

Review of biomechanical studies of arteries and their effect on stent performance



Aleksandra Fortier^{a,*}, Vikranth Gullapalli^a, Reza A. Mirshams^b

^a Mechanical and Energy Engineering Department, University of North Texas, 3940 N Elm Street, Denton, TX 76207, United States

^b Engineering Technology Department, University of North Texas, 3940 N Elm Street, Denton, TX 76207, United States

ARTICLE INFO

Article history:

Received 14 April 2014

Accepted 20 April 2014

Available online 26 April 2014

Keywords:

Artery mechanics

Biomechanics

Stent implants

Stent failure

Deformation

Femoral artery

Cardiovascular diseases

Curvature

ABSTRACT

Factors such as aging, atherosclerosis, hypertension, genetic defects and diabetes mellitus have been known to cause arteries to develop various shapes and characteristics in patients such as tortuosity, kinking, twisting, elongation, contraction, and curving. The change in artery mechanics can cause a variety of cardiovascular diseases among men and women. The improvement in technology and techniques has allowed access to different therapies such as balloon angioplasty or stenting. Stents are permanent implants that undergo repetitive deformations as a result of patient daily activities such as walking, flexing, sitting, climbing stairs, and getting into a car. Often, these deformations imposed on the stents result in stent failures. It is imperative that the biomechanics environment of the arteries causing stent failure is well understood and the stents be evaluated under multiple loading modes for increased life-cycle. As a result, this paper aims to summarize part of the available literature that reports studies on biomechanical environment in healthy and diseased arteries using various analytical methods.

© 2014 The Authors. Published by Elsevier Ireland Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/3.0/>).

1. Introduction

Heart diseases are playing a major cause of death with about 600,000 deaths per year. Among heart diseases, coronary heart disease alone kills more than 350,000/year and it costs \$108.9 billion for the United States each year which includes the cost of health care services, medications and lost productivity [1]. In spite of significant advancements in clinical care and education for public, cardiovascular diseases (CVDs) are a leading cause of death and disability to the nation. Cardiovascular diseases (CVDs) include peripheral artery disease (PAD), high blood pressure (HBP), coronary heart disease (CHD), heart failure (HF) and stroke. According to the latest statistical data, CVDs are the number one cause of morbidity and mortality in countries of the western world [1]. Nearly 2400 Americans die of CVDs each day (an average of 1 death every 37 s) [2]. The causes of CVD include mainly atherosclerosis, syphilis, atheroma, heart attacks, congenital defects, obesity, smoking, hypertension,

trauma, and hereditary conditions as well as hemodynamic and biomechanical factors. Atherosclerosis is a common disorder of the arteries, characterized by the accumulation of cells, lipids, connective tissue, calcium, and other substances inside the inner lining of the arterial wall. This fatty tissue – known as atheroma – can cause hardening of the arteries, rupture or erosion of the arterial wall, and eventually reduction or complete blockage of the blood flow. Atherosclerosis appears preferentially at sites of complex geometry (e.g., along the outer portions of the bifurcation), most often in the abdominal aorta, iliacs, coronaries, femorals, popliteals, carotids, and cerebrals. The atherosclerotic process starts early in life and advances throughout adulthood. In CVD the first line of defense is prevention by taking some strategies whereas sometimes it cannot be effective due to its advanced stages which are cured only by treatment. The treatment is being done by angioplasty, an invasive procedure where a balloon-tipped catheter is inserted into the narrowing and expanded which is also called stenosis. It helps in the widening of the vessel lumen and makes the flow of blood effective. By using this technique there are some complications like closing of the vessel after few days or weeks. In order to overcome issues during treatment a metal mesh tube called stent (Fig. 1) is used which is expandable and remains inside the vessel even after expanding and prevents it from closure [2–6]. There were issues associated with the stent treatment as well like tissue growing inside the stent after few days or

* Corresponding author.

E-mail addresses: Aleksandra.Fortier@unt.edu (A. Fortier),

Vikranth.Gullapalli@unt.edu (V. Gullapalli), Reza.Mirshams@unt.edu (R.A. Mirshams).

few weeks which make the tube narrow inside and thereby restenosis occurs. Now the stent models are improved in certain aspects like fabrication techniques, strut shapes and the placement of stent is also considered depending upon the flexibility of the target vessel. Recently the stents are being improved with the drug eluting stents (DES) where they release the drug which regulates the metabolic activity of the vascular tissue and prevents the tissues from growing inside the stents [7].

Even though stents are good alternative to treat artery disease they undergo significant deformations during daily activities that patients perform especially in larger arteries like those in the limbs. During everyday body function, parts of the legs are exposed to multiaxial deformations with up to 60% rotation and 20% contraction as the leg is bent from an extended position [6]. As a result stent deployed in the intersection of the femoral and popliteal arteries is exposed to significant multiaxial displacements due to the motion as well as bending, torsion, tension, and compression during walking cycle [7]. This can lead to fracture of the metal stent in this region, which aligns with the fact that stents fracture at a measurable rate of more than 50%. Even the treatment procedures alone affect the vessels mechanically. As a result, understanding in details the mechanical environment of the arteries (with special interest on the large arteries in the limbs such as superficial femoral artery (SFA) and popliteal artery (PA)) imposing deformations in stents and the stent failures under cycle-mode is imperative for the improvement of the outcome of these treatments. In an effort to do

so, this paper aims to summarize part of the available literature that reports studies on biomechanical environment in healthy and diseased arteries using various analytical methods.

2. Characteristics of healthy arterial wall

All blood vessels consist of three distinct layers or tunicae: the tunica intima, tunica media and tunica adventitia (Fig. 2).

The intima is a thin endothelial layer that lines the inside walls, and sits on a very thin (~80 nm) basal lamina of a net-like type IV collagen in young human. Endothelial cells, typically elongated in the direction of the blood flow, act as a semipermeable membrane, through which nutrients and chemical signals can reach the cells in the vessel wall from the bloodstream. The intima has also a key role in regulating the active response of the vessel through which pressure regulating agents reach the media. Additionally, in order to help control the vascular tone the intima produces NO (nitric oxide), which relaxes smooth muscle cells in the media. Despite its great functional importance, due to its small thickness in young arteries the intima is usually neglected when considering the different layer contributions to the global mechanical resistance of the vessel wall. A fenestrated sheet of elastin called internal elastic lamina separates the intima from media [10].

The media is formed primarily by smooth muscle cells (SMC) that are embedded in an extracellular plexus of elastin and collagen (mainly types I and III) and an aqueous ground substance that also contains proteoglycans. Depending on the internal arrangement of the smooth muscle cells in the media, it is distinguished between elastic arteries and muscular arteries. The former tend to be large-diameter vessels close to the heart, and include the aorta, the main pulmonary artery, the common carotid and common iliac arteries. Their most characteristic histological feature is the so-called lamellar unit, a sandwich-like 'sublayer' of smooth muscle cells and thin elastic laminae. Elastic arteries have concentric ring-like structures that are tied together by radially oriented collagen. In muscular arteries, the media appears as a single thick ring of smooth muscle cells. The SMC are embedded in a loose connective tissue matrix and arranged as a sequence of concentric layers of cells, which can reach numbers of 25–40 in larger vessels like in the femoral artery [10].

The adventitia is the outermost layer of the vessel wall. It consists of a dense network of type I collagen fibers with scattered fibroblasts, elastin and nerves. In medium and large arteries there is also the vasa vasorum, an intramural network of arterioles, capillaries and venules that supply large vessels where the distance from the main bloodstream to the outer sections of the wall does not allow for proper interchange of O₂, CO₂, nutrients and metabolites. The presence of nerves in the adventitia allows innervation of smooth muscle in the outer media, via the diffusion of neurotransmitters. As for the fibroblasts, they are responsible for collagen production, particularly type I, and thus regulate the connective tissue. At higher pressures, the fibers gradually straighten, confirming the hypothesis that the adventitia serves as a protective sheath, preventing rupture of the vessel due to an acute increase in pressure [10].

3. Mechanics of arteries

The mechanical behavior of blood vessels has been a subject of research for many years with first few reports dating back to the end of the 19th century [11,12]. The first characteristic of arterial mechanics is the presence of residual stresses where it has been reported that if arterial ring is cut radially it springs open and an axial strip excised from the artery bends away from its vessel axis which signals the presence of residual stresses both in axial and circumferential directions [10,13–17]. Further studies report that the luminal part is under compression and the external part is under tension where the internal pressure equilibrates these stresses and they have been reported as a positive feature as part of the compatible growth and remodeling and not of physical

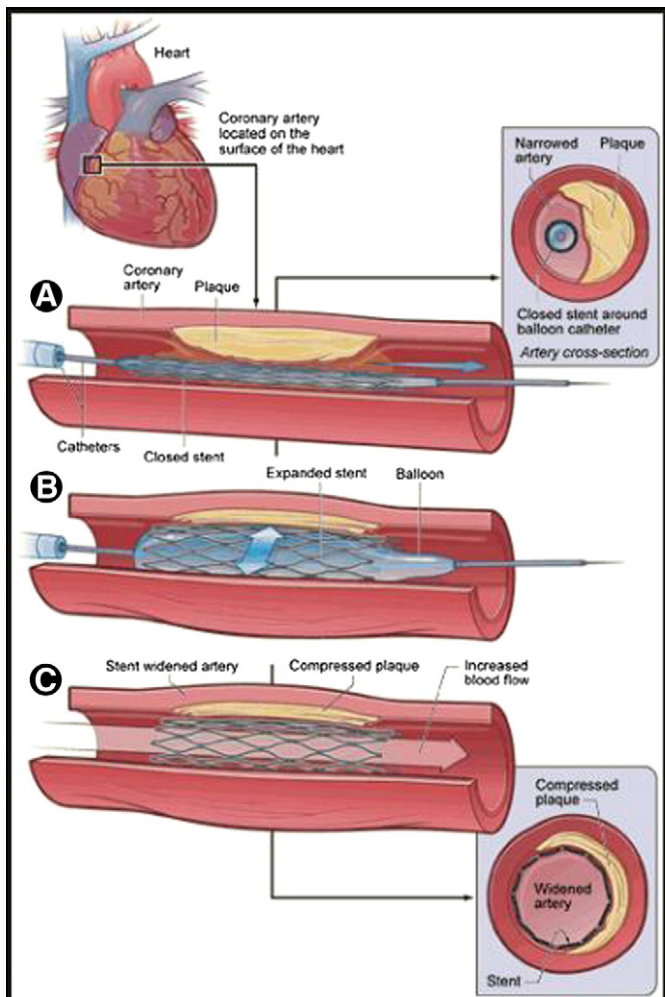


Fig. 1. Schematic showing stent implant into artery obstructed by plaque [8].

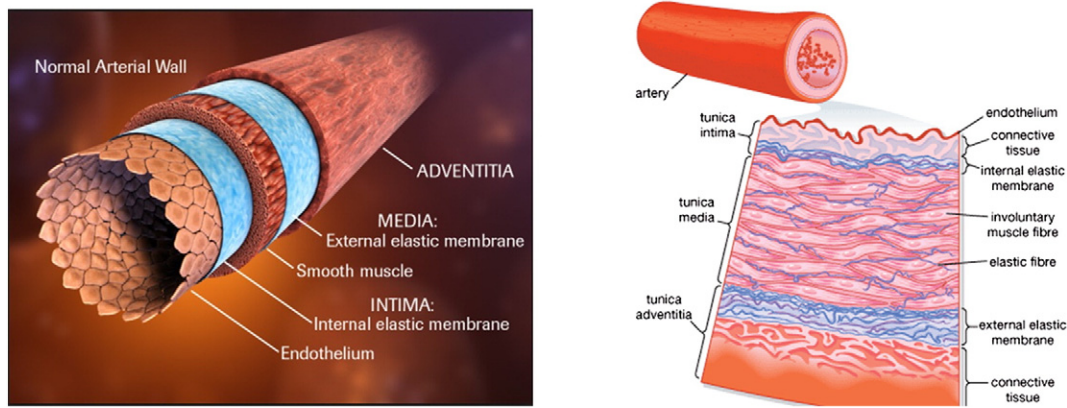


Fig. 2. Schematic representation of distinct layers of arterial wall left: top view of layers in artery [8] and right: cross-sectional view of layers in artery [9].

deformation [18–20]. Another fundamental characteristic reported of the vascular tissue is anisotropy under load-free configuration, which notes different properties of the tissue in circumferential and axial directions [21,22]. Because of high water content of the vascular wall (70–80%) another characteristic that is concluded is incompressibility even though there are some exceptions in cases with large deformations [23]. Further reports show that nearly all soft tissues present a certain degree of visco-elastic response, which is revealed by the stress relaxation they suffer when subject to sustained deformations and by the hysteresis they display under cyclic loads. This may be attributed in part to fluid transport within the solid matrix, and to the friction between its fluids and solid constituents. After being preconditioned, the tissue displays highly repetitive behavior, so that it can be considered pseudoelastic, that is elastic but behaving differently in loading and unloading [10,24]. Many additional studies report on the type of behavior that the abovementioned arterial layers experience under high loads, well outside of the physiological range but layer-specific data on the behavior of the human vessel is scarce due to the complexity of the layer separation and the difficulty in obtaining samples, mainly because of ethical concerns [25–38]. In summary, the observation among studies is that aged arteries are typically stiffer than younger arteries and that this could be related to fracture of the elastic laminae due to fatigue in the media, and in the adventitia due to cross linking among collagen fibers derived from the remodeling process [10].

4. Mechanics of arteries under forces

Arteries are subject to significant mechanical forces from internal blood flow and contiguous tissue tethering [39] especially arteries subject to one or more diseases. Furthermore, the implanted devices such as the stent simultaneously alter the biochemical and biomechanical environment of the cardiovascular system, triggering acute and chronic changes, and are in turn inherently affected by the physiological environment of the body. Even though the safety and efficacy of the implanted device have been studied extensively the surrounding forces affecting the device performance have not been studied in details. As a result, recent research has been directed toward *in vivo* arterial deformation under loading. This paragraph will summarize selected literature on this topic. Choi et al. report [40] quantified data regarding *in vivo* deformation of the abdominal aorta and common iliac arteries (CIAs) caused by musculoskeletal motion. Using magnetic resonance angiography (MRA) seven healthy patients, with age range of 24–50 years, were examined. Due to maximum hip flexion shortening of about 5%, twisting of about $0.45^\circ/\text{mm}$, and curvature changes of about 0.015 mm^{-1} of the CIA were observed. The angle between CIAs also increased by about 18° ,

and the abdominal aorta experienced shortening ($\sim 3\%$) and twisting ($0.07^\circ/\text{mm}$) due to hip flexion. As far as the movement, the iliac arteries move preferentially in the superior direction relative to the aortic bifurcation, which would induce compression and bending, thus increasing curvature and angle between the CIAs. This study included only few healthy subjects but it concluded that musculoskeletal motion (specifically hip flexion) can cause significant *in vivo* morphological changes (shortening, twisting, and bending) of the arteries [40]. In an alternative study related to aging Cheng et al. report on geometric deformation of superficial femoral artery (SFA) due to aging during hip and knee flexion in older patients. Seven healthy subjects between the ages of 50 and 70 were studied. Compared to the previous report on the deformation of arteries in healthy young subjects [40] this study highlights significant (almost double in some segments) shortening, twisting, and curvature increase of the SFA in the older group of patients most likely due to loss of arterial elasticity with age [41]. Further, Choi et al. report on novel method for quantifying 3D dynamic arterial deformation due to pulsatile and nonpulsatile forces. More specifically in this study, they introduce a systematic framework for generating a centerline of the vessel and segmentation techniques. Once the vessel has been analyzed and segmented, the geometry of the vessel has been reported such as: longitudinal strain, axial twist, and curvature changes. Same methods were applied to quantify similar geometries for several other arteries: coronary artery, abdominal aorta, common iliac artery, and SFA since these arteries are prone to disease and are frequent sites of stent implants [42]. Extensive work in the area of the biomechanical modeling on deformation of arteries such as twisting, kinking and tortuosity due to aging and hypertension using finite elements methods theoretically and computationally has been developed by Han et al. [43–57]. This pioneering work provides adequate models that can predict various mechanical parameters such as critical load as a result of buckling, geometric parameters in tortuous veins, angles of kinked and twisted arteries, strain, and stress that can lead to better treatment of hypertension and to postpone aging. Klein et al. report on quantitative assessment of change of femoropopliteal artery (a long vessel that encompasses the superficial femoral artery (SFA) and popliteal artery (PA); see Fig. 3) during leg movement in patients with PAD undergoing peripheral angiography in two positions, straight-leg and crossed-leg [58]. This study uses algorithms to generate 3D models of the *in-vivo* human femoropopliteal artery and measure length, curvature, torsion, twist angle, and creation of new flexion angles between both positions. Results show that significant changes in length, curvature, and twist occur in the PA and significant but more modest changes in length and twist occur in the SFA during movement from the straight-leg to the crossed-leg position [58]. This data reports good insight toward the development of improved endovascular

therapies. Similar studies have been previously reported specifically on axial and twisting deformations in the SFA under maximum hip and knee flexion when the patient is in supine and fetal positions with SFA especially undergoing drastic deformations during supine position, and a study on hinge point development in vessels during compression and movement is suggesting that these situations impose fracture mechanism on the stent itself [6,59].

Curvature and tortuosity as direct effects on the development of peripheral artery diseases were also studied in superficial femoral artery in men and women [60]. In relation to increased body surface area, body mass index and weight it seems that tortuosity and curvature were significantly greater (up to 5 times more) in men than in women which can lead to increased risk for peripheral artery disease in the lower limbs. In the recent years many papers have been reporting on using modeling algorithms and software to generate three dimensional (3D) models of the femoropopliteal artery in order to study in-vivo deformation of the same. Kelin et al. report on in vivo 3D models of femoropopliteal (FP) artery in patients with different leg positions who have peripheral arterial disease (PAD). They use acquired paired angiographic images of the FP artery, and angiography-based 3D modeling algorithms to generate the models in order to quantify the effects of physical forces on the native and stented FP artery which can provide important insights for future stent design at this location [61].

5. Stent behavior inside the arteries and types of stents

In addition, a large number of literature report on stent deformation, fracture and the environment causing stents to decrease in performance. There are various reports in the literature that describe experimental and theoretical methods for measuring forces on stents. These include some in-vitro [62–70] and ex-vivo studies [71] as well as computational modeling methods [72]. Among the imaging studies, high accuracy in measuring the diameter (error < 0.1 mm) and length (error < 0.3 mm) was achieved with micro-CT [66]. Smouse et al. report findings of stent deformation under biomechanical forces when stent is placed in the femoropopliteal arterial segment [73]. The study reports

that the importance of stent fracture in the drug-eluting stent trials covers three aspects: (1) stent fractures could disrupt a drug delivery system, (2) fractured stents may result in vessel injury, and (3) the mechanical stress found in this arterial segment may delay vessel healing and stent incorporation. Furthermore, the SFA and popliteal arteries undergo unique and severe conformational changes that can literally pull apart a metal device (stent). Given this environment, incorporating implanted stents into the SFA and popliteal arteries will likely take longer than similar stents implanted into more stable environments, such as the coronary circulation. It was concluded that the SFA undergoes bending and axial compression during hip flexion and knee movement specifically behind the knee, also axial rigidity or stiffness, and when stent is placed it can alter this axial rigidity in the artery. Depending on the stent type, the rigidity may be drastically increased, and this increase may severely reduce the arteries' ability to accommodate foreshortening. This lack of accommodation adds stress to the stent and the adjacent unstented artery, possibly contributing to stent kinking or fracturing (see Fig. 4) [73].

Comparative test studies of seven different stent designs for the superficial femoral artery were done between different stent manufacturers to evaluate critical stent zones that could lead to fracture using fatigue tests and it was concluded that stent design might play a major role in the appearance of stent strut fracture related to restenosis and reocclusion [74,75]. Ganguly et al. report in-vitro and in-vivo imaging devices for the analysis of the deformation of nitinol stents in femoral artery which results in good base information on the types of deformation that a stent undergoes. However, these studies provide an effective method for testing the accuracy of the image acquisition, reconstruction, segmentation, and analysis framework. The stent used for imaging was a single nitinol stent in each study from a specific manufacturer. These same tests need to be performed for stents from different manufacturers to provide a broad range of data for greater clinical relevance [62,76]. Similarly, Nikanorov et al. report on testing multiple self-expanding nitinol stents used as implant in superficial femoral artery (SFA) from different manufacturers under in-vitro stressed environment replicating intravascular conditions. In this study Nikanorov et al. summarize that the use of stents in the superficial femoral artery continues to be controversial because many believe that the biomechanical forces exerted on the vessel through standing and walking are unfavorable to chronically indwelling devices. The goal of

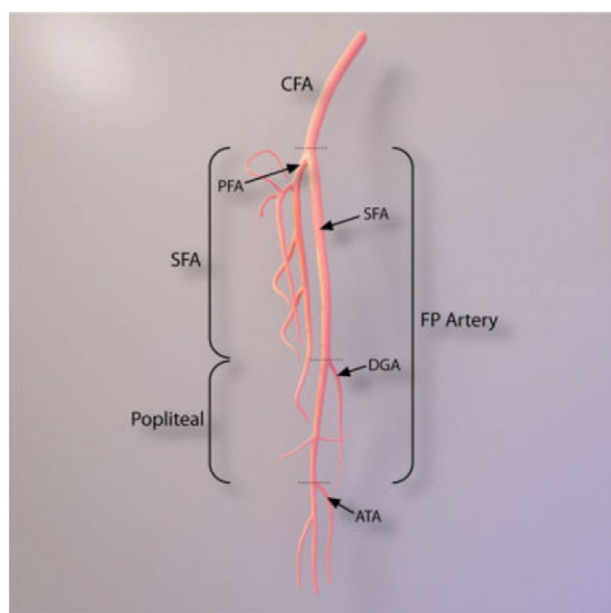


Fig. 3. Anatomy of the femoropopliteal (FP) artery. CFA, common femoral artery; PFA, profunda femoral artery; SFA, superficial femoral artery; DGA, descending genicular artery; ATA, anterior tibial artery [58].

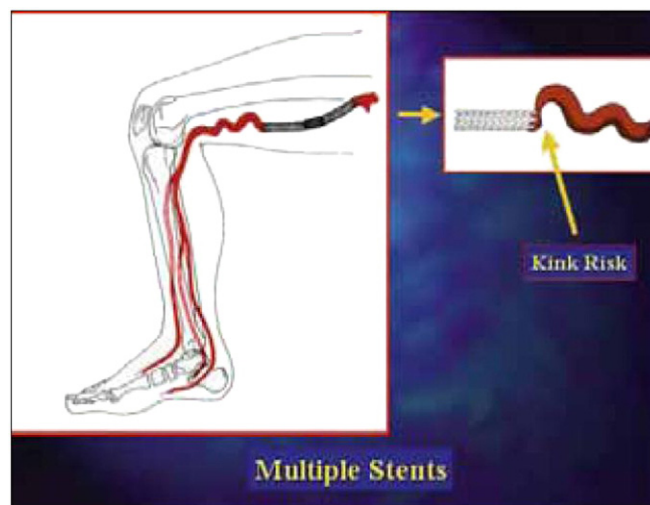


Fig. 4. As stents are placed into the artery, its ability to bend and compress is reduced. The adjacent unstented artery bends more, possibly resulting in kinking at the margin of the stent [73].

the study was to (1) use a human cadaver model to characterize the types and ranges of stent distortion produced by extremity movement and (2) use these ranges as parameters for in vitro fatigue testing of commercially available self-expanding stents. The results show that stents are indeed subjected to measurable axial and bending deformations in the cadaveric superficial femoral artery and that currently available stents exhibit a variable ability to withstand chronic deformation depending on stent design and the type of deformation applied [77].

5.1. Types of stents

A stent is a tubular device, comprised of a special fabric supported by a rigid structure usually metal. It is completely a metal mesh with no covering but coated by a polymer which supports the bio life. It is mostly used in endovascular surgery which supports the weak points in arteries. These weak points are generally known as aneurysms. These stents act like a false lumen in the passage of blood flow instead of flowing through the aneurysm sack. There are different types of stents used such as bare-metal stent, a drug eluting stent, a bio-absorbable stent, and a dual therapy stent (combination of both drug and bioengineered stent) [78].

5.1.1. Bare-metal stent (BMS)

It is a vascular stent without a coating of drug (generally used in drug-eluting stents) (see Fig. 5). It looks like a mesh tube of thin wire. Bare metal stents are the ones used in the cases of cardiac arteries and are often made from 316 L stainless steel.

Metal stents have a tubular lattice structure and can be assembled from a range of metals like nitinol, stainless steel and cobalt chromium. Ideally it should be flexible and spring like, conforming to the shape of the arterial wall. The goal is to hold the inner wall in its newly compressed position without changing the diameter. The diameter of the stents can range from 2 mm to 4 mm depending upon the vessel, condition and the type of disease. The length ranges from 8 mm to 38 mm depending upon the length of the disease. The materials differ in degrees of strength and flexibility. According to engineers specific material and designs can create greater resistance to stent fracture and also these materials are radiopaque and biocompatible. Radiopaque helps the physicians in visualizing the stent while implanting by using a fluoroscope. For example, a cobalt chromium stent material is more radiopaque and durable than stainless steel. Manufacturers are also introducing a lot of designs like multicellular corrugated, coil and serpentine. Some of these designs are included with a lining of carbon, platinum and heparin in order to decrease the potential of thrombosis [78].

Usage of bare metal stents has decreased the elastic recoil effect after the balloon angioplasty surgery. Thereby the incidence of restenosis has been dropped to around 25% within the 3 to 6 months after the surgery. However, laterally stents fracture because of the biomechanical environment of the vessels. Mainly stents in patients with peripheral artery disease (PAD) where there is a movement like sitting, running, walking and standing were associated with stent fracturing. Stent fracture rate has been approximated to around 65% in patients with PAD and thereby leading to restenosis [78].

5.1.2. Drug-eluting stent (DES) (Fig. 6)

It is a stent placed mainly in the narrowed, diseased peripheral and coronary arteries that slowly releases a drug to block cell proliferation. This prevents fibrosis that, together with clots (thrombus), could otherwise block the stented artery, a process called restenosis [79,80]. Food and Drug Administration (FDA) has approved DES after clinical trials showing superior performance to BMS to treat narrow arteries and decreased number of major adverse cardiac events (MACE). MACE, is generally defined as death, myocardial infarction, or the need for repeated revascularization procedures [79]. DES consists of three parts:

Stent platform: The basic stent platform will be the BMS which has expansion, flexibility and more radio-opaque. Cobalt chrome alloy is stronger, thinner and radio-opaque and it is less allergenic. Mostly DES is based upon the BMS [79].

Coating: Typically it is a polymer which holds and releases the drug into the arterial wall by contact. Primarily there were few durable coatings which have been replaced by new coatings that can be biodegradable after the drug has been released. These coatings are generally dip coated or spray coated. There can be one or more layers depending upon the requirement. For example the first layer for adhesion, next layer for holding the drug and the third coat can be to slow down the release of the drug and increase its effectiveness [79].

Drug: As explained above the drug's function is mainly to inhibit the neointimal growth and suppress the cause of restenosis. Neointimal hyperplasia is the proliferation of the smooth muscle cells during the inflammation of the balloon. Hence in order to suppress this growth immunosuppressive and antiproliferative drugs are used. Drugs like sirolimus and paclitaxel have been used primarily but now new drugs are being used in order to prevent current problems [79].

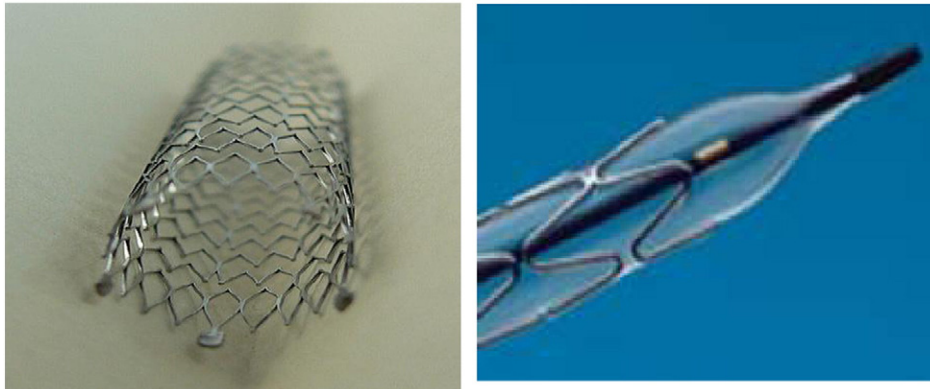


Fig. 5. Left: bare metal stent and right: bare metal stent with inflated balloon [78].

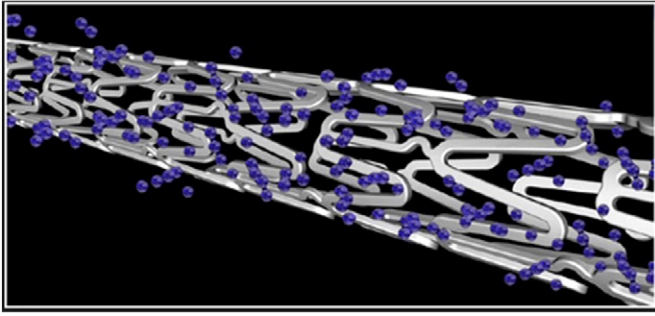


Fig. 6. Drug eluting metal stent [80].

6. Conclusion

The association of target vessel restenosis with stent fractures has led to an emergence of interest in understanding the mechanical properties of stents and the environment causing stent fracture. Reduction of these fractures requires an understanding of the biomechanical forces at the implantation site and the mechanical properties of the stent. Other factors predisposing to stent fractures include lengthy coronary stents, overlapping stents, saphaneous vein graft stents, and right coronary artery lesions treated with sirolimus-eluting stents.

Repetitive compression, creep deformation due to axial and radial stresses, kinking and shear stresses during movement in patients may also cause metal fatigue and subsequent fracture. Thrombosis is thought to occur from exposure of the strut to blood which can lead to platelet aggregation and subsequent clotting. Maldistribution of the drug due to stent architecture malfunction is implicated in restenosis. All the studies mentioned in this review directly relate toward the improved performance of the stent implants as part of the arterial environment imposing additional loading. There is no perfect stent and one which exhibits all the ideal properties required and therefore a range of stents are available so that all lesions are to be addressed. In summary, in order to minimize stent fracture and improve life-cycle of stent implants detailed systematic study for understanding the artery state and environment, stent manufacturing, deployment, fracture classification and management is crucial. This detailed review provides a summary of literature that leads a step forward toward addressing the problem on stents with short life-cycle.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

References

- [1] Kochanek KD, Xu JQ, Murphy SL, Miniño AM, Kung HC. Deaths: final data for 2009. *National vital statistics reports*, 60(3); 2011.
- [2] Rosamond W, Flegal K, Furie K, Go A, Greenlund K, Haase N, et al. Heart disease and stroke statistics – 2008 update, volume 117. A report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee; 2008.
- [3] Schillinger M, Sabeti S, Dick P, et al. Sustained benefit at 2 years of primary femoropopliteal stenting compared with balloon angioplasty with optional stenting. *Circulation* 2007;115:2745–9.
- [4] Schillinger M, Minar E. Past, present and future of femoropopliteal stenting. *J Endovasc Ther* 2009;16(Suppl. 1):147–52.
- [5] Krankenberg H, Schluter M, Steinkamp HJ, et al. Nitinol stent implantation versus percutaneous transluminal angioplasty in superficial femoral artery lesions up to 10 cm in length: the femoral artery stenting trial (FAST). *Circulation* 2007;116:285–92.
- [6] Cheng CP, Wilson NM, Hallett RL, Herfkens RJ, Taylor CA. In vivo MR angiographic quantification of axial and twisting deformations of the superficial femoral artery resulting from maximum hip and knee flexion. *J Vasc Interv Radiol* 2006;17:979–87.
- [7] Kelin AJ, Chen SJ, Messenger JC, et al. Quantitative assessment of the conformational change in the femoropopliteal artery with leg movement. *Catheter Cardiovasc Interv* 2009;74:787–98.
- [8] <http://www.medivisuals.com/an-arterial-wall-604089r-02x.aspx>.
- [9] Encyclopedia Britannica Inc. 2008.
- [10] Sommer G. Mechanical properties of healthy and diseased human arteries. [Dissertation] Austria: Verlag der Technischen Universität Graz; 2010.
- [11] Marey EJ. Pressione et vitesse du sang. *Physiol Exp* 1876.
- [12] Roy CS. The elastic properties of the arterial wall. *J Physiol* 2008;3(125–159):1880–2.
- [13] Bergel DH. The visco-elastic properties of the arterial wall. [PhD thesis] University of London; 1960.
- [14] Fung YC. On the foundations of biomechanics. *J Appl Mech* 1983;50:1003–9.
- [15] Vaishnav RN, Vossoughi J. Estimation of residual strains in aortic segments. In: Hall CW, editor. *Biomedical engineering II: recent developments*. New York: Pergamon Press; 1983. p. 330–3.
- [16] Chuong CJ, Fung YC. On residual stress in arteries. *J Biomech Eng* 1986;108:189–92.
- [17] Takamizawa K, Hayashi K. Strain energy density function and uniform strain hypothesis for arterial mechanics. *J Biomech* 1987;20:7–17.
- [18] Fung YC. *Biomechanics. Mechanical properties of living tissues*. 1st ed. New York: Springer-Verlag; 1981.
- [19] Skalak R, Dasgupta G, Moss M, Otten E, Dullemeijer P, Vilmann H. Analytical description of growth. *J Theor Biol* 1982;94:555–77.
- [20] Skalak R, Zargaryan S, Jain RK, Netti PA, Hoger A. Compatibility and the genesis of residual stress by volumetric growth. *J Math Biol* 1996;34:889–914.
- [21] Patel DJ, Fry DL. The elastic symmetry of arterial segments in dogs. *Circ Res* 1969;24:1–8.
- [22] Von Maltzahn W, Warriyar RG, Keitzer WF. Experimental measurements of elastic properties of media and adventitia of bovine carotid arteries. *J Biomech* 1984;17:839–47.
- [23] Dobrin PB, Rovick AA. Influence of vascular smooth muscle on contractile mechanics and elasticity of arteries. *Am J Physiol* 1969;217:1644–51.
- [24] Fung YC. *Biomechanics. Mechanical properties of living tissues*. 2nd ed. New York: Springer-Verlag; 1993.
- [25] Cox RH. Three-dimensional mechanics of arterial segments in vitro: methods. *J Appl Phys* 1974;36:381–4.
- [26] Cox RH. Arterial wall mechanics and composition and the effects of smooth muscle activation. *Am J Physiol* 1975;229:807–12.
- [27] Cox RH. Effects of norepinephrine on mechanics of arteries in vitro. *Am J Physiol* 1976;23:420–5.
- [28] Cox RH. Mechanics of canine iliac artery smooth muscle in vitro. *Am J Physiol* 1976;230:462–70.
- [29] Cox RH. Passive mechanics and connective tissue composition of canine arteries. *Am J Physiol* 1978;234:H533–41.
- [30] Cox RH. Regional variation of series elasticity in canine arterial smooth muscles. *Am J Physiol* 1978;234:H542–51.
- [31] Cox RH. Comparison of carotid artery mechanics in the rat, rabbit and dog. *Am J Physiol* 1978;234:H280–8.
- [32] Cox RH. Differences in mechanics of arterial smooth muscle from hindlimb arteries. *Am J Physiol* 1978;235:H649–56.
- [33] Dobrin PB, Doyle JM. Vascular smooth muscle and the anisotropy of dog carotid artery. *Circ Res* 1970;27:105–19.
- [34] Dobrin PB. Isometric and isobaric contraction of carotid arterial smooth muscle. *Am J Physiol* 1973;225:659–63.
- [35] Dobrin PB. Mechanical properties of arteries. *Physiol Rev* 1978;58:397–460.
- [36] Dobrin PB. Vascular mechanics. In: Shepherd JT, Abboud FM, editors. *Handbook of physiology. Section 2: the cardiovascular system, vol. III*. Bethesda: American Physiological Society; 1983. p. 65–102.
- [37] Dobrin PB, Canfield TR. Elastase, collagenase, and the biaxial elastic properties of dog carotid artery. *Am J Physiol* 1984;247:H124–31.
- [38] Dobrin PB. Biaxial anisotropy of dog carotid artery: estimation of circumferential elastic modulus. *J Biomech* 1986;19:351–8.
- [39] Han HC, Fung YC. Longitudinal strain of canine and porcine aortas. *J Biomech* 1995;28(5):637–41.
- [40] Choi G, Shin LK, Taylor CA, Cheng CP. In vivo deformation of the human abdominal aorta and common iliac arteries with hip and knee flexion: implications for the design of stent-grafts. *J Endovasc Ther* 2009;16:531–8.
- [41] Cheng CP, Choi G, Herfkens RJ, Taylor CA. The effect of aging on deformations of the superficial femoral artery due to hip and knee flexion: potential clinical implications. *J Vasc Interv Radiol* February 2010;21(2):195.
- [42] Choi G, Cheng CP, Wilson NM, Taylor CA. Methods for quantifying three-dimensional deformation of arteries due to pulsatile and nonpulsatile forces: implications for the design of stents and stent grafts. *Ann Biomed Eng* Jan 2009;37(1):14t–33t [Epub 2008 Nov 11].
- [43] Han HC, Chesnutt JKW, Garcia JR, Liu Q, Wen Q. Artery buckling: new phenotypes, models and applications (invited review). *Ann Biomed Eng* 2013;7:1399–410 [online Nov 29, 2012].
- [44] Garcia JR, Lamm SD, Han HC. Twist buckling behavior of arteries. *Biomech Model Mechanobiol* 2013;5:915–27.
- [45] Liu Q, Han HC. Mechanical buckling of arterioles in collateral development. *J Theor Biol* 2013;316:42–8.
- [46] Han HC. Twisted blood vessels: symptoms, etiology, and biomechanical mechanisms. *J Vasc Res* 2012;49(3):185–97.
- [47] Lee AY, Han B, Lamm SD, Fierro CA, Han HC. Effects of elastin degradation and surrounding matrix support on artery stability. *Am J Physiol Heart Circ Physiol* 2012;302(4):H873–84.
- [48] Liu Q, Han HC. Mechanical buckling of arteries under pulsatile pressure. *J Biomech* 2012;45(7):1192–8.
- [49] Chesnutt JKW, Han HC. Tortuosity triggers platelet activation and thrombus formation in microvessels. *ASME J Biomech Eng* 2011;133(12):121004.

- [50] Han HC. Determination of the critical pressure of artery buckling using the potential energy approach. *Ann Biomed Eng* 2011;39(3):1032–40.
- [51] Jin Y, Han HC, Berger J, Dai Q, Lindsey ML. Combining experimental and mathematical modeling to reveal mechanisms of macrophage-dependent left ventricular remodeling. *BMC Syst Biol* 2011;5:60.
- [52] Lee YU, Luo J, Sprague EA, Han HC. Comparison of artery organ culture and coculture models for studying endothelial cell migration and its effect on smooth muscle cell proliferation and migration. *Ann Biomed Eng* 2010;38(3):801–12.
- [53] Martinez R, Fierro CA, Shireman PK, Han HC. Mechanical buckling of veins under internal pressure. *Ann Biomed Eng* 2010;38(4):1345–53.
- [54] Lee YU, Hayman D, Sprague EA, Han HC. Effects of axial stretch on intimal thickness and cell proliferation in arteries in organ culture. *Cell Mol Bioeng* 2010;3(3):286–95.
- [55] Han HC. Blood vessel buckling within surrounding tissue generates tortuosity. *J Biomech* 2009;42(16):2797–801.
- [56] Han HC. The theoretical foundation for artery buckling under internal pressure. *J Biomech Eng* 2009;131(12):124501.
- [57] Han HC. A biomechanical model of artery buckling. *J Biomech* 2007;40(16):3672–8.
- [58] Klein AJ, Chen SJ, Messenger JC, Hansgen AR, Plomondon ME, Carroll JD, et al. Quantitative assessment of the conformational change in the femoropopliteal artery with leg movement. *Catheter Cardiovasc Interv* 2009;74:787–98.
- [59] Diaz JA, Villegas M, Tamashiro G, Miceli MH, Enterrios D, Balestrini A, et al. Flexions of the popliteal artery: dynamic angiography. December 2004;16(12).
- [60] Wood NB, Zhao SZ, Zambanini A, Jackson M, Gedroyc W, Thom SA, et al. Curvature and tortuosity of the superficial femoral artery: a possible risk factor for peripheral arterial disease. *J Appl Phys Lett* 2006;101:1412–8.
- [61] Klein AJ, Casserly IP, Messenger JC, Carroll JD, James Chen SY. In vivo 3D modeling of the femoropopliteal artery in human subjects based on x-ray angiography: methodology and validation. *Med Phys* February 2009;36(2).
- [62] Ganguly A, Simons J, Schneider A, Keck B, Bennett NR, Fahrig R. In-vitro imaging of femoral artery nitinol stents for deformation analysis. *J Vasc Interv Radiol* 2011;22:236–43.
- [63] Duda SH, Wiskirchen J, Tepe G. Physical properties of endovascular stents: an experimental comparison. *J Vasc Interv Radiol* 2000;11:645–54.
- [64] Dyet JF, Watts WG, Ettles DF, Nicholson AA. Mechanical properties of metallic stents: how do these properties influence the choice of stent for specific lesions? *Cardiovasc Intervent Radiol* 2000;23:47–54.
- [65] Jedwab MR, Clerc CO. A study of the geometrical and mechanical properties of a self-expanding metallic stent—theory and experiment. *J Appl Biomater* 1993;4:77–85.
- [66] Nikolov HN, Pelz DM, Lownie SP. Micro-CT-compatible technique for measuring self-expanding stent forces. *J Vasc Interv Radiol* 2008;21:562–70.
- [67] Kalmar G, Hubner F, Voelker W. Radial force and wall apposition of balloon-expandable vascular stents in eccentric stenoses: an in vitro evaluation in a curved vessel model. *J Vasc Interv Radiol* 2002;13:499–508.
- [68] Maintz D, Kugel H, Schellhammer F, Landwehr P. In vitro evaluation of intravascular stent artifacts in three-dimensional MR angiography. *Invest Radiol* 2001;36:218–24.
- [69] Maintz D, Seifarth H, Raupach R. 64-slice multidetector coronary CT angiography: in vitro evaluation of 68 different stents. *Eur Radiol* 2006;16:818–26.
- [70] Nuutinen JP, Clerc C, Tormala P. Theoretical and experimental evaluation of the radial force of self-expanding braided bioabsorbable stents. *J Biomater Sci Polym Ed* 2003;14:677–87.
- [71] Grenacher L, Ganger E, Lubienski A, Dux M, Kauffmann GW, Richter GM. Experimental functional analysis of self-expanding stents using a new developed ex vivo model. *Invest Radiol* 2004;39:374–83.
- [72] Howell BA, Kim T, Cheer A, Dwyer H, Saloner D, Chuter TA. Computational fluid dynamics within bifurcated abdominal aortic stent-grafts. *J Endovasc Ther* 2007;14:138–43.
- [73] Smouse HB, Nikanorov A, Laflash D. Biomechanical forces in the femoropopliteal arterial segment. *Endovascular Today*; June 2005.
- [74] Muller-Hulsbeck S, Schafer PJ, Charalambous N, Yagi H, Heller M, Jahnke T. Comparison of second-generation stents for application in the superficial femoral artery: an in vitro evaluation focusing on stent design. *J Endovasc Theory* 2010;17:767–76.
- [75] Schmidt W, Wissgott C, Andresen R, Behrens P, Schmitz K-P. Performance characteristics of modern self-expanding nitinol stents indicated for SFA. *Fortschr Röntgenstr* 2011;183:818–25.
- [76] Ganguly A, Simons J, Schneider AB. In-vivo imaging of femoral artery nitinol stents for deformation analysis. *J Vasc Interv Radiol* 2011;22:244–9.
- [77] Nikanorov A, Smouse HB, Osman K, Bialas M, Shrivastava S, Schwartz LB. Fracture of self-expanding nitinol stents stressed in vitro under simulated intravascular conditions. *J Vasc Surg* 2008;48(2):435–41.
- [78] <http://en.wikipedia.org/wiki/Stent>.
- [79] http://en.wikipedia.org/wiki/Drug-eluting_stent.
- [80] <http://www.alvimedica.com/index.php/en/products/drug-eluting-stents/coraxel-des>.