2021 43rd Annual International Conference of the
IEEE Engineering in Medicine & Biology Society (EMBC)
Oct 31 - Nov 4, 2021. Virtual Conference

Coupled FEA Model with Continuum Damage Mechanics for the Degradation of Polymer-based coatings on Drug-Eluting Stents

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Abstract— **Drug-Eluting Stents (DES) are commonly used in Coronary angioplasty procedures to reduce the phenomenon of restenosis. Numerical simulations are proven to be a useful tool to the Bioengineering community in computing the mechanical performance of stents. BioCoStent is a research project aiming to develop a DES with retinoic acid (RA) coating, in the frame of which FEAC is responsible for the *in silico* numerical simulation of the coating's degradation in terms of Finite Element Analysis (FEA). The coatings under study are poly(lactic-co-glycolic acid) (PLGA) and polylactide (PLA). The FEA is based on the Continuum Damage Mechanics (CDM) theory and considers a mechanistic model for polymer bulk degradation of the coatings. The degradation algorithm is implemented on the NX Nastran solver through a user-defined material UMAT subroutine. This paper describes the developed numerical model to compute the degradation of biodegradable coatings on DES. The transient numerical model provides useful insight into the critical areas with regards to the scalar damage of the coatings. The FEA results present a complete degradation of polymers after several weeks.**

I. Introduction

Drug-Eluting Stents (DES) are lately used in angioplasty due to their controlled drug delivery mechanism to inhibit vascular smooth muscle cell (VSMC) growth after stent placement [1]. DES utilizes the technology of biodegradable materials, whose use in Coronary Artery Disease (CAD) treatment is frequent. Results present that polymer-based coatings such as paclitaxel and sirolimus can reduce in-stent restenosis below 10% after the DES placement [2].

Another method to prevent artery remodeling is by using biodegradable stents made of i. metal alloys or ii. aliphatic polyesters. This type of stent has been extensively studied and relies on biodegradable materials as well absorbed by the human body through complex physical and chemical reactions. The theory of Continuum Damage Mechanics (CDM) is widely used to study the corrosion process on biodegradable stents.

i. Regarding metal-based biodegradable stents, an overview of several studied corrosion mechanisms is elucidated in [3]. More specifically, based on stress and uniform micro-galvanic corrosion process, the structural behavior of bioabsorbable magnesium and zinc alloy is described in [4,5]. In an attempt to implement a dimensionless pitting parameter through the Weibull probability distribution, a phenomenological corrosion model is developed in [6]. The coupled formulation of uniform and stress corrosion along with dynamic cyclic is presented in [7].

ii. Regarding polymer-based biodegradable stents, they are frequently used aiming mainly at drug delivery to the human body [8]. A thermodynamically constitutive model is developed to study the degradation rate of poly-l-lactide (PLLA) [9] based on an exponential function with five materials constraints, calculated after fitting on experimental results. The evolution of Young's Modulus due to polymer hydrolysis is studied in terms of numerical analysis [10] while a degradation model for aliphatic polyesters according to a first-order hydrolytic process is introduced [11].

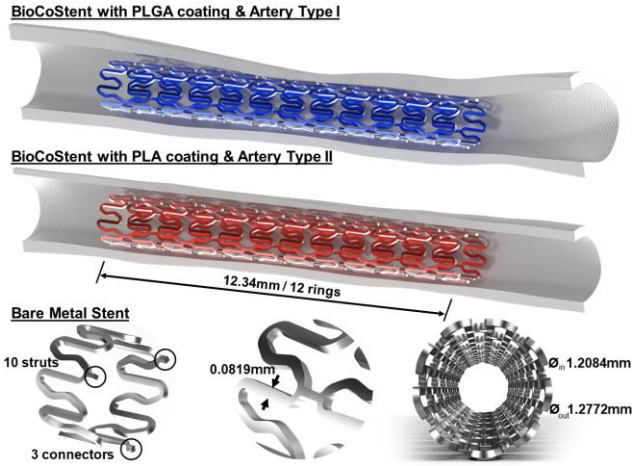

Figure 1. The DES geometry with its variants of polymer-based coatings and arterial walls. The stent design includes 10 struts along its periphery with 3 connectors, 12 rings resulting in an overall length of 12.34mm, and an inner and outer diameter of 1.2084mm and 1.2772mm respectively. Each strut is 0.0819 mm wide and 0.0688 mm thick. 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], equals 28,6%. The inner and outer thickness of the coating equals 0.0017mm and 0.0041mm for the poly(lactic-co-glycolic acid) (PLGA) and 0.003mm and 0.0071mm for the polylactide (PLA) respectively.

The main objective of this work, as part of the BioCoStent project, is to study the mechanical behavior of polymer-based

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coatings used in DES, by implementing an innovative degradation algorithm in a numerical framework. The developed Finite Element Model (FEM) leverages the CDM theory to study a stent design of Rontis with two polymeric coatings of different thicknesses: i. PLGA and ii. PLA, on two real arterial segments of rabbits (Fig. 1). University of Ioannina (UoI) provides the 3D arterial reconstruction, achieved by the fusion of Optical Coherence Tomography (OCT) and angiography.

The developed Finite Element Analysis (FEA) focuses on the phase of the stent's life after its inflation and deflation in the artery.

II. Damage Model For Hydrolysis

The CDM theory describes the materials' stiffness reduction caused by damage accumulation [4]. To illustrate the mechanical strength decrease of the material, a relationship between the effective stress tensor (σ) and the undamaged stress tensor ($\bar{\sigma}$) is introduced and expressed as

$$\sigma = (1 - D)\bar{\sigma} \quad (1)$$

Initially, D=0 indicates an intact material state, while D=1 describes a completely degraded material without any load-bearing capacity.

The developed CDM algorithm is based on bulk degradation caused by the bond scission during the chemical reaction. The diffusion of water inside the body is considered to occur instantaneously and therefore not taken into account. Hydrolytic degradation is included, describing the slow drug release of the DES attempting to block cell proliferation. It starts homogeneously along the polymer's thickness, as the coating's thickness is small. Hydrolysis is the main mechanism for polymer-based DES coatings degradation, leading to reduced molecular weight (MW) and mechanical properties [11].

Based on a mechanistic model for drug release in PLGA DES coatings, the average MW change can be defined as

$$M_w = M_{w,0} e^{-kt} \quad (2)$$

where $M_{w,0}$ is the initial weight-average MW, k is obtained through the half-time for weight-average MW decay and is acquired as $k = 7.5 * 10^{-7}$ (s^{-1}) for the PLGA polymer [14]. In the frame of BioCoStent, it is assumed that the k value of the PLGA and PLA polymers is identical.

The phenomenon of hydrolysis due to water absorption generates the polymer's stiffness reduction. A scalar damage parameter (D), accounting for MW loss, is expressed as

$$D = \frac{M_w}{M_{w,0}} \quad (3)$$

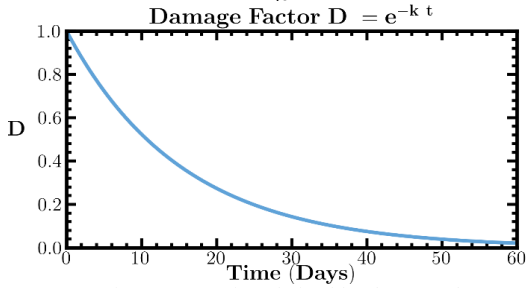

Figure 2. Damage factor versus time derived by the MW change according to a degradation model [14] calibrated with experimental data sets.

III. CDM Algorithm & Numerical Model

A. CDM Algorithm

The degradation process, accounting for a coupled CDM algorithm with the structural FEA model, is implemented in the integrated environment of SIEMENS PLM Simcenter 3D [15], by utilizing a User-Defined Material (UMAT) subroutine. The numerical model is solved with the NX Nastran solver.

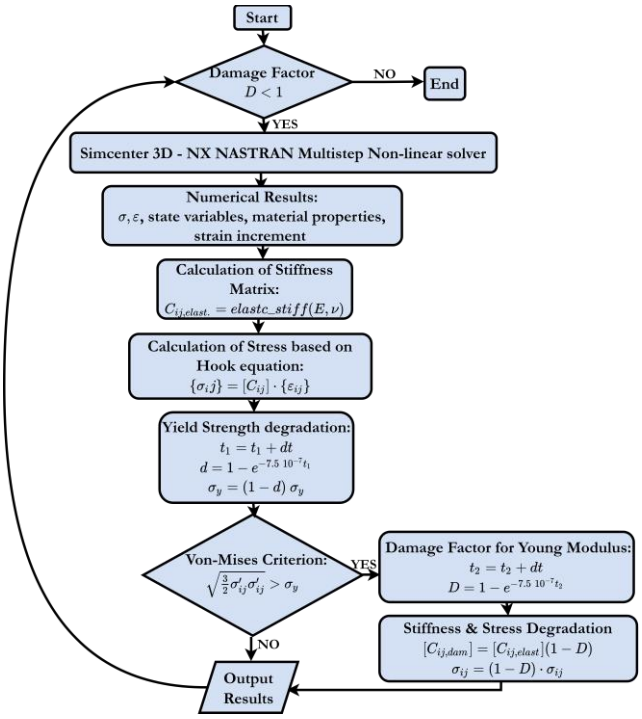

Figure 3. Logical flowchart of the degradation model process. Polymers present a transition from brittle to ductile behavior at high strain rates [11]. In the same manner, the instantaneous balloon expansion used for the DES deflation generates large strains at the polymer-based coating, resulting in a more brittle behavior. Thus, the proposed CDM model does not account for permanent plastic strains of the polymer-based coating.

Fig. 3 presents the flowchart of the UMAT subroutine. Firstly, the isotropic elastic stiffness matrix (C_{ij}) is calculated, and the Cauchy stress tensor (σ) is derived through the strain results (ε). The Yield Strength (σ_y) degradation follows leading to the Von-Mises Criterion. Depending on whether the criterion is satisfied or not, the hydrolytic Damage of the Young Modulus (E) is calculated, and the stiffness and stress values are decreased. The results are passed to NX Nastran to continue with the next iteration. The flowchart applies to each node of the coating, calculating the scalar damage factor, D.

B. Numerical Model

The Cobalt-Chromium (Co-Cr) alloy bare-metal stent (BMS) is described by a multi-linear stress-strain curve with Von-Mises criterion and isotropic hardening rule. The PLGA (poly-lactic-co-glycolic Acid) and PLA (polylactic acid) DES coatings are defined with isotropic properties. The hyperelastic material used to define the non-linear behavior of the artery is described by a five parameter, Mooney-Rivlin model [16].

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
	PLA	1.2	1,325	5	0.36
		Coefficients [MPa]			
	C_{10}	C_{01}	C_{20}	C_{11}	C_{30}
Artery	0.0189	0.00275	0.08572	0.59047	0

Meshing the DES components is a key step for obtaining accurate results in an FEA. The mesh consists of linear hexahedron solid elements (3D). The discretization of the artery is denser towards its inner wall, to numerically enhance the artery-DES contact interface. The resulting high-quality mesh improves the numerical convergence and performance (Fig. 4).

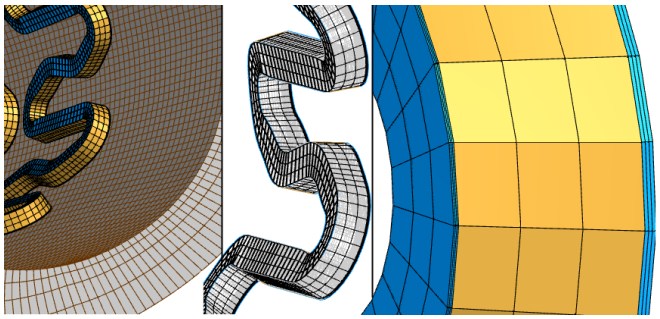

Figure 4. Mesh grid of the DES geometry. Three elements through the thickness are used to model the external and internal polymer-based coatings.

The highly-non linear transient FEM includes geometrical nonlinearity in terms of large displacements and large strains. Material nonlinearity is set up to describe the plasticity of the stent and the hyperelasticity of the artery.

IV. RESULTS AND DISCUSSION

TABLE II
EXPANSION, RECOIL & DEGRADATION FEA RESULTS OF STENTS

Design	Press. (MPa)	Phase	Von-Mises Stress σ_{max} (MPa)		Strain ε_{max} (mm/mm)		Radial Disp. d_{max} (mm)
			Eng.	True	Eng.	True	
BioCoStent with PLGA & ArteryI	8.5	Exp.	891	1050	0.14	0.13	0.44
		Rec.	591	721	0.13	0.12	0.39
		Degr.	580	716	0.13	0.12	0.38
BioCoStent with PLA & ArteryII	8	Exp.	839	962	0.12	0.11	0.35
		Rec.	604	665	0.11	0.10	0.3
		Degr.	592	660	0.11	0.10	0.29

The FEA results of the DES inflation and deflation are provided by UoI. The stress, strain, and displacement distribution after the stent's recoil are mapped on the current mesh grid (Fig. 4) and constitute the initial conditions of the degradation phase. Table II presents an overview of the maximum computed results, in terms of engineering and true values [17] of the two design scenarios. The stiffness of the polymer is insignificant compared to the one of CoCr, resulting in a minor change on the stent's stress field as the degradation evolves and polymer material is removed. No further recoil is observed. The Damage Factor (D) is more critical in the high-stressed regions at the strut's curvatures, as those regions experience the highest deformations. The drug is primarily released in those regions from both the internal and external coating, as presented in Fig. 5.

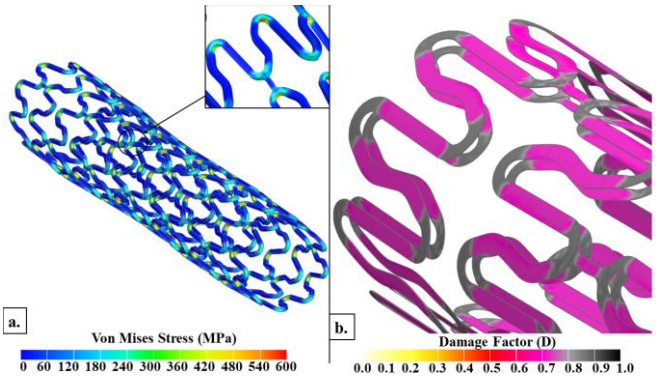

Figure 5. a. Engineering Von Mises stress distribution on the stent at the end of the recoil phase. b. Damage Factor (D) contour on the PLGA polymer coating after 1 month.

A high D value leads to an increased quantity of drug released and corresponds to a low remained polymer quantity (RPQ). The complete loss of PLGA's load-bearing capacity occurs at the end of the 2nd month, as most of the elements are fully degraded with D approaching 1 (Fig. 6).

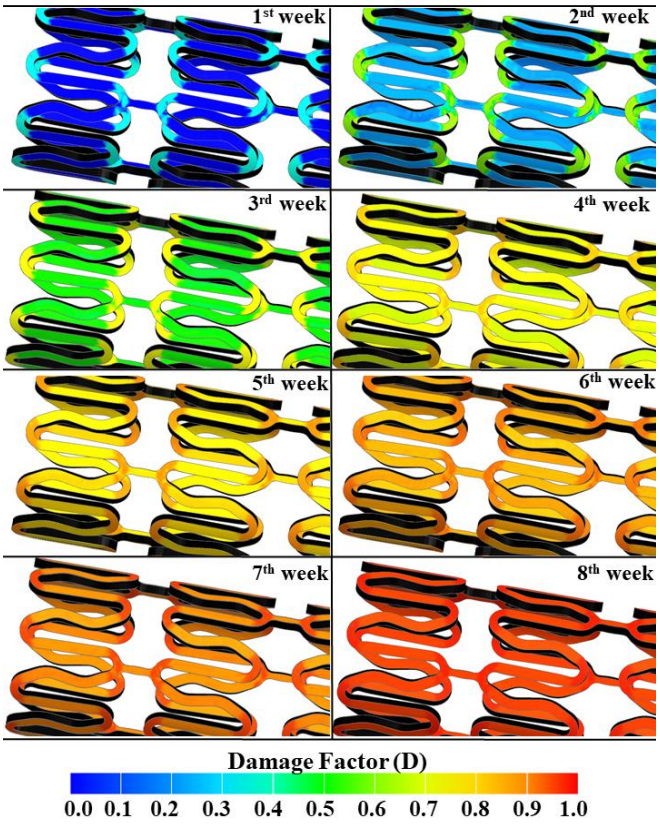

Figure 6. Evolution of the Damage Factor (D) on the first three struts of the stent, at the end of each week. The figure concerns the scenario with the PLGA coated stent inside Artery I.

The evolution of *D* on the PLGA and PLA coatings is very similar due to the assumption that their hydrolytic rates are identical and the stresses after recoil are very similar between the two designs (Table II). Fig. 7 presents the remained polymer quantity (RPQ) on the stent's coating according to the evolution of *D*. The differentiation in the coatings' thicknesses and their respective stiffness (Fig. 1, Table I) generates minimal deviations in the minimum, mean and maximum RPQ.

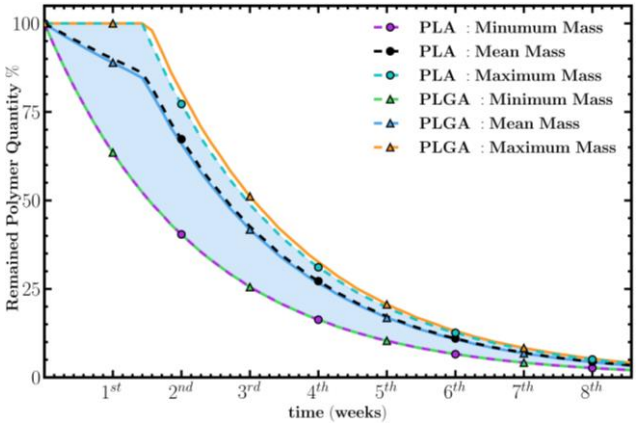

Figure 7. Evolution of the RPQ on the DES. The plot presents the evolution of the minimum, maximum, and mean values of RPQ, obtained on the coating with respect to time. The function of the maximum RPQ shows an undamaged area during the 1st&2nd week concerning the elements with the minimal D values. The evolution of the RPQs relies heavily on the D values at each timestep.

After the 1st and 2nd week, a significant undamaged area of the DES' coating can be observed with a plateaux value of minimum *D* equals 0. The remaining damaged area presents a maximum *D* value of about 0.3 (Fig. 6). The resulting mean RPQ derived by the average value of the minimum and maximum, explains the nearly linear behavior during the 1st and 2nd week (Fig. 7). The trend of the minimum RPQ rate of both polymers follows the exponential form of the function proposed in Eq. 3: it decreases exponentially during the 1st month with a high rate, while after the 7th week the rate is almost linear (Fig. 7). The greatest mass loss of the polymers is observed between the 2nd & 3rd week corresponding to 25% of the initial mass, while the minimum mass loss is observed between the 7th & 8th week corresponding to 4%.

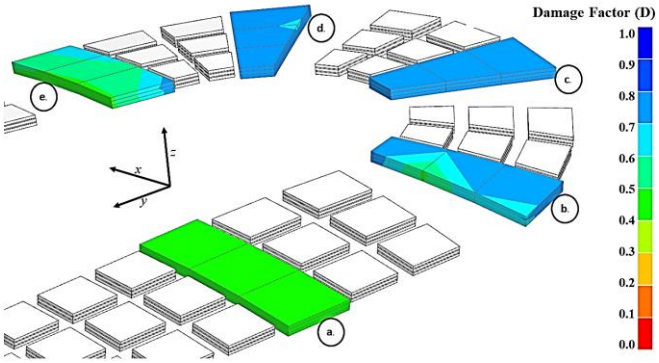

Figure 8. The Damage Factor (*D*) distribution on the PLGA coating. The elemental groups b & e present a high variation of the *D* value, whereas the groups a, c & d show a constant *D* contour.

The developed stress field along the struts can be distinguished in a low-stress region, in its straight part, and a high-stress region, in its curved part (Fig. 5a). These regions present a uniform stress field which also explains why groups a,c & d (Fig. 8) have a relatively constant *D*. The transition region in between the straight and curved part of the struts (Fig. 5a), from a low to a high stressed region, is the one that presents variations in terms of *D*. The distribution of *D* is uniform in the radial direction of the DES due to the coating's small thickness (Fig. 8).

V. Conclusions

Within the framework of the BioCoStent project, a detailed mechanical model describing the degradation of the DES polymer-based coating is presented in terms of FEA and CDM theory. The degradation of the polymeric coatings is applied through the definition of a UMAT subroutine in SIEMENS Simcenter 3D. The developed transient, non-linear, numerical model simulates the molecular weight loss due to hydrolysis. The stiffness degradation is calculated based on the reduction of the polymers' Young's Modulus and Tensile Strength. The results show that the DES maintains its radial displacement during the degradation and the stent's structural results after recoil remain unaffected. The FEM describes the hydrolytic evolution along with the DES coatings' lifecycle and predicted a complete degradation after 2 months for the PLGA and PLA polymers.

The precise behavior determination of implanted devices with biodegradable parts, under complex and multi-physics phenomena, is clearly not predictable *a priori*. Nonetheless, the developed numerical model described in this paper, constitutes a useful and innovative tool in the prediction of the remained drug quantity on the DES coatings, by taking into account the hydrolytic degradation.

All in vivo tests in the frame of the BioCoStent project are approved by UoI and future steps include experimental procedures to validate amongst others the developed CDM model.

Acknowledgment

This paper is supported by the BioCoStent research project, co-financed by Greece and the European Union within the "Competitiveness, Entrepreneurship and Innovation" (EpanEK) Operational Program [13]. The author would like to thank all members of the consortium (FEAC [18], UoI [19], Rontis [20], UTH [21], BRFAA [22]).

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