Effects of Residual Stress, Axial Stretch, and Circumferential Shrinkage on Coronary Plaque Stress and Strain Calculations: A Modeling Study Using IVUS-Based Near-Idealized Geometries

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Accurate stress and strain calculations are important for plaque progression and vulnerability assessment. Models based on in vivo data often need to form geometries with zero-stress/strain conditions. The goal of this paper is to use IVUS-based near-idealized geometries and introduce a three-step model construction process to include residual stress, axial shrinkage, and circumferential shrinkage and investigate their impacts on stress and strain calculations. In Vivo intravascular ultrasound (IVUS) data of human coronary were acquired for model construction. In Vivo IVUS movie data were acquired and used to determine patient-specific material parameter values. A three-step modeling procedure was used to make our model: (a) wrap the zero-stress vessel sector to obtain the residual stress; (b) stretch the vessel axially to its length in vivo; and (c) pressurize the vessel to recover its in vivo geometry. Eight models were constructed for our investigation. Wrapping led to reduced lumen and cap stress and increased out boundary stress. The model with axial stretch, circumferential shrink, but no wrapping overestimated lumen and cap stress by 182% and 448%, respectively. The model with wrapping, circumferential shrink, but no axial stretch predicted average lumen stress and cap stress as 0.76 kPa and -15 kPa. The same model with 10% axial stretch had 42.53 kPa lumen stress and 29.0 kPa cap stress, respectively. Skipping circumferential shrinkage leads to overexpansion of the vessel and incorrect stress/strain calculations. Vessel stiffness increase (100%) leads to 75% lumen stress increase and 102% cap stress increase. [DOI: 10.1115/1.4034867]

Keywords: residual stress, opening angle, circumferential shrinkage, axial stretch, plaque rupture, IVUS

1 Introduction

It is well-accepted that mechanical forces play an important role in atherosclerotic plaque progression and rupture [1–8]. Accurate calculations of plaque stress/strain values are critical to plaque progression and vulnerability investigations. Thin fibrous cap (threshold cap thickness of 0.065 mm) and high cap stress are most reported key risk factors for plaque rupture research. Finet et al. used computational modeling method to calculate cap stress and reported that 300 kPa could be used as a stress threshold value for vulnerable plaques [9]. This stress value has been widely cited as a distinctive feature to identify vulnerable plaques. In this paper, we would like to draw people's attention to the fact that plaque stress value may be influenced considerably by residual stress, axial stretch, and circumferential shrinkage. Models including residual stress, axial stretch, and circumferential shrinkage may provide more accurate stress/strain calculations which could serve as the basis for further plaque research including mechanism research, vulnerability assessment, or in vitro experimental design where mechanical stress/strain environment is needed.

Image-based models have been used to calculate mechanical stress and strain and investigate their role in biological processes, including plaque remodeling, progression, and rupture. Medical image technologies such as intravascular ultrasound (IVUS), optical coherence tomography (OCT), and magnetic resonance imaging (MRI) have been constantly improving and are able to provide plaque morphology and differentiate plaque components under in vivo conditions [5–8,10]. However, computational plaque

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models often need to start from a stress-free state which is not available directly from medical images. In Vivo image data are obtained when the blood vessel is under pressure and axially stretched. So, the vessel image data should be shrunk circumferentially (radially) and axially to obtain its no-load state. The no-load geometry needs to be cut open to release the residual stress to obtain its stress-free state [11]. Implementation of those steps for real plaque models may not be practical due to the complexity of plaque geometries. In this paper, we will use IVUS-based near-idealized human coronary plaque geometries to investigate the impact of residual stress, circumferential, and axial shrinkages on stress/strain calculations.

Residual stress, defined as the stress remaining in the ex vivo no-load vessel ring, was first discovered by Fung and coworker [11–12]. It is evidenced by the fact that when the vessel ring was cut open, it would open up into a sector. Each sector is characterized by an opening angle. The sector obtained by releasing the residual stress under no-load state represents the stress-free geometry of the blood vessel. This conventional opening angle description was used by many study groups to take care of the residual stress when calculating the stress/strain distributions. Using the opening angle method in human carotid model for quantifying residual stress, Delfino et al. claimed that the circumferential stress throughout the wall was much more uniform with residual stress included [13]. Ohayon et al. showed that peak strain in the thick fibrous cap was overestimated by a factor of as much as 4 without residual stress involved [14].

Two other equally important but less well-known factors related to obtaining stress-free state are axial and circumferential shrinkages. If we take a vessel segment from its in vivo state, it will shrink in axial and circumferential directions to come to its no-load shape. Based on the simulation result from in vivo MRI data, Huang et al. indicated that maximum principal stress (stress- P_1) and maximum principal strain (strain- P_1) at the plaque cap increased 23.7% and 25.9%, respectively, under 10% axial stretch and patient-specific circumferential shrinkage [15]. Speelman et al. adopted a backward incremental method to account for the initial stress in the blood vessel in vivo and found that abdominal aortic aneurysms wall stresses as computed with initial stress considered were higher than the ones without initial stress [16]. Holzapfel et al. investigated the residual deformation by considering the arteries as a three-layer blood vessel and claimed that the

deformation caused by the residual stress was layer-specific and axially dependent, and this method was implemented by Pierce et al. to simulate the residual stresses/stretch in patient-specific abdominal aortic aneurysms model [17,18]. Gee et al. demonstrated two finite deformation-based methods to find out the unknown blood vessel geometry under certain physiological conditions based on geometry from in vivo images under known external load [19].

In this paper, patient-specific coronary plaque IVUS data and IVUS movie data were acquired from a patient to obtain in vivo plaque morphology and vessel material properties. Eight computational models were constructed using IVUS-based near-idealized geometries to quantify the effects of residual stress and axial and circumferential shrinkages in stress/strain calculations. After a coronary vessel segment obtained from in vivo IVUS image was shrunk axially and circumferentially and cut open, a three-step process was taken to make the model: (a) wrap the stress-free open sector to form a vessel segment to return to its no-load shape with its residual stress; (b) stretch the vessel segment axially to its length in vivo; and (c) pressurize the vessel segment to fully recover its in vivo geometry with the final stress/strain distributions. It should be noted that the three-step process is truly three-dimensional because axial shrink and stretch and circumferential shrink are linked and cross section morphology will change which cannot be achieved by plane strain. Models of a healthy vessel and a more severely diseased plaque were also made for comparisons. The details are given below.

2 Data, Models, and Methods

2.1 In Vivo IVUS Data Acquisition. Patient-specific material properties are normally not available for modeling use. As a novel approach, in vivo IVUS movie data at fixed vessel locations were acquired and used to determine patient-specific material parameter values for the computational model. In Vivo IVUS data of human coronary were acquired from a patient (male, age 58) at the Zhongda Hospital, Southeast University, Nanjing, China, with informed consent obtained. IVUS data acquisition followed standard procedure described in Ref. [5]. A 20 MHz, 2.9 F phased-array transducer catheter (Eagle Eye Platinum, Volcano Corp., Rancho Cordova, CA) was used. The original gray scale of IVUS image had an axial resolution of 150–200 μm and a lateral resolution of 150–300 μm [20]. The IVUS-VH (IVUS Virtual Histology, Volcano S5, Volcano Corp., Rancho Cordova, CA) was created by using autoregressive models to provide four classified tissue components [21]. The IVUS-VH data for model construction has 20 μm pixel resolution. To obtain IVUS movie data which would be used to determine vessel material parameter values, the catheter paused 5–10 s at five locations during its pull-out. When the catheter was paused, IVUS images of the vessel at the fixed location with diameter variations were recorded. The location of the catheter was recorded by angiography (Allura Xper FD10 System, Philips, Bothell, WA). Figure 1 shows the stacked contours of the IVUS-VH data set and a selected slice from IVUS movie with maximum and minimum lumens. It should be noted that IVUS-VH and IVUS movie contours appear slight differently because different segmentation methods were used.

2.2 Material Model and Patient-Specific Parameter Value Determination. Structure-only models will be used in this paper for stress/strain calculations. The governing equations and boundary conditions can be found in our previous publication [22]. The anisotropic Mooney–Rivlin material model was used to describe the material properties of the blood vessel tissue. The strain energy density function for the anisotropic Mooney–Rivlin material is

$$W = c_1(I_1 - 3) + c_2(I_2 - 3) + D_1[\exp(D_2(I_1 - 3)) - 1] + (K_1/K_2)\exp[K_2(I_4 - 1)^2 - 1] \quad (1)$$

Fig. 1 A human coronary plaque sample together with IVUS movie to determine vessel material properties: (a) stacked IVUS-VH contours showing 3D view of the plaque and (b) IVUS movie slices at a location corresponding to maximum and minimum pressure. Minimum circumference = 11.85 mm and maximum circumference = 12.53 mm.

Fig. 2 Stress-stretch curves from Mooney-Rivlin models using parameter values determined from IVUS movie, 200% stiffness (2×in vivo), and ex vivo biaxial testing of human coronary plaques. Parameter values are listed in Table 2.

$$I_1 = \sum C_{ii}, I_2 = 1/2[I_1^2 - C_{ij}C_{ij}] \quad (2)$$

where I_1 and I_2 are the first and second invariants of right Cauchy-Green deformation tensor $\mathbf{C}$ defined as $\mathbf{C} = [C_{ij}] = \mathbf{X}^T \mathbf{X}$, $\mathbf{X} = [X_{ij}] = [\partial x_i / \partial a_j]$, (x_i) is the current position, (a_i) is the original position, $I_4 = C_{ij}(\mathbf{n}_c)_i(\mathbf{n}_c)_j$, $\mathbf{n}_c$ is the unit vector in the circumferential direction of the vessel, and c_1 , c_2 , D_1 , D_2 , K_1 , and K_2 are the

material constants [23–26]. Plaque components (specifically, the necrotic lipid core in this study) were assumed isotropic, and the isotropic Mooney-Rivlin material model was used to describe its material properties.

A three-dimensional thin-slice model and Cine IVUS data were used to determine vessel material parameter values from one selected IVUS slices (see Fig. 1). The thin-slice model was made by adding a thin-slice thickness to the 2D slice so that the model becomes 3D and axial stretch could be applied, mimicking the axial stretch in full 3D models. Axial shrinkage was set at 5% because atherosclerotic vessels were stiffer than healthy vessels. An iterative procedure (see Ref. [27] for details) was followed to adjust the parameter values in the modified Mooney-Rivlin model (1) and the circumferential shrinkage rate to match both maximum and minimum lumen circumferences corresponding to patient-specific systolic and diastolic pressures, respectively. The parameter values $c_1 = -1312.9$ kPa, $c_2 = 114.7$ kPa, $D_1 = 629.7$ kPa, $D_2 = 2.0$, $K_1 = 35.9$ kPa, and $K_2 = 23.5$ obtained from one ex vivo plaque sample were used as the initial guess in our iterative procedure in this paper. Initial circumferential shrinkage rate was set as $S = 5\%$. The in vivo vessel slice was shrunk circumferentially with shrinkage rate S , and with vessel area/volume conserved. Then, the minimum pressure was applied to lumen so that the vessel would be inflated and the lumen circumference would match in vivo minimum circumference from Cine IVUS data. If not, the shrinkage (S) is adjusted to obtain good matching agreement (matching in vivo circumference with error $< 0.1\%$). After that, the maximum pressure is applied to the lumen to see if the lumen circumference would match in vivo maximum circumference data (with error $< 0.1\%$). If not, the material parameter values are adjusted to get better agreement (until error $< 0.1\%$). The whole iteration is repeated by adjusting both the circumferential shrinkage and material constants until good agreements at both

Fig. 3 The IVUS slice and wrapping-up process: (a) the in vivo IVUS-VH image, (b) the segmented contour, (c) contour plot after smoothing and merging small lipid pools to a combined one; (d) overlapped contours at in vivo state (blue), no-load state (black), and stress-free state (magenta), circumferential shrinkage was applied; and (e) 3D view of the blood vessel geometry at no-load state and in vivo state

Table 1 All the sets of material constants and Young's modulus for tissue and lipid component

Model/tissue type	C_1 (kPa)	C_2 (kPa)	D_1 (kPa)	D_2	K_1 (kPa)	K_2	YM_c (kPa)	YM_a (kPa)
Set 1: In Vivo data	−262.58	22.94	125.94	2.0	7.18	23.5	326	188
Set 2: 2× In Vivo stiffness	−525.16	45.88	251.88	2.0	14.36	23.5	652	375
Set 3: Ex Vivo ME testing	−1312.9	114.7	629.7	2.0	35.9	23.5	1631	938
Necrotic lipid core	0.5	—	0.5	1.5	—	—	10	10

YM_c : Young's modulus in circumferential direction and YM_a : Young's modulus in axial direction.

Table 2 Eight models with different wrapping, stretch, shrink, and material assumptions

Model	Wrapping	Axial stretch (%)	Material	Circumferential shrink
M1	Yes	10	In Vivo material	Yes
M2	No	10	In Vivo material	Yes
M3	Yes	5	In Vivo material	Yes
M4	Yes	0	In Vivo material	Yes
M5	Yes	10	In Vivo material	No
M6	Yes	0	In Vivo material	No
M7	Yes	10	200% stiffness	Yes
M8	Yes	10	Ex Vivo data	Yes

minimum and maximum pressure conditions are obtained. The iterative procedure was set to stop if the relative changes of the shrinkage and parameter values were less than 0.01 (1%). The parameter values determined from this procedure are given in Table 1. Three sets of material constants were used in this paper for comparisons. Parameter values were doubled to get set 2

values (the stiffer case). Set 3 parameter values were obtained from our earlier ex vivo biaxial test data [22,28]. Figure 2 shows the stress–stretch curves of the three materials. The approximate Young's modulus (YM) for axial and circumferential directions on the interval [1.0, 1.1] was determined for easy comparison.

2.3 Obtaining Stress-Free Geometry From an In Vivo Segment. Since it is technically difficult to perform the opening-up, axial shrinking–stretching, and circumferential shrinking and pressurization to plaques with complex components, curvature and branching, one slice from the in vivo IVUS data set was chosen to make a straight vessel segment for our modeling use. The slice was extended to a hypothetical 20 mm in vivo vessel segment. This segment was then shrunk axially and circumferentially (with volume conservation) to obtain its no-load geometry which would be restored to in vivo geometry after axial stretching and pressurizing. The no-load geometry was opened up to a sector with an opening angle of 120 deg (the average of eight human coronary samples) based on real human coronary study in Kural et al. [28] (see Fig. 3). The opening-up process was performed under two assumptions: (1) vessel wall volume was conserved and (2) the

Table 3 Average values of stress- P_1 and strain- P_1 on lumen at systolic pressure (130 mm Hg) and the circumferential shrinkage for all the eight models

Model	Circumferential shrinkage	Lumen	Out boundary	Whole slice	Cap stress
Average stress- P_1 value (kPa)					
M1	Lumen: 8.5%; out boundary: 4.5%	42.53	161.49	83.70	29.00
		100%	100%	100%	100%
M2	Lumen: 7.8%; out boundary: 4.2%	119.94	68.66	84.43	159.34
		282%	42.5%	101%	548%
M3	Lumen: 11.3%; out boundary: 5.9%	10.31	162.59	63.88	−3.86
		24.2%	101%	76.3%	−13.3%
M4	Lumen: 13.4%; out boundary: 6.9%	0.76	166.94	59.56	−15.01
		1.7%	103%	71.1%	−51.7%
M5	Lumen: 0%; out boundary: 0%	53.51	173.09	95.94	39.63
		126%	107%	115%	137%
M6	Lumen: 0%; out boundary: 0%	20.88	184.03	81.82	−1.88
		49.1%	114%	97.8%	−6.48%
M7	Lumen: 4.7%; out boundary: 2.5%	74.35	209.87	119.92	58.65
		175%	130%	143%	202%
M8	Lumen: 2.5%; out boundary: 1.3%	176.24	383.73	233.00	160.75
		414%	238%	278%	554%
Average strain- P_1 value					
M1	Lumen: 8.5%; out boundary: 4.5%	0.1058	0.1764	0.1261	0.1051
		100%	100%	100%	100%
M2	Lumen: 7.8%; out boundary: 4.2%	0.1547	0.1063	0.1212	0.1841
		146%	60.3%	96.1%	175%
M3	Lumen: 11.3%; out boundary: 5.9%	0.0721	0.2158	0.1320	0.0513
		68.1%	122%	105%	48.8%
M4	Lumen: 13.4%; out boundary: 6.9%	0.0619	0.2504	0.1516	0.0131
		58.5%	142%	120%	12.5%
M5	Lumen: 0%; out boundary: 0%	0.1119	0.1824	0.1343	0.1051
		106%	103%	107%	100%
M6	Lumen: 0%; out boundary: 0%	0.0925	0.2578	0.1756	0.0685
		87.4%	146%	139%	65.2%
M7	Lumen: 4.7%; out boundary: 2.5%	0.1051	0.1309	0.1090	0.1051
		99%	74.2%	86.4%	100%
M8	Lumen: 2.5%; out boundary: 1.3%	0.1051	0.1069	0.1053	0.1051
		99%	60.6%	83.5%	100%

Fig. 4 Stress/strain plots from M1 and M2 showing impact of residual stress. $p = 130$ mm Hg. (a) M1: stress- P_1 , (b) M2: stress- P_1 , (c) M1: strain- P_1 , and (d) M2: strain- P_1 .

circumference of the middle line of the vessel wall remains unchanged. Figure 3 shows (a) an in vivo IVUS-VH slice; (b) segmented contour; (c) contour plot after smoothing and merging lipid pools; (d) overlapped contours at in vivo state, no-load state, and stress-free state; and (e) 3D view of the opening-up process.

2.4 Comparative Study Using Models With Different Assumptions. Eight 3D structure-only models were made for our study. The baseline model (M1) was constructed from the stress-free geometry obtained in Sec. 2.3 with wrapping, 10% axial stretch, pressurization, and the in vivo vessel material parameter values. Table 2 gives definitions of the eight models with various combinations of wrapping, axial stretch, circumferential shrinkage, and different vessel material properties. All the eight models were constructed and solved by a commercial finite-element package ADINA (ADINA R & D, Watertown, MA) to obtain stress/strain distributions for analysis. Since stress and strain are tensors, maximum principal stress (stress- P_1) and strain (strain- P_1) values were used as the scalar representative stress/strain values (referred to as stress and strain for simplicity) for easy comparison.

3 Results

Since both axial stretch and wrapping affect lumen/out boundary shrinkage needed to recover in vivo geometry, the lumen/wall shrinkages used to obtain in vivo length of lumen circumference were different from model to model, due to different stretch and wrapping conditions. Table 3 lists the lumen and out boundary shrinkages for the eight models, together with average stress and strain values for model comparisons. Average stress/strain values from lumen, out boundary, plaque cap, and the entire vessel were

Fig. 5 Stress and strain plots from M1, M3, and M4 showing impact of axial stretch. $p = 130$ mm Hg. (a) M1: stress- P_1 , (b) M3: stress- P_1 , (c) M4: stress- P_1 , (d) M1: strain- P_1 , (e) M3: strain- P_1 , and (f) M4: strain- P_1 .

Fig. 6 Stress and strain plots from M1, M5, and M6 showing impact of circumferential shrinkage. $p = 130$ mm Hg. (a) M1: stress- P_1 , (b) M5: stress- P_1 , (c) M6: stress- P_1 , (d) M1: strain- P_1 , (e) M5: strain- P_1 , and (f) M6: strain- P_1 .

included to observe stress/strain variations on different parts of the vessel. More details are given in Secs. 3.1–3.7.

3.1 Effect of Residual Stress on Stress/Strain Distributions. The baseline model M1 included wrapping, axial stretch, and pressurization. M2 included axial stretch and pressurization, but did not include wrapping. Figure 4 gives plots of stress- P_1 and

strain- P_1 distributions from M1 and M2 on the vessel cross section under systolic pressure condition ($p = 130$ mm Hg). Due to the wrapping, maximum stress and strain values from M1 appeared on the out boundary of the vessel, while the maximum stress/strain values from M2 appeared on the inner side of the vessel. Table 3 shows that the average lumen stress and strain from M2 were 182% and 46% higher than those from M1, i.e.,

Table 4 Comparison of stress/strain values between diseased and healthy vessels

Model	Circumferential shrinkage	Lumen	Out boundary	Whole vessel	Cap stress
Average stress- P_1 value (kPa)					
M1	Lumen: 8.5%; out boundary: 4.5%	42.53	161.49	83.70	29.00
		100%	100%	100%	100%
M2	Lumen: 7.8%; out boundary: 4.2%	119.94	68.66	84.43	159.34
		282%	42.5%	101%	548%
M9	Lumen: 10.7%; out boundary: 8.0%	111.85	192.98	148.06	—
		263%	120%	177%	—
M10	Lumen: 11.8%; out boundary: 8.1%	181.04	123.35	147.46	—
		426%	76.4%	176%	—
M11	Lumen: 15.6%; out boundary: 11.6%	104.91	183.78	143.98	—
		247%	114%	172%	—
Average strain- P_1 value					
M1	Lumen: 8.5%; out boundary: 4.5%	0.1058	0.1764	0.1261	0.1051
		100%	100%	100%	100%
M2	Lumen: 7.8%; out boundary: 4.2%	0.1547	0.1063	0.1212	0.1841
		146%	60.3%	96.1%	175%
M9	Lumen: 11.3%; out boundary: 5.9%	0.1224	0.2006	0.1622	—
		116%	114%	129%	—
M10	Lumen: 13.4%; out boundary: 6.9%	0.2007	0.1320	0.1644	—
		190%	74.8%	130%	—
M11	Lumen: 15.6%; out boundary: 11.6%	0.2001	0.2774	0.2395	—
		189%	157%	190%	—

$p = 130$ mm Hg.

Fig. 7 Stress and strain plots from M1, M7, and M8 showing impact of material stiffness changes. $p = 130$ mm Hg. (a) M1: stress- P_1 , (b) M7: stress- P_1 , (c) M8: stress- P_1 , (d) M1: strain- P_1 , (e) M7: strain- P_1 , and (f) M8: strain- P_1 .

neglecting residual stress leads to overestimation of lumen stress and strain. On the other hand, out boundary average stress and strain from M2 were lower and were only 42.5% and 60.3% of those from M1. The slice average stress and strain from M1 and M2 were about the same (differences less than 4%). Cap average stress and strain from M2 were 448% and 75% higher than those from M1. Again, neglecting residual stress leads to huge overestimation of cap stress and strain values.

3.2 Effect of Axial Stretch Combined With Wrapping on Stress/Strain Calculation. M1, M3, and M4 had 10%, 5%, and 0% axial stretch with all the other conditions held equal to study the effect of axial stretch on stress/strain calculations. Figure 5 gives stress and strain plots of the three models showing differences of stress/strain distributions. Because all the three cases have wrapping which created compression on the lumen side, average lumen stress values from M3 and M4 were only 24% and 1.7% of that from M1. Average lumen strain values from M3 and M4 were 68.1% and 58.5% of that from M1. Average cap stress values from M3 and M4 were negative, indicating that vessel was under compression from the wrapping. Slice average stress values from M3 and M4 were 24% and 29% lower than that from M1, while slice average strain values from M3 and M4 were 5% and 20% higher than that from M1. For out boundary averages, stress values from the three models were almost the same, while strain values from M3 and M4 were 22% and 42% higher than that of M1. Axial stretch combined with wrapping has great impact on lumen and cap stress/strain calculations. It should also be noted that results from M1, M3, and M4 would be different if wrapping was not included. The comparison of results from M1, M3, and M4 would also be different under those conditions.

3.3 Effect of Circumferential Shrinkage on Stress/Strain Calculation. M5 had wrapping, 10% axial stretch, but no circumferential shrinkage. M6 had wrapping, no axial stretch, and no

circumferential shrinkage. We compared M1 with M5 and M6 to investigate the influence of circumferential shrinkage on stress/strain calculations. Figure 6 gives stress and strain plots of the three models showing differences of stress/strain distributions. Average lumen, out boundary, slice, and cap stresses stress values of M5 were 26%, 7%, 15%, and 37% higher than those of M1, respectively. This happens because the blood vessel in M5 expanded more and became thinner and thus easier to deform. Average stress values of M6 showed mixed results, Average lumen, out boundary, slice, and cap stresses stress values of M6 were 49.1%, 114%, 97.8%, and -6.48% of those from M1. Differences on strain values were more modest. There were only slight differences (smaller than 7%) in average strain values between M1 and M5 on lumen, out boundary, slice, and cap nodes. For M6, average lumen and cap strain values were 12.6% and 34.8% smaller than those from M1, but average out boundary and slice strain values were 46% and 39% higher than those from M1. Impact of circumferential shrinkage is closely linked to wrapping and axial stretch.

3.4 Effect of Material Stiffness on Stress/Strain Calculation. M1, M7, and M8 used in vivo stiffness, 200% in vivo stiffness, and ex vivo stiffness (500% of in vivo stiffness) tissue material with the same three-step process applied to study the effect of material stiffness on stress/strain calculations. Figure 7 gives the stress and strain plots of the three models showing differences of stress/strain distributions. Stiffer materials lead to overall higher stress. Average lumen stress values of M7 and M8 were 75% and 314% higher than that from M1. The results on out boundary, slice, and cap nodes from M7 and M8 were all higher than those from M1, with cap stress from M8 454% higher than that from M1. The differences on average strain values were much smaller. M1, M7, and M8 had the same average cap strain values. Both M7 and M8 had the same average lumen strain values as 99% of that from M1. Average wall strain values of M7 and M8 were 74.2% and 60.6% of that from M1, while average

slice strain values of M7 and M8 were 86.4% and 83.5% of that from M1. This demonstrates that material stiffness with wrapping involved has a slight negative impact on strain calculation. Overall, material stiffness increase leads to higher stress values but had very small impact on strain values (except lower maximum strain on out boundary).

3.5 Effect of Residual Stress on Stress/Strain Distributions for Healthy Vessel. Three more models were made to investigate the effect of residual stress on stress/strain distributions for a healthy vessel. M9 and M10 used the same model assumptions as M1 and M2, respectively, with a thinner vessel wall (see Fig. 8). M11 used the same model assumptions as M9 with vessel stiffness reduced by 50%. Figure 8 gives the stress and strain plots from M9 to M11. Table 4 compares average stress and strain values on lumen, out boundary, whole vessel, and cap from M1 to M2 and M9 to M11 at systolic pressure (130 mm Hg). Overall, the stress and strain levels from M9 to M11 were higher than those from M1 to M2. For the healthy vessel, stress and strain differences between lumen and out boundary were much smaller than those from M1 to M2.

Comparing M11 with M9, it is worth noting that 50% reduction of material stiffness leads to large strain increases (63% increase for lumen), but very modest stress change (a 6% decrease for lumen). That is consistent with our earlier report [27].

3.6 Effect of Residual Stress on Stress/Strain Distributions for an Eccentric Plaque With a Lipid Core. Models M12–M13 were constructed to consider an eccentric plaque case. M12 and M13 used the same model assumptions as M1 and M2,

respectively. Figure 9 shows the eccentric plaque geometry and stress/strain plots from M12 to M13. Table 5 provided average stress and strain values on lumen, out boundary, whole vessel, and cap from M12 to M13 systolic pressure (130 mm Hg). Compared to M12 which included residual stress, M13 (model without residual stress) overestimated average lumen and cap stress values by 86.5% and 239.8%, respectively. The overestimation for average lumen and cap strain values was 29.4% and 32.4%, respectively.

3.7 Sensitivity of the Cut Location. To check if our results would be sensitive to the location of the cut position, Model M14 was made with a different cut position. The cut position and stress/strain plots are shown in Fig. 10. Table 6 provided comparison of average stress and strain values between M1 and M14. Differences were all under 5%.

4 Discussion

4.1 The Zero-Stress Issue and Related Factors. The zero-stress issue is of vital importance if we want to construct models based on in vivo data and obtain stress/strain solutions correctly. The residual stress concept is well known. The axial shrink–stretch has also been accepted by the biomechanical research community. The circumferential shrinkage is often done together with axial shrink–stretch process, but has drawn less attention. The main purpose of this paper is to quantify the impact of zero-stress related factors, mainly residual stress, axial shrinkage, and circumferential shrinkage. This is, in a sense, to expand the residual stress concept and handle the zero-stress issue with wrapping, circumferential, and axial shrinkages combined at 3D level. Since plaque morphology, component, and material

Fig. 8 Stress and strain plots from M9 to M11 showing modeling results for a healthy vessel. $p = 130$ mm Hg. (a) M9: stress- P_1 , (b) M10: stress- P_1 , (c) M11: stress- P_1 , (d) M9: strain- P_1 , (e) M10: strain- P_1 , and (f) M11: strain- P_1 .

Fig. 9 Stress and strain plots from M12 and M13 showing the impact of residual stress for an eccentric plaque case. $p = 130$ mm Hg. (a) in vivo geometry, (b) in vivo and open-up geometrics, (c) M12: stress- P_1 , (d) M12: strain- P_1 , (e) M13: stress- P_1 , and (f) M13: strain- P_1 .

properties all play important roles in plaque stress/strain distributions, we used an IVUS data set of a human coronary plaque in our model construction. IVUS-based near-idealized geometries were used for the models in this paper. Our results included eight models with different combinations of four factors, i.e., residual stress (wrapping), axial shrink, circumferential shrink, and material stiffness change. Stress and strain on lumen, cap, out boundary, and whole slice were reported.

Residual stress was discovered in the process of finding the stress-free state from an ex vivo artery ring. For models based on in vivo data, the in vivo artery morphology needs to be shrunk to its no-load state (equivalent to the ex vivo ring). Due to volume conservation law, axial shrink has to be accompanied by radial shrink (or expansion) to keep vessel volume conserved. In fact, vessel out boundary and inner boundary need to have different shrinkage rates (vessel cross section area becomes larger after

axial shrink). The volume conservation law was used to calculate vessel inner and out boundary shrinkages.

Considering the impact of each single factor, wrapping changes stress/strain distributions in a way that it increases stress/strain on out boundary and decreases stress/strain on the lumen, especially the cap over a lipid core. So, previous models without wrapping probably overestimated stress/strain levels on the lumen. Axial stretch increased plaque stress for the whole slice modestly. But it raised lumen and cap stresses by 312–400%. And it changed cap stress from negative to positive. Basically, axial stretch and pressure worked together to counter the compression caused by wrapping. Circumferential shrinkage, if not performed, the vessel would expand under pressure and its lumen would become bigger than its in vivo shape, leading to stress/strain overestimation. Stiffness increase leads to considerable increased stress values on lumen (75% and 314%), out boundary (30% and 138%), cap

Table 5 Impact of residual stress on stress/strain calculations for an eccentric plaque

Model	Circumferential shrinkage	Lumen	Out boundary	Whole vessel	Cap stress
Average stress- P_1 value (kPa)					
M12	Lumen: 9.5%; out boundary: 4.0%	54.84	102.1	71.38	28.72
		100%	100%	100%	100%
M13	Lumen: 8.5%; out boundary: 4.5%	102.3	57.17	69.27	97.59
		186.5%	56.00%	97.04%	339.8%
Average strain- P_1 value					
M12	Lumen: 9.5%; out boundary: 4.0%	0.1111	0.1207	0.1146	0.1051
		100%	100%	100%	100%
M13	Lumen: 9.5%; out boundary: 4.0%	0.1438	0.1056	0.1133	0.1392
		129.4%	87.49%	98.87%	132.4%

M12: model including residual stress and M13: model without residual stress. $p = 130$ mm Hg.

Fig. 10 Cut position has very modest impact on stress and strain calculations: (a) M1: stress- P_1 , (b) M14: stress- P_1 , (c) M1: strain- P_1 , and (d) M14: strain- P_1

(102% and 454%), and the whole vessel (43% and 178%). These results are different from what we reported earlier [27].

4.2 Use of IVUS-Based Near-Idealized 3D Geometry Model. One of the limitations of the study is that we used a 3D cylinder model made from one IVUS slice, not a full 3D plaque model using multiple IVUS slices as we used before [5,22]. The main reason is that the available methods are not able to wrap a plaque segment with curvature and complex morphology. Even though we are realizing the importance of including residual stress in plaque models, how to construct full 3D models with wrapping, circumferential shrink, and axial shrink/stretch remains to be a big challenge for our future effort.

It should be emphasized that the opening angle concept is only applicable to a circular vessel ring which will open with uniform circumferential relaxation. A real physical plaque slice will open with different degree of relaxations at different locations, depending on vessel thickness, plaque components, composition, shape, and its 3D locations. When we cut open a physical plaque slice, we would need to record the exact shape and opening angle (opening angle itself is not enough to define how a noncircular plaque slice would open or close). Then, location-specific displacements would need to be imposed to wrap up the slice (reverse of the opening process) to obtain residual stress/strain correctly. Since we did not have real physical plaque slice open data, our paper assumed uniform circumferential relaxation which is an

approximation. For nonuniform asymmetric plaques with large components, the open-angle assumption will no longer be adequate.

4.3 Model Construction Cost for the Models With the Wrapping-Up Process. An extra iterative procedure is required to determine the circumferential shrinkage for the models with a wrapping-up process. The convergence rate of the iterative procedure is decided by how restricted the convergence criterion is and which iterative method is used. Even though the secant method is used to find the proper circumferential shrinkage, still it normally needs four steps (some models three steps) to find the convergent shrinkage that satisfies the given criterion. It means the time cost for a model involving wrapping-up process is quadrupled (or tripled) compared to a model without a wrapping-up process. This time-consuming feature of the wrapping-up process may hinder the popularity of applying this technique to large-scale patient study.

4.4 Other Plaque Samples and Healthy Vessels. Models were constructed to demonstrate the impact of residual stress on stress/strain calculations for other plaque samples and healthy vessels. Residual stress is complicated for real plaques. It would be really hard to try to get real coverage for plaques in general. Each real plaque would open up in its own way, depending on its components, morphology, and material properties. And, 3D plaque would open up to a 3D shape that we do not have techniques to handle at present time. This remains to be a future challenge.

5 Conclusion

Eight models based on in vivo IVUS-VH and IVUS movie data of a human coronary plaque were constructed to quantify the impact of residual stress, axial shrink/stretch, and circumferential shrinkage, the three factors related to zero-stress status. A three-step procedure was introduced to bridge the gap between the in vivo plaque geometry obtained under in vivo condition and the stress-free state geometry needed for computational models to start simulation. The in vivo geometry should be shrunk axially and circumferentially, and then cut open to obtain its zero-stress state. Starting from here, the residual stress was introduced into the model using a wrapping-up process; and axial stretch and pressurization were done to recover the in vivo blood vessel geometry associated with its in vivo stress/strain distributions. Our model comparison studies indicated that wrapping leads to reduced lumen and cap stress; axial stretch leads to increased overall stress level and can also counter the compressive stress caused by wrapping; and skipping circumferential shrinkage leads to over expansion of the vessel and incorrect stress/strain calculations. The impact of the zero-stress related factors on stress/strain calculations can vary from 30% to 500%. Different combinations of these factors can lead to huge stress/strain differences. Stiffer material leads to high stress values. More vigorous validation and large-scale studies based on more IVUS slices with various plaque morphology and vessel geometry are needed to establish and further improve our model accuracies.

Table 6 Comparison of average stress and strain values between M1 and M14

Model	Circumferential shrinkage	Lumen	Out boundary	Whole slice	Cap stress
Average stress- P_1 value (kPa)					
M1	Lumen: 8.5%; out boundary: 4.5%	42.57	161.49	83.70	29.15
		100%	100%	100%	100%
M14	Lumen: 8.5%; out boundary: 4.5%	44.13	157.20	85.35	30.59
		103.7%	97.34%	102.0%	104.9%
Average strain- P_1 value					
M1	Lumen: 8.5%; out boundary: 4.5%	0.1058	0.1764	0.1261	0.1051
		100%	100%	100%	100%
M14	Lumen: 8.5%; out boundary: 4.5%	0.1063	0.1786	0.1281	0.1051
		103.2%	101.2%	101.6%	100%

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