Iliac Veins Are More Compressible Than Iliac Arteries: A New Method of Testing

Margaret Brass
Department of Biomedical Engineering,
Indiana University Purdue University,
Indianapolis, IN 46202

Ghassan S. Kassab[1]
Department of Biomedical Engineering,
California Medical Innovations Institute,
San Diego, CA 92121
e-mail: gkassab@calmi2.org

Incompressibility implies that a tissue preserves its volume regardless of the loading conditions. Although this assumption is well-established in arterial wall mechanics, it is assumed to apply for the venous wall without validation. The objective of this study is to test whether the incompressibility assumption holds for the venous wall. To investigate the vascular wall volume under different loading conditions, inflation-extension testing protocol was used in conjunction with intravascular ultrasound (IVUS) in both common iliac arteries (n = 6 swine) and common iliac veins (n = 9 dogs). Use of IVUS allows direct visualizations of lumen dimensions simultaneous with direct measurements of outer dimensions during loading. The arterial tissue was confirmed to preserve volume during various load conditions (p = 0.11) consistent with the literature, while the venous tissue was found to lose volume (about 35%) under loaded conditions (p < 0.05). Using a novel methodology, this study shows the incompressibility assumption does not hold for the venous wall especially at higher pressures, which suggests that there may be fluid loss through the vein wall during loading. This has important implications for coupling of fluid transport across the wall and biomechanics of the wall in healthy and diseased conditions. [DOI: 10.1115/1.4044227]

Keywords: incompressibility assumption, biomechanics, mechanical testing, filtration, IVUS, volume, fluid transport

Introduction

Current knowledge of venous tissue biomechanics is substantially lagging behind arterial tissue in both healthy and diseased states [1,2]. Although the basic concepts of vascular biomechanics are well established, the investigation of biomechanical properties of the venous tissue is relatively limited [3–8]. Biomechanical studies assume the vein to be a viscoelastic, nonlinear, homogeneous, anisotropic, and incompressible cylinder that is capable of large deformation [9–12]. These assumptions are adapted from arterial wall mechanics and some may not translate from arteries to veins since veins are hemodynamically, functionally, and structurally different from arteries [1,5,13–15]. For example, the incompressibility assumption is used in venous mechanics without validation [16–23].

This study examined whether the incompressibility assumption can be applied to venous wall which is well established in arterial wall mechanics. The incompressibility assumption implies that a tissue preserves its volume regardless of the loading conditions. The physical motivation behind this assumption is that water is nearly incompressible. Since vascular tissues are largely composed of water, their walls may be assumed to be nearly incompressible in the physiological loading range, although no material remains perfectly incompressible under all loads. The analytical and experimental simplification afforded by the assumption of incompressibility is thought to outweigh the small error that arises due to the nearly incompressible assumption [6,24].

If a vessel segment is assumed to be incompressible, the mechanical properties in the axial and circumferential directions are obtained using the inflation-extension test [2,9,11,12,15,25–27]. The force, pressure, and outer diameter are measured at each length and internal pressure in the conventional inflation-extension protocol. The outer diameter of the vessel is determined with either a laser beam micrometer [25,26] or a video dimension analyzer combined with a camera [9,11,12,27]. Incompressibility assumes that the relative dimensional changes in all the directions (axial, circumferential, and radial) are equal to one, at a given load [12]. This allows the calculation of the loaded vessel inner diameter from the measured outer diameter and reference thickness. Currently, biomechanical tests do not measure both inner and outer diameters simultaneously during the inflation-extension test and hence use incompressibility to calculate one diameter from measurement of the other. Here, we introduce a new method to measure the inner and outer diameters simultaneously in the loaded states to understand how vessels distribute their volume at different loads in order to test the incompressibility assumption.

Materials and Methods

The common iliac vein of nine control mongrel dogs of either sex weighting 24.8 ± 2.5 kg (mean ± standard deviation (SD)) and the common iliac artery of six control domestic swine of either sex weighting 61.8 ± 19.0 kg (mean ± SD) were used in this study [28]. The canine [29] and swine animals had been used for other unrelated physiological experiments, performed in accordance with national and local ethical guidelines including the Institute of Laboratory Animal Research guidelines, Public Health Service policy, the Animal Welfare Act, and were approved by Institutional Animal Care and Use Committee at Indiana University Purdue University, Indianapolis.

Following sacrifice, the vessels were exposed and a suture was placed at the proximal end of the vessel as close to the bifurcation from the inferior vena cava or aorta as possible for the veins and arteries, respectively. Another suture was placed six to eight centimeters distal from the first. Once both ends of the vessel were tied off, all visible branches were ligated and the in situ length was

[1]Corresponding author.

Manuscript received February 13, 2019; final manuscript received June 10, 2019; published online August 2, 2019. Assoc. Editor: Haichao Han.

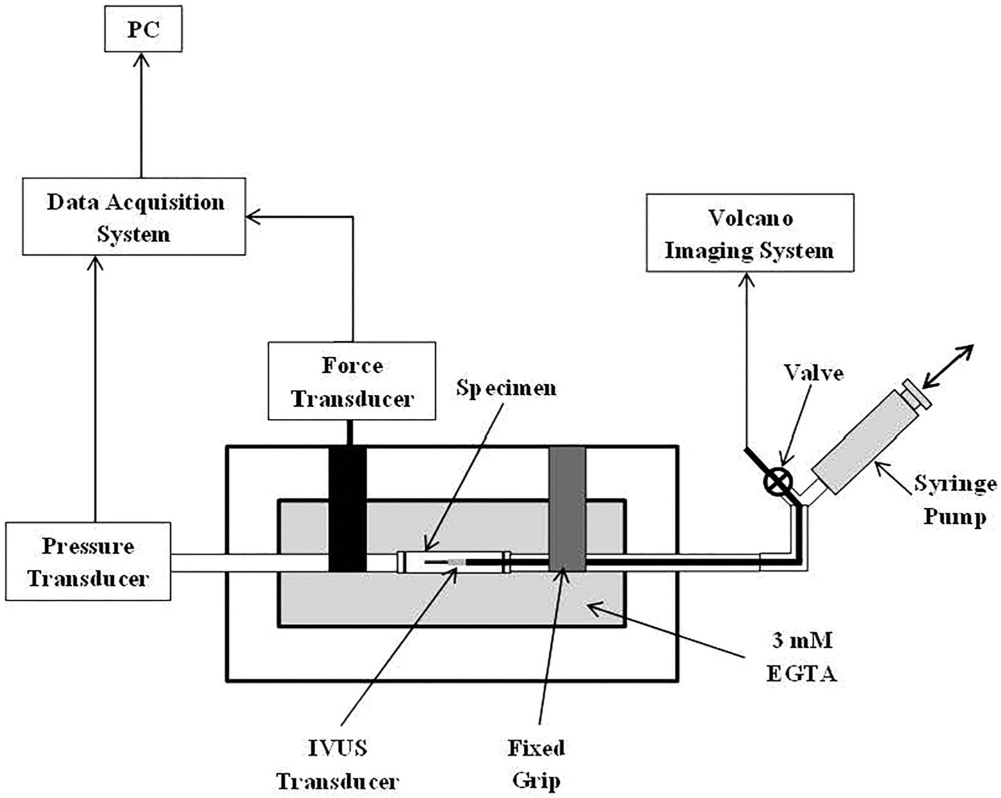

Fig. 1 Schematic of the experimental setup. Schematic of the experimental setup integrating IVUS with the conventional inflation-extension protocol.

measured. The vessel was then excised, rinsed in room temperature saline, and the ex vivo length was measured from a digital image using NIH Image J after calibration of image with a ruler. The vessel was stored in normal saline at 4 °C until biomechanical testing. All biomechanical tests were performed within 24 h of tissue harvest. Prior to biomechanical testing, the loose adventitia was carefully cleaned under a stereomicroscope (SMZ660, Nikon; Melville, NY). Care was taken to leave the dense adventitia intact and to not overstretch or mechanically traumatize the vessel. For the common iliac veins obtained from the control dogs, a two-centimeter portion of the proximal end of the vessel was removed prior to biomechanical testing (reducing the length of the biomechanical testing specimen to approximately 4–6 cm) and was fixed in 10% formalin for histological examinations to measure wall thickness. Each of these two-centimeter segments was cut into two 1 cm long rings. One segment was used for basic morphology, while the other one was used for wall thickness measurements.

Inflation-Extension Test. The experimental setup (Fig. 1) was used for the inflation-extension bi-axial testing on both veins and arteries. Each tubular specimen was mounted in a bath filled with 3 mM EGTA (ethylene glycol tetraacetic acid; calcium chelator to prevent contraction of vessel) solution kept at room temperature to prevent contraction of the vessel. A manual syringe pump was used to apply internal pressure to the specimen. The pressure was measured with a fluid-filled pressure transducer (TSD104A, BIOPAC Systems; Coleta, CA), the force was measured with a force transducer (Fort1000, World Precision Instruments; Sarasota, FL), and the inner and outer diameters were determined using an VISIONS PV .018 intravascular ultrasound (IVUS) imaging catheter (86700, Volcano; San Diego, CA) in conjunction with the s5i imaging system (S5iVC01, Volcano; San Diego, CA).

Once mounted, an axial load was applied to the vessel by extending it to its physiologic length, which was measured by two axial markers placed on the surface of the vessel in situ before harvest. The vessel was then preconditioned at the axial loaded state by means of several inflation-deflation loops where no significant further changes occurred. The veins were preconditioned using an inflation-deflation loop in the range of 0 and 60 mmHg (5, 10, 15, 20, 30, 40, 50, and 60 mmHg), while the arteries were preconditioned using an inflation-deflation loop in the range of 0 and 120 mmHg (20, 30, 40, 50, 60, 80, 100, and 120 mmHg). Once the pressure–diameter curve was reproducible, the vessels were perfused by a syringe pump with 3 mM EGTA solution at the various perfusion pressures. Data were captured at each of the eight specific intraluminal pressures. At each condition of interest, the pressure and force measured by the transducers were recorded and an image was captured with IVUS. Figure 2 is an example of the raw data produced during each inflation cycle for the canine vein.

Biomechanical Analysis. The principal stretch ratios are the primary deformations associated with the radial (λ_r), circumferential (λ_θ), and axial (λ_z) directions due to loading [24]. The three principal stretch ratios were calculated using the experimental data and the following equations with the 5 and 20 mmHg (to ensure circular cross section of veins and arteries, respectively) as the reference condition

$$\lambda_\theta(r) = \frac{2\pi r}{2\pi R} = \frac{r_{\text{out}} + r_{\text{in}}}{R_{\text{out}} + R_{\text{in}}} \tag{1}$$

$$\lambda_z = \frac{l}{L} \tag{2}$$

$$\lambda_r = \frac{\Delta r}{\Delta R} = \frac{r_{\text{out}} - r_{\text{in}}}{R_{\text{out}} - R_{\text{in}}} \tag{3}$$

where r_{in} and r_{out} are the inner and outer radii at the loaded condition, respectively; and where r_{in} and r_{out} are the inner and outer

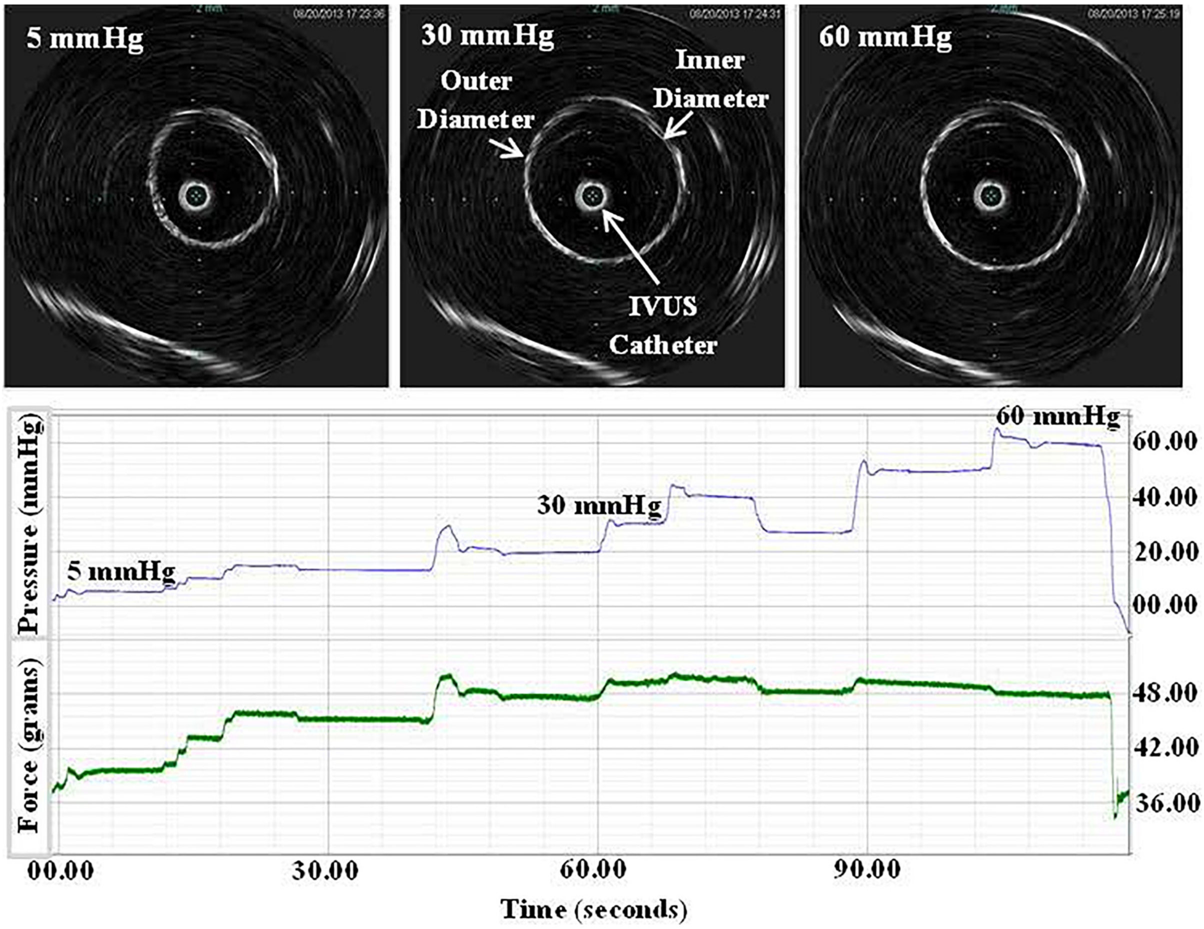

Fig. 2 Raw data produced for one inflation cycle at physiologic length extension in control common iliac vein. The three images on the top panel illustrate the IVUS images captured by the Volcano imaging system at 5, 30, and 60 mmHg. The middle panel shows the real-time pressure as well as the corresponding axial force (bottom panel) during the inflation cycle.

radii at the loaded condition, respectively. The axial length at the loaded condition is l, while L is the length at the reference condition. Last, R_{in} and R_{out} are the inner and outer radii of the vessel at the reference condition. By use of IVUS during the inflation-extension protocol, the inner and outer radii can be directly measured at all loading conditions. Thus, allowing for the differential of the radial direction to be measured in both the loaded and reference conditions as: $\lambda_r =$. The values of r_{in}, r_{out}, R_{in}, and R_{out} were obtained from IVUS images for all the loaded conditions. Similarly, the circumferential and axial stretch ratios can be directly measured using experimental data based on Eqs. (1) and (2), respectively. If we assume the vessel wall is incompressible, we have

$$\lambda_r \lambda_\theta \lambda_z = 1 \tag{4}$$

Equation (4) allows the test of the incompressibility assumption as each of the three principle stretch ratios can be determined in our experimental setup.

Intravascular Ultrasound Versus Digital Camera. To determine the agreement between digital camera and IVUS, the outer diameter of the specimen was measured with both IVUS and the digital camera during the inflation-extension tests. Five specimens consisting of two control canine common iliac vein and three control swine common iliac arteries were used. A digital camera (PC1742, Canon; Melville, NY) was added to the experimental setup and placed vertically above the specimen. At each point of interest, the pressure and force were measured by the transducers and recorded. In addition, two still images were captured concurrently using IVUS and digital camera. The outer diameter was measured for each image using an image analyzer (ImageJ, NIH) after a ruler was used to calibrate the image. The Bland–Altman method was used to measure the agreement between IVUS and the digital camera.

Wall Thickness Measurement. To validate the wall thickness measurements obtained using IVUS, thickness measurements of the common iliac vein were obtained from images captured for basic morphology on six of the nine control canine veins used for biomechanical analysis. The histologic microscopy images were captured using a Spot Insight Color digital camera (Diagnostic Instruments) attached to a histological microscope (Eclipse E600; Nikon), and wall thickness measurements were made from these images using ImageJ (National Institutes of Health). In order to obtain the wall thickness, the light microscopy image was imported into an image analyzer (ImageJ, NIH).

Water Content. The common iliac veins of five swine were used to determine the total water content. After rinsing with saline, the vessel was longitudinally cut, excess water was removed from the surface, and the wet weight was recorded. The vessel was then placed in a precision compact oven (PR305225G, Thermo Scientific) at 37 °C for 8 h and the dry weight was subsequently recorded. The total water content was then determined using the wet to dry weight ratio.

Statistical Analysis. All data are expressed as mean ± standard error (SE) unless otherwise specified. A student's t-test was

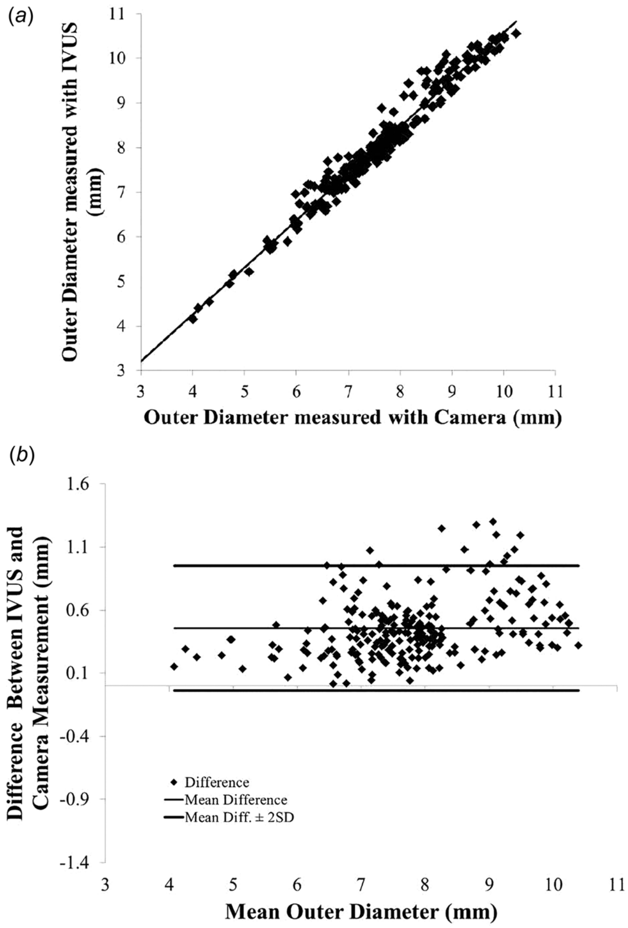

Fig. 3 Accuracy of IVUS in measuring the outer diameter of the vessel: (*a*) the identity relationship between the IVUS measurement and the digital camera measurement, with the solid black line as the identity line and (*b*) Bland–Altman analysis. SD—standard deviation. Figure shows grouped average for $n = 240$ (48 images per vessel for 5 vessels).

used to detect possible differences between the calculated volume change and the theoretical volume change for both veins and arteries. Significance was defined as $p < 0.05$.

Results

The agreement between the conventional experimental method (digital camera) and the proposed method (IVUS) for measuring the outer diameter was tested in five vessels. Outer diameter measurements were obtained with the digital camera and IVUS at 48 data points per animal ($n = 240$). Figure 3(*a*) shows the relationship between the IVUS measurement and the digital camera measurement. The relationship is described by $y = 1.05x + 0.06$ with an R^2 value of 0.96. The y-intercept indicates that IVUS overestimated the outer diameter by 6.5%. Figure 3(*b*) is the Bland–Altman analysis. The Bland–Altman shows the difference and average values of the outer diameters measured by IVUS and the digital camera. The bias between the two methods was 0.46 mm with a root-mean-square (rms) of 0.25 mm.

The agreement between IVUS and histological microscopy for measuring the wall thickness of the vein was tested in six vessels. The average wall thicknesses obtained from the IVUS and microscopy (camera) were 0.46 ± 0.03 mm and 0.46 ± 0.05 mm, respectively. There was no statistical significance found between the two imaging methods ($p = 0.99$).

The product of the three principal stretch ratios ($\lambda_\theta \lambda_z \lambda_r$) indicates the change in volume. If a vessel is incompressible, then the change in volume is equal to one; i.e., volume at any load remains equal to reference volume. The radial stretch ratio (λ_r), the circumferential stretch ratio (λ_θ), and the axial stretch ratio (λ_z) were experimentally obtained for six control swine common iliac arteries and six control canine common iliac veins. Since both arteries and veins were studied, the 5 mmHg loaded condition was used as the reference configuration for the veins while the 20 mmHg loaded condition was used as the reference configuration for the arteries required to maintain circular cross section. The product of the three stretch ratios was determined at physiologic axial length as shown in Fig. 4. A one-sample t-test was performed with a hypothesized mean of 1. There was significance between the experimental mean of both the veins and the hypothesized mean ($p < 0.05$), but there was no significance found between the experimental mean of the artery and the hypothesized mean of 1 ($p = 0.11$). The change in volume for arteries was 0.97 ± 0.02. There was a significant decrease in the change in volume, however, between arteries and veins (0.64 ± 0.04). All experimental results produced ($\lambda_\theta \lambda_z \lambda_r$) values that were < 1.

The total water content was determined using the wet and dry weights. The average wet weight was 0.16 ± 0.05 g, while the average dry weight was 0.04 ± 0.01 g. The total water content of the common iliac vein was found to be $77.9 \pm 3.33\%$ (mean $\pm$ SD).

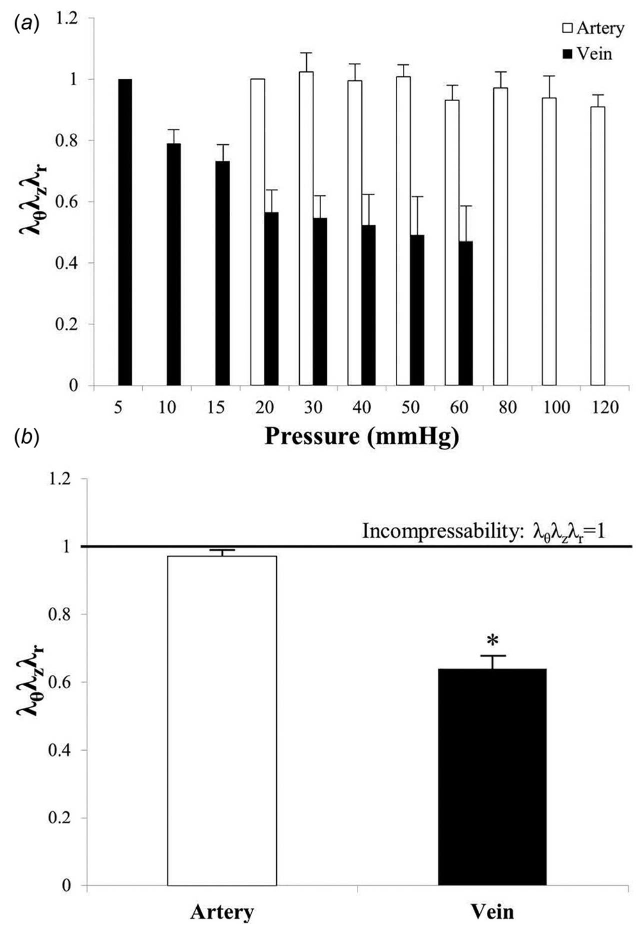

Fig. 4 Change in wall volume (compressibility) of arteries and veins: (*a*) product of the three directional stretch ratios (change in volume) at each loaded condition at physiologic length and (*b*) mean change in volume at physiologic length. The 5 mmHg loaded condition was used as the reference state in veins. The 20 mmHg loaded condition was used as the reference state in arteries. Figures shows grouped average for $n = 6$ dogs. Mean $\pm$ SE and $n = 6$ swine. *$p < 0.05$ versus hypothesized mean of 1.

Discussion

Prior to this study, veins were assumed to be incompressible in order to analytically and experimentally simplify the mechanical analysis [12]. The incompressibility assumption allows for the inner diameters to be theoretically calculated using the loaded outer diameter and the zero-stress thickness. Using IVUS in conjunction with an inflation-extension protocol allowed for the inner diameter to be directly measured in each loaded condition and the incompressibility assumption to be tested. Using the experimentally obtained inner and outer diameters, the wall volume was found to change under each loaded condition in iliac veins but not iliac arteries (Fig. 4(*a*)).

If the wall of a vessel is incompressible, the change in wall volume will remain equal to 1, despite the applied load. It was found that the mean volume change in iliac arteries at physiologic length was not significantly different from 1 (Fig. 4(*b*)). This finding supports the literature, which has established that incompressibility is a reasonable assumption in arterial wall mechanics [6,30,31]. Unlike arteries, the veins did show a mean volume change significantly lower than 1. A decrease in volume indicates that either water was expelled from the venous tissue during the loading procedure or that the total water content within venous tissue is significantly less than arterial tissue. A significant decrease in volume due to water being expelled may suggest that, under the loaded conditions studied, the venous wall is more permeable to water than the arterial wall. Permeability is the ability of the vessel wall to allow liquid to pass through it and is inversely proportional to the wall thickness [32]. A predominant structural difference between the veins and arteries is the overall thickness of the vessel wall [1]. This suggests that the arterial wall has a lower permeability than the venous wall, since arteries are thicker than veins. Sarelius et al. demonstrated that the permeability of control venules is significantly greater than that of control arterioles [33]. Further work is needed to determine the filtration dynamics that can affect the compressibility of the vein wall.

The total water content of the common iliac vein was found to be $77.9 \pm 3.33\%$, while Cox and Detweiler [34] reported the total water content of the common iliac artery in greyhound dogs to be $76.4 \pm 0.2\%$. Compared to Cox et al., there is no significant difference in total water content between arteries and veins ($p = 0.35$).

The compressibility phenomena due to fluid loss may not be limited to veins. The myocardium, for example, squeezes out the coronary volume during cardiac contraction and should have some degree of compressibility over the cardiac cycle. Indeed, we found there is significant volumetric deformation in the left ventricle wall during the ejection based on previously published data [35]; e.g., the wall volume decreases by about 15% (unpublished data). This degree of volume change is reasonable as the coronary volume represents approximately 15% of the left ventricle volume [36].

Limitations of Study. Certain limitations with the methodology of this study need acknowledgment. The possible effect of surrounding the tissue on the compressibility of the vessel wall should be noted. In this study, the surrounding tissue was dissected away and the mechanical contribution and external forces exerted by the surrounding tissues in vivo were not considered [33,37–39]. Although it is not known the degree to which the presence of external force will prevent volume change, it is unlikely the presence of external forces would render the venous wall incompressible given the volume change observed in vitro.

Intravascular ultrasound was found to overestimate the outer diameter of both veins and arteries by 6.5% when compared with measurements made by digital camera. This bias or overestimation, however, was not found to affect the thickness measurement when compared to other imaging methods. Therefore, the overestimation produced by IVUS cannot be used to explain the degree of compressibility observed. Furthermore, it was assumed that the axial stretch was unchanged during the inflation process, which was confirmed experimentally.

The observation of compressibility of veins in this study was serendipitous. In the original study, the focus was on understanding the remodeling of canine iliac vein in venous hypertension/reflux [29]. During the testing, we found the unexpected volume change of vein wall during loading as we utilized a novel method of mechanical testing that directly measures wall thickness. Since incompressibility of arteries is well known, we did not feel it was necessary to sacrifice additional dogs to prove the point. Hence, we utilized control swine iliac veins (under identical testing protocol) routinely available in our laboratory from other terminal swine studies.

Since the analysis relies on the three principle stretches to calculate compressibility (Eq. (4)), the assumption of axisymmetry is invoked. At zero pressure, this assumption (especially for veins) does not hold. Hence, the lowest pressures considered for veins and arteries were 5 and 20 mmHg, respectively, to ensure cylindricity. Furthermore, the cylindricity assumption does not hold at points of bifurcations.

Finally, although EGTA was used to prevent contraction of the vessel segments and hence maintain a passive geometry, we did not use a buffer to ensure neutral fluid exchange. Although the use of EGTA without a buffer is a limitation since we did not control ion flux and hence the fluid exchange of these tissues, both arteries and veins were subjected to the same solution and we did not observe any obvious dimensional changes of the vessel segments. Clearly, the water content balance of vessel wall requires further studies where the wet to dry ratio and filtration experiments that can be performed systematically to verify the fluid exchange differences between arteries and veins.

Conclusion

This study confirms that integrating IVUS with the conventional inflation-extension protocol verifies the incompressibility assumption for arteries but not the veins. Future investigations are needed to explain the detailed filtration mechanism for decrease of venous wall volume during loading and the implications on venous wall mechanics.

Acknowledgment

This paper is dedicated to my mentor Prof. Y. C. Fung in celebration of his centennial birthday. Prof. Fung's work has been very seminal in the field [40]. During his four decades of contributions to biomechanics, he established a solid foundation for the field in the areas of microcirculation, blood flow, cell mechanics, constitutive laws, residual stress, morphometry of vasculature, and growth and remodeling of soft tissue, to name a few. In the process, he questioned old established theories ranging from blood flow in the lung capillaries that had been assumed to have cylindrical flow to the zero-stress states, which had been assumed to be equivalent to the no-load state. In the former, he proposed a novel sheet flow theory while on the latter, he showed the existence of residual stress in tubular organs. These developments became foundational to the field where many researchers continue to build on this strong foundation. In this paper, the incompressibility of blood vessels (experimentally proven for arteries) has been axiomatic in biomechanics and researchers have assumed that veins follow suit. Here, we show that this assumption is at odds with experimental data and hence call for the need to revise this assumption for veins, which are far less studies than arteries. We hope future studies will continue to study the biomechanics of veins and lymphatic vessels to reach the heights of our understanding of the arterial system as the vascular system can only be well understood if each of its components (arteries, veins, and lymphatics) is equally illuminated.

Funding Data

- NIH (Grant No. U01 HL118738; Funder ID: 10.13039/100000002).

References

[1] Attinger, E. O., 1969, "Wall Properties of Veins," IEEE Trans. Biomed. Eng., **4**, pp. 253–261.

[2] Sokolis, D. P., 2008, "Passive Mechanical Properties and Constitutive Modeling of Blood Vessels in Relation to Microstructure," Med. Biol. Eng. Comput., **46**(12), pp. 1187–1199.

[3] Chuong, C., and Fung, Y., 1984, "Compressibility and Constitutive Equation of Arterial Wall in Radial Compression Experiment," J. Biomech., **17**(1), pp. 35–40.

[4] Fung, Y., 1984, "Structure and Stress-Strain Relationship of Soft Tissue," Am. Zool., **24**(1), pp. 13–22.

[5] Fung, Y., Fronek, K., and Patitucci, P., 1979, "Pseudoelasticity of Arteries and the Choice of Its Mathematical Expression," Am. J. Physiol.-Heart Circ. Physiol., **237**(5), pp. H620–H631.

[6] Humphrey, J. D., 2002, *Cardiovascular Solid Mechanics: Cells, Tissues, and Organs*, Springer, New York.

[7] Kassab, G. S., 2006, "Biomechanics of the Cardiovascular System: The Aorta as an Illustratory Example," J. R. Soc., Interface, **3**(11), pp. 719–740.

[8] Watts, S. W., Rondelli, C., Thakali, K., Li, X., Uhal, B., Pervaiz, M. H., Watson, R. E., and Fink, G. D., 2007, "Morphological and Biochemical Characterization of Remodeling in Aorta and Vena Cava of Doca-Salt Hypertensive Rats," Am. J. Physiol.-Heart Circ. Physiol., **292**(5), pp. H2438–H2448.

[9] Desch, G. W., and Weizsäcker, H. W., 2007, "A Model for Passive Elastic Properties of Rat Vena Cave," J. Biomech., **40**(14), pp. 3130–3145.

[10] Dobrin, P. B., Littooy, F. N., Golan, J., Blakeman, B., and Fareed, J., 2006, "Mechanical and Histologic Changes in Canine Vein Grafts," J. Surg. Res., **44**, pp. 740–746.

[11] Hayashi, K., and Naiki, T., 2009, "Adaptation and Remodeling of Vascular Wall; Biomechanical Response to Hypertension," J. Mech. Behav. Biomed. Mater., **2**(1), pp. 3–19.

[12] Wesly, R., Vaishnav, R. N., Fuchs, J., Patel, D. J., and Greenfield, J., 1975, "Static Linear and Nonlinear Elastic Properties of Normal and Arterialized Venous Tissue in Dog and Man," Circ. Res., **37**(4), pp. 509–520.

[13] Dilley, R. J., McGeachie, J. K., and Prendergast, F. J., 1988, "A Review of the Histologic Changes in Vein-to-Artery Grafts, With Particular Reference to Intimal Hyperplasia," Arch. Surg., **123**(6), pp. 691–696.

[14] Stooker, W., Gok, M., Sipkema, P., Niessen, H. W., Baidoshvili, A., Westerhof, N., Jansen, E. K., Wildevuur, C. R., and Eijsman, L., 2003, "Pressure-Diameter Relationship in the Human Greater Saphenous Vein," Ann. Thorac. Surg., **76**(5), pp. 1533–1538.

[15] Vito, R. P., and Dixon, S. A., 2003, "Blood Vessel Constitutive Models: 1995–2002," Annu. Rev. Biomed. Eng., **5**(1), pp. 413–439.

[16] Brossollet, L. J., and Vito, R. P., 1995, "An Alternate Formation of Blood Vessel Mechanics and the Meaning of the In Vivo Property," J. Biomech., **28**(6), pp. 679–687.

[17] Glagov, S., Vito, R., Giddens, D. P., and Zarins, C. K., 1992, "Micro-Architecture and Composition of Artery Walls: Relationship to Location, Diameter and the Distribution of Mechanical Stress," J. Hypertens., **10**(6), pp. S101–S104.

[18] Holzapfel, G. A., Gasser, T. C., and Ogden, R. W., 2000, "A New Constitutive Framework for Arterial Wall Mechanics and a Comparative Study of Material Models," J. Elasticity Phys. Sci. Solids, **61**(1/3), pp. 1–48.

[19] Liu, Y., Zhang, W., and Kassab, G. S., 2008, "Effects of Myocardial Constraint on the Passive Mechanical Behaviors of the Coronary Vessel Wall," Am. J. Physiol.-Heart Circ. Physiol., **294**(1), pp. H514–H523.

[20] Liu, Y., Wen, H., Gorman, R. C., Pilla, J. J., Gorman, J. H., Buckberg, G., Teague, S. D., and Kassab, G. S., 2009, "Reconstruction of Myocardial Tissue Motion and Strain Fields From Displacement-Encoded MR Imaging," Am. J. Physiol. Heart. Circ. Physiol., **297**(3), pp. H1151–H1162.

[21] Monos, E., Kauser, K., Contney, S., Cowley, A., Jr., and Stekiel, W., 1991, "Biomechanical and Electrical Responses of Normal and Hypertensive Veins to Short-Term Pressure Increases," *Cellular Aspects of Hypertension*, Springer, NY, pp. 51–57.

[22] Monos, E., Lóránt, M., Dörnyei, G., Bérczi, V., and Nádasy, G., 2003, "Long-Term Adaptation Mechanisms in Extremity Veins Supporting Orthostatic Tolerance," Physiology, **18**(5), pp. 210–214.

[23] Sassani, S. G., Theofani, A., Tsangaris, S., and Sokolis, D. P., 2013, "Time-Course of Venous Wall Biomechanical Adaptation in Pressure and Flow-Overload: Assessment by a Microstructure-Based Material Model," J. Biomech., **46**(14), pp. 2451–2462.

[24] Holzapfel, G. A., and Ogden, R. W., 2009, "On Planar Biaxial Tests for Anisotropic Nonlinearly Elastic Solids: A Continuum Mechanical Framework," Math. Mech. Solids, **14**(5), pp. 474–489.

[25] Kritharis, E. P., Kakisis, J. D., Giagini, A. T., Manos, T., Stergiopulos, N., Tsangaris, S., and Sokolis, D. P., 2010, "Biomechanical, Morphological and Zero-Stress State Characterization of Jugular Vein Remodeling in Arteriovenous Fistulas for Hemodialysis," Biorheology, **47**(5–6), pp. 297–319.

[26] Rezakhaniha, R., and Stergiopulso, N., "A Structural Model of the Venous Wall Considering Elastin Anisotropy," ASME J. Biomech. Eng., **130**(3), p. 031017.

[27] Weizsäcker, H. W., 1988, "Passive Elastic Properties of the Rat Abdominal Vena Cava," Pflűgers Archiv, **412**(1–2), pp. 147–154.

[28] Brass, M., 2014, "Biomechanical and Morphological Characterization of Common Iliac Vein Remodeling: Effects of Venous Reflux and Hypertension," MS dissertation, IUPUI, Indianapolis, IN.

[29] Brass, M., Berwick, Z. C., Zhao, X., Chen, H., Krieger, J., Chambers, S., and Kassab, G. S., 2015, "Remodeling of Canine Common Iliac Vein in Response to Venous Reflux and Hypertension," J. Vasc. Surg.: Venous Lymphat. Dis., **3**, pp. 303–311.

[30] Carew, T. E., Vaishnav, R. N., and Patel, D. J., 1968, "Compressibility of the Arterial Wall," Circ. Res., **23**(1), pp. 61–68.

[31] Chuong, C., and Fung, Y., 1986, "Residual Stress in Arteries," *Frontiers in Biomechanics*, Springer, New York, pp. 117–129.

[32] Truskey, G. A., Yuan, F., and Katz, D. F., 2004, *Transport Phenomena in Biological Systems*, Pearson/Prentice Hall, Upper Saddle River, NY.

[33] Sarelius, I. H., Kuebel, J. M., Wang, J., and Huxley, V. H., 2006, "Macromolecule Permeability of In Situ and Excised Rodent Skeletal Muscle Arterioles and Venules," Am. J. Physiol., **290**(1), pp. H474–H480.

[34] Cox, R. H., and Detweiler, D. K., 1988, "Comparison of Arterial Wall Properties in Young and Old Racing Greyhounds," Mech. Ageing Dev., **44**(1), pp. 51–67.

[35] Monos, E., Contney, S. J., Cowley, A., and Stekiel, W. J., 1989, "Effect of Long-Term Tilt on Mechanical and Electrical Properties of Rat Saphenous Vein," Am. J. Physiol.-Heart Circ. Physiol., **256**(4), pp. H1185–H1191.

[36] Kassab, G. S., Lin, D., and Fung, Y. C., 1994, "Morphometry of the Pig Coronary Venous System," Am. J. Physiol. Heart Circ. Physiol., **267**(6 Pt 2), pp. H2100–H2113.

[37] Boutouyrie, P., Bézie, Y., Lacolley, P., Challande, P., Chamiot-Clerc, P., Benetos, A., Renaud de la Faverie, J. F., Safar, M., and Laurent, S., 1997, "In Vivo/In Vitro Comparison of Rat Abdominal Aorta Wall Viscosity Influence of Endothelial Function," Aeterioscler., Thromb., Vasc. Biol., **17**(7), pp. 1346–1355.

[38] Choy, J. S., and Kassab, G. S., 2006, "Non-Uniformity of Axial and Circumferential Remodeling of Large Coronary Veins in Response to Ligation," J. Biomech., **39**, p. S316.

[39] Masson, I., Boutouyrie, P., Laurent, S., Humphrey, J., and Zidi, M., 2008, "Characterization of Arterial Wall Mechanical Behavior and Stresses From Human Clinical Data," J. Biomech., **41**(12), pp. 2618–2627.

[40] Kassab, G. S., 2004, "Y.C. "Bert" Fung: The Father of Modern Biomechanics," Mech. Chem. Biosystems, **1**(1), pp. 5–22.