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FEA of Drug-Eluting Stents and Sensitivity Analysis of a Continuum Damage Model for the Degradation of PLGA Coating

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Abstract— **Drug-Eluting Stents (DES) are commonly used in coronary angioplasty operations as a solution against artery stenosis and restenosis. Computational Bioengineering allows for the *in-silico* analysis of their performance. The scope of this work is to develop a DES Digital Twin, focusing on the mechanical integrity of its biodegradable coating throughout the operational lifecycle. The implementation leverages the Finite Element Method (FEM) to compute the developed mechanical stress field on the DES during the inflation/deflation stage, followed by the degradation of the polymer-based coating. The simulation of the degradation process is based on a Continuum Damage Mechanics (CDM) model that considers bulk degradation. The CDM algorithm is implemented on the NX Nastran solver through a user-defined material (UMAT) subroutine. For benchmarking purposes and to compare with the baseline design of the BioCoStent project, this conceptual study implements an alternative stent design, to study the effect of the geometry on the developed stresses. Additionally, the effect of the degradation rate on the polymer-based coating's lifecycle is studied via sensitivity analysis.**

I. Introduction

Arteriosclerosis, also known as Coronary Artery Disease (CAD), is a common cardiovascular disease generated mainly by the build-up of cholesterol and other fatty substances, leading to plaque formation and potentially to heart attack incidents. To restore patency, intravascular Bare-Metal Stents (BMS) of various designs are used in angioplasty processes attempting to prevent arterial elastic recoil. However, early smooth muscle cell (SMC) migration and proliferation generate in-stent restenosis (ISR) within three to six months after angioplasty [1]. Drug-Eluting Stents (DES) with coatings out of biodegradable polymer-based materials are used to resolve restenosis, due to the drug release mechanism acting as a shield against neointimal hyperplasia [2].

The development of robust methods that accurately represent the degradation mechanisms of bioabsorbable materials is a topic of research in the bioengineering community [3]. *In silico* modeling approaches provide significant advantages over the costly and time-consuming *in vivo* and *in vitro* tests. In the frame of the BioCoStent project, a state-of-the-art numerical model simulating the degradation of DES coatings made of PLGA (poly-lactic-co-glycolic) and PLA (polylactic acid) is presented [4]. The developed computational process, in terms of the Finite Element Method (FEM) model coupled with the Continuum Damage Mechanics (CDM) theory, describes the hydrolytic degradation highlighting the evolution of the damage accumulation on the polymer-based coating. The results present a complete degradation of the polymer-based coating within 2 months.

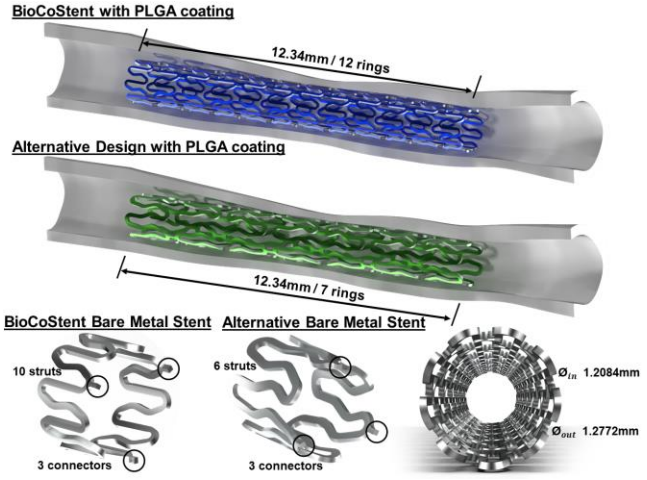

Figure 1. The two variants of DES geometries within the same arterial wall. Both designs are 12.34mm long, with an inner and outer diameter of 1.2084mm and 1.2772mm, respectively. BioCoStent includes 12 rings and 10 struts of 0.0819mm width with 3 connectors. The alternative stent design includes 7 rings and 6 struts of 0.1204 width with 3 connectors as well. The metallic surface area (MSA) derived by the ratio among the mass of the stent and the mass of an ideal hollow tube as described in [12] for the BioCoStent equals 28.6% compared to 32.6% of the alternative design. The coating in both designs consists of PLGA with an inner and outer thickness of 0.0017mm and 0.0041mm, respectively.

The main objective of this work is to develop a Digital Twin of a DES aiming at the study of the biodegradable coating's mechanical behavior. The FE model encompasses the entire lifecycle of the DES including its expansion/recoil followed by the coating's degradation, that utilizes the CDM model developed in [4]. For benchmarking purposes and to compare with BioCoStent's baseline stent, an alternative stent is designed with similar parameters (Fig. 1). The alternative design is a scaled-down version of a larger BMS of Rontis

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which operates at a radial expansion of 11mm. The results provide useful insight into the effect of the i. stent's developed stress field and ii. the PLGA's hydrolysis rate on the degradation behavior of the DES coatings.

II. Numerical Model

The Finite Element Analysis (FEA) model is prepared in the integrated environment of SIEMENS PLM Simcenter 3D [7]. The alternative stent geometry is designed in NX and the transient numerical model is developed and solved with the SOL402 non-linear NX Nastran solver. The bi-directional interface of the Simcenter 3D platform between the Computer-Aided Design (CAD) and Computer-Aided Engineering (CAE), enables the simultaneous definition of geometrical and FEM parameters.

A. FEA Mesh

The discretization of the two models consists of a full-hex mesh with three elements through the thicknesses of the stents and the coatings. The artery's mesh is denser towards its inner arterial wall, to numerically enhance the artery-DES contact interface. The high-quality mesh guarantees the solver's convergence and significantly reduces the simulation time.

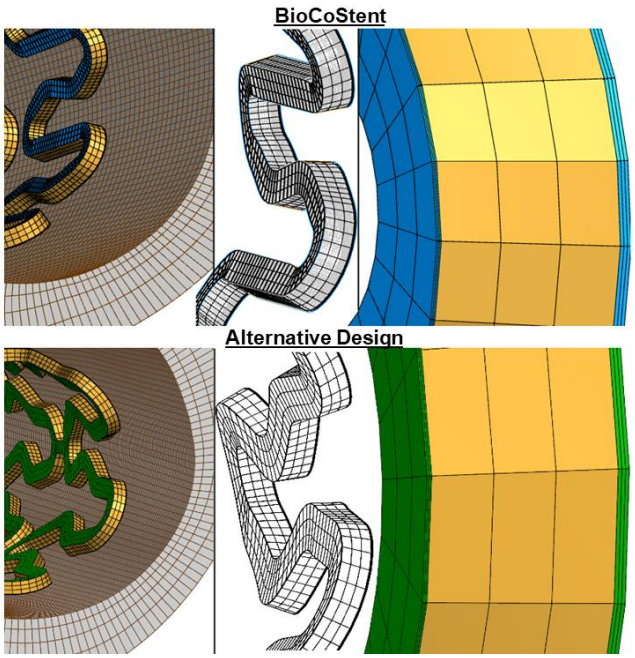

Figure 2. Mesh grid of the DESs geometries. The baseline stent of BioCoStent and the alternative stent design are discretized with 70820 and 30700 elements, respectively. The internal and external coatings of the BioCoStent DES include 141640 elements, and 61420 for the alternative, as well. The artery mesh consists of 263000 elements both for the BioCoStent and the alternative DES.

B. Material Properties

The assigned material properties are identical to those used in the BioCoStent project [4], to facilitate the comparison of the two designs. To accurately model the non-linear behavior of the DES, a multi-linear true stress-strain curve describes the Cobalt-Chromium (CoCr-MP35N) alloy stent with Von-Mises criterion and isotropic hardening rule. The PLGA (poly-lactic-co-glycolic acid) coating is defined as an isotropic material, while the hyperelastic material of the artery is described by a five parameter, Mooney-Rivlin model [8].

TABLE I
Material Properties

Part	Material	Young Modulus [GPa]	Density [kg/m^3]	Yield Stress [MPa]	Poisson's ratio
Stent	CoCr-MP35N	235	8,430	500	0.32
Coating	PLGA	1.64	1,300	5	0.33
		Coefficients [MPa]			
	C_{10}	C_{01}	C_{20}	C_{11}	C_{30}
Artery	0.0189	0.00275	0.08572	0.59047	0

C. Boundary Conditions

Boundary conditions are necessary to ensure a numerically well-defined problem and to realistically represent the physical phenomenon. A time-dependent pressure field is used to model the balloon expansion. To prevent rigid body motion leading to unrealistic translational and rotational movements, certain degrees of freedom (DoFs) of specific nodes at each ring are constrained. The stent is free to expand and shrink in the radial and longitudinal directions. The arterial wall is fixed on the distal faces and the drug is attached on the stent by sharing common nodes. Contact definition is established to implement the connection between the outer face of the external coating and the inner arterial wall.

D. Solver Settings

A transient, multi-step solution is set up, including three main steps: 1. DES inflation, 2. DES deflation, 3. Polymer degradation during the DES operational phase. Each step considers as a starting point the end condition of the previous step. The contact algorithm checks the contact force convergence and the penetration between the artery and the stent. The sliding behavior is updated at each iteration to account for geometry changes. NX Nastran Sol402 is set to consider the material non-linearities of the elasto-plastic and the hyperelastic materials of the stent and the artery respectively. Due to significant deformations of DES compared to its initial geometry, the large displacements and large strain theories are included in the FEA. A User-Defined Material (UMAT) interferes with NX Nastran SOL402 to implement the developed degradation algorithm, by coupling a CDM algorithm with the structural FEA model [4].

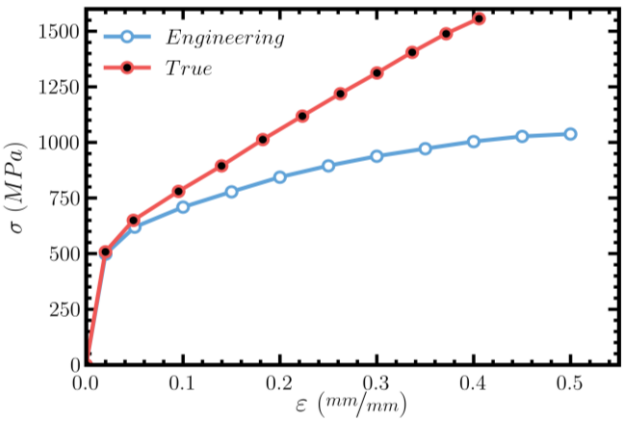

Figure 3. Engineering and true stress-strain curve of Cobalt-Chromium (CoCr-MP35N) [9].

III. Results and Discussion

A. Expansion & Recoil

TABLE II
EXPANSION, RECOIL & DEGRADATION FEA RESULTS OF STENTS

DES	Press. (MPa)	Phase	Von-Mises Stress σ_{max} (MPa)		Strain ε_{max} (mm/mm)	
			Eng.	True	Eng.	True
BioCo Stent	8.5	Exp.	891	1050	0.140	0.130
		Rec.	591	721	0.130	0.120
		Degr.	580	716	0.130	0.120
Alt. Design	6.6	Exp.	767	850	0.107	0.102
		Rec.	640	705	0.101	0.096
		Degr.	635	695	0.101	0.096

The expansion pressure of the alternative design is derived after trials until the radial deformation equals the baseline's at the end of recoil, to achieve similar starting conditions for the degradation phase. The alternative design presents lower true stress and strain values at the expansion phase with respect to the baseline design, and similar true stress values at the end of the recoil (Table II). As expected, the degradation of the coating has a minor effect on the mechanical behavior of the stents, due to PLGA's low stiffness compared to CoCr.

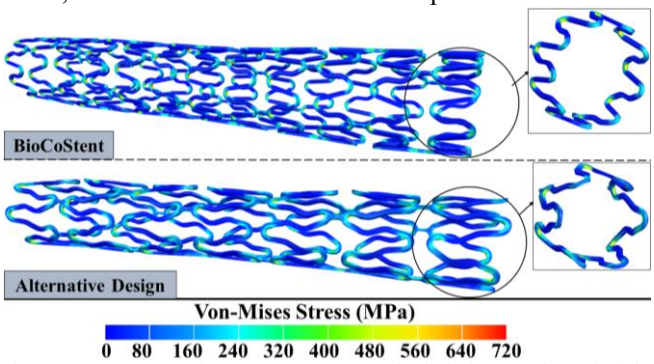

Figure 4. True Von-Mises stress contours on both designs, at the end of the recoil phase. The stress distribution along the rings is periodic, due to the repeated pattern of the designs.

The peak stress on both designs is located on the curved areas of the struts, while the minimum values are in the straight sections. The connectors of the rings on the alternative stent present higher stress values compared to the baseline (Fig. 4).

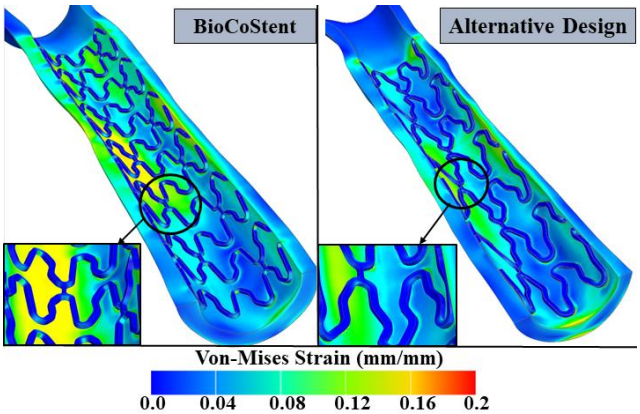

Figure 5. True Von-Mises strain contours on both DESs after the recoil. Similar to Fig. 4, the curved areas of the struts present the peak strain values.

After the recoil phase, the remained Von-Mises strain distribution on the stents indicates the locations with plastic deformation (Fig. 5). The plastic strains in the curved areas of the struts resist the arterial pressure and prevent the stent from recoiling. Concerning the artery, the baseline design presents greater strain values on the arterial wall compared to the alternative, due to its design with denser rings and struts. The peak strain values in the artery illustrate the locations of possible injury of the lumen and neointimal hyperplasia, leading to future restenosis [10].

TABLE III
PERFORMANCE PARAMETERS OF THE STENTS

DES	Radial Recoil RR (%)			Dogboning Ratio DR	
	pl.1	pl.2	pl.3	pl.1& pl.2	pl.3&pl.2
BioCoStent	16.6	16.2	11.4	0.08	0.38
Alt. Design	24.6	26.4	19.1	0.12	0.42
$RR\ \% = \frac{D_{exp}^{distal} - D_{rec.}^{distal}}{D_{exp}^{distal}}$				$DR = \frac{D_{exp}^{distal} - D_{exp}^{central}}{D_{exp}^{distal}}$	

Where D: radial displacement [11]

Table III presents the performance parameters of both DESs designs. The necessary maximum displacement values are computed in three planes, at the extremities and the center of each stent (Fig. 6). The radial recoil performance parameter shows that the baseline stent shrinks less from the expanded diameter to its deflated state. It is also less stretched in the extremities with respect to its mid-plane in terms of the dogboning ratio performance parameter. The alternative design presents higher radial recoil and dogboning ratio values.

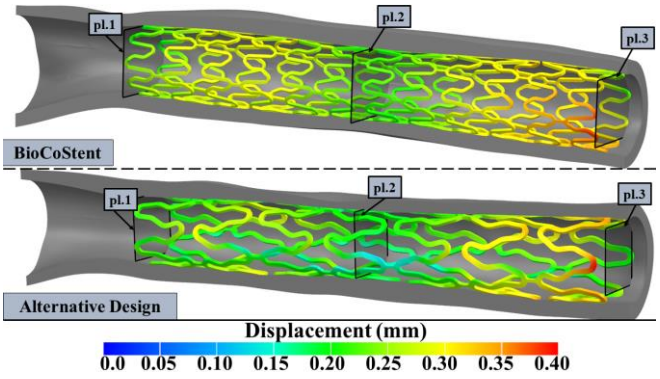

Figure 6. Displacement contours of both DESs at the end of the recoil phase. The distribution is similar for both designs. The maximum value occurs on the right extremity of the DESs while the minimum occurs at the center, where the arterial stenosis is higher.

B. Degradation FEA

The transient degradation analysis starts directly after the recoil. The CDM algorithm is implemented on the PLGA coating, to compute the evolution of the Damage Factor (D). The mathematical definition of D and the CDM model is presented in [4]. The hydrolytic degradation distribution on the polymer-based coating of both DES is similar at the end of the 1st and 2nd month, as the peak stresses at both DESs are of the same order after the recoil phase (Fig.7). As expected, the maximum D values are observed in the high-stressed areas

of the stents (Fig. 4). The damage factor, *D*, ranges between 0.65 - 0.8 at the end of the 1st month. The complete hydrolytic degradation (D ≈ 1) is observed at the end of the 2nd month (Fig. 7).

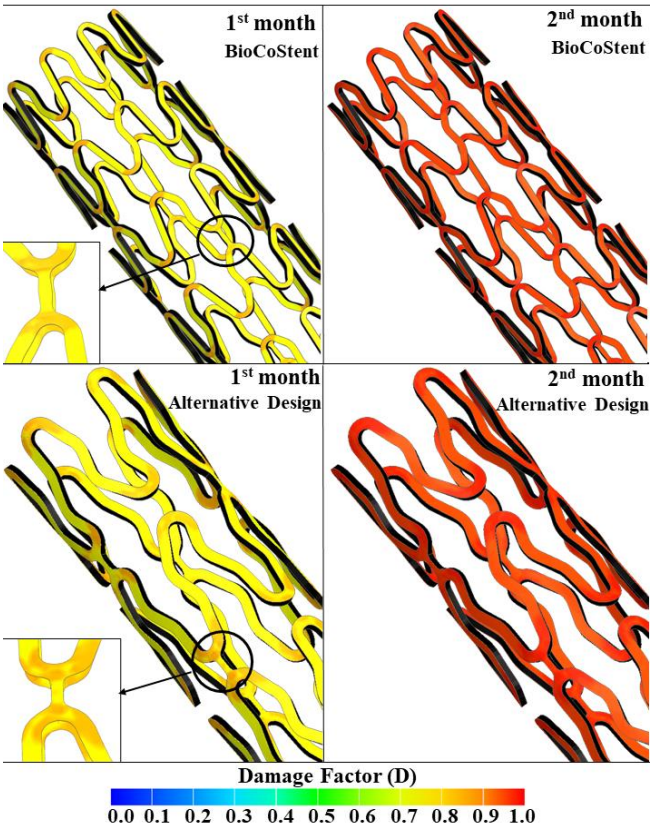

Figure 7. Evolution of the Damage factor (D) on the PLGA coating of the DESs, at the end of the 1st and 2nd month. In the curved areas of the struts, the alternative design has a larger degradation area compared to the baseline, as the high stresses spread over a wider area (Fig. 4). A PLGA hydrolytic rate of k = 7.5e^{-7} (s^{-1}), similar to the BioCoStent project [4], is used.

C. CDM Model Sensitivity Analysis

The exact determination of the hydrolytic rate (*k*) of various polymers is a difficult task and is thus prone to inaccuracies. A sensitivity analysis in the CDM model is conducted, to study the effect of the hydrolytic rate in the degradation evolution of BioCoStent's PLGA coating, with values ranging between 6.5e^{-7} - 15e^{-7} (s^{-1}).

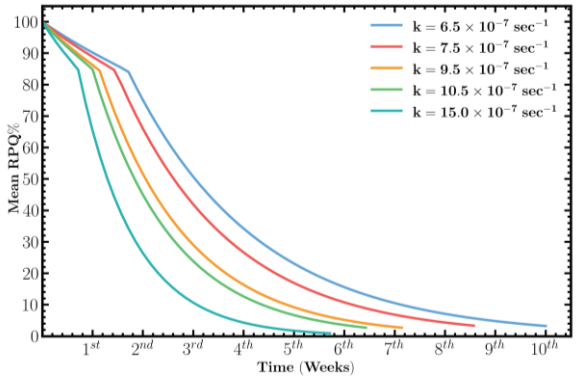

Figure 8. Mean Remained Polymer Quantity (RPQ %) on the PLGA coating of the baseline design. An increase of 130% in the k value (k = 6.5e^{-7} (s^{-1}) to k = 15e^{-7} (s^{-1})) causes a reduction of 42% (70 to 40 days) in the lifetime of the PLGA coating.

Fig 8. presents the strong coupling between the hydrolytic rate (*k*) and the mean RPQ versus time on the DES polymer-based coating. The evolution of the RPQs, derived by the average value of the maximum and minimum *D*, shows a significant undamaged area of the DES's coating during the 1st and 2nd week, resulting in a nearly linear behavior. As time evolves further, the coating's degradation spreads over the whole stent area and the minimum D is non-zero while the maximum D constantly rises [4]. Consequently, the behavior of the mean RPQ changes abruptly. The increase of the *k* accelerates the coating's hydrolytic degradation. The mean RPQ illustrates a complete polymer degradation between the middle of the 6th and 10th week depending on the hydrolytic rate.

IV. CONCLUSIONS

A multi-step, fully parametric numerical model coupled with the CDM model for the polymer-based coating degradation has been carried out to describe the mechanical behavior of two DESs. The goal to design an alternative stent, based on an existing Rontis BMS design with similar characteristics compared to BioCoStent DES, has been achieved.

The alternative design requires less inflation pressure compared to BioCoStent, to achieve an equal radial deformation after the recoil phase. The developed peak stress/strain values during expansion are lower than the baseline design. After recoil, the peak stress values are of the same order between the two designs. Consequently, the starting condition of the degradation process is similar for both designs resulting in comparable scalar *D* distribution on the rings of the DES. BioCoStent presents better performance parameters in contrast to the alternative design. The sensitivity analysis of BioCoStent's CDM model demonstrates the inverted proportional relationship between the hydrolysis rate and the coating's lifetime.

In the frame of BioCoStent, the experimental procedures involving animal subjects are approved by UoI. The next phase includes in vivo tests to validate amongst others the developed numerical model.

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