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An overview of superelastic stent design

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Summary

The purpose of this paper is to contrast the performance of self-expanding and balloon-expandable stents. While both approaches to stenting have proven to be successful in treating a wide range of vascular disease, there are significant differences in the philosophy behind and properties of the two types of stents. Many of these differences, such as strength, stiffness (or compliance), recoil, dynamic scaffolding, vessel conformity and fatigue resistance will be highlighted by studying the mechanics of the stent alone, and then of a stent within a vessel. These differences can be summarised by observing that self-expanding stents provide more anatomically-correct scaffolding, while balloon-expandable stents provide rigid and uncompromising reinforcement. Other differences, such as corrosion resistance, placement accuracy and visibility, will also be briefly summarised.

Keywords

Nitinol, stents, superelasticity

Introduction

Superelasticity refers to the ability of Nitinol and certain other metals to return to their original shape after severe deformations. As such, it is an extension of the conventional elasticity that all metals exhibit to varying degrees: stainless steel (SS) can return to its original length if stretched up to 0.3% of its original length, extremely elastic titanium alloys up to 2%, and superelastic Nitinol, over 10%.

While a superelastic material appears macroscopically to be simply 'very elastic', in fact the mechanism of deformation is quite different from conventional elasticity, or simply the stretching of atomic bonds. When a stress is applied to Nitinol, and after a rather modest elastic deformation, superelastic Nitinol changes its crystal structure from austenite to martensite. The austenite, or 'parent' crystal structure is cubic in nature; the martensitic 'daughter' structure is a complex monoclinic structure. This 'stress assisted' phase transition allows the material to change shape as a direct response to the applied stress. When the stresses are removed, the material reverts to the original austenite and recovers its original shape.

Nitinol, a nearly equiatomic composition of nickel and titanium, is one of very few alloys that is both superelastic and biocompatible. Moreover, the narrow temperature range within which Nitinol's superelasticity is exhibited includes body temperature. Thus, Nitinol has become the 'material of choice' for designers of self-expanding (SE) stents. SE stents are manufactured with a diameter larger than that of the target vessel, crimped and restrained in a delivery system, then elastically released into the target vessel. Performance of SE stents is therefore limited by the ability of the material to store elastic energy while constrained in the delivery system, making Nitinol the ideal choice. While the exact mechanisms of superelasticity in Nitinol are well understood [1], the use of Nitinol in stents is relatively new [2].

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The most dramatic and demonstrable attribute of Nitinol stents is their 'crush recoverability'. Most, if not all, Nitinol stents can be crushed fully flat and still elastically recover their original shape without clinically-relevant loss of lumen diameter. This attribute is important in superficial indications subject to external crushing, such as the carotid artery. Crush recoverability is surely the easiest way one can distinguish Nitinol from SS, but differences between balloon-expandable (BE) and SE stents are far more numerous and important.

Terminology and definition of forces

As a preamble, it is necessary to define some terminology regarding vascular forces and cylindrical shapes in general. Blood vessels experience loads from a variety of sources, such as the pulse pressure of the cardiac cycle, spasms, angioplasty balloons, the placement of a stent, etc. Pressures applied to any cylindrical structure, such as a blood vessel, result in hoop, or circumferential-loading of the vessel (Figure 1a). Both the applied pressure and the resulting hoop stress have units of 'force per unit area', but differ in direction. 'Pressure' refers to the force normal to the vessel wall, divided by the surface area of the lumen, while 'hoop stress' is the circumferential load in the vessel wall divided by the cross-sectional area of the vessel wall (length times wall thickness). By analogy, water pressure within a pipe results in a tensile hoop stress within the metal pipe itself. The pressure (p) and the hoop stress (σ) in a thin-walled cylindrical object such as a vessel or stent are related by:

$$\sigma = p\,\phi/2\,t \qquad (1)$$

where 'ϕ' is the vessel diameter and t the vessel wall thickness. We can describe the hoop force 'F_θ' in a vessel wall as:

$$F_\theta = \sigma\, t\, L = p\,\phi\, L/2 \qquad (2)$$

where 'L' is the stent length. In fact, it is more convenient to define hoop force per unit length as:

$$f_\theta = F_\theta / L = \sigma\, t = p\,\phi/2 \qquad (3)$$

As an example, a blood pressure of p = 100 mmHg would apply a hoop force (or hoop load) on an 8 mm diameter vessel of:

$$f_\theta = (100\ \text{mmHg})\,[1.33 \times 10^{-4}\ (\text{N mm}^{-2})\text{mmHg}^{-1}]\,(8\ \text{mm})\,/\,2 = 0.053\ \text{N mm}^{-1} \qquad (4)$$

where 1.33×10^{-4} (N mm^{-2})/mmHg is the conversion from mmHg to N mm^{-2} or MPa. Thus, each mm of vessel length experiences a tensile load in the hoop direction of 0.053 N.

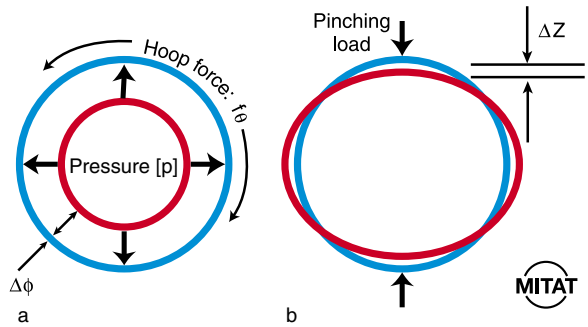

Figure 1. The two most common loading modes for stents are **(a)** radial or hoop and **(b)** pinching.

Hoop or radial strength

While hoop stress, total hoop force and pressure are all equivalent descriptors of vessel forces, we find f_θ to be most convenient because it best correlates to strength, or the maximum hoop load that can be carried without failure. In the case of a vessel or pipe, failure is suitably defined as burst, or rupture. Failure would occur when the hoop stress exceeds the ultimate tensile strength (UTS) of the material used to manufacture the vessel or pipe.

All the same concepts apply to a stent within a vessel. Pressures acting on the vessel result in hoop-loading of the stent that is being used to scaffold, or support, the vessel. The concept of 'failure', however, now becomes illusive. A stent is intended to hold the vessel open, not to prevent rupture. A stent may fail to perform its intended function and still be fully intact, so the concept of fracture as the failure criteria is no longer relevant. 'Failure' is often defined as the onset of permanent, or plastic, deformation ('yielding'). In BE stents there exists some pressure that causes plastic deformation of the stent, thus providing a basis for defining the strength of the stent. Radial strength can, however, and often is used instead of hoop strength, with the two quantities related through equation 3. In contrast to BE stents, however, Nitinol knows no such limitations: it cannot be deformed or broken due to clinically-relevant external stresses. It is important to note that Nitinol therefore has no physically-appropriate hoop or radial strength limit.

Radial or hoop stiffness

While we therefore cannot compare the strength of a SE stent to a BE stent, we can and should compare their stiffness. 'Stiffness' measures the elastic response of a device to an applied load and thus will

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reflect the effectiveness of the stent in resisting diameter loss due to vessel recoil and other mechanical events. Just as above, the choice of radial or hoop stiffness is only one of terminology, but we prefer the mathematics of hoop stiffness because of its more direct correlation to design. More specifically, we can define the hoop stiffness of a stent or a vessel as the hoop force per unit length required to elastically change its diameter, or:

$$k_\theta = f_\theta / \Delta\phi \quad (5)$$

Note that stiffness is the inverse of another commonly used term, 'compliance', or diameter change at a specific applied pressure. Vessel compliance (C) is usually reported as the percent diameter change at a given pressure, P_o. Thus hoop stiffness is related to radial compliance through:

$$k_\theta = P_o / 2C_o \quad (6)$$

With the commonly-assumed pressure of P = 100 mmHg (0.0133 N mm^{-2}), we have k_θ = (0.00665 N mm^{-2}) / $C_{100mmHg}$.

Using analytical mechanics [3] we can estimate the stiffness of a conventional diamond or z-strut (Figure 2). While we need not concern ourselves with the detailed calculations, it is interesting to summarise trends. The change in stent diameter due to an applied load is related to the stent geometry by:

$$\Delta\phi \propto f\phi \; n L_s^3 / E w^3 t \quad (7)$$

or, substituting equation (3), the change in stent diameter may be related to an applied pressure load by:

$$\Delta\phi \propto p \phi \; n L_s^3 / E w^3 t \quad (8)$$

where 'L' is the length of a z-strut or half-diamond, 'w' the strut width, 't' the thickness of the stent, 'n' the number of struts around the circumference, and 'E' is the elastic modulus of the material. It follows from equations (3) and (8) that the stiffness per unit length (k_θ) can be determined by:

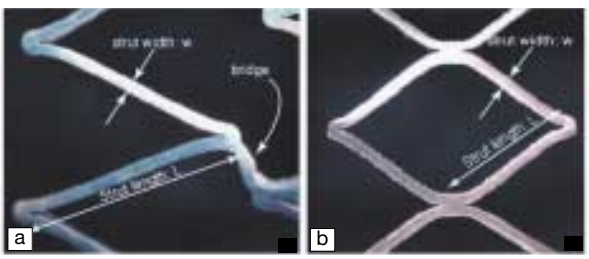

Figure 2. Most stents are variations on either **(a)** 'z's or **(b)** diamonds.

$$k_\theta \propto E w^3 t / n L_s^3 \quad (9)$$

However, equations (7) through (10) are only good approximations for small linear deflections, within the linear elastic range of the material; larger deformations and more complicated geometry require other techniques such as finite element analysis (FEA).

The stiffness of a stent does have clinical significance in reducing acute recoil and in determining fatigue life (both discussed below).

Pinching loads and buckling

Important in equation (9) is the cubic relationship of hoop or radial stiffness to strut width. If instead a stent is squeezed between two fingers or platens, the stent is subjected to a pinching load (Figure 1b). Pinching loads subject struts to out-of-plane bending, i.e., the struts are not bent around the circumference, as in radial compression. The dependence deflection of a stent on geometry is rather complex and includes tension, torsion and bending components, but we can approximate the primary bending component as follows:

$$k_{pinching} \propto E t^3 w / n L_s^3 \quad (10)$$

Note that under a pinching load, strut width now demonstrates only a linear contribution, while thickness shows a cubic dependence, precisely the opposite of hoop strength, for which strut width has the dominate role. Thus, the stiffness of a stent determined by flattening has little to do with the clinically-relevant stiffness of the stent. In fact, design changes aimed at increasing crush resistance may well decrease radial stiffness. Pinching loads and deflections are far easier to measure than hoop, therefore one must be vigilant not to erroneously use this as a gauge of stent strength or stiffness.

Buckling refers to unstable deformation, meaning that an applied load can be reduced by increasing deformation. Most objects loaded in compression are potentially subject to buckling, such as a walking cane that might bend suddenly if leaned on too hard. Once a structure buckles its stiffness is generally dramatically reduced. A stent experiences circumferential compression and may, in cases, become unstable and buckle outside the circumferential plane into a half-moon shape. This can be exacerbated if the compression loads are not radially symmetric, as in the 'kissing' stent grafts shown in Figure 3. Being an out-of-plane deformation, buckling is resisted by the pinching stiffness, described in equation 10. Thus, a lower hoop stiffness but more stable shape can be obtained by maximising thickness and minimising width. One must be careful to balance the two stiffnesses.

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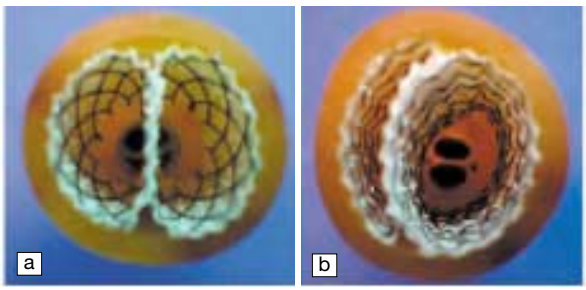

Figure 3. Two 'kissing' Nitinol stent grafts of equivalent radial stiffness, both shapes set to the same circular cross-section, but with different pinching stiffness. The design on the left can be crushed in any direction and will return to the desired shape shown. The design on the right prefers to buckle out of plane and return to a half-moon geometry, occluding one of the branches.

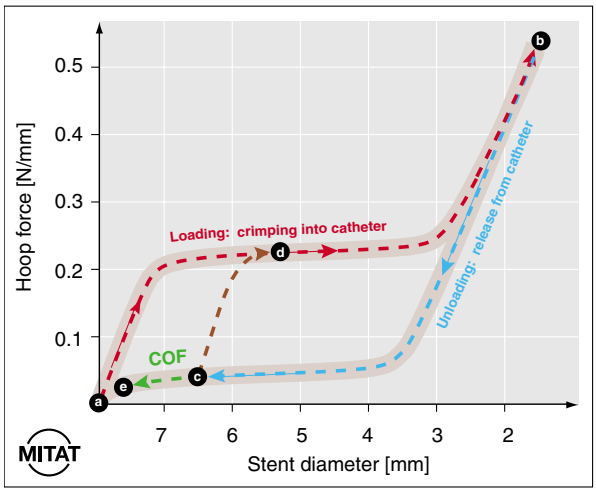

Figure 4. A typical superelastic stress–strain curve is transposed onto a hoop force–diameter diagram, illustrating the concept of 'biased stiffness'. An 8 mm stent is compressed into a catheter **(b)**, then released to a diameter **(c)**. Further deformation forces are resisted by the 'radial resistive force' **(d)**, while the opening 'chronic outward force' (COF) remains constant and gentle **(e)**.

Elastic modulus and biased stiffness

Next we consider the elastic modulus, E, in equations 7–10, a simple constant for conventional materials, but an enormously complex concept in Nitinol [1]. The modulus of all SS stents is approximately 200 GPa; variations in device stiffness result only from the geometry variations described in equation 9. Nitinol, however, is a non-linear, path-dependent and temperature-dependent material, making E anything but a constant. One certainty, however, is that E is always lower in Nitinol than it is in SS, thus a SS stent will always be stiffer, or less compliant, than a Nitinol stent made to the same design. In fact, a BE stent will be at least three times as stiff as an identical Nitinol SE stent. Clearly this has important implications for recoil, which will be reviewed later in this paper.

The hysteresis or path dependence of Nitinol results in another very important feature termed 'biased stiffness'. This concept is illustrated in Figure 4. Shown in grey is a typical schematic superelastic stress–strain curve for Nitinol, illustrating both non-linear response and hysteresis. Superimposed on the curve is the crimping and deployment of a SE stent. The axes have been changed from stress–strain to hoop force–stent diameter. This particular schematic stent has been manufactured with an 8 mm diameter ('a' in Figure 4), crimped into a delivery catheter (point 'b'), then packaged, sterilised and shipped. After insertion to the target site, the stent is released into a vessel, expanding from 'b' until movement is stopped by impingement with the vessel (point 'c'). Having reached equilibrium with the vessel, recoil pressures are resisted by forces dictated by the loading curve (brown trace towards point 'd') which is substantially steeper (stiffer) than the unloading line (green trace towards point 'e').

In the next section we will examine this 'impingement' in more detail, but already we can see some of the significance of Nitinol's unusual elastic hysteresis. This biased stiffness means that the continuing opening force of the stent acting on the vessel wall, or 'chronic outward force' (COF) remains very low through large deflections and oversizing. Meanwhile the forces generated by the stent to resist compression, or 'radial resistive force' (RRF), increase rapidly with deflection until a plateau stress is reached. As a matter of definition, we again find it most convenient to define both RRF and COF as hoop forces per unit length of stent, thus allowing a constant value within a family of stents of varying diameter and length. We will discuss the clinical relevance of COF and RRF in later sections, but in general, stent designers should strive for as high an RRF with as possible, with as low a COF as possible. Figure 5 shows actual measurements of hoop force versus diameter for a commercially-available 10 mm Nitinol stent. The actual diameter of the stent is closer to 10.5 mm and it is typical that SE stents are larger than their nominal diameter. Since the consequence of oversizing is substantially less than the consequence of under-sizing, a 'one-sided tolerance' is often applied.

The device is crimped to 2 mm and deployed into an emulated 8.5 mm vessel diameter (data at diameters < 4 mm is not recorded). At 8.5 mm, the RRF is recorded by crimping the stent back to 7.5

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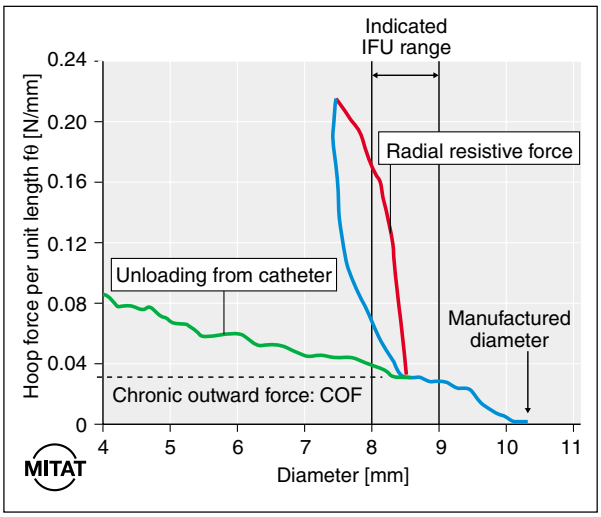

Figure 5. Hoop forces are measured during the release of a commercially-available, laser-cut Nitinol SE stent with a nominal 10 mm diameter. The release is halted at the centre of the intended diameter range of 8–9 mm, at which point the stent is compressed 1 mm in order to demonstrate biased stiffness. After the compression, the stent is again unloaded, quickly returning to the original unloading path, but with a small hysteresis.

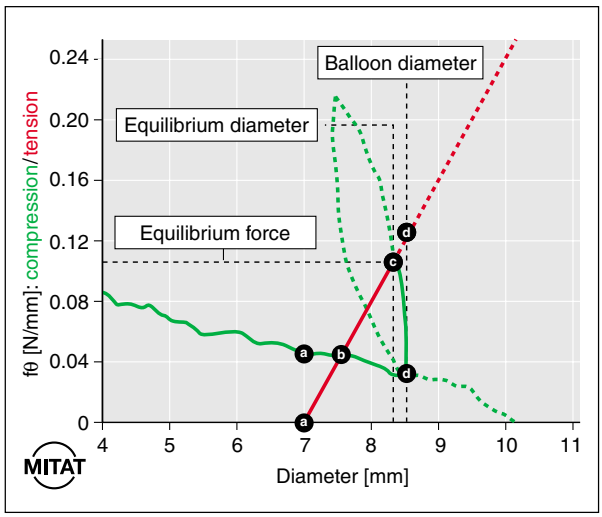

Figure 6. The interaction of a vessel with a typical SE stent is illustrated by examining the delivery process and post-dilatation. (Note that the stent forces are compressive, while the vessel forces are tensile.) The stent is released from the delivery system, making vessel contact at **(a)**, then reaching a stress equilibrium at **(b)**. Post-dilatation further unloads the stent, and stretches the vessel, to points **(c)** and, finally, deflation of the balloon loads the stent and relaxes the vessel to the final equilibrium points **(d)**.

mm, then the stent is unloaded entirely to its original diameter. One can see that the COF is quite constant at 0.035 N mm^{-1} throughout the indicated diameter range (8–9 mm). The RRF increases sharply as the stent is deformed from the equilibrium diameter, reaching 0.22 N mm^{-1} after a 1 mm deflection. Continued deformation would indicate a plateau at approximately 0.24 N mm^{-1}. Note that the RRF is not a property of the stent, but must be defined by applying some relevant diameter change, in this case, 1 mm. Also note that unloading (in blue) does not follow the same line as loading, but instead shows additional hysteresis, rejoining the original unloading line at the point at which loading began. With cycling, this hysteresis will reduce to nearly zero and the RRF slope will decrease.

Post-dilatation and acute recoil

Having described the behaviour of a stent alone, we can now examine the 'impingement' and interaction of the stent with the vessel during deployment. To illustrate this, Figure 6 follows the same 10 mm stent illustrated in Figure 5, as it contacts a 7 mm vessel with a hoop stiffness of 0.11 N mm^{-2} (6% compliance at 100 mmHg). During this sequence, the vessel will experience tensile hoop forces, with the stent in compression, although, for reasons of convenience, they are plotted on the same axis. The stent is released from the delivery catheter and unloads to meet the vessel wall (shown by the solid green traces). The stent contacts the vessel at 'a' and reaches an initial equilibrium diameter at point 'b'. Note that this equilibrium diameter is dictated by an equilibrium between the compressive stent COF and the tensile hoop forces in the vessel wall. The stent is then balloon dilated to 8.8 mm, forcing stent and vessel to diameter 'c'. Finally, the balloon is deflated, allowing the vessel to recoil, achieving a new stress equilibrium, at point 'd'. During dilation the stent is unloaded and during recoil it is loaded. Since the stent is now being loaded to the final diameter, equilibrium is now determined by the RRF of the stent, rather than the COF. Except for the biased stiffness of Nitinol, post-dilatation of a healthy elastic vessel would be completely ineffective and return to the original equilibrium diameter at point 'b'. We should note that there is at least one SS SE stent on the market, made of braided wire. While SS doesn't inherently provide biased stiffness, friction between braided wires can emulate this effect.

It is interesting to compare Figure 6 with the same scenario carried out with a BE stent (Figure 7). The vessel is the same in Figures 6 and 7, but now it is superimposed with the hoop force versus diameter characteristics of a typical peripheral BE stent. (Note that the sense of the forces for stent and vessel are reversed, just as in Figure 6, and that the scale below the axis is much coarser than that above.) In this

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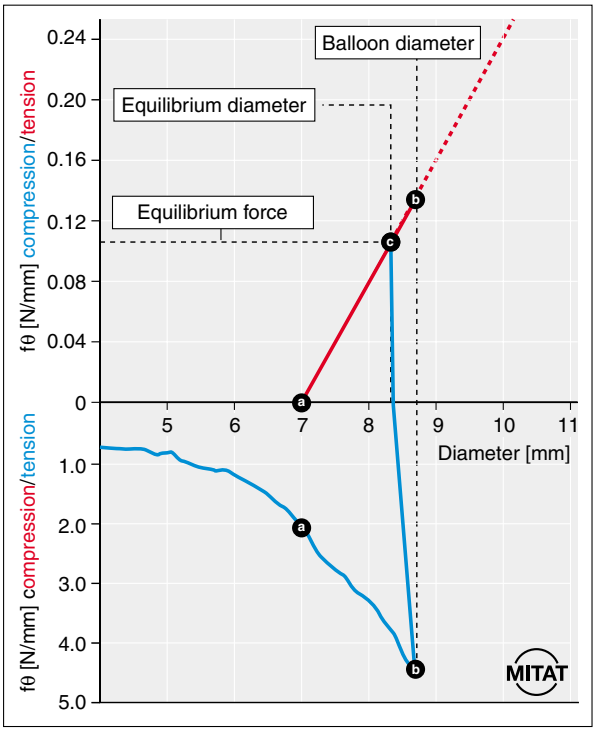

Figure 7. The same vessel as shown in Figure 6 is now stented with a typical SS laser-cut stent rated for use up to 9 mm and mounted on a non-compliant balloon. Inflation pressures far in excess of those shown in Figure 6 are required to bring balloon and stent to 9 mm **(c)**. Deflation unloads the stent, then loads it in compression to the final equilibrium **(b)**. (Note that the scale below the axis is much coarser than above.)

case, the BE stent is plastically deformed to 8.8 mm by the balloon pressures. Vessel contact is made in passing point 'a', after which both vessel and stent are stretched to 'b'. During deflation, the tensile hoop forces in the stent are relieved until a stress equilibrium with the vessel is achieved at 'c'.

Both BE and SE stents recoil to a diameter less than that of the balloon. Scenarios exist in which the BE and SE stents exhibit greater recoil, depending upon geometry, vessel compliance and oversizing. Similarly, the equilibrium interference stresses resulting from BE and SE stenting are approximately the same, as is hypotensive risk. The most obvious difference is the enormous difference in balloon pressures used to achieve the final result. While this should cause no damage to a straight vessel, inflation requires stiffer, higher-pressure balloons and this may increase acute damage to vessels, particularly in tortuous anatomy, where high-pressure balloons temporarily straighten the vessel, creating trauma at the balloon ends.

Dynamic scaffolding and cyclic effects

The above analysis shows there are only minor static and acute differences between the BE and SE stents, but now we turn our attention to the post-implant dynamics and chronic outcome. Here we will see large and important differences. We begin by examining responses to vessel diameter changes. Figure 8 will be used to illustrate some important concepts by superimposing the stiffness curves of the BE and SE stents of Figures 6 and 7, with both the original nominal vessel, as well as an expanded and a contracted native vessel. These vessel diameter changes can arise from the systolic–diastolic cycle, or from other sources. While somewhat simplistic, this model is a useful way of understanding how the intersection points, or equilibrium diameters and stresses, change as the native vessel undergoes change.

On the horizontal axis, one sees that the equilibrium diameter of the SE stented vessel changes far more than that of the BE stented vessel, in other words, the BE stent is more effective in preventing diameter change. On the other hand, the Nitinol stent dynamically scaffolds or supports the vessel, meaning that if the vessel were to move away from the stent, the stent would follow and continue to apply a force. Support from the BE stent would quickly dissipate and could, in fact, end up within the vessel lumen. Dynamic scaffolding may play a particularly important role in drug and radiation therapy, where the vessel lumen may actually increase over time. While these differences are marked, it is not clear if a better clinical outcome results from rigid or compliant scaffolding. It is, however, clear that the greater diameter change experienced by the Nitinol device creates a complex and severe fatigue environment (discussed later).

To complete the picture, the changes in equilibrium stress indicate that the BE stents experience larger variations in hoop strength and thus contact pressure, which may contribute to pressure necrosis, or atrophy of the smooth muscle layer. Thus, while the BE stent reduces the compliance of the vessel, it does so by applying highly localised pressure. Figure 8 understates this effect because of its over-simplistic approach. Again, however, the clinical relevance of this difference is not clear.

Time-dependent effects

While the cyclic differences between BE and SE stents are significant, the most important differences arise from the time dependency of the vessel–stent equilibrium. The properties of Nitinol itself are not time dependent, but those of the tissue are. For short

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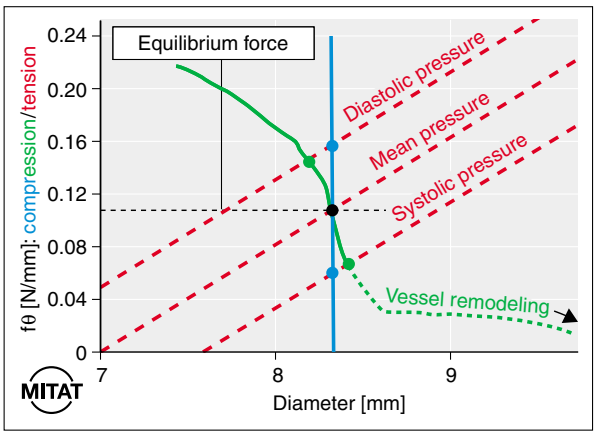

Figure 8. Dynamic effects on the vessel–stent interaction are exemplified by considering the effect of variations in the native vessel diameter on the equilibrium forces and equilibrium-stented vessel diameter. The red curves represent three native vessel diameters (diastolic, mid-cycle and systolic, for example). The blue circles illustrate the stented vessel equilibrium forces and diameters corresponding to a BE stent. The green circles correspond to an SE stent.

Figure 9. View of an SE stent 4 months after implantation in an internal carotid artery, illustrating that the stent is scaffolding the vessel from the outside of the vessel wall.

times, vessels can be reasonably modeled as elastic tubes, but over longer time periods, tissue remodeling occurs in response to the interference stresses. BE interference stresses are applied only over a very short distance and thus stresses are very quickly dissipated, without detectable stent migration. A BE stent quickly becomes an inert, stiff prosthesis, maintaining a diameter very close to its original diameter. The COF of SE stents, however, acts over a relatively long distance and thus an SE stent migrates towards the outside of a vessel (see the dashed line in Figure 8). Angiographic evidence for migration is commonly observed during follow-ups (Figure 9). While no studies of COF versus migration rate have been published, it would seem logical to believe that migration rates are determined by the contact pressure of the stent (the radial force divided by the footprint, or contact area of the stent).

While we know of no definitive studies of COF and migration, limited data from animals provides some qualitative insights (to be published, D Wilson *et al.*). There appear to be times when the stent reaches an equilibrium position at the outside of the vessel wall and other times when the outside diameter of the vessel is barreled out. There also appears to be only a weak dependence of stent growth on oversizing, perhaps indicating a second chronic stress equilib-rium is reached once the stent has migrated to the outer layers of the vessel wall. It also appears that the majority of the outward growth occurs during the first 2 weeks of implantation. It is important to note that even this premature evidence is based on 'healthy' animal vessels and not calcified vessels.

Concerns have been expressed about excessive stent oversizing, leading to vessel perforation, pressure necrosis, or a stress-related complication, such as Horner's Syndrome. We know of no clinical evidence of this. In fact, animal studies of exaggerated oversizing have demonstrated that the ends of stents can protrude as much as 2 mm outside the adventitia, but remain covered by connective tissue, exhibiting no adverse clinical reaction (Figure 10). Still, it would seem prudent to limit oversizing and reduce COF. Typically, when an SE stent migrates outwards, the lumen does not necessarily follow, but instead hyperplasia occurs and the original lumen diameter is maintained. This contrasts sharply to hyperplasia in BE stents, in which hyperplasia represents true lumen loss. Thus, one must be careful in viewing histology slides, such as Figure 10; one cannot simply assume that hyperplasia is problematic.

In summary, there are three noteworthy time-dependent differences between BE and SE stents:

PETITIONER ARTHREX
EX. 1010

Figure 10. Histology slides 6 months after implantation of a 9 mm SE sent in a 5 mm porcine sub clavian artery shows that the original lumen is maintained, although the stent has migrated well into the vessel wall. The view on the right shows two struts at the end of the stent that have migrated outside the vessel itself.

- BE stents tend to support from within the lumen, while SE stents support near the outside of the adventitia, imbedded deeply in the smooth muscle.
- Hyperplasia is not indicative of restenosis or lumen-loss in an SE stent, as it is in a BE stent.
- SE stents may exhibit chronic lumen opening, while BE-stented lumens can only become constricted with time.

Clearly, more research must be done to fully understand the effects of COF and oversizing regimes on stent growth, particularly in diseased vessels. One can envision that perhaps direct stenting will be possible without post-dilatation — just relying on the COF to gently open the vessel over a period of time. Of course, the acute result may not be as aesthetically pleasing as one would obtain with aggressive pre- or post-dilatation, but certain indications may profit from such gentler treatment. Thus, our earlier assumption that one wants to minimise COF and maximise RRF is conservatively based on regulatory considerations and the lack of a proper study, and may, in fact, be incorrect.

Conformability and wall apposition

'Conformability' refers to the ability of a stent to adopt the tortuous path of a vessel, rather than forcing the vessel to straighten. Intuitively, one might expect that SE stents conform better to tortuous anatomies. Indeed, many SE stents are very conformable, but there are no technical grounds for this. Conformability depends far more on the design of the stent than on the flexibility of the material from which it is made: segmented, helical and flexible bridge patterns all tend to provide conformability, and can be incorporated equally well into BE and SE designs. Of course, the far greater balloon pressures experienced during BE stenting cause an initial straightening and attendant vessel trauma, but after deflation a well-designed BE stent should relax to the vessel morphology.

'Wall apposition' refers to the ability of a stent to remain in close contact with the wall of the vessel. Separation from the wall can occur if the vessel cross-section is eccentric, when the vessel changes diameter along its length, or at a bifurcation. A BE stent takes on a rigid cylindrical character during balloon expansion and is quite forceful in dictating a circular vessel cross-section — thus the acute appearance is typically perfect, with good apposition and an excellent lumen. An SE stent, on the other hand, will tend to conform to the native cross-section and axial shape, and fill the available lumen without forcing acute change — the result is often not as aesthetically pleasing, but less invasive. Moreover, if the vessel morphology changes due to remodelling, flexing or crushing, an SE stent will move to fill the changing lumen, while the BE stent remains static.

While the self-expanding process is generally a gentler and physiologically more correct process, we need to be careful not to assume that all SE stents are the same in this regard. Designs with a low pinching stiffness will tend to conform better than very stiff designs (although, as mentioned earlier, buckling can occur). As an extreme example, Figure 11 shows two commercially-available SE stents of the same diameter deployed into flattened lumens. Note that the same results are obtained if one deploys the stents into a circular cross-section then flattens them, thus apposition is both a static and dynamic design consideration. The stent on the left has a higher pinching stiffness and a lower radial stiffness than the stent on the right, and thus is very insistent in maintaining a circular cross-section.

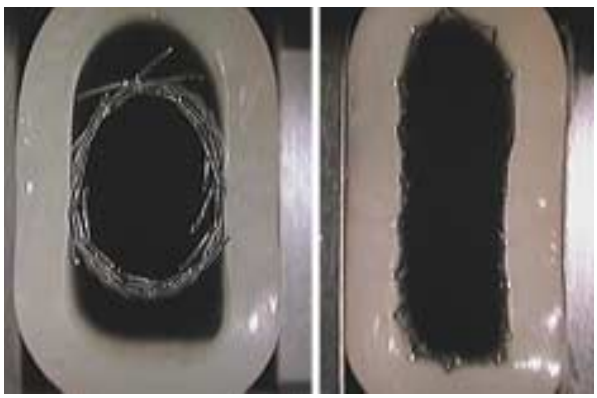

Figure 11. Two commercially available SE stents of the same nominal diameter are deployed into a flattened lumen. The stent on the right exhibits excellent wall apposition, while the one on the left does not.

PETITIONER ARTHREX
EX. 1010

Pulsatile fatigue

Native vessels undergo diameter changes of approximately 3–10% when subjected to 100 mmHg pulse pressures [4]. A stent placed in these environments is usually expected to remain patent for 10 years, or 40 billion systolic cycles. This is no easy task and, again, BE and SE stent design philosophies are in juxtaposition. SS stents cannot survive such large diameter changes, but are sufficiently rigid to prevent the vessel from 'breathing' due to the pulse pressure. Vessels stented with BE stents generally pulse < 0.25% of their diameter, making fatigue essentially a stress-controlling problem. As shown in Figure 8, Nitinol stents are generally similar in compliance to a healthy vessel and thus undergo much larger pulsatile diameter changes (albeit somewhat reduced from those of the native vessel). Fortunately, the displacement-controlled fatigue lifetime of Nitinol far exceeds that of ordinary metals and stents are able to survive this harsh environment. It should be noted that it is possible to design an SE stent so that it is as stiff as a BE stent, in which case fatigue can be ignored. But we have assumed here that a high compliance is a desirable feature of an SE stent.

The FDA currently requires that a statistically-relevant number of stents is tested to 400 million cycles under clinically-relevant condition and that no failures are observed. It is rather parochial to think that one can understand and predict life without causing failure. Ideally, one should test to failure and project a safety margin with respect to an endurance limit. This can be done theoretically by using a strain-based Goodman approach, approximating survival by considering a pulsatile strain ($\Delta\varepsilon$ cyclic pulse amplitude due to pulse pressure) and a mean strain (ε_m the strain at mid-pulse). Assumptions regarding pulse pressure (Δp) and the stented vessel compliance yield a value for $\Delta\varepsilon$, the principal driver for fatigue damage. Mean strains in SE stents can be estimated from assumptions concerning equilibrium diameters, vessel compliance, tortuosity and over-sizing. Such approaches are also used to evaluate the life of BE stents, but there are no substantial over-sizing strains in BE stents — instead, mean strains arise from residual strains from the plastic deformation. Analyses such as these are complex and beyond the scope of this paper.

Intensive work is underway to better understand the effects of mean strain on fatigue lifetime [5–8]. All studies indicate that the lifetime of Nitinol at high mean strains is far better than one would expect using classical Goodman analysis techniques. This is particularly important in tortuous anatomies, since static bending tends to increase mean strains but have little effect on pulsatile strain. Ultimately, we cannot say that the pulsatile life of Nitinol stents is better or worse than BE stents, just that their diametrically-opposed approaches may suit individual indications in different ways.

Crushing and bending fatigue

A host of other fatigue influences, including crushing and bending, are often ignored. These influences might be experienced under the inguinal ligament, or in the popliteal. Tensile and bending fatigue can also occur in the coronary vessels, as a result of the systolic expansion of the heart. Particularly challenging is the first of these, anatomy that severely flexes and/or buckles a very large number of times and that cannot practically be prevented from doing so by reinforcement with a stiff BE stent. Nitinol performs far better than any other known metal in displacement-controlled environments such as these but, even so, such severe dynamic cycling may exceed even the limitations of existing Nitinol stents.

The second type of fatigue condition (bending) also warrants some discussion. As the heart expands and contracts, the topology of the surface undergoes large changes, exposing vessels to both high cycle bending and stretching. First-generation BE stents were very rigid, and would locally reinforce to the extent that bending and stretching fatigue was not an issue. The market is demanding increasingly flexible stents, however, and even though these later BE devices are radially stiff, they are typically very compliant in bending and tension, and are thus subject to these fatigue modes. Ultimately, this may lead to advantages for the more fatigue-resistant Nitinol.

Thermal response and A_f control

The origins of superelasticity were briefly outlined in the introduction of this paper. While a complete mechanistic description is unnecessary to the task at hand, it is important to note that the transformation between austenite and martensite is driven by temperature, as well as by stress. When no stress is applied, we define A_f to be the temperature at which martensite is completely transformed to austenite upon heating. (This is a somewhat simplified definition, which ignores several complexities that are important, but have no bearing on this specific context.)

Within a limited range, alloy producers can control the A_f temperatures of Nitinol. The higher the A_f temperature, the lower the stress needed to induce the transformation to martensite. Thus, the difference between body temperature and the A_f temperature

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EX. 1010

dictates the material properties of the material and, therefore, the apparent stiffness of the stent. For each degree that A_f is below body temperature, the tensile loading and unloading stresses of Nitinol increase by approximately 4 Nmm^{-2}. These are very important concepts that can be vividly demonstrated simply by 'feeling' a Nitinol stent at room temperature and body temperature. Figure 12 illustrates the temperature dependence, by comparing the unloading–loading–unloading cycle for a 10 mm Nitinol stent at three different temperatures. Note that the COF is increased by nearly 50% in warming from just 30°C to 37°C!

Choosing and controlling the A_f temperature of a stent is one of the most important tasks facing design engineers. A_f must be below body temperature to assure the stent will fully deploy. The lower A_f is set, the stiffer the stent; but a very low A_f can lead to unacceptably high COF values. A designer can compensate for a low A_f by designing a weaker structure (e.g. reducing strut width), but this will severely reduce RRF. In fact, the most efficient combination of RRF and COF is obtained by using A_f temperatures as close to body temperature as possible (without running the risk of being above body temperature).

Still another important consideration, illustrated in Figure 12, relates to elevated temperature exposure during shipping, storage, or sterilisation. As ambient temperature is increased, the forces applied by the stent on the delivery system increase. If the temperature becomes too great, either the stent will damage the delivery system, or the stent will damage itself and fail to recover fully to its prescribed diameter once released [9]. It is necessary, therefore, to control both the stent A_f and the temperatures to which it may be exposed after crimping. Some manufacturers have put thermal markers on packaging to assure that the stent system is not exposed to temperatures above tested limits.

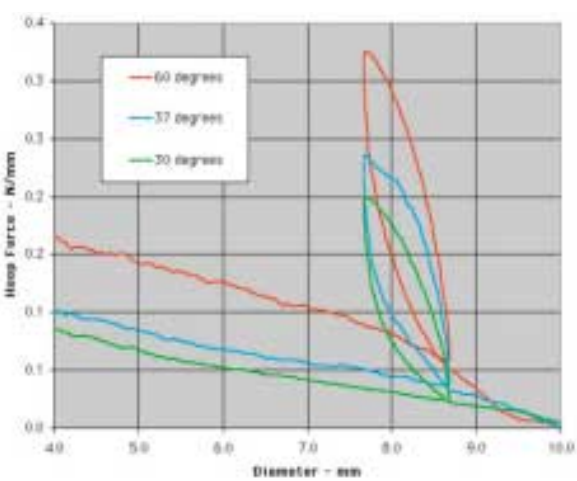

Figure 12. A commercially available 10 mm stent is unloaded in the same cycle as shown in Figure 5, but at three different temperatures. Note that the COF forces are increased by nearly 50% as the stent is warmed from 30° to 37°C.

Deployment precision and foreshortening

Stent performance is critically dependent upon getting the stent to the target location and accurately deploying it once there. There are a variety of factors that contribute to accuracy.

Foreshortening refers to the fact that the opening of the geometry of Figure 1 results in geometric shortening. If there is uncertainty in the direction of the foreshortening, this can lead to large inaccuracies in deployment. There are a variety of ways to reduce this effect. One can design stents where stretching of bridges compensates for strut shortening (see Figure 1). Other designs exist which make use of wave designs, such that diamonds or struts initially lengthen during expansion, then shorten. Foreshortening can be somewhat more easily eliminated in BE stent design, but is clearly a design, not material, issue.

As the leading end of the stent begins to emerge from the constraint, there is a natural tendency for it to spring forward. In the extreme, the stent can jump completely out of the delivery catheter. Several attributes influence this tendency, including bridge design, longitudinal stiffness, pinching stiffness and friction. While this tendency can be reduced to a minimum in an SE stent, this potential source of inaccuracy simply does not exist in a BE stent.

Finally, most SE delivery systems consist of an inner and outer member that are axially stressed during delivery. Since designers strive towards flexibility in delivery catheters, these members are generally not rigid and thus they either stretch or compress. Experienced deployment and the application of some pre-stress to the delivery system will mitigate these effects, but again this is an issue that is peculiar to SE stents.

In summary, while the accuracy of SE stenting has improved dramatically and will probably continue to improve, it would appear that BE stents will continue to be more accurate than SE stents.

X-ray and MR visibility

The X-ray density of Nitinol is very similar to SS (Figure 13). Differences in perceived opacity are a result of stent design, as well as the resolution and energy of the imaging equipment. As stents continue to evolve towards lower mass and finer features, so imaging

PETITIONER ARTHREX
EX. 1010

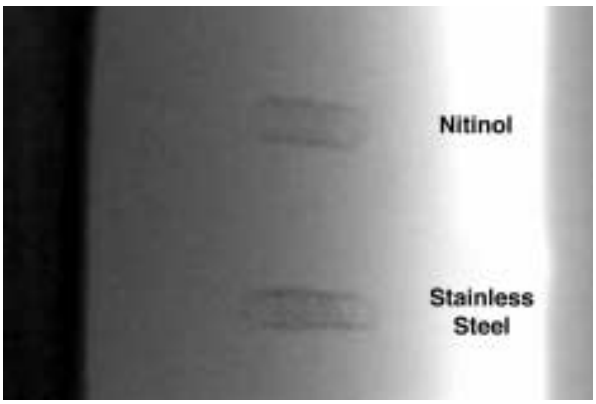

Figure 13. Two geometrically identical stents are viewed radiographically.

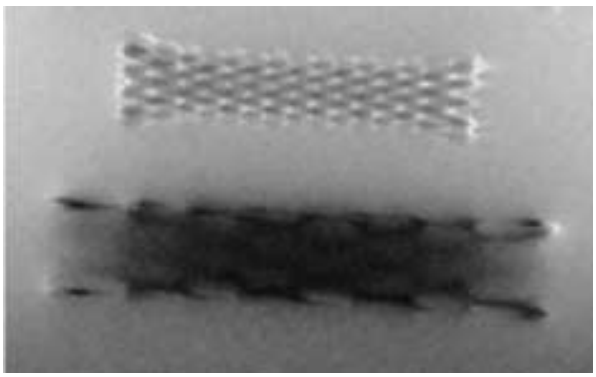

Figure 14. Two different commercially available Nitinol SE stents shown by MR imaging, illustrating the importance of surface finish and design on MR compatibility.

equipment will need to improve. Some stent manufacturers have resorted to using coatings, or markers, to improve visibility. This is not a straightforward solution: as discussed below, dissimilar metal contact can dramatically impact the corrosion resistance of Nitinol. Gold and platinum in particular are ill-advised materials to use.

MR visibility, however, is quite different between SS and Nitinol. SS interacts strongly with the MR field and can create artifacts, making imaging of nearby areas difficult. With appropriate surface treatment, Nitinol exhibits a very low magnetic susceptibility and provides clean detailed images. Interestingly, Nitinol is not universally MR compatible, due to differences in surface treatment and design (Figure 14). Certain common surface conditions can be magnetic and can interfere with imaging.

Thrombogenicity and biocompatibility

These attributes have been discussed in detail in other publications [10,11]. In short, both thrombogenicity and corrosion-resistance of Nitinol are superior to SS, but it appears unlikely that these differences are of clinical significance — or at least no firm evidence of this has been presented. Still, a few questions are often asked and should be summarised.

There is often concern expressed regarding Ni allergies and the 50% nickel content of Nitinol. Although SS contains less nickel, the nickel is released at a more rapid rate than from Nitinol. The reasons for this relate to the extremely high-energy bonds formed between nickel and titanium, and the chemistry of the surface. The surface of properly treated Nitinol is the same, very stable TiO_2, that is formed on pure titanium [12].

Dissimilar metal contact has already been mentioned. Theoretically, whenever two dissimilar metals are in contact there is a galvanic couple, causing one of the two metals to corrode at an accelerated rate, the other at a retarded rate. The galvanic potentials of SS and Nitinol are very similar, making this effect almost unmeasurable. Tantalum and Elgiloy are both galvanically similar to Nitinol and have been shown to be safe to use. This does not mean, however, that there is never an issue. Contact with noble metals, such as gold or platinum, should be avoided unless the coated areas are completely protected from corrosive media. SS corrosion performance can also be dramatically deteriorated by contact with gold.

Concerns have been expressed about scratches. The concern revolves around the fact that both SS and Nitinol resist corrosion through the formation of a passive oxide layer that seals and protects the reactive metal from the corrosive media. When damaged, these passive layers reform and re-protect the base material. The concern is whether the layer can heal itself if no oxygen is present, or if the device is immersed in a corrosive environment when damaged. In short, there does not appear to be a significant difference between SS and Nitinol stents. In general, however, any fretting opportunities should be avoided whenever possible, regardless of the stent material used: this includes braided wire stents and designs that incorporate interlocking features.

Finally, various Nitinol stent manufacturers produce different surface finishes, ranging from dark blue oxides to highly polished and bright surfaces. Most recent work indicates that highly polished surfaces with no coloration are preferred [13].

Martensitic Nitinol

While the vast majority of Nitinol stents are superelastic and self-expanding, three other types of Nitinol stents have been proposed:

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EX. 1010

- Stents that are installed cold, then thermally recover their specified shape when exposed to body temperature [14]
- Stents that recover their desired diameter by heating above body temperature after insertion into the body [15]
- BE Martensitic stents that can be heated to cause shrinkage to assist in removal [16].

The last of these is probably the most interesting, but has not yet been commercially successful. In addition to removability, these stents offer more uniform expansion, but at a price: Martensitic Nitinol is inherently weak and requires large, bulky structures. Moreover, Martensitic Nitinol is not superelastic and thus offers none of the typical advantages of Nitinol SE stents.

Conclusions

SE and BE stents differ in many respects but, thematically summarising, SE stents become part of the anatomy and act in harmony with native vessels, while BE stents change the geometry and properties of the anatomy. SE stents assist, BE stents dictate. Clearly, there is a place for both in radiology suites. Perhaps the most important unknown regarding SE stenting concerns the effect of COF or chronic outward growth of a stent. Physicians are beginning to experiment with eliminating post-dilatation and relying on chronic outward force to slowly remodel the vessel to the desired diameter. While acute results may not be as good, the lessened trauma may lead to a better chronic outcome.

References

1 Duerig TW, Melton KN, Wayman CM. *Engineering aspects of shape memory alloys*. Boston: Butterworth-Heinemann,1990.

2 Lau KW, Sigwart U. Intracoronary stents. *Indian Heart J* 1991;**43(3)**:127.

3 Tolomeo DE, Duerig TW. Criteria for fatigue resistant design of superelastic stents. In press.

4 Pederson OM, Aslaksen A, Vik-Mo H, Ultrasound measurement of the luminal diameter of the abdominal aorta and iliac arteries in patients without vascular disease. *J Vasc Surg* 1993; 596–601.

5 Berg B. ICOMAT-99, Barolocia, Argentina. In press.

6 Santinoranont M, Davidson S, Tolomeo DE, Cyclic properties of superelastic Nitinol: design implications. In: *Proceedings of shape memory and superelastic technologies 2000*. In press.

7 Perry K, Kugler C. Non-zero mean fatigue test protocol for NiTi. In: *Proceedings of shape memory and superelastic technologies 2000*. In press.

8 Harrison W, Lin Z. The study of Nitinol bending fatigue. In: *Proceedings of shape memory and superelastic technologies 2000*. In press.

9 Martynov V, Basin F, Effect of constraining temperature on the post-deployment parameters of self-expanding Nitinol stents. In: *Proceedings of shape memory and superelastic technologies 2000*. In press.

10 Venugopalan R, Trepanier C. Corrosion of Nitinol. In: *Proceedings of shape memory and superelastic technologies 2000*. In press.

11 Thierry B, Merhi Y, Trepanier C, *et al.* Blood compatibility of Nitinol compared to stainless steel. In: *Proceedings of shape memory and superelastic technologies 2000*. In press.

12 Chan CM, Trigwell S, Duerig T. Oxidation of an NiTi alloy. *Surface Interface Anal* 1990;**15**:349.

13 Trepanier C, Tabrizian M, Yahia L'H *et al.* Effect of the modification of the oxide layer on NiTi stent corrosion resistance. *J Biomed Mat Res* 1998;**43**:433–40.

14 Balko A, Piasecki GJ, Shah DM *et al.* Transfemoral placement of intraluminal polyurethane prosthesis for abdominal aortic aneurysm. *J Surg Res* 1986;**40**:305.

15 Alfidi RJ, Cross WB, inventors. *Vessel implantable appliance and method of implanting it*. US patent 3,868,956. 1975.

16 Hess RL. Removable heat-recoverable tissue supporting device. US patent 5,197,978. 1993.

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