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In a Preliminary Simulation Data, Stent with Thinnest Strut Beta Crystalline Titanium Gold Alloy (β-Ti-Au) Outperforms Typical Implants

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Abstract **Background:** Large volume of data support the overall safety of coronary stents for cardiovascular disease. Yet, one cannot lose sight of their shortcomings such as restenosis; hence stents continue to evolve in lattices, materials, and drugs. Studies outlining the successful use of titanium gold alloy stents to counter these issues are lacking. **Methods**: In this analysis we obtained available historical manufacturing records on routinely used stents to compare to two revolutionary titanium-gold alloy stents. By using a 3D CAD finite element analysis space, each stent type was tested for flexibility, rigidity, and radial forces. Except for lengths and diameter, each type was held to their own strut geometry and thickness. Our analysis focused on using Von Mises Stress and resulting deformation or expansion. Our assessments were performed by using discrete changes and Pearson's chi-squared statistics to obtain significance of our findings. Three lengths: 15mm,27.5mm and 40mm were tested for each type. Comparisons were obtained from the mean percentage length or diameter (3.5mm) changes. ***Results:*** β-Ti-Au alloy in our hexagonal mesh was significantly more expansive (78.29 percent gain in diameter under 7 atm. than Orsiro Hybrid (the baseline). $p < 0.001$. The best performance in vertical crush testing was obtained from our second original structure, titanium – gold alloy stent 1 (0.8 percent vs control). Nobori was the most longitudinally flexible in that testing category but was closely matched by beta titanium – gold alloy (1.97 percent vs 2.19 percent) with promus PREMIER's performance serving as the zero-reference point. In radial strength testing, our opened and closed titanium-gold structures first and second designs respectively came second and third to Orsiro (10.03 percent >9.09 percent >7.80 percent). Maximum changes in displacements, 0.19 and 0.25. Both values were significant. (95% CI 0.11-0.27, 0.17-2.33). **Conclusion:** Routine use of Titanium in coronary stents has been hindered by its low density, elastic modulus and strength; contrary these results suggest that by mixing titanium with gold and on the right structure the alloy can be constructed with a thin strut for percutaneous coronary intervention.

Keywords: *beta crystalline titanium gold alloy (β-Ti-Au), coronary artery disease, cardiac catheterization, percutaneous coronary intervention, coronary stents, drug-eluting stents, atherosclerotic heart disease, cardiovascular disease, interventional cardiology, nitinol, titanium, cobalt chromium, stent technology, myocardial infarction*

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1. Introduction

Hypertension, obesity, hypercholesterolemia, and endothelial dysfunctional factors, in a milieu of familial predispositions outcomes coronary plaques that affect millions of people around the globe hence the use of coronary stents as one of the effective reperfusion modalities. In the past, intense research has been devoted to various stents using AISI 316L (the low carbon version of stainless steel 316), AISI 316F (with chromium, carbon, nickel), L-605 (Cobalt-chromium alloy), Nitinol, MP35N, titanium-nitride-oxide, among the many ranks since the inception of coronary and vascular stents. [1]

Despite significant advances made from bare metal to drug-eluting stents (DES), there is a persistent challenge of obviating present stent problems such as impairment of re-endothelization, restenosis, fracturing, and late stent thrombosis [2] with one that is definitive after implantation, even in longer and tortuous vessels such as the right coronary artery or the obtuse marginal.

Besides the operator, this definitive performance portends from numerous properties such as the stent's excellent coronary intimal apposition, radio-opacity, strut conformability - flexibility, rigidity and biocompatibility not only to the goal, but also in minimizing inflammation post balloon expansion. These qualities can be fundamentally accomplished by carefully choosing a material composition that can be modeled into a specific structural connectivity [3] and perhaps a dual bolus-maintenance coating strategy.

Table 1. Alloy Properties and Comparison

Stent Alloy	Nitinol [4,5]	316L [6] Stainless Steel	L-605 [7] Cobalt-Chromium Alloy	MP35N [7] Cobalt chromium alloy with nickel
Density (g/cm^3)	6.45	8	9.22	8.414691
Tensile Strength Yield (MPa)	690	205	414	345
Tensile Strength Ultimate (MPa)	895	515	1035	758
Modulus of Elasticity (GPa)	83	193	243	233
Elongation at Break	25.00%	60.00%	50.00%	60.00%
Reduction of Area		55.00%	40.00%	70.00%
Specific Heat (J/g-°C)	0.837	0.500	0.385	0.502
Hardness, Vickers	326	155	148	220
Volume per 100g of material (cm^3)	15.50	12.50	10.85	11.88

Titanium, labeled in astrological geographic observations as metal of the Gods is perhaps due to its relative abundance on the moon; gold the 79th element on the other hand, is an earthly metal that not only adorned the wrists and necks of Homo sapiens and in their electronics, but also constituents of its bulk and nanoparticles have been explored as a therapeutic armamentarium in the cure for diseases such as arthritis and cancer; this perhaps by exploiting its conduit or anti-inflammatory properties. [8,9] Titanium alloys for stenting such as **A**lpha/**B**eta ASTM F1295 have been investigated, but with concern for exceeding ultimate tensile strength, and low density regardless of their excellent biocompatibility and visibility on imaging. [10] Its density of 4.51 g/cm^3 in pure form, has not made it a striking element for stent-makers; the current gold alloy offers a perfect salvage in increasing its specific strength as well as elongation. While the proportions and processing methods can shift the phase of Ti-Au (titanium gold alloy), the mixture approximates many ideal metallurgical properties for stenting in several respects; first, the combination takes a strength that is radially stable without compromising a trial of thin strut. In our statistical analysis software, we can achieve an ideal meshing alloy in a range of 8.9 – 10.8 g/cm^3. This makes it desirable for flexibility, deliverability and amenable for smaller occlusive lesions. While elongation is improved, unlike nitinol's and chromium cobalt's elasticity, self-expansibility is a property that is yet to be known. As will be shown further, radial force stresses are better resisted by β-Ti-Au than stainless steel stents, another property gained from its tensile strength.

We posit that this futuristic balloon expandable β-Ti-Au coronary stent because of its inherent desirable characteristics when modeled on the right structure will have an overall better preclinical testing performance.

2. Methods

We scouted the following databases; MEDLINE, PubMed, Embase, manufacturers URL's and ScienceDirect for work containing engineering data on stents used in interventional cardiology. Nobori (Stainless Steel, Terumo Europe), Promus PREMIER (Platinum Chromium, Boston Scientific) and Orsiro (Cobalt Chromium, Biotronik) to be compared to the β-Ti-Au Stent 1 (this was our first structural design) and β-Ti-Au Stent 2 (the second). From manufacturer's data, identical categorical testing representations of the stents were created for finite element testing in the 3D CAD. This was done by holding each stent to their own design geometry and material composition. This way the data was consistent and comparable across all types. The parameters examined included: *longitudinal flexibility, radial strength, rotational stress*, *vertical crush* testing and *expansibility* at 5 to 14 atmospheres of balloon pressure.

The simulation software output Von Mises Stress values, 1st Principal Stress (Tensile Mpa), and with maximum displacements. This procedure was validated with prior study [11] using stainless steel 316l output of Von Mises stress. Although several real-world implantation variances [12] are not accounted for, this method of computational analysis of stents provide a close surrogate in such preliminary studies. Under each simulation, three respective lengths were tested for each stent. Our values were input into a spreadsheet to resolve the percentage change for diameter and lengths. In non-radial testing, these variables would change depending on the requirements of the stent itself, while the value kept constant would be 3.5mm for luminal diameter.

Stents have integral connectors and overall multipart strut necessitating the vertical crush test, a simplified loading test which gives an indication of the integral stability of the meshing assembly when acted upon by a vertical force. This is achieved by holding one end constrained, while the opposite is collapsed by a weight thereby noting the resulting deformation. Preservation of the luminal diameter to more than 50% is essential if any buckling occurs. Coronary stenting techniques require a stent which is flexible, yet rigid at certain points. The *longitudinal flexural* testing is a bending deflection test representing easy deliverability of stent to the area of interest and the ability of the stent to mitigate the intimal contours with less mechanical and cytotoxic cascades. This test can be performed in several ways; in our approach, we held one end constrained, while the upper quartile was acted on by a perpendicular force. In operation, this longitudinal flexibility test is also crucial factor in overlapping stents especially with different grades and sizes. *Rotational Flexibility* test measures the ability for the scaffold to resist a twist deformation. FDA recommends measuring the torque strength of the stent delivery system when the distal tip is not free to rotate, by rotating the proximal end of the catheter until failure. [13] Atherosclerosis being a global vascular phenomenon, radial *strength or stiffness test* comes in handy to measure the ability for the stent to endure external peripheral crushing forces as in say reperfusion of severe peripheral arterial disease. The test holds both ends of the stent constrained while six forces act perpendicular to the tangent of the design near the midpoint noting the stress onto the outer circumference. Expansion test measures the ability for the stent to enlarge after crimping under a balloon-deployable condition. The test holds both ends of the stent constrained, while a catheter balloon of pressure 5 atm, 7 atm and 14 atm are used to determine the degree of expansibility. All testing was performed bare metal. Fatigue durability was not tested.

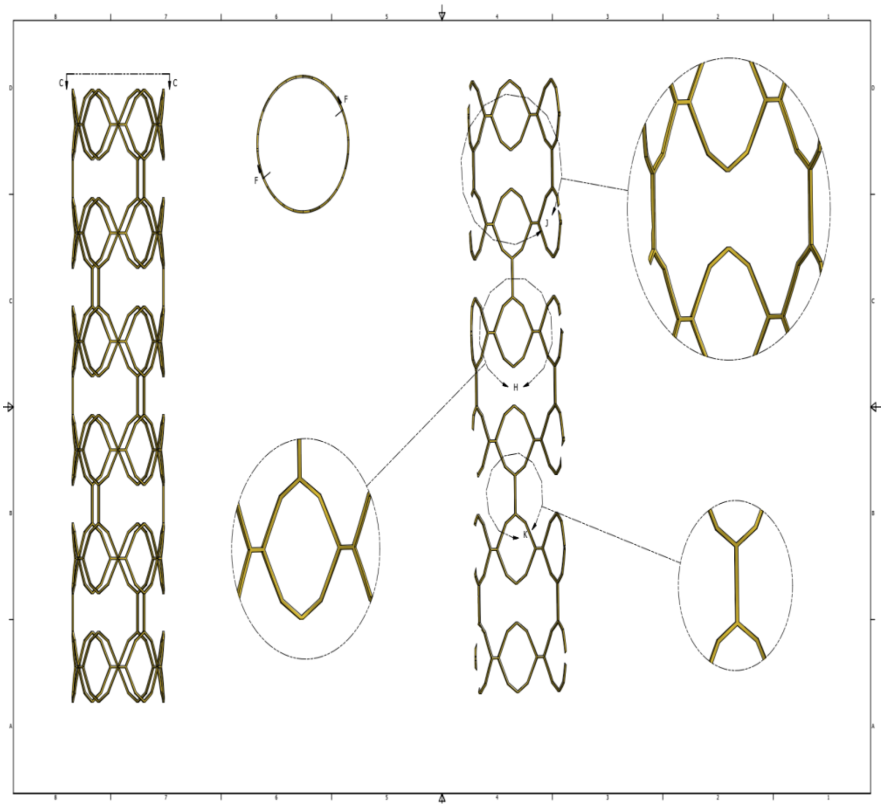


Figure 1. β-Ti-Au Stent 1 Design

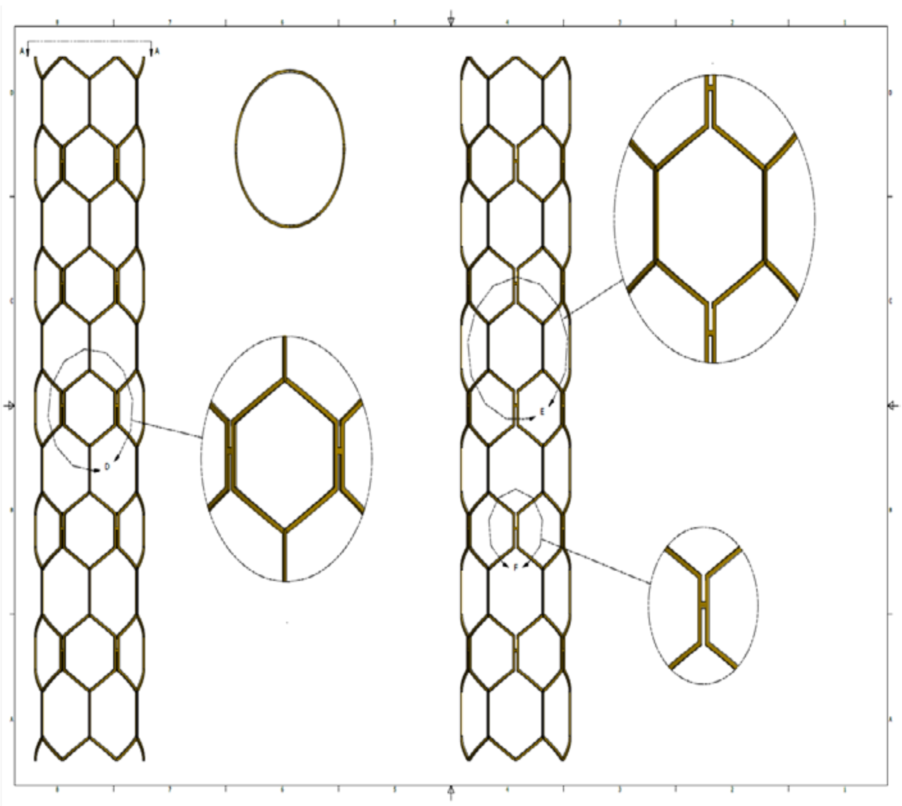


Figure 2. β-Ti-Au Stent 2 Design

Cross-sectional View

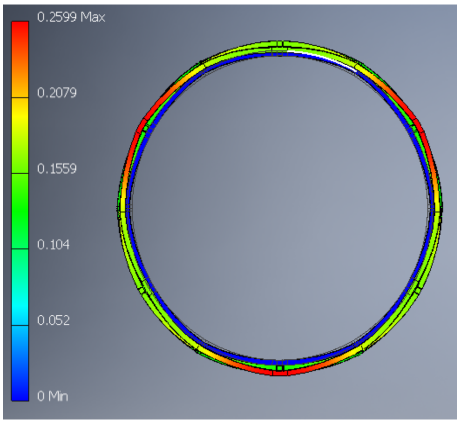


Figure 3. Cross-Sectional View of Vertical Crush Test β-Ti-Au Stent 2

Side View

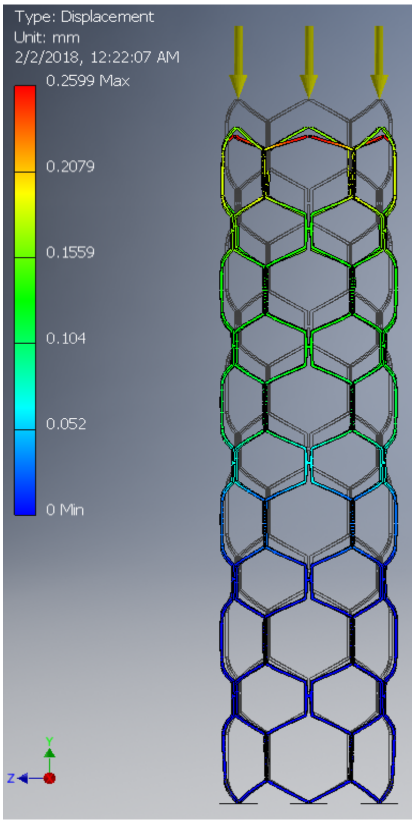


Figure 4. Side View of Vertical Crush Test β-Ti-Au Stent 2

Top down

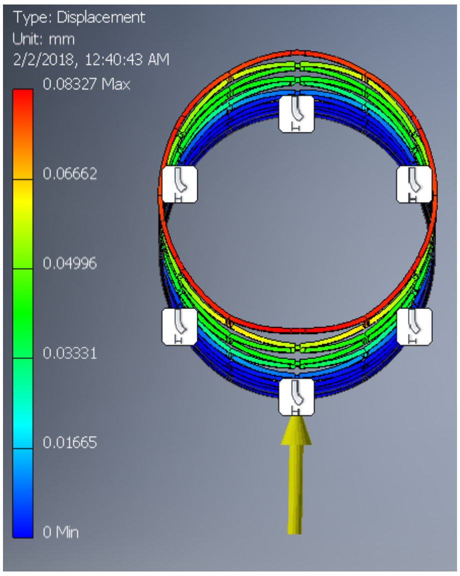


Figure 5. Cross-Sectional (Top-Down) view of Longitudinal Flexibility Test β-Ti-Au Stent 2

Side View

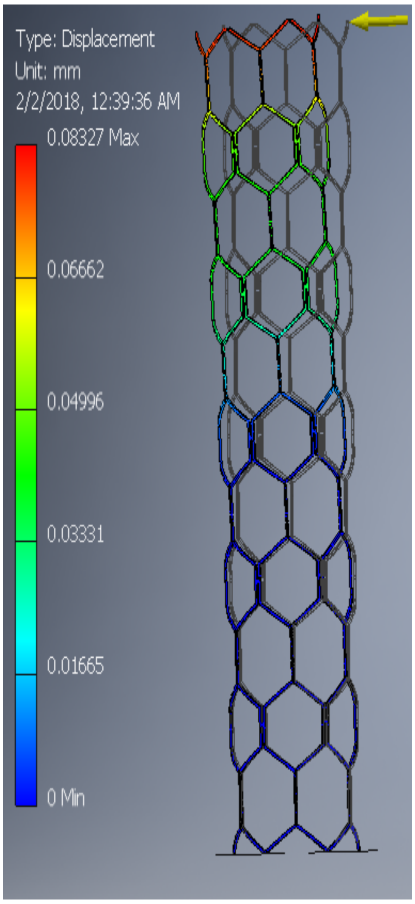
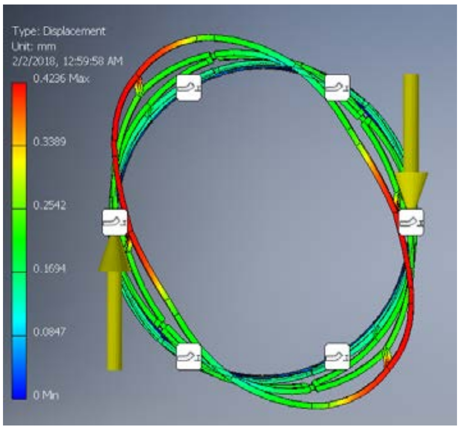
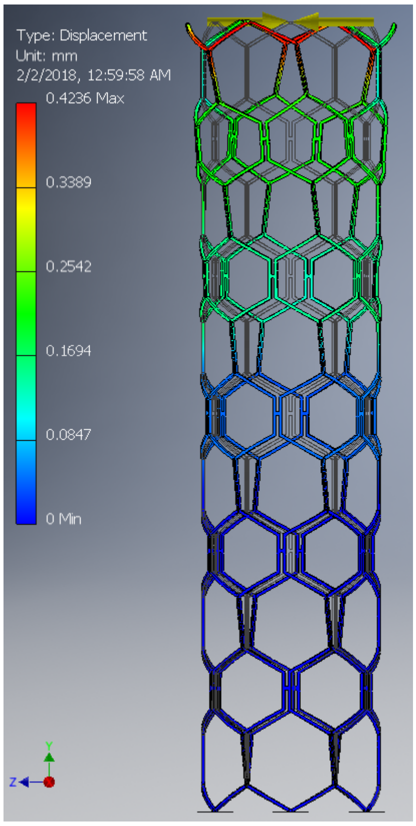


Figure 6. Side View of Longitudinal Flexibility Test β-Ti-Au Stent 2

Cross-sectional View	Side View
 **Figure 7.** Cross-Sectional (Top-Down) view of Rotational Flexibility Test β-Ti-Au Stent 2	 **Figure 8.** Side view of Rotational Flexibility Test β-Ti-Au Stent 2

3. Statistical Analysis

In a total of five stents, three characteristically unique commercial stent types were compared to our proprietary-modeled, slotted and meshed designs. The stent diameter and lengths were similar among the groups. Three lengths: 15mm, 27.5, and 40mm were tested for each type. In the expansion test, each type was tended to three pressures. Altogether 105 simulations were completed. We studied their performances by using percentage increments and Pearson's chi-squared test to derive statistical power. As appropriate, baseline characteristic was assigned to the stent with the lowest discrete value in that testing category. The findings have been summarized in the figures below.

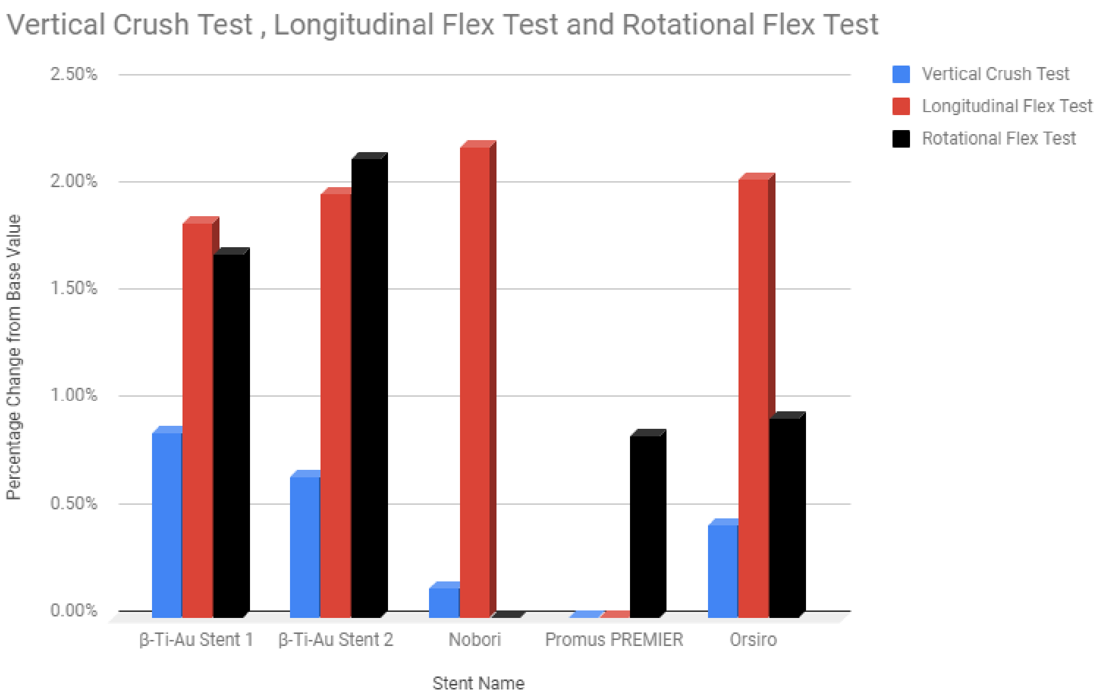


Figure 9. Vertical Crush Test, Longitudinal Flex Test and Rotational Flex Test

4. Results

In the vertical crush test, distinct improvement was observed in β-Ti-Au Stent 1 and had the highest performance of all the five types. This was followed by β-Ti-Au Stent 2. 0.86 percent vs. 0.66 percent. Promus Premier the control deformed by a mean of 0.611 mm. vs 0.38 mm of β-Ti-Au Stent 1 ($p < 0.001$), significant. With a 2.1 percent improvement from the base value, the Nobori stent, outperformed the rest of the group in Longitudinal flexibility test. However, it is worthy to note that both Stent 1 and 2, fell within the upper two standard deviations from the group mean (0.083mm), and whilst Nobori was the most longitudinally flexible, it ended up with inverse rotational flexibility capabilities thereby forming the control in the later testing category.

Stent 1 and Stent 2 had the smallest strut sizes; counterintuitively the overall achievement targets for resisting radial compression was slightly below Orsiro the highest in the group. In radial strength testing, our opened and closed titanium-gold systems first and second designs respectively came second and third to Orsiro (10.03 percent >9.09 percent >7.80 percent). Maximum changes in displacements, 0.19 and 0.25. Both significant. (95% CI 0.11-0.27, 0.17-2.33).

Balloon expansion at 7 atmospheres was responded with 66.03 and 78.29 percent improvements in Stent 1 and Stent 2 respectively. In this simulation comparison, both outperformed the nadir of the testing group. $P < 0.001$ with respect to the expansion test group. The trend correlated well with balloon pressure increments. Corresponding diameters are indicated on each circular loop.

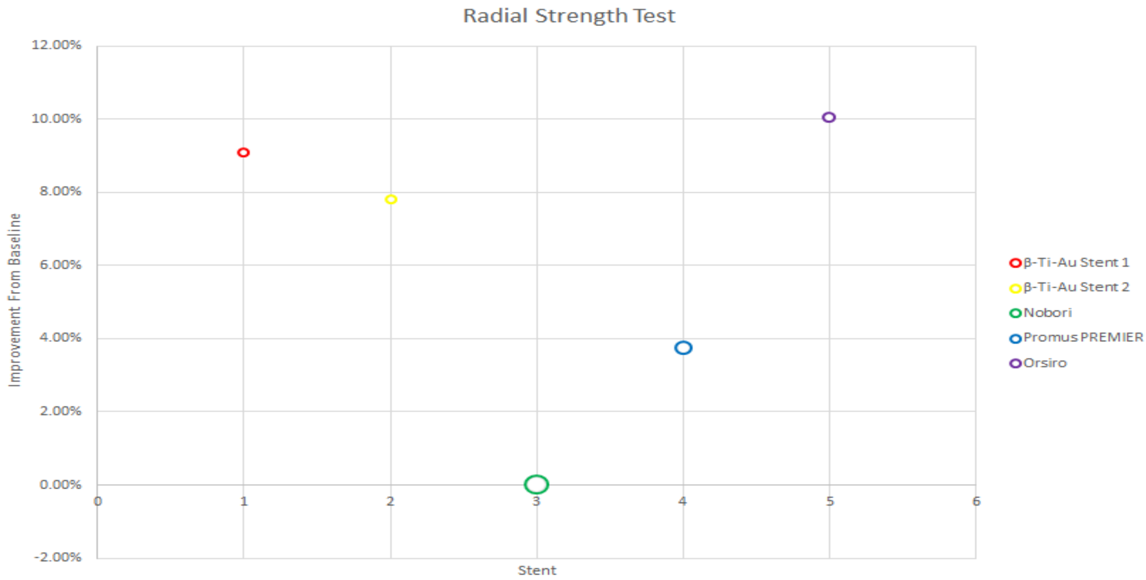


Figure 10. Radial Strength Test

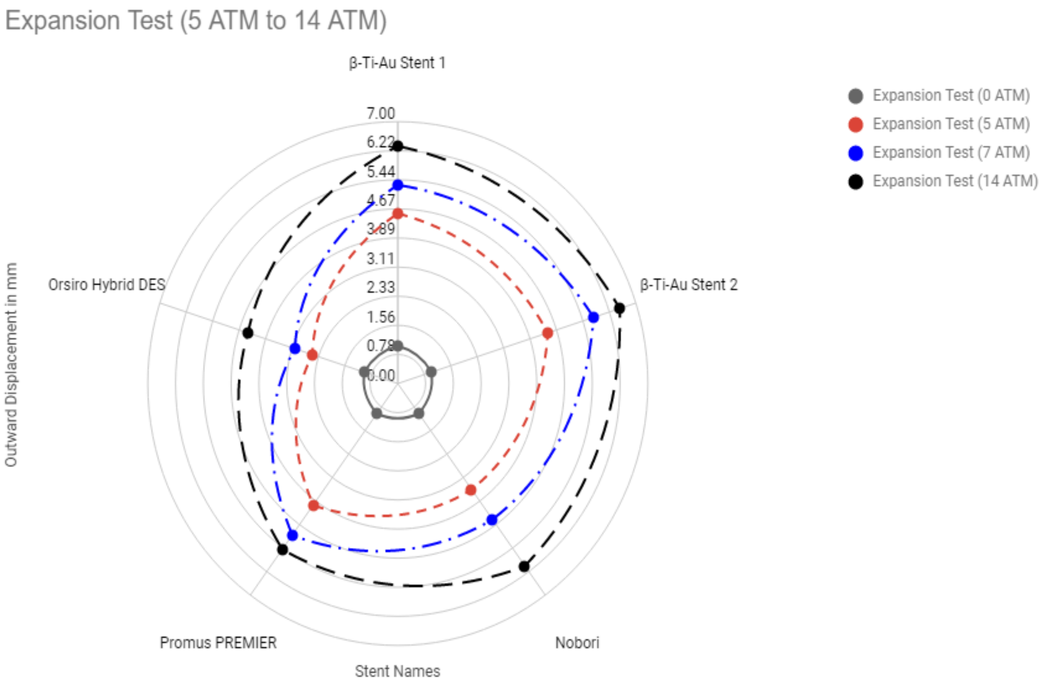


Figure 11. Expansion Test

5. Discussion

Our finite element preimplantation testing supports enhancement of all tested properties in beta titanium gold alloy as a stent material. The better end-points achieved signal high performance, and reductions in strut fracture or late stent thrombosis. Besides the intrinsic desired properties of the alloy, other imperative balances of the stent such as arrangement of connectors and their strut played into these results. Ultimate arrival at the outcomes were achieved with careful attention to safety - although being thin, considerations such as surface smoothing, addition of drug coating and chamfering approaches for trackability were considered. We achieved increments in function. In a framework of real-world implantation limitations, the aims of our study, the sparse manufacturing record available to us, these data represent significant advances from what is currently used. We accomplished the primary targets that refutes the null hypothesis thus meriting further testing.

6. Conclusion

Once stents continue to be key devices in percutaneous coronary intervention, there will always be yet another inspiring pursuit towards unravelling their limitations either by some esoteric platform in combination with an exceptional material or by changing the entire approach such as was tried with scaffolding stents. [16] Despite remaining questions, we captured the essential testing requirements and the major findings in this interesting study is that Beta titanium gold alloy is resilient to crushing yet expansive without remarkable compromises in other coronary stent testing matrices.

References

[1] O'Brien B, Zafar H[2], Ibrahim A, Zafar J, Sharif F. Coronary Stent Materials and Coatings: A. Technology and Performance Update. Ann Biomed Eng. 2016 Feb; 44(2): 523-35.

[2] Gregory D. Curfman, et al. Drug-Eluting Coronary Stents — Promise and Uncertainty. NEW Engl J Med 2007; 356:1059-1060.

[3] Shuichi Yoneda. Comparison of Stent Performance Between ZES and EES. Circulation. 2018;134: A13902.

[4] “Nitinol Technical Properties”. http://jmmedical.com/resources/221/Nitinol-Technical-Properties.html Accessed April 12, 2018.

[5] Stoeckel, Pelton, Duerig, Self - Expanding Nitinol Stents, Material and Design Considerations. European Raiology. 2003. http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.542.9850&rep=rep1&type=pdf. Retrieved 7/29/18.

[6] Stent platforms and materials. Journal of American College of Cardiology. JACC 1996; 27: 53.

[7] Technical Data, Physical and Chemical Properties of Cobalt Chromium. Medical Devices Certification Data. http://www.3trpd.co.uk/wp-content/uploads/2013/03/cobalt-chrome-alloy-co28-cr6mo-2012.pdf Retrieved 6/28/2018.

[8] Bagheri S, Yasemi M, Safaie-Qamsari E, Rashidiani J, Abkar M, Hassani M, Mirhosseini SA, Kooshki H. Using gold nanoparticles in diagnosis and treatment of melanoma cancer. Artif Cells Nanomed Biotechnol. 2018 Jan 26:1-10.

[9] Kubota T, Kuroda S, Morihiro T, Tazawa H, Kagawa S, Fujiwara T. [Novel HER2-Targeted Therapy Combined with Gold Nanoparticles. Gan To Kagaku Ryoho. 2016 Oct; 43(10): 1237-1239.

[10] P. PONCIN, J. PROFT. Stent Tubing: Understanding the Desired Attributes. Materials & Processes for Medical Devices Conference 8-10 September 2003.

[11] Trina Roy, Abhijit Chandra. Computational Modeling and Analysis of Latest Commercially Available Coronary Stents During Deployment, Science Direct. Procedia Materials Science 5(2014) 2310-2319.

[12] Hongxia Li, Tianshuang Qui, Bao Zhu, Jinying Wu, and Xichheng Wang. Design Optimization of Coronary Stents Based On Finite Element Models. The Scientific World Journal. Volume 2013 Article ID 630243.

[13] U.S. Food and Drug Administration. Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems - Guidance for Industry and FDA Staff. April 18, 2010.

[14] Kastrati A, Mehilli J, Dirschinger J, et. Al. Intracoronary Stenting and Angiographic Results Strut Thickness Effect on Restenosis Outcome (ISAR-STEREO) Trial]. Vestn Rentgenol Radiol. 2012 Mar-Apr; (2): 52-60.

[15] John A. Ormiston, Mark W.I. Webster, Peter N. Ruygrok. Stent Strut Thickness and Restenosis. Mar 2018Circulation. 2018; 105: e12.

[16] Harold L. Dauerman. The Magic of Disappearing Stents. Journal of the American College of Cardiology Oct 2011, 58 (15) 1589-1591.