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ORIGINAL PAPER

On the mechanical behaviour of carotid artery plaques: the influence of curve-fitting experimental data on numerical model results

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Abstract Computational models of diseased arteries are advancing rapidly, and a need exists to develop more accurate material models of human atherosclerotic plaques. However, intact samples for in vitro mechanical testing are not readily available. Most plaque samples are harvested from carotid endarterectomies where the geometries are not suitable for the boundary parameters necessary for classical uniaxial tensile testing. Experimental studies of biological tissue, particularly human plaque tissue, have not specified the minimum width-to-length (WL) ratio necessary for appropriate tensile testing. This study proposes either tensile or planar shear testing on whole specimen samples depending on the WL ratio. However, a "grey-area" of WL ratios exists which are unsuitable for either test, between 0.5:1 and 4:1 WL ratio. Eighteen plaque samples are investigated in this study, and according to classical approaches, two of the plaque samples have WL ratios suitable for tensile testing and four are suitable for planar shear testing. The remaining twelve samples fall in the grey-area of WL ratio. The study analyses which test method is suitable for the samples in this grey-area and what effect using the incorrect test method has on results from a computational model. The study highlights that tissues above a WL ratio of 2:1 are suitable for planar shear testing, and samples below 1:1 are more suited for tensile testing. Therefore, the "grey-area" can be reduced with certain limitations applied by the minor strain assumption which need to be taken into account during experimental testing. This study also demonstrates the influence of curve-fitting experimental results using tensile- and planar shear–based boundary parameters from eighteen plaque samples.

Keywords Carotid artery disease · Plaque properties · Mechanical characterisation · Modelling approaches

1 Introduction

Stroke is a sudden necrosis of brain cells caused by an interruption of normal perfusion to the brain. Stroke has the potential to cause irreversible damage to an array of neurological functions in 22–25 % of victims and death within one year for 25 % of victims (Medtech-Insight 2011). One of the main instigators of a stroke event is the presence of atherosclerotic plaque in the carotid arteries (Guyton 1991). Atherosclerosis refers to a condition in which the walls of an artery thicken due to an accumulation of fatty deposits consisting mainly of lipid and connective tissue matrix. Over time, these deposits harden and form a fibrous cap which can rupture and cause an occlusive thrombosis reaction that can prevent normal blood flow to the brain and lead to a stroke event. Carotid artery stenting (CAS) is a minimally invasive technique of mechanically widening a diseased carotid artery, by deploying a stent at the site of stenosis, compressing the atherosclerotic plaque and widening the lumen to increase blood perfusion. Despite the numerous advantages of CAS over carotid endarterectomy such as increased accessibility, decreased trauma and absence of general anaesthetic (Roffi et al. 2009), it accounts for only 26 % of stroke prevention procedures performed due to the lack of knowledge on the mechanical effect of stents on the plaque structure (Paraskevas et al. 2009).

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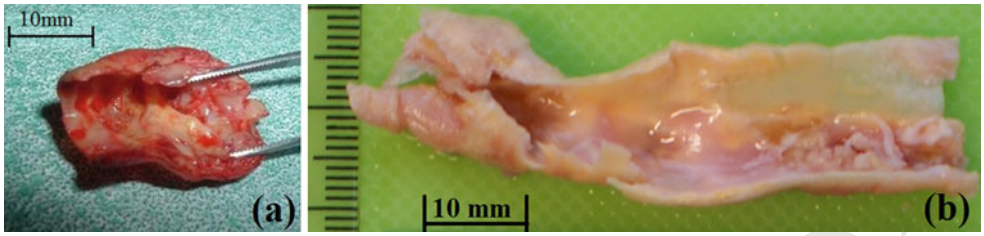

Fig. 1 **a** Fresh whole specimen CAP from the Lawlor et al. (2011) study and **b** a defrosted sample from an ongoing study which highlights the variability in plaque geometry, material and location in the artery

Computational studies of atherosclerotic arteries under physiological conditions have evaluated the stress distribution within the plaques to analyse the biomechanical response to certain geometrical, structural and material variations (Li et al. 2008; Kiousis et al. 2009; Creane et al. 2010; Franquet et al. 2011). A limited number of studies have also examined the biomechanical structural alterations of the plaque to the deployment of stents to improve the design of the stent (Takashima et al. 2007; Cui et al. 2010; Auricchio et al. 2011; Scherer et al. 2011). Computational studies of diseased coronary arteries are more common than the carotid (Cilla et al. 2012; Huang et al 2001; Versluis et al. 2006) and a main limitation in these studies is the material properties representing the plaque model which are developed from experimental data based on a small sample size of human plaque from the aorta (Beattie et al. 1998; Lendon et al. 1993; Loree et al. 1994a), limiting the reliability of the stress values from these studies. The computational simulations of diseased carotid arteries also base the material properties of the carotid plaque on experimental data of atherosclerosis from other parts of the vasculature which have different morphologies and potentially different mechanical responses to stent deployment (Herisson et al. 2011), excluding Creane et al. (2010) which is based on uniaxial tensile data of fresh human carotid plaques undertaken by Maher et al. (2009).

Ideally for improved material properties of diseased tissue, in vivo mechanical characterisation of carotid atherosclerotic plaque (CAP) would be carried out on a patient to develop a specific constitutive material model and apply it to their diseased artery geometry. However, there is no fully validated method of carrying out this in vivo mechanical characterisation procedure. Current studies that mechanically characterise CAPs use in vitro mechanical test procedures developed for engineering materials with specific geometry requirements to satisfy the minor strain assumptions such as pure tension and equi-biaxial testing. Limitations when mechanically characterising any type of excised intact plaque tissue are the random geometry and variance in mechanical response, making it difficult to test the CAP specimen as a whole in pure tension (a common test method for mechanically characterising biological tissue when using a strain energy function (SEF)). Figure 1 highlights the geometrical difference between CAPs excised after a carotid endarterectomy, Fig. 1a is from Lawlor et al. (2011) which is a fresh human CAP tested immediately after excision from the common carotid. Figure 1b is a defrosted human CAP from the carotid bifurcation (left-side) through to the common carotid. There are many limitations to in vitro mechanical characterisation of biological tissue such as the deleterious effect on the structure and residual stresses within the plaque during excision, damage to tissues from clamping and inhomogeneity of the CAP tissue material for an ideal failure at the centre of the specimen.

In vitro studies, testing human and animal biological tissue in tension, range the width-to-length (WL) ratio from 0.5:1 to 0.167:1 in both the circumferential and longitudinal directions, Table 1 (excluding ASTM-International (2009) which is a standard based on engineering materials). Specifically examining the studies of human plaque, the WL ratio varies from 0.3:1 to 0.21:1. The shortest gauge lengths used in these tensile test studies were 3 and 4 mm, Richardson (2002) and Maher et al. (2009), respectively, where it was stated that such a small distance between the clamps can affect the stress distribution within the material during testing. Excluding this gauge length, the experimental plaque studies range from 7 to 15.9 mm in gauge length where in theory this length should be much longer to allow for a larger uniform stress distribution for the governing equations of major and minor strains to hold true when applying the experimental data to a SEF. However, as the tissue contains interconnected fibres, this cutting can deleteriously affect the structure of the fibres as well as alter the global mechanical properties of the plaque. For an immediate improvement in the constitutive material models of CAPs, it is necessary to mechanically characterise the whole plaque specimen as separating the specimen into smaller sections can potentially underestimate the global mechanical properties (Lawlor et al. 2011; Borschel et al. 2003).

Due to the nature of the CAP geometry, when excised from the artery, this study investigates the limitations that geometric ratios associated with excised plaque specimens (WL ratios) have when mechanically tested in either pure tension or planar shear. A "grey-area" of unsuitable WL ratios is created between the correct ratios for tensile and planar

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Table 1 List of experimental studies using tensile tests on biological tissue which also detail the gauge lengths and widths of the samples tested

Author	Length (mm)	WL	Tissue type
Stemper et al. (2005)	15.9	0.5:1	Human carotid artery
Lally et al. (2004)	9.38	0.37:1	Porcine coronary artery
Hanuza et al. (2010)	30	0.33:1	Human aortic artery
Holzapfel et al. (2004)	7–17	0.31–0.13:1	Human iliac plaque
Loree et al. (1994a)	15.9	0.3:1	Human aortic plaque
Raghavan et al. (1996)	40	0.25:1	Human aortic aneurysm
Wang et al. (2001)	40	0.25:1	Human aortic thrombus
ASTM E8	N/A	0.25:1	Tensile testing standard
Maher et al. (2009)	4	0.25:1	Human carotid plaque
Xiong et al. (2008)	20–25	0.25–0.2:1	Human aortic aneurysm
Teng et al. (2009)	9	0.22:1	Human carotid plaque
Lendon et al. (1993)	7	0.21:1	Human aoritc plaque
Silver et al. (2003)	10	0.2:1	Porcine carotid artery
Guinea et al. (2010)	10	0.2:1	Human aortic artery
Di Martino et al. (1998)	22	0.2:1	Human aortic artery
Veronda et al. (1970)	45.7	0.167:1	Cat skin
Richardson (2002)	3	0.167:1	Human coronary plaque

Table 2 List of WL ratios used in a number of experimental studies using mechanical tests on biological tissue in planar shear

Author	Length (mm)	WL	Tissue type
Davis (2004)	N/A	4:1	Shear standard
Gao et al. (2009)	11	4.6:1	Porcine liver
Hollenstein et al. (2011)	10	6:1	Porcine skin

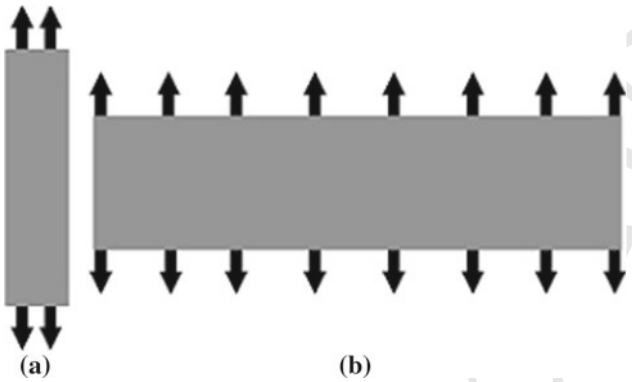

Fig. 2 Idealised computational models of tensile and planar shear uniaxial tests. **a** WL 0.25:1 suitable for tensile testing and **b** WL 4:1 suitable for planar shear testing

shear testing. Currently this "grey-area" is between WL 0.5:1 and 4:1 according to Davis (2004). Unfortunately for whole specimen testing of CAP tissue excised from carotid endarterectomies, the sample geometry can fall into this area. Therefore, there is a need to investigate the feasibility of reducing this area and investigate the errors involved when testing inside this "grey-area". These findings will aid in understanding the effect of changing the governing equations of principal stretches, to suit either tensile or planar shear tests for 18 carotid plaques, on a computational model of an idealised stenosed carotid artery. An understanding of the limitations and percentage error from theoretical minor strains for CAP samples in the grey-area will aid in improved experimental methods when testing whole CAP specimens and more accurate constitutive material models (Table 2).

2 Materials and methods

2.1 Ratio analysis

A computational analysis of the stresses in a test specimen with varying geometric ratio (WL 0.1:1–10:1) was carried out with a consistent hyperelastic material property. By examining the effect of the WL ratio on the resolved stresses and minor strain of the test specimens, the errors involved when the WL ratio is in the "grey-area" for suitable mechanical testing, 0.5:1 to 4:1, were identified. Figure 2 illustrates two of the twelve computational models employed in this study. Figure 2a shows an ideal geometry for tensile testing with a WL ratio of 0.25:1, (b) illustrates a model with a WL ratio of 4:1 suitable for planar shear testing. Comparison of the minor strain at the centre of gauge length

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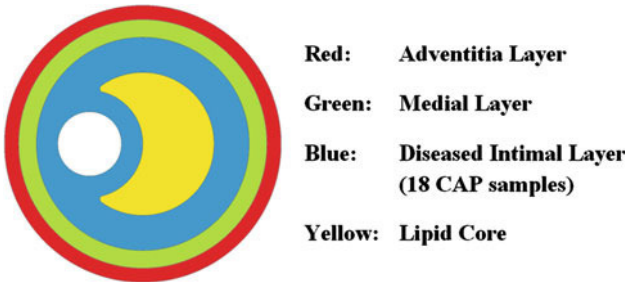

Fig. 3 Dimensioned diagram of the idealised 2D planar model of a diseased carotid artery

of each geometric ratio to the theoretical minor strain will highlight in an idealised computational uniaxial setup the errors involved for geometric ratios within the "grey-area" of 0.5:1–4:1 WL ratios. The "grey-area" is the range of WL ratios which are theoretically unsuitable for tensile or planar shear testing for engineering materials. However, for whole specimen biological tissue testing, this grey-area is too large and needs to be redefined to a smaller range as the current area significantly reduces the number of samples suitable for testing.

2.2 Idealised diseased artery

A two-dimensional cross-section of an idealised atherosclerotic artery was modelled using geometries analogous to work carried out by Li et al. (2008) and Franquet et al. (2011). The geometric model contains a large lipid core which is surrounded by a diseased intimal layer with a fibrous cap of 0.6 mm, Fig. 3. The internal diameter of the artery is 6 mm which was based on Franquet et al. (2011) and reiterated in experimental work by Krejza et al. (2006). The lumen diameter was chosen to be 30 % of the artery diameter, 1.8 mm, which is based on the typical minimum stenosis of a diseased artery which undergoes carotid endarterectomy. The 0.9 mm thickness of the carotid wall was based on Delfino et al. (1997), but can vary up to 1.5 mm (Li et al. 2008). The artery wall was divided into the medial and adventitial layers according to Holzapfel et al. (2000), 0.4 and 0.5 mm, respectively. The lipid core size and shape were based on Franquet et al. (2011). A peak physiological systolic pressure value of 18 kPa was applied uniformly to the wall of the lumen for each model (Cilla et al. 2012).

Grid independence was established using a 6-noded free triangular mesh applied throughout the whole finite element (FE) model. Hybrid formulation, used for incompressible and large deformation problems, and plane strain were applied to this model. Elements were concentrated around the lumen and fibrous cap region, but with at least 6 elements through the thickness of the medial and adventitial layer.

2.3 Material properties

The CAP properties were based on the experimental data of fourteen CAP samples from Lawlor et al. (2011) as well as data of four CAP samples from that study which were not included due to the unsuitablility of the WL ratios for tensile testing. The stress-strain data of each plaque were fitted to a third-order reduced polynomial SEF, the Yeoh form, using an optimisation technique developed with Matlab (r2009a, Natick, MA; The Mathworks Inc., 2009) to minimise the difference in stress values between the Yeoh SEF and the experimental data . The optimisation technique was carried out for each CAP sample using both tensile and planar shear principal stretches leaving 36 material models in the numerical study.

$$\Psi(I_1) = \sum_{(i=1)}^{3} C_{i0}(I_1 - 3)^i \tag{1}$$

The Yeoh SEF is suitable for characterising hyperelastic materials using uniaxial mechanical data, in tension or planar shear, as the function does not depend on the second strain invariant of the Cauchy Green deformation tensor, I_2. C_{i0} are the material coefficients, and I_1 is the first-strain invariant which is based on the principal stretch ratios, Eq. 2.

$$I_1 = \lambda_1^2 + \lambda_2^2 + \lambda_3^2 \tag{2}$$

The principal stretches (λ_1, λ_2 and λ_3) change depending on the uniaxial test, tensile or planar shear, where in both cases λ_1 is the stretch in the loading direction. For tensile testing, the principal stretches are:

$$\lambda_1 = \lambda, \lambda_2 = \lambda_3 = \frac{1}{\sqrt{\lambda}} \tag{3}$$

For planar shear testing:

$$\lambda_1 = \lambda, \lambda_2 = 1, \lambda_3 = \frac{1}{\lambda} \tag{4}$$

The WL ratio governs the degree of deformation that the minor stretch ratio component (λ_2) undergoes during a tensile or planar shear test. During a planar shear test, the minor principal stretch ratio (λ_2) is considered to be 1 which equates to zero strain in the transverse direction. According to Davis (2004), the minor strain is 0.05 times the major strain when the WL ratio is 4:1 which is close to the plane strain condition necessary for the test (Palmieri et al 2009). However, any WL ratio lower than this can lead to a larger deviation from the zero strain assumption in the minor direction. For tensile testing, the minor axis experiences compressive, negative strains, as the principal strain is positive. This study developed two constitutive material models for each of the eighteen plaques based on the Yeoh form, using the tensile and planar shear boundary parameters, and analysing

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Table 3 List of the SEF parameters used for the adventital and medial layers in this study taken from Cilla et al. (2012)

Layer	μ (kPa)	k_1 (kPa)	k_2 (kPa)	κ
Adventita	8.44	547.67	568.01	0.26
Media	1.4	206.16	58.55	0.29

the effect that the WL ratio can have on the stress distribution and mechanical response in an idealised FE model. The lipid core was based on Akyildiz et al. (2011), where the lipid core is treated as a very soft and nearly incompressible tissue, with a Young's Modulus of 1 kPa and Poisson's ratio of 0.45 rather than an incompressible liquid, which is based on experimental work carried out by Loree et al. (1994b). Other approaches (Loree et al. 1994b) have treated the lipid core as a nearly incompressible fluid which is not able to sustain shear stress. The effects of the 1 kPa assumption on the trends presented in this study were evaluated and discussed in the limitations section. The arterial media and adventitia layers were modelled using an anisotropic SEF developed by Gasser et al. (2006). The strain energy per unit of reference volume is represented as Ψ.

$$\Psi = \mu(I_1 - 3) + \frac{k_1}{k_2}(\exp(k_2[\kappa(I_1 - 3) + (1 - 3\kappa)(I_4 - 1)]^2) - 1) \tag{5}$$

From Eq. 5, μ, k_1, k_2 and κ are material parameters, I_1 and I_4 are invariants of the Cauchy Green strain tensor. The parameter kappa ($0 \leq \kappa \leq 1/3$) describes the level of dispersion in the fibre directions. The parameters for adventitial and medial layers were based on readily available data of arterial tissue from Cilla et al. (2012), listed in Table 3. The model was assumed incompressible, by setting the compressibility value (D) to zero for each material property, to simplify the material model (Holzapfel et al. 2000).

3 Results

3.1 Ratio analysis

Table 4 lists the different gauge lengths, WL ratios and plaque type of the CAP samples tested, highlighting the size and random nature of the CAP specimens. Figure 4 illustrates the percentage error of the minor strains of each WL ratio, from 0.1:1 to 10:1, from the theoretical minor strain suitable for either tensile (red area) or planar shear (blue area) testing. For example, any WL ratio less than 0.5:1 has minor strain values 100 % in error for planar shear testing and WL ratios greater than 4:1 has minor strain values 100 % in error for tensile testing making any of these ratios unsuitable for those test methods.

Table 4 List of gauge length, WL ratios and plaque type for each CAP sample

Plaque	Length (mm)	WL	Type
1	16	1.19:1	Mixed
2	7.8	2.25:1	Soft
3	4.72	3.51:1	Soft
4	5.8	0.45:1	Mixed
5	3.1	5.55:1	Mixed
6	7.98	1.04:1	Hard
7	10.05	1.32:1	Soft
8	3.96	5.02:1	Soft
9	6.1	1.93:1	Hard
10	5.6	2.55:1	Soft
11	6.42	2.02:1	Mixed
12	6.11	2.05:1	Soft
13	5.18	2.53:1	Soft
14	4.57	0.44:1	Mixed
15	6.89	4.50:1	Mixed
16	7.08	1.90:1	Mixed
17	2.88	4.01:1	Soft
18	9.89	1.95:1	Mixed

Using current standard approaches and the WL ratios in Table 4, only two CAP samples are suitable for tensile testing (4 and 14) and four CAP samples are suitable for planar shear testing (5, 8, 15 and 17) leaving twelve CAP samples unsuitable for either test. Excluding twelve CAP samples from this experimental study is not ideal due to the difficulty of acquiring these human CAP samples and the desire not to deleteriously cut the samples into smaller sections which could significantly alter the global mechanical properties. Therefore, it was decided to assess the current "grey-area" WL ratios to determine the theoretical minor strain errors involved with test samples in this area.

FE analysis of WL ratios from 0.1:1 to 10:1 shows that ratios less than 0.5:1 and greater than 4:1 are suitable for tensile and planar shear testing, respectively, as the minor strain is correct within 5 % for more than 80 % of the gauge length, Fig. 5c, d. However, for the ratios that fall between 0.5:1 and 4:1, the minor strains are less than 80 % of the gauge length, Fig. 5a, b (1:1 and 2:1, respectively). From Fig. 4, the percentage error from the theoretical minor strain of 2:1 WL is 65 and 32 % from tension and planar shear, respectively, indicating that planar shear testing is more suitable. However, this is only true for 55 % of the gauge length area, Fig. 5b. Again looking at Fig. 4 for the WL ratio 1:1, the percentage error is 12 and 85 % from tension and planar shear, respectively, indicating that tensile testing is more suitable.

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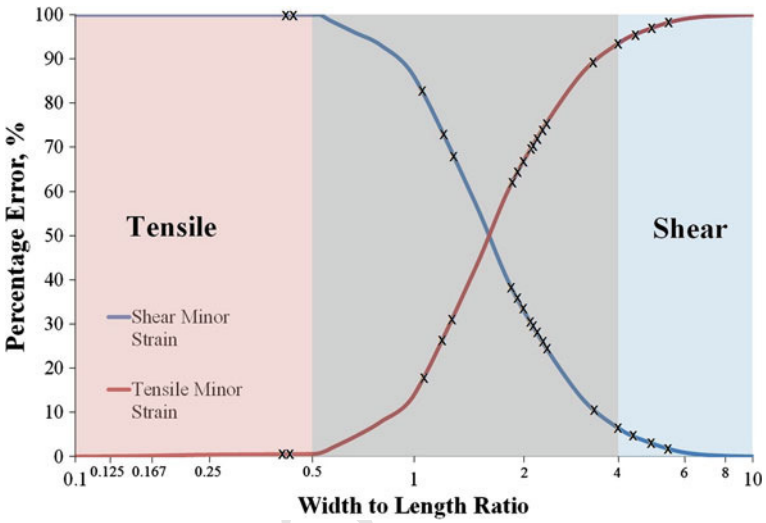

Fig. 4 The percentage error of each CAP sample (*black X*) from the theoretical minor strain suitable for tensile (*dark red line*) and planar shear (*dark blue line*) for each geometric ratio that is suitable for tension (0.1:1–0.5:1), for planar shear (4:1–10:1) and in the "*grey-area*" (0.5:1–4:1)

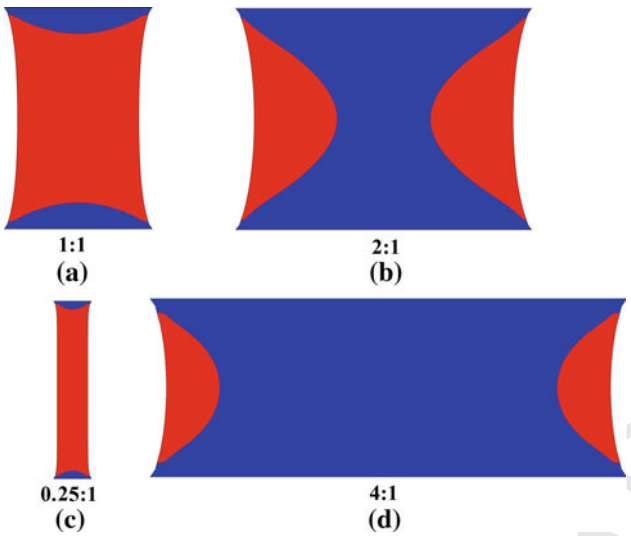

Fig. 5 Minor Strain plots for tension and planar shear of samples with different WL ratios: **a** 1:1, **b** 2:1, **c** 1:1 and **d** 4:1, where *red* denotes minor strain suitable for tension (**a**, **c**) and *blue* is suitable for planar shear (**b**, **d**)

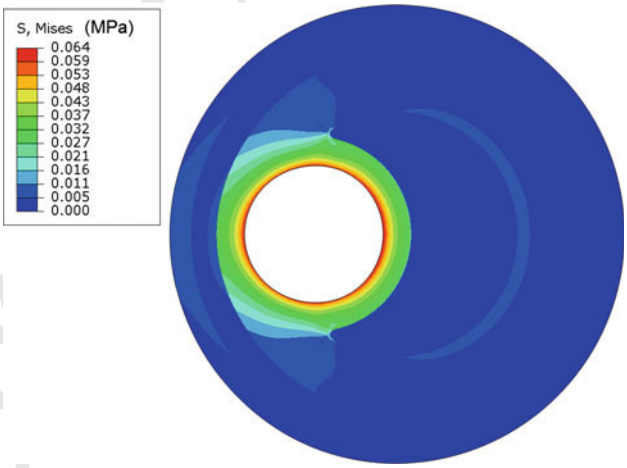

Fig. 6 Von Mises stress (MPa) distribution in an idealised stenosed artery. Peak stresses occur on the lumen closest to the lipid pool and the shoulder regions of the lipid pool

However, again this is only true for 70 % of the gauge length, Fig. 5a.

3.2 Idealised diseased artery

An example of the von Mises stress distribution of a 2D plane strain–idealised diseased artery model is shown in Fig. 6, CAP sample 7, using material model developed from planar shear principal stretches (Eq. 4). The peak von Mises stress typically occurs at the point on the lumen closest to the lipid pool. The peak von Mises, maximum principal stresses and radial displacement were recorded. A constitutive model was developed for each of the CAP samples in both tension and planar shear, based on Eqs. 3 and 4, respectively. The results demonstrated that the peak stress and displacement values were typically larger in the FE models using the planar shear–based SEF.

Figure 7 quantitatively shows the difference in radial displacement from the lumen centre along a horizontal centreline through the stenosed artery model. This graph highlights the similar behaviour of both models, but the larger radial displacement of the planar shear SEF through each section of the model of CAP sample 8. Figure 8 illustrates the difference in peak radial displacement between the tensile-based SEF model (a) and the planar shear model (b) of CAP sample 8 where the planar shear model has larger displacements for this particular sample and for all samples, excluding sample 6. CAP sample 8 was chosen as the geometry of the specimen suggested that it should be characterised in planar shear rather than tension, and the sample best illustrates the underestimation in radial displacement for a tensile-based FE model shown in Fig. 8a.

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Figures 9, 10 and 11 are data plots of the radial displacements along the circumference of the lumen, where the start point (0 °) is at the right side of the lumen closest to the lipid core and continues counter clockwise. These figures compare the radial displacement of the undeformed original lumen to the deformed lumen of both the tensile and planar shear models of CAP samples 8, 14 and 13, respectively. CAP samples 8 and 14 were chosen as the WL ratios of each are suitable for planar shear and tension, respectively. CAP sample 13 has a WL ratio of 2.53:1 which places the sample in the grey-area and creates a reduced percentage difference in lumen area between the planar shear and tension.

Each of the CAP samples were assigned to averaged WL ratios, which ranges from 0.5:1 (suitable for tensile testing) to 5:1 (suitable for planar shear) in increments of 1, and the percentage difference of the radial displacements of the lumen area between the tensile and planar shear models were analysed in Fig. 12. Figure 12 highlights that the percentage difference between the tensile and planar shear models of each CAP sample is higher at the WL ratios suitable for tensile, 0.5:1, and planar shear, 4:1 and 5:1. This suggests that reassessing the "grey-area" can alter the WL ratios limits to a maximum of WL 1:1 for tensile testing and a minimum WL of 2:1 for planar shear where only 6 of the 18 (33 %) of the CAP samples are unsuitable for testing, Fig. 13.

4 Discussion

Recent computational studies aim to simulate the deployment of stents in diseased carotid arteries and to evaluate the stress distribution in vivo throughout the plaque. These studies make it imperative to understand the global mechanical properties of carotid plaques. Idealised FE analysis of different WL ratios highlighted the significant errors in the minor strain associated when testing a specimen outside of the suitable ratios for tensile and planar shear testing.

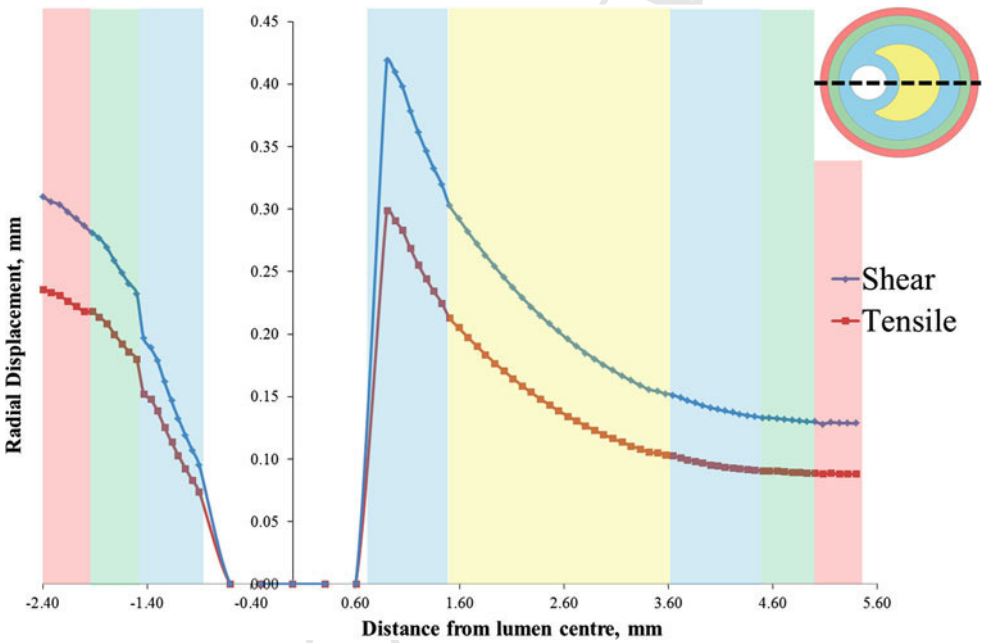

Fig. 7 Radial displacement from lumen centre along *dashed line* (*inset*) of stenosed artery for both the tensile (*red*) and planar shear (*blue*) models for CAP sample 8. *Shaded regions* on plot match the material sections outlined in Fig. 3 (*inset*)

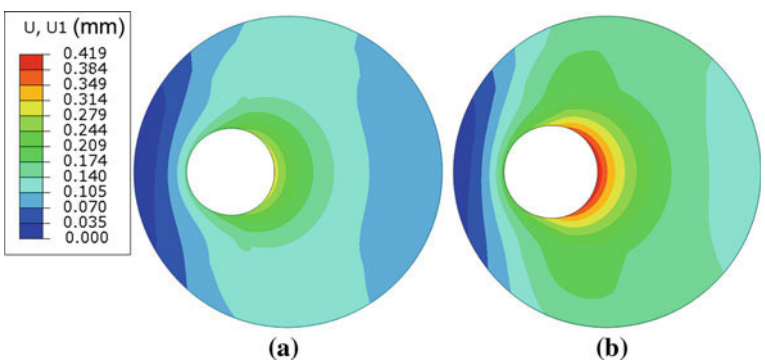

Fig. 8 Contour of radial displacement (mm) from lumen centre in an idealised stenosed model of plaque sample 8 with a material model based on tensile (**a**) and planar shear (**b**) principal stretches

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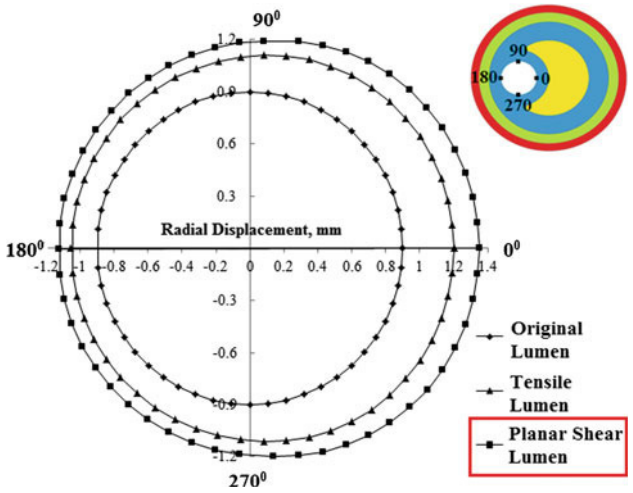

Fig. 9 Radial displacement (mm) along lumen circumference of the original lumen diameter and the deformed lumen for the tensile and planar shear models for CAP sample 8, where the WL ratio (5.02:1) is suitable for planar shear testing, *red box*

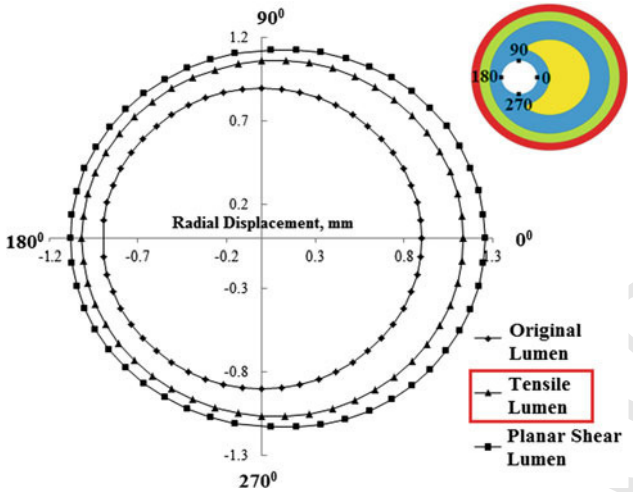

Fig. 10 Radial displacement (mm) along lumen circumference of the original lumen diameter and the deformed lumen for the tensile and planar shear models for CAP sample 14, where the WL ratio (0.44:1) is suitable for tensile testing, *red box*

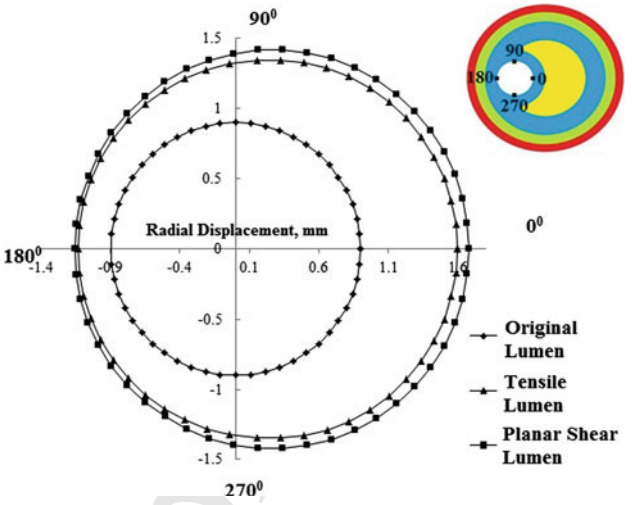

Fig. 11 Radial displacement (mm) along lumen circumference of the original lumen diameter and the deformed lumen for the tensile and planar shear models for CAP sample 13, where the WL ratio (2.53:1) falls in the "*grey-area*" of testing

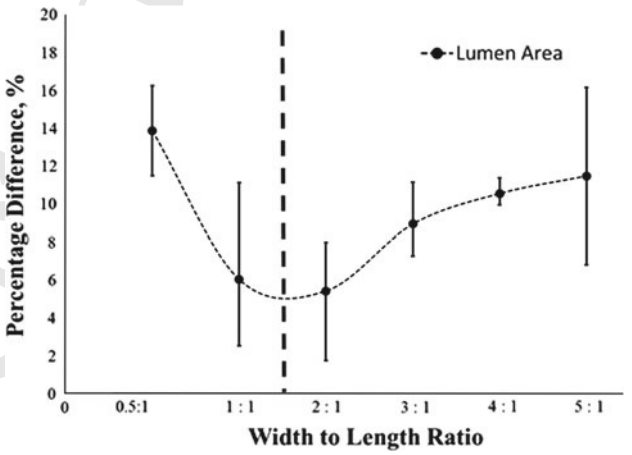

Fig. 12 Percentage difference between lumen areas of material models based on tensile or planar shear principal stretches for each plaque sample (grouped by WL ratio). The dashed line indicates the lowest percentage error and cut-off point between using tensile and planar shear tests

Unlike engineering materials, biological tissue cannot be altered to suit the required geometrical parameters needed for the boundary conditions to analytically develop constitutive material models, without changing the global mechanical behaviour of the sample. The acquisition of whole human CAP specimens is difficult and limited which makes it imperative to mechanically test every available specimen even when the WL ratio does not fall within current standards. Twelve of the eighteen plaques were theoretically unsuitable for either tensile or planar shear testing, Table 4. However, a precise knowledge of the errors involved and a reduction of this "grey-area" can aid in improved experimental methods and more accurate material models for FE analysis of stent deployment without wastage of CAP samples.

4.1 Ratio analysis

The geometric ratio analysis carried out in this study illustrates the large error in minor strain between WL ratios 0.5:1 and 4:1 for both tensile and planar shear testing, Fig. 4. This analysis highlights the limitation when testing specimens in this "grey-area". However, as twelve of the eighteen plaque specimens are in this area, it is a common and unavoidable issue. The use of contactless measurement of the strain in an

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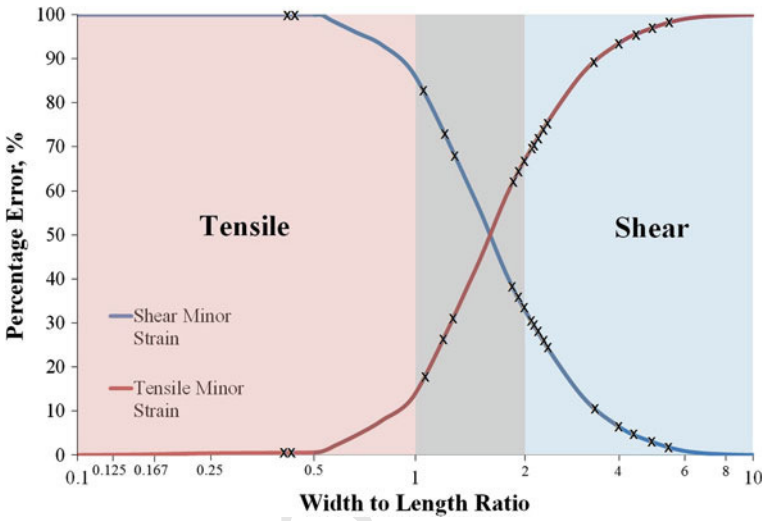

Fig. 13 The percentage error of each CAP sample (*black X*) from the theoretical minor strain suitable for tensile (*dark red line*) and planar shear (*dark blue line*) where the limits have been reassessed to reduce the "*grey-area*" from WL 0.5:1–4:1 to WL 1:1–2:1

area of the sample where the minor strain is known to be suitable for pure tension or planar shear throughout the whole test could improve the accuracy of the results. For example, WL 2:1 ratio the minor strain at 50 % strain is in planar shear for only 55 % of the gauge length from the vertical centre, Fig. 5b, whereas for WL 1:1 ratio the minor strain is correct for tension in only 70 % of the gauge length at 50 % strain, Fig. 5a. The contactless strain measurement would have to take into account this limited area for each ratio in the area throughout the test. This is necessary to ascertain accurate global mechanical behaviour of CAP samples for improved SEF material models to be used in future FE studies.

4.2 Idealised diseased artery

The computational study on the idealised stenosed artery evaluated the effect of changing the principal stretches, to tensile or planar shear, had on the numerical model through the altered SEF. The peak von Mises stress values typically occurred at the point on the lumen closest to the lipid core due to the soft and deformable nature of the core material. The peak maximum principal stress was located on the lumen closest to the lipid core for twelve of eighteen (66 %) samples and at the shoulder cap region of the lipid core for six of the eighteen (33 %) samples. The difference between the peak stress at each location was no greater than 12 % for these CAP models for either the tensile or planar shear approaches. The peak stress values were typically larger for the planar shear–based models. The largest deformation of the lumen occurred in CAP samples 2 and 17 due to the soft nature of these samples allowing for a large displacement.

In theory, the planar shear-based SEF is expected to be stiffer than the tensile-based version when using the same experimental data. The results from the numerical model reiterate this theoretical expectation as there is decreased stress and radial displacement in CAP sample models that should be based on planar shear test rather than tensile, Fig. 8. This emphasises the incorrect assumption of characterising samples in the grey-area that have greater width than length to a tensile-based SEF. This assumption can lead to numerical models underestimating the realistic global mechanical behaviour of the CAP samples with these geometric ratios, Figs. 9, 10 and 11. Figure 10 shows sample 14 which is suited for tensile testing only and that the FE model using the planar shear–based SEF overestimates the lumen displacement and vice versa for Fig. 9.

Assigning the CAP sample models to WL ratios in the "grey-area", which ranges from 0.5:1 (suitable for tensile testing) to 4:1 (suitable for planar shear) in increments of 1, the greatest percentage error between lumen area occurred at the extremities, 0.5:1 and 5:1, as these ratios are farthest from the specified geometrical ratio needed for the respective test method, Fig. 12. For certain samples between, 1:1 and 2:1 the percentage difference between the lumen areas is reduced; as expected from Fig. 4 the percentage errors are similar from tension and planar shear for these WL ratios. Results show that characterising experimental data of a CAP sample with a geometric ratio unsuitable for either uniaxial test to a SEF has a significant effect on the numerical analysis. However, as acquisition of human CAP specimens suitable for in vitro mechanical testing is limited, it is necessary to characterise these particular CAP samples. Prior to this study, the "grey-area" was not clearly defined for unsuitable geometric ratios of biological soft tissues for tensile testing as some studies used WL ratios as low as 0.4:1, but according to engineering standards, the grey-area can be between 0.25:1 and 4:1.

This study demonstrates that planar shear testing can be carried out on samples with WL ratios as low as 2:1 with certain errors in the minor strain involved and for samples below 1:1 tensile testing is suitable, but again with certain

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limitations involved for ratios that fall within the "grey-area". Therefore, the "grey-area" is reduced from 0.5:1 ≤ WL ≤ 4:1 to 1:1 ≤ WL ≤ 2:1 (Fig. 13). It is also proposed that if a CAP sample has a WL ratio that falls within this new "grey-area" the gauge length should be altered when mounting the specimen in the clamps to achieve a WL ratio outside this "grey-area" avoiding the larger errors involved and improving the accuracy of the material model developed to characterise the CAP sample.

4.3 Limitations

The simplified computational analysis of the idealised ratios with uniform thickness was carried out to highlight the errors theses geometric ratios contain when compared to theoretical minor strain. The idealised 2D plane strain models were used in the numerical study is an over-simplification of a diseased artery. However, as this was a comparative study, this setup was deemed suitable as was the exclusion of residual strains and geometrical variations of the CAP samples. The effects of the 1 kPa assumption on the trends of this study were evaluated by varying the Young's Modulus of the lipid core down to zero and this affected the peak von Mises stress, peak displacement and deformed lumen area results by 3.33, 6.08 and 1.57 %, respectively. The CAP samples were characterised using the Yeoh SEF which assumes the material is isotropic and homogenous. However, as the main priority of this study is to analyse the plaque behaviour in the circumferential direction, the authors believe that an isotropic and homogenous assumption for the material properties is appropriate. This methodology of intact plaque testing is not without its own limitations, and the authors ultimately wanted to assess the strength of these tissues as a whole. Biaxial testing of plaque samples is necessary in future studies that aim to understand the anisotropic behaviour of carotid plaques (Holzapfel et al. 2004). The sample size of CAPs used in this study was small, but this limitation further highlights the need to redefine the ratios grey-area that can be used for uniaxial testing as well as taking into account the experimental errors to improve the data needed for curve fitting of SEFs.

5 Conclusion

This study highlights that using the incorrect boundary parameters in a SEF can affect the peak stress and radial displacement values in a numerical model. The percentage error radial displacement is largest for CAP samples with WL ratios of 0.5:1 and 5:1 between the constitutive models developed for tensile and planar shear. It is important to characterise the sample using the correct boundary conditions, tensile or planar shear, for samples with certain geometrical ratios. However, as many whole CAP specimens typically do not have the required geometric ratio to suit these parameters, this study suggests to characterise samples to a SEF that have a WL ratio of 1:1 or less using tensile parameters and for samples greater than WL 2:1 to a planar shear setup. There are significant limitations when following these assumptions, and the use of contactless strain measurement in an area of the sample where the minor strain is known to be correct is imperative for more accurate experimentation of these CAP samples in the grey-area.

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