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Residual strains in conduit arteries

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Abstract

Residual strains and stresses are those that exist in a body when all external loads are removed. Residual strains in arteries can be characterized by the opening angle of the sector-like cross-section which arises when an unloaded ring segment is radially cut. A review of experimental methods for measuring residual strains and the main results about the variation of the opening angle with arterial localization, age, smooth muscle activity, mechanical environment and certain vascular pathologies are presented and discussed. It is shown that, in addition to their well-established ability to homogenize the stress field in the arterial wall, residual strains make arteries more compliant and thereby improve their performance as elastic reservoirs and ensure more effective local control of the arterial lumen by smooth muscle cells. Finally, evidence that, in some cases, residual strains remain in arteries even after they have been cut radially is discussed.

Keywords: Opening angle; Residual stress; Remodeling

1. Introduction

It has been known for at least 40 years (Bergel, 1960) that when a ring segment is cut from an artery and a radial cut is made in the ring, it uncoils like a watch spring. In 1983 Vaishnav and Vossoughi and Chuong and Fung noted that this implied the existence of circumferential residual strains and therefore stresses, which remained in the vessel even when it was free of all external loads and were revealed only when it was cut. Using data from the rabbit thoracic aorta, Chuong and Fung showed that the ratio of maximum circumferential stress to its mean value was about 1.4 when residual stress was taken into account, whereas in the absence of residual stress the ratio was 6.5. (Chuong and Fung, 1986). They suggested that residual stress developed in growing arteries so as to reduce stress gradients across the wall thickness. An alternative approach, termed the *uniform strain hypothesis*, was adopted by Takamizawa and Hayashi (1987) who started from the assumption that, under physiological conditions, the circumferential strain is constant across the thickness of a blood vessel wall. From in vitro measurements of transmural pressure, external diameter and axial force they derived the stress–strain relation for the dog carotid artery and, using a logarithmic form of the strain energy density function to calculate the stress distribution, they found that the radial distribution of circumferential stress was almost uniform under physiological conditions. This implied the existence of residual stresses and strains within the wall when free of all external loads. Subsequent studies have demonstrated circumferential residual strains in conduit and muscular arteries from a variety of mammals including man, as well as in other tubular structures such as the left ventricle (Omens and Fung, 1990; Summerour et al., 1998; Weis et al., 2000), veins (Liu and Fung, 1992; Pang et al., 2001), trachea (Han and Fung, 1991), ureter (Hansen and Gregersen, 1999), oesophagus and the gastrointestinal tract (Gregersen et al., 2000; Lu and Gregersen, 2001).

In spite of the increasing body of experimental and theoretical studies on vascular residual stress and strain a number of outstanding problems remain. The aims of this paper are (i) to review recent studies of residual stress and strain in arteries and to identify those experimental reports about which there is little disagreement and those which present conflicting results; (ii) to review current methods for the measurement of residual

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strains; (iii) to present some new ideas about the effect of residual strain on vessel dimensions and compliance under physiological conditions and; (iv) to suggest possible directions for future studies.

2. Methods

2.1. Measurement of residual strains

By definition residual strains are defined as those that exist in a solid when all externally acting loads are removed. To quantify residual strains we must know the displacement field, which describes the transformation of the zero-stress configuration into the unloaded one. Chuong and Fung (1986) suggested that a single radial cut in the ring is sufficient to yield the zero-stress state. This configuration is close to a circular sector and is completely described by the inner and outer arc lengths and the angle α between two lines joining the midpoint of the inner arc of the cross-section to its tips, known as the *opening angle* (Fig. 1a). In the no load configuration the cross-section is considered to be a circular ring (Fig. 1b). However, this information is still not sufficient to calculate the distribution of the residual strains across the wall thickness because it does not specify the deformation of an arbitrary point within the wall. Chuong and Fung (1986) assumed that the transformation of the circular sector into a circular ring is a plane strain deformation, and exploited the incompressibility of arterial tissue. Then, the residual circumferential stretch ratio λ_θ, defined as ratio of the length of an arc in the no load state to the corresponding length of the arc in the zero-stress state, is

$$\lambda_\theta = \frac{\pi r}{(\pi - \alpha)R},$$
$$r = \sqrt{r_i^2 + \frac{(\pi-\alpha)}{\pi}[R^2 - R_i^2]}, \quad R_i \leqslant R \leqslant R_o, \tag{1}$$

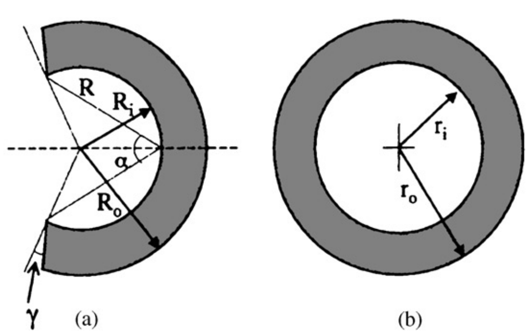

Fig. 1. A cut arterial ring in its zero-stress state. The opening angle α, a frequently used measure of circumferential residual strain, is defined as the angle subtended at the mid-point of the inner circumference by its two ends (Chuong and Fung, 1986). The edge angle γ (Li and Hayashi, 1996) may also be used for this purpose.

where r and R are the radii of an arbitrary point and r_i and R_i the inner radii in the no load and zero-stress state, respectively (Fig. 1). R_o is the outer radius in the zero-stress configuration. The corresponding residual circumferential Green strain is

$$e_\theta = \tfrac{1}{2}(\lambda_\theta^2 - 1). \tag{2}$$

It follows from Eq. (1) that the residual strains can be completely determined if the geometry of the zero-stress configuration and the inner radius of the arterial ring segment in the no load state are recorded. Evidently residual strains exist only if the opening angle (subsequently abbreviated "OA") is not zero. Although the magnitude of the residual strains depends also on the other geometrical dimensions of the zero-stress configuration, the magnitude of the opening angle itself is often used to characterize residual strains.

In the majority of reports, photographic or video images of the vessel in its unloaded state and, subsequently in the zero-stress state, are obtained and required geometrical parameters are determined by manual or computerized measurement of the two images. In a typical experiment rings from excised vessels are placed in a neutrally buoyant medium and an image of the unloaded state is obtained. The ring is then cut, replaced in the medium and an image of the putative zero-stress state is captured. It is possible that the movement of the segment as it approaches the zero-stress state may be impeded by surface tension and/or drag between the vessel and the base of the container. There have been no reports of attempts to quantify these effects, although our own (unpublished) observations suggest they may account for the rather large variability in OA between adjacent ring segments from the same vessel. Matsumoto et al. (1996) have described an ingenious solution to this problem in which the cut ring is suspended in medium attached to the tip of a micropipette by suction.

In practice, the cut specimens rarely take the form of circular segments, however this technique remains popular, presumably because of its technical simplicity. Pictures of the zero-stress state clearly show that many, perhaps the majority, of cut vessel specimens open in an asymmetric fashion. In order to avoid the problem of non-circularity which is worse still in diseased vessels due, for instance, to remodeling in the vicinity of atheromatous plaques, Matsumoto et al. (1995) described a technique in which the vessel profile is divided into 32 segments and residual strains were derived from the local curvature and dimensions of each segment. More recently Li and Hayashi (1996) have reported an alternative approach based on the measurement of the *edge* angle (γ in Fig. 1a, defined by equation 3 in their paper). The authors argue that values of residual strain calculated from measurements of the OA may be in error if the edge angle is not small. This effect may well be important in thick walled muscular arteries, although as the OA increases the edge angle becomes smaller. In measurements on rabbit aorta, carotid and femoral arteries the edge angle never exceeded 9°, which suggests that measurement errors might significantly affect the correction term which depends on the tangent of the edge angle.

Debes and Fung (1995) sprayed excised canine pulmonary arteries with ink and measured surface strains directly by optically tracking the displacement of groups of three spots. A similar approach was used to measure residual strains using black ink micro-dots sprinkled on the cross section of uncut rings (Han and Fung, 1996). This elegant technique, a modification of which was later used by Zhao et al. (2000), on the adventitial surface of the vessel allows direct measurement of the local strain distribution although it is obviously limited to measurements at exposed surfaces only.

When an arterial ring is cut it springs open rapidly and continues to open more slowly reaching a constant OA after 20–30 min. In a number of studies (Vaishnav and Vossoughi, 1987; Liu and Fung, 1989; Hong et al., 1995; Matsumoto et al., 1995; Hong et al., 1997) where this effect may not have been accounted for, the degree of residual strain would therefore have been underestimated. The effect of temperature on OA has rarely been discussed. Liu (1990) (cited in Liu and Fung, 1992) in measurements on systemic and pulmonary arteries in the rat, and Frobert et al (1998) on pig coronary arteries observed no significant change of residual strain in the range 25–40°C. Our own observations on the rat aorta confirm this in the range 10–37°C (Badrek-Amoudi et al., 1996). In studies on the effect of vascular smooth muscle activity on residual strain, temperature and the composition of the surrounding medium should, of course, be carefully controlled.

2.2. Calculation of residual stress

In contrast to strains, which can be directly determined from measurable quantities, residual stresses must be calculated. The required input information is the geometry of the zero-stress configuration and a description of the mechanical properties of arterial tissue in terms of appropriate constitutive equations. Chuong and Fung (1986) have calculated the residual strains and stresses in the rabbit thoracic aorta using the solution of axisymmetric plane strain deformation of a circular sector (Green and Adkins, 1970). The arterial wall was considered to be a homogeneous, incompressible, orthotropic and elastic material. Then the constitutive equations that relate stresses and strains follow from a strain-energy density function. This is a function of the Green strains determined with respect to the zero-stress configurations and contains material constants that must be determined from inflation-extension experiments on arterial segments. It is worth noting that, given the zero-stress configuration and the strain energy density function, the inner radius of the unloaded ring segment can also be calculated solving the boundary value problem for no traction on the isolated ring. The residual circumferential stretch ratios and the strain are calculated from Eqs. (1) and (2).

3. Results and discussion

3.1. Effects of residual strains

As mentioned above, the first experimental results quantifying residual strains were reported by Vaishnav and Vossoughi (1983) for pig and cow aortas, showing that residual strains estimated in terms of a classical strain tensor are negative at the inner part of the arterial wall and positive at the outer part. Independently, Chuong and Fung (1986) calculated the residual strains and stresses from the geometry of the opened-up configuration and the strain energy function of a rabbit thoracic aorta. The dimensions in the zero-stress state (Fig. 1a) are: inner arc length $L_i = 9.75$ mm; outer arc length $L_o = 11.25$ mm; OA $\Phi = 108.6°$. The strain energy function took the form $W = 0.5c\exp[b_1e_\theta^2 + b_2e_z^2 + b_3e_r^2 + 2b_4e_\theta e_z + 2b_5e_ze_r + 2b_6e_\theta e_r]$, where e_r, e_θ and e_z, are Green strains in the radial, circumferential and axial directions and $c, b_1, \ldots, b_6$ are experimentally determined constants as follows: $c = 22.40$ kPa, $b_1 = 1.0672$, $b_2 = 0.4775$, $b_3 = 0.0499$, $b_4 = 0.0903$, $b_5 = 0.0585$, $b_6 = 0.0042$. The axial (off-plane) stretch ratio is taken to be one. The distribution of the residual stretch ratios and residual Cauchy stresses are shown in Fig. 2.

Two points deserve special consideration. First, the values of circumferential and radial residual strains are close to one and the corresponding residual stresses are

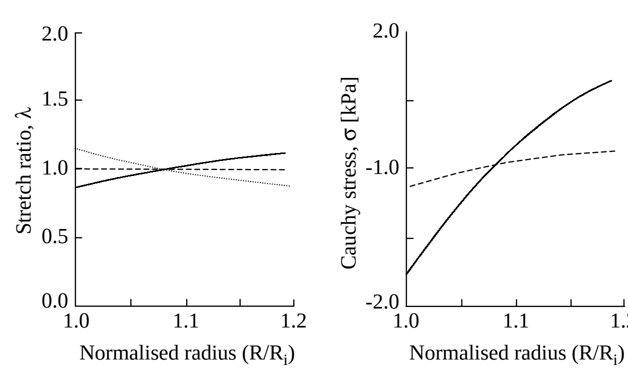

Fig. 2. Distributions of principal stretch ratios (left hand panel) and residual stresses (right) in the unloaded thoracic aorta of the rabbit. (dotted line refers to the radial direction; solid lines to circumferential direction; and dashed lines to axial direction) (Redrawn from Chuong and Fung, 1986, with permission).

small. Second, assuming that the axial stretch ratio is constant across the wall thickness and is equal to one, it is not possible strictly to satisfy the condition that the unloaded configuration is traction free. To realise the transformation of the circular sector into a circular ring by the prescribed plane strain deformation, axial residual stresses σ_z must be applied (Fig. 2b). Moreover, the condition of zero axial traction is not satisfied in an integral form across the whole cross section, as suggested by Humphrey (1995) and Rachev (1997). However, strictly satisfying this condition yields a value of the axial stretch ratio very close to one (Humphrey, 1995), which justifies the value adopted by Chuong and Fung (1986). Exactly determining the residual strain and stress distribution in an unloaded arterial segment remains an open problem which may be successfully attacked using 3-D finite element methods elaborated for an orthotropic elastic solid undergoing finite deformations. On the other hand, in the particular case of relatively thin-walled arteries, residual strains can be approximately calculated using beam theory, assuming constancy of the wall thickness and mid-wall arc length when a sector bends into a circular ring (Rachev et al., 1995).

Fig. 3 illustrates the distribution of the circumferential stretch ratios and stresses under physiological conditions (internal pressure, 16 kPa (120 mmHg) and axial stretch ratio, ($\lambda_z = 1.691$) when residual strains are taken into account. When compared to their previous results (Chuong and Fung, 1983) concerning three-dimensional stress distribution in arteries, consideration of residual strains strongly reduces the gradient of the circumferential stress across the wall thickness. It is worth noting this effect cannot be directly explained by a superposition of the small residual stresses on much larger circumferential stresses caused by inflation of the thick-walled tube, although such an interpretation, adopted from the classical theory of elasticity, is often used for illustrative purposes. The effect is better

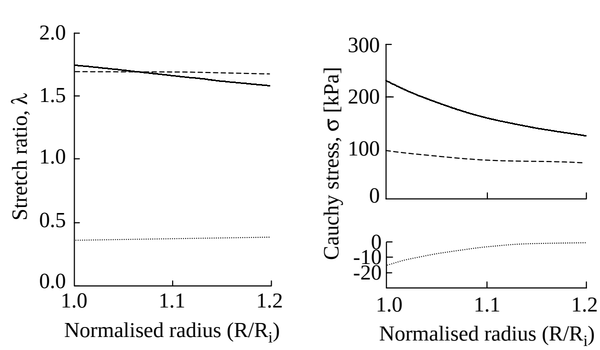

Fig. 3. Distributions of principal stretch ratios (left hand panel) and residual stresses (right) in the rabbit thoracic aorta at a transmural pressure of 120 mmHg and axial stretch ratio 1.691. (solid line, λ_θ; dashed line, λ_z; dotted line λ_r. Redrawn from Chuong and Fung, 1986, with permission).

understood when the strain measures are considered. Residual circumferential strains correspond to stretch ratios slightly smaller than 1 at the inner arterial surface and slightly greater than 1 at the outer surface (Fig. 2a) while the arterial pressure and axial forces extending the artery to its in situ length cause large elastic deformations (Fig. 3a). It is easy to see that the circumferential stretch ratio under physiological conditions calculated with respect to the zero-stress configuration is a product of the stretch ratio corresponding to the deformation from the zero-stress state to the unloaded state, and the stretch ratio corresponding to the subsequent finite deformation in the physiological state. As a result, residual strains decrease the magnitude of the circumferential stretch ratio at the inner surface and increase it at the outer surface compared to the values calculated when residual strains are neglected. Because arterial tissue exhibits a pronounced mechanical non-linearity over the range of physiological deformations, even small alterations in the stretch ratios cause significant changes in the corresponding stresses.

The idea that residual strains homogenize the circumferential stress distribution was formulated by Fung (1983) as a manifestation of the "principle of optimal operation". According to this principle uniform stress distribution ensures the optimal performance of an artery as a load-bearing thick-walled structure. Moreover, it provides a uniform local mechanical environment for vascular smooth muscle cells throughout the arterial wall, thus optimizing their performance. Assuming that the mechanical environment plays an important role in vascular morphology (Fung, 1993a) the principle of optimal operation is in keeping with the small differences in scleroprotein in vascular smooth muscle cell content across the wall thickness found in some arteries (Stergiopulos et al., 2001).

We used the geometrical and mechanical data for a rabbit aorta, given in Chuong and Fung (1986) to calculate the pressure/inner radius relationship with and without accounting for residual strains (Fig. 4). The axial stretch ratio was kept at its in situ value of 1.691. We found that, at a given pressure, residual strains increase the arterial lumen when compared to its size in the absence of residual strains. According to the Laplace law, the mean circumferential stress in the arterial wall is

$$\langle \sigma_\theta \rangle = \frac{Pr_i}{h},$$

where P is the arterial pressure and h is the deformed wall thickness. Residual strains increase the wall tension and increase the mean circumferential stress but homogenizes the stress distribution. The change in the magnitude of the mean circumferential stress results from the mechanical non-linearity of arterial tissue and geometrical non-linearity of the deformation process. If the effect of residual stresses is studied using the classical

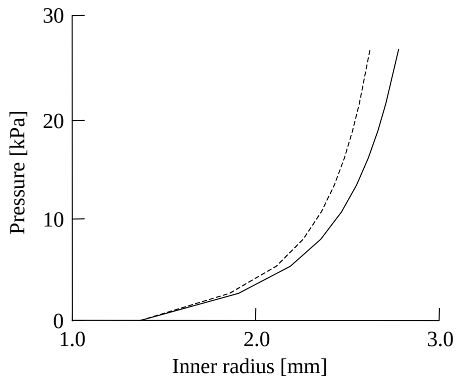

Fig. 4. Pressure–radius relationship of the rabbit thoracic aorta. The continuous curve refers to the case when the residual strains were taken into account; the dashed curve, when the unloaded configuration is taken as a stress-free.

theory of elasticity, they will manifest solely as a change in the stress distribution.

In addition, according to Poiseuille's formula for flow-induced shear stress at the inner arterial surface:

$$\tau = \frac{4\mu Q}{\pi r_{\mathrm{i}}^3},$$

where μ is the blood viscosity and Q is the mean flow rate, residual strains decrease the wall shear due to the increase in deformed radius mentioned above. For the case of the rabbit aorta the shear stress decreases by a factor of 0.86. Because low shear stress at the arterial endothelium is considered a primary mechanical event that triggers processes leading to intimal hyperplasia, (Glagov, 1994) one might speculate that residual strains do not have a beneficial effect on arterial function as far as blood flow is concerned.

Finally, we calculated the arterial compliance at the physiological state (transmural pressure, 120 mmHg; axial stretch ratio, 1.691) using the formula

$$C = \frac{\Delta r_{\mathrm{i}}}{r_{\mathrm{i}} \Delta P_{\mathrm{i}}},$$

where Δr_{i} is the small change in radius corresponding to a small change in pressure ΔP. It was found that the compliance calculated when accounting for residual strains ($8.42 \times 10^3\,\mathrm{kPa}^{-1}$) is higher than that calculated if they are not considered ($7.25 \times 10^3\,\mathrm{kPa}^{-1}$). This implies that residual strains make elastic arteries more compliant and thereby improve their performance as elastic reservoirs. In smaller arteries, increased compliance enhances the effect of changes in smooth muscle tone allowing easier control of vessel lumen.

3.2. Effects of mechanical environment

Arteries are subjected to pulsatile pressure, to axial forces caused by the surrounding tissue and to flow-induced shear force due to friction between the wall and the blood. Adopting an appropriate mathematical model for the loading, geometry and deformation processes, the strain and stress at any point in the arterial wall can be determined, and these specify the local mechanical environment of the cells at this point. Like all tissue exposed to mechanical forces, arteries are sensitive to alterations in their mechanical environment. If changes in this environment persist, the long-term response is a gradual change in geometry, structure and composition of the vessel. Irreversible changes in arterial geometry and structure also occur during development and maturation. The process is determined by genetic factors which may include vessel size, topology and any inherent tendency towards developing occlusive and degenerative diseases, together with epigenetic factors including changes in the mechanical environment in prenatal and early antenatal life (foetal programming) and age-related changes in arterial blood pressure and flow. Changes of arterial geometry are termed growth or geometrical remodeling (Fung, 1993b). Growth is regarded as a local response caused by a changed proliferative and secretory function of vascular cells in response to local mechanical stimuli. As has been pointed out by Skalak (1981), when considering tissue as collection of growing elements, an additional deformation is required to maintain its continuity. Under no load conditions this deformation gives rise to strain and stress fields which by definition are termed residual strains and stresses.

Therefore, residual strain and stress in arteries and the opening angle that reveals their existence in the no load state are the result of volumetric growth ensuring the optimal performance of arteries. From this perspective some of the observed changes in the opening angle of large arteries which accompany changes in the local mechanical environment are described and discussed below.

3.3. Regional variations in arterial opening angle

It is generally agreed that there are steady changes in residual strain along the arterial tree and that the detailed pattern of these changes is species dependent. In many experiments residual strain per se has not been measured rather, opening angle has been used as a surrogate. Along the aorta of the adult rat, for instance the opening angle falls from around 180° near the heart to a minimum of between 20° and 50° at the diaphragm and increases again to 100° approaching the tail (Liu and Fung, 1989, 1988; Saini et al., 1995; Badrek-Amoudi et al., 1996). In the pig a similar pattern is seen although the maxima at each end of the aorta are smaller, as is the minimum in the centre (Han and Fung, 1991). Direct measurements of residual strain in the rabbit also show a minimum in the abdominal aorta

(Hayashi et al., 1995; Hong et al., 1997). In larger animals there are, as yet, few data although inspection of the images in Vaishnav and Vossoughi (1987) shows little variation along the aorta, an observation confirmed by a single study of the aorta in man (Saini et al., 1995). In the rat lung there is a steady decrease in OA from around 300° in the main pulmonary artery to 100° in muscular vessels of 60 μm in diameter (Fung and Liu, 1991; Liu and Fung, 1992), and in man a similar fall towards the periphery has been found although measurements of major vessels near the heart were not described (Huang and Yen, 1998). In the coronary circulation of the pig (Frobert et al., 1998), in man (Valenta et al., 1999) and in muscular arteries of the gut and leg (Fung and Liu, 1992; Liu and Fung, 1992) the general pattern is a fall in opening angle towards the periphery.

The reasons for these complex regional differences in opening angle are not yet known. It has been shown that, in the large conduit arteries excluding the ascending aorta and main pulmonary vessels, OA correlates well with the ratio of medial thickness to lumen radius (h/r) (Fung and Liu, 1992; Liu and Fung, 1992; Badrek-Amoudi et al., 1996; Frobert et al., 1998; Han et al., 1998; Lu et al., 2001). Because all these factors, as well as the mechanical properties of arteries, affect the residual stress it might be speculated that the opening angle varies such that the resulting stress distribution under physiological conditions is close to uniform elsewhere along the arterial tree, a statement that remains to be proved.

3.4. The effects of smooth muscle

Early investigations suggested that the effect of changing smooth muscle tone on OA was small (Fung and Liu, 1989a, b, 1991; Han and Fung, 1991; Fung and Liu, 1992). However, when due care was taken to control temperature it was found that in the rat aorta, carotid (Fridez, 2000) smooth muscle contraction produced an increase in OA; while relaxation decreased it, when compared to the control value. Similarly, Matsumoto et al. (1996) concluded that residual strains increased with muscle contraction and further reduced the stress distribution compared to the passive case.

A mathematical model of the effects of smooth muscle contraction on the stress and strain distribution in arteries was proposed by Rachev and Hayashi (1999). The artery was assumed to be a thick-walled tube made of non-linear orthotropic incompressible material. Contraction of smooth muscle cells generates an active circumferential stress, which acts in parallel with the stress borne by the passive structural components of arterial wall. The model predicted that increased muscular tone causes an increase in opening angle and an increase of arterial pressure at which the circumferential strain distribution is uniform across the arterial wall. The results were in agreement with the experimental findings of Matsumoto et al. (1996) and support the conclusions that the basal muscular tone contributes to the nearly uniform distribution of strains under physiological conditions (Hayashi and Li, 1993). The model also supports the conclusion that the myogenic response tends to restore the strain distribution in the arterial wall and the flow-induced wall shear stress to baseline values. Finite element modeling and numerical simulation of the artery in the active state was also performed by Yamada et al. (1999), predicting an increasing of the opening angle with muscle contraction.

Contrary to the experimental results of Masumoto et al. Zeller and Skalak (1998) found that vasodilatation of rat saphenous arteries increased rather than decreased the opening angle. The authors suggested that smooth muscle tone could affect the residual stress, and thus the configuration of the zero-stress state, by altering the interconnections between smooth muscle cells and extracellular matrix components. To what extent the vascular smooth muscle contributes as an active load-bearing constituent and/or alters the wall structure affecting the passive mechanical properties is not known. Further experimental investigations accompanied by a detailed morphological and histological analysis of the arterial wall of different species and locations are needed.

3.5. Ageing

Remarkably few studies have considered the effect of growth and development on arterial residual strain. In the rat aorta opening angle (OA) falls from the age of 20 days until puberty (6–8 weeks) and increases steadily thereafter until 56 weeks (Badrek-Amoudi et al., 1996) showing that the artery grows non-uniformly across the wall thickness. The reduction in OA during early life may be related to the fact that most of the rapid aortic growth during this period is directed towards an increase in lumen area at the expense of a fall in thickness/radius ratio, h/r. After puberty h/r increases as does OA, a change that results in the maintenance of constant circumferential stress distribution as growth continues (Rachev et al., 1995). A similar age-related increase in OA has been observed in the human aorta from subjects aged between 3 months and 87 years (Saini et al., 1995). At all ages OA in females was less than that in males, a difference not seen in rats.

3.6. Hypertension

When hypertension is induced acutely by aortic banding (Fung and Liu, 1989a, b; Liu and Fung, 1989; Fridez, 2000), or in the lung by hypoxia (Fung and Liu, 1991), OA increases rapidly within minutes reaching a maximum a few days after the intervention and then returns to normal or lower than normal values. A similar pattern of the OA changes was obtained when arterial segments were subjected to a sustained increase in pressure in organ culture systems (Waliszewski et al., 1999).

A rapid increase in OA indicates that the inner part of the artery grows more than the outer. Therefore the dynamics of the OA reflect the non-uniform remodeling of the arterial wall. On the other hand, increased internal pressure causes changes in the magnitude and distribution of the circumferential wall stresses characterized by a more pronounced increase of stress at the inner arterial surface. Therefore, the observed changes in OA can be considered as consequences of remodeling caused by the deviation of circumferential wall stress from its optimal value and distribution. This response reflects a negative feedback between stress and growth, proposed in a general form by Fung (1991) as a stress-growth law. Matsumoto and Hayashi (1996) investigated the histology of the aortic wall in hypertensive rats. They found that the thickening, which occurs mainly in the media, is due to smooth muscle hypertrophy and an increase in ground substance produced by the cells. They showed that these effects are more pronounced in the inner lamellar units of media. These observations and the accompanying stress analysis of the arterial wall support the hypothesis that remodeling is induced and driven by wall stress and tends to restore the circumferential stress distribution to normal.

A detailed morphometric study (Fridez, 2000) has shown that the continuing increase in OA reflects remodeling of the media with growth predominantly in the inner half, where the circumferential stress gradient was greatest. The subsequent return to normal or below normal angles was associated with a more sustained growth on the adventitial side of the media tending to produce a compressive stress and thus to reduce the OA. Other models of hypertension, such as that arising spontaneously or produced surgically, in which blood pressure increases gradually, reveal a correspondingly gradual increase in OA and no tendency for it to return to normotensive values (Zonglai et al., 2000).

Finally, theoretically predicted dynamics of the opening angle consistent with experimental observations were used to justify the applicability of the proposed stress-growth and remodeling rate equations for arteries subjected to sustained high or variable pressure (Rachev et al., 1996; Taber and Eggers, 1996; Rachev et al., 1998; Taber, 1998).

3.7. Increased flow

In a detailed study of flow overload in the rat femoral artery, Lu et al. (2001) showed that OA had fallen by approximately 20% 12 weeks after the production of an arterio-venous fistula, although this reduction was not apparent in the first 4 weeks. The decrease in OA was explained by the suggestion that the vessel remodels by increasing its lumen so that flow-induced shear stress returns to control values while the vessel wall becomes thinner and a smaller OA is sufficient to make the stress distribution across the wall thickness uniform. Though this is a logical interpretation of the consequences of the observed eccentric remodeling, the question remains: what is driving stimulus for such a pattern of remodeling?

3.8. Atheroma/atherosclerosis and diabetes

The intimal growth associated with the onset of atheroma and the related changes due to diabetes both lead to an increase in residual strain. In general, this is associated with increased OA (Matsumoto et al., 1995; Saini et al., 1995; Hong et al., 1997), although the non-uniform distribution of lesions around the circumference may lead to local variations in curvature, which are best quantified by local measurements. As calcification ensues, residual stress remains elevated (Hong et al., 1995), although measurements on the coronary arteries of four subjects suggest that calcification is associated with reduced residual strains (Valenta et al., 1999). The induction of diabetes by STZ treatment leads to a gradual increase of OA over 20 days throughout the arterial system, followed by a return towards normal values over the next 20 (Liu and Fung, 1992; Zhao et al., 2000), suggesting that the intimal changes associated with the onset of hyperglycaemia are followed by slower remodeling in the rest of the media.

3.9. Does a single radial cut relieve all residual stress in the arterial wall?

If we accept that residual strains and stresses result from non-uniform growth which tends to make or maintain optimal arterial function, it seems reasonable to ask how residual stresses and strains can be completely relieved. In general, stresses due to a volumetric growth can be released if a body is cut into infinitesimal elements. However, a more practical form of the question is what is the minimum number of cuts required to release all (or at least most) of the residual stress in an unloaded ring segment. Fung and Liu (1989a, b) have shown that, having made a single radial cut, subsequent radial cuts do not affect the opened-up configuration, which may therefore be regarded as stress-free. In this case the OA is the only parameter that indicates the existence of residual strains, which together with thickness/radius ratio, allow the calculation of their distribution across the wall thickness. Subsequently, however, Vossoughi et al. (1993) found that the opened-up configuration changes when an additional circumferential cut is made to separate the vessel wall into two halves. The inner layer becomes a sector having a larger OA compared to the outer layer, indicating that the opened-up configuration still contains residual strains and stresses.

By stepwise removal of the inner or outer layers of the porcine carotid artery by matching frozen specimens, we have shown that the true stress-free state can only be reached by partial destruction of the vessel wall (Greenwald et al., 1997) and that different layers of the wall may each have different zero-stress states. It was also found that enzymatic digestion of elastin reduces residual strains; whereas removal of collagen or destruction of VSMC had little effect, and it was speculated that the relationship between OA, position and elastin content might be associated with non-homogeneity in the structure and/or composition of the vessel wall.

Recently, Stergiopulos et al. (2001) have studied the elastic properties of porcine aortic media and found a significant difference in the opening angles between the inner and outer halves of the media, having separated them by lathing frozen specimens. The strains required to reassemble the layers, assuming that each is in a state of zero-stress, depend not only on the mismatch of the opening angles but also on the difference between the arc lengths that are in contact before the layers were separated. Moreover, the thinner the arterial layer the smaller is its bending rigidity and the lesser is the contribution of the OA to the magnitude of the residual strains. It was shown that there is little difference in the strain distribution across the wall thickness in an intact artery under physiological pressures when the vessel is considered composed of two stress-free layers and when the configuration arising after a single cut is taken to be stress-free. The mechanical properties of both layers, estimated by the stress–strain relationships agreed closely, which is in keeping with the observed uniform radial distribution of scleroprotein and vascular smooth muscle cells. Therefore, the study suggested that, at least for the porcine aorta, a single radial cut is sufficient to release practically all residual strains and stresses.

Even when a single radial cut to produce the opened-up configuration fails to remove all residual strains, the opening angle remains an informative and useful variable in assessing differential growth and remodeling across the thickness of the arterial wall.

Assuming material incompressibility, the distribution of strains in the arterial wall due to an axisymmetric plane deformation depends on the dimensions of the zero-stress and the deformed states. However, the stress distribution also depends on the mechanical properties of arterial tissue. In their recent paper Taber and Humphrey (2001) have shown that the residual strains and the OA associated with a uniform stress distribution under physiological conditions depend strongly on the heterogeneity of the mechanical properties. Using the observation that gradual removal of wall material in the bovine carotid artery alters the OA (Greenwald et al., 1997), the authors suggested that the mechanical properties must change continuously across the wall and that the growth of the artery during development and maturity is modulated by wall stress. We believe that growth-induced residual strains and material heterogeneity are two possible mechanisms for achieving the optimal performance of an artery, which complement one another but can contribute differently to the short and long term response to changes in the mechanical environment.

Vossoughi (1992) has shown that a rectangular strip cut along the length of a bovine aorta curves axially, indicating the existence of longitudinal residual strains in the vessel. These too probably originate from non-uniform longitudinal growth. The contribution of these strains to the stress field under physiological conditions remains to be investigated.

4. Conclusion

The number of studies on arterial residual stress and strain has increased steadily in recent years. During this time, much experimental data concerning their distribution within the arterial wall, their association with vascular smooth muscle activity and scleroprotein composition and their role in vascular growth and remodeling has accumulated. The presence and origin of residual strain has been incorporated in several theoretical models of arterial growth and remodeling. However, many questions still remain open. We have attempted to formulate some of them in the hope they will stimulate further experimental and theoretical investigations.

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