 0.0198
Monte Carlo (1000)	0.813 – 0.0242
Monte Carlo (500)	0.818 – 0.0339
Importance Sampling (505)	0.784 – 0.0126
Technique (samples)	**Probability of Success**
Mean Value Method (7)	0.796
First Order Reliability Method (355)	0.797

4. Discussion

In this study, FEA in combination with statistical and probabilistic techniques was used to examine the effect of various manufacturing tolerances and boundary conditions on robustness of stent design. Isight framework was used to perform these simulations which proved to be robust. Also, access to scripting interface and parametric modeling in CAE served as a useful tool.

Isight provided access to various Six Sigma techniques which were applied to the stent design for comparison. Mean value method used lowest sample size to accurately predict probability of success and importance sampling resulted in tighter confidence interval. Monte Carlo simulations which were based on completely random distribution of points showed sensitivity to sample size as expected and also required largest sample size for converged results.

Various other tools like Pareto plots helped in identifying wire diameter and stent height to be the most critical design parameters.

Since, all the Six Sigma techniques were based on approximations, they ran fairly quickly (less than a minute) on a single CPU whereas the 200 model DOE took 4 hours on a Linux cluster with 4 cores. A large DOE was selected to minimize error in the approximation generated based on the results of this DOE. Errors were found to be less than 1%.

It should be noted that several components of this model may need further investigation to validate this approach against manufactured stents as limited radial force data was available from bench test. In addition, more realistic vessel modeling could help in accurately capturing the in vivo environment.

Next step of this analysis could be modeling other components like delivery system parts and graft material to better predict the delivery system and implanted device performance.

5. Conclusion

This study showed that FEA in combination with probabilistic modeling techniques can help us examine the effect of various manufacturing tolerances and boundary conditions on robustness of a stent design. Most sensitive parameters can be identified and tighter tolerance could be used to reduce performance variability. This approach can also be used to determine the limits within which current design would satisfy intended use thus reducing the risk of re-design during design verification testing.

Most device manufacturers already perform FEA analysis for design evaluations and the regulatory agencies have also recognized the importance of such analysis in determining the device performance. With these additional techniques of statistic and probabilistic analysis, the stochastic nature of device manufacturing, deployment and in situ conditions could be incorporated for in-depth evaluation of robustness of the design.

6. References

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