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A Decade of Evolution in Stent Design

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Proceedings of the International Conference on Shape Memory and Superelastic
Technologies, SMST-2003

2003

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SMST-2003

Proceedings of the International Conference on

Shape Memory and Superelastic Technologies

5 May to 8 May 2003

Asilomar Conference Center

Pacific Grove, California, USA

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Published by:
SMST Society, Inc.
c/o SRI M/S AA287
333 Ravenswood Avenue
Menlo Park, California 94025
USA
Telephone: (650) 879-6476
E-mail: info@smst.org
Website: www.smst.org

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Printed and bound in the United States of America

Library of Congress Control Number: 2004102781

Publisher's Cataloging in Publication Data

SMST-2003: proceedings of the international conference on shape memory and superelastic technologies / edited by Alan R. Pelton and Tom Duerig.

xvi; 746 p.; 26 cm

Includes bibliographical references and index.

ISBN 0-9660508-3-5

1. Alloys—Congresses. 2. Alloys—Thermomechanical properties. 3. Shape memory effect. I. Pelton, Alan (Alan R.) II. Duerig, Tom (Thomas W.)

TN690.S675 2004
669'.94—dc20

Production Services by TIPS Technical Publishing, Inc.

A DECADE OF EVOLUTION IN STENT DESIGN

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ABSTRACT

Stents have been commercially available for vascular and nonvascular applications for well over a decade. In this time, hundreds of designs have evolved utilizing a vast array of materials and fabrication techniques, assuming myriad forms and geometries and including various additions. These categories of distinctions are presented as a pyramid of stent design options, highlighting key advantages or compromises within each category. Most commercial stent designs have attempted to differentiate themselves on the basis of stent geometry, so this diverse category receives particular attention. These categories are used to present an organized taxonomy of past, present, and future stent designs.

KEYWORDS

Stents, Design, Materials, Fabrication, Geometry, Nitinol

INTRODUCTION

The intravascular stent first rose to prominence in 1994 with the launch of the Palmaz-Schatz Coronary Stent. This new device transformed the practice of interventional cardiology, selling one million units in less than two years and creating a \$700 million annual market nearly overnight. Today, the market for coronary stents alone has more than doubled to \$1.5 billion, and is expected to immediately double yet again to \$3 billion with the advent of drug eluting stents. The rapid growth of this market attracted hundreds of innovators, each seeking to match their perceived design advantages with a clinical need. This fertile environment spawned hundreds of clever, simple, revolutionary, and uninspired designs: “stent” appears in 5063 issued US Patents, 1225 times in the title. A recent survey uncovered 157 commercial stent designs, and countless others have certainly escaped the attention of this author and his able research team. The following pages will attempt to bring order to this menagerie of designs and offer insight into the design choices made by stent developers.

1977: PRE-STENTING

The word “stent” is attributed to Charles R. Stent, a nineteenth century English dentist, and was originally used to describe a mold for keeping a skin graft in place [2]. In a more modern context, the word “stent” refers to an implantable device used to provide structural support to a circulatory vessel or other luminal passage in human anatomy. Vascular stents evolved as an adjunct to balloon angioplasty, which was pioneered by surgeon Andreas Gruentzig in 1977. Minimally invasive angioplasty techniques became an important alternative to open heart surgery, but acute success and long term durability of such procedures was limited. Restenosis, or reclogging of treated arteries, was commonplace. This clinical problem was the impetus for developing stents and more exotic devices like intravascular lasers and drill-like burrs designed to ablate or remove the offending blockage. The first coronary stent implantation is credited to Jacques Puel and Ulrich Sigwart of Toulouse, France, in 1986.

The Palmaz stent would ultimately become the first to be proven successful in meeting the restenosis challenge. Dr. Julio Palmaz began his design exploration using the readily available resources of the day. His first stent prototype was created from copper wire and solder obtained from a local Radio Shack (Figure 2A). Knowing this design had its limitations, and inspired by the metal mesh used by a contractor doing plaster work in his house, Palmaz realized that similarly staggered slots could be applied to stent design. This would allow for fabrication from a single tube without overlapping filaments or solder points. Dr. Palmaz did not know how to go about creating such a slotted tube, so he did the only sensible thing: he consulted a rocket scientist in the rural woods of California. The retired German rocketeer suggested the second innovation, electrical discharge machining (EDM). These two central distinctive innovations of the Palmaz design led to its clinical success. Dr. Palmaz filed for a U.S. patent in November of 1985. After being rejected by every major medical device company in the field, he and his partners ultimately found an unlikely suitor for this controversial new technology. Johnson & Johnson had no experience in interventional therapy, but would ultimately become the first to commercialize this transformational new technology.

1994: RADIAL STRENGTH

In the early 1990s, there were a handful of stents in trials and commercially available. The primary types: The Wallstent, fabricated from braided wire of a cobalt alloy called elgiloy; The Wiktor stent, fabricated from tantalum wire formed into a helical ring structure; the Gianturco-Roubin Flex-Stent, fabricated from stainless steel wire in a clamshell design; and finally the Palmaz and Palmaz-Schatz stents, fabricated from slotted stainless steel tubes [2]. At this point, there were a growing variety of design options from which to choose (see Table 1).

Like most other experimental therapies of the day, three of the above designs were not successful in combating restenosis. But the Palmaz-Schatz stent proved to be different than the rest. In 1995, the BENESTENT trial clearly demonstrated the benefits of stenting; at last, interventional cardiologists had a tool that dramatically improved their success rates [3]. The slotted tube construction derived from the plasterer’s mesh was the foundation for the stent’s superior strength and clinical efficacy. As with most things unique and successful, the marketplace quickly responded with designs that attempted to emulate the attributes of the Palmaz-Schatz stent, while improving upon some of the shortcomings inherent in this first generation product.

Table 1 Stent Design Options

	Wallstent	Wiktor	GR Flex-Stent	Palmaz/Palmaz-Schatz
Material	elgiloy	tantalum	stainless steel	stainless steel
Form	wire	wire	wire	tube
Fabrication	braid	bend	bend	EDM
Geometry	braid	helical rings	clamshell	slotted tube
Figure	2B	N/A	2E (2nd generation)	2C

1995: FLEXIBILITY

By the mid 1990s, it was clear that stents were an essential (and profitable) new technology, and substantial resources were invested in development of next generation devices. From a clinical perspective, the strength lesson was clear, but strength often came at the expense of flexibility. Stent designers became focused on creating designs that would be more maneuverable in tortuous coronary anatomy, but still strong enough to provide adequate scaffolding for diseased vessels. EDM machining only worked well for straight slots, which made for a rather inflexible stent. It became clear that new technologies would be required if stents were to be made more flexible. Laser machining and photochemical etching answered the call, unlocking a virtually infinite world of geometrical possibilities for slotted tube stent designs.

Dr. Kobi Richter adapted the photochemical (PC) etching technology used in the electronics industry for stent manufacturing. His company, Medinol, went on to develop the NIR stent, which was PC etched from sheets of stainless steel, then wrapped into a cylindrical form and welded into a stent. The PC etching process allowed for the addition of flexible connector elements in the stent geometry, and also offered compelling economies of scale in production.

Also at this time, laser-machining capabilities were advancing rapidly. Laser micromachining quickly became the preferred fabrication technique for tube based stents, and remains so today. Laser fabrication technology allowed for virtually limitless variations in geometry, and became readily available to the stent development community through system integrators or vendors. Laser micromachining capabilities spawned the diverse variety of stent designs that have been created through the years.

While most of the stent designs in the second wave relied upon these new technologies for creating flexible and strong geometries, there is at least one notable exception. Arterial Vascular Engineering (AVE) developed a coronary stent of the very simplest construction, wire rings (Figure 2H), welded at some but not all junction points between adjacent bends. This perfectly simple construction proved to be quite successful. Its successors share the same construction and remain quite successful today. This design was one of the first to employ an open cell structure (Figure 1B) to achieve a successful balance of strength and flexibility.

1997: GEOMETRY

In October of 1997, Guidant received FDA approval for its MultiLink stent and became the first competitor to challenge J&J's 90% share of the U.S. market. Within 45 days, the MultiLink stent commanded 70% of the market. The Boston Scientific NIR stent and AVE MicroStent II followed in 1998, and these three new designs combined to render J&J's new Crown stent an insignificant player. It is worthwhile to consider the unique aspects of geometry that contributed to their fates.

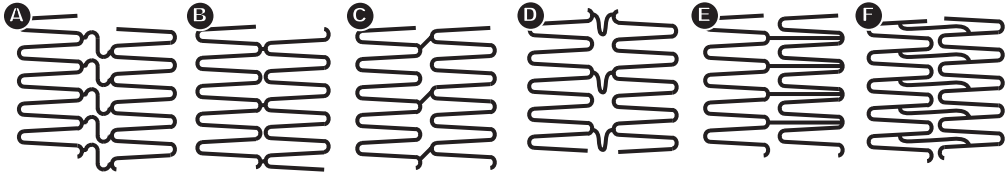


Figure 1 Typical stent constructions: (A) closed cell, peak-peak, flex connector, (B) open cell, nonflex connector, peak-peak, (C) open cell, nonflex connector, peak-peak, (D) open cell, flex connector, peak-peak, (E) open cell, nonflex connector, peak-valley, and (F) open cell, nonflex connector, midstrut.

First, a primer on stent construction: most stent designs have two fundamental constituents—expandable ring elements and connecting elements (Figure 1). Expandable rings are typically comprised of some number of struts arranged in a zigzag pattern with inflection points (tips or elbows) located at the end of each strut. Connecting elements (bridges), connect adjacent rings together, and may be described as flex or nonflex connectors, based on their shape. Connecting elements may also be described by the points at which they join with the ring elements. The terms, “peak-to-peak,” “peak-to-valley,” and “midstrut” can be used to describe these connection points. Stent designs may be classified as being open or closed cell, based on the arrangement of the connecting elements. A design may only be considered closed cell if each internal inflection point is connected peak-to-peak with a corresponding inflection point on the adjacent expandable ring. In this configuration, the closed area formed by two pairs of struts and two bridges is considered a cell. Any other configuration will feature some internal inflection points that are unconstrained, and the open cell would span one or more of these inflection points. Closed and open cell structures and a variety of bridge connection strategies are highlighted in Figures 1A–F [4].

The original Palmaz-Schatz stent and its successor, the “Crown” design are both examples of closed cell, nonflex connector, peak-to-peak designs which define the most inflexible of any possible stent configuration. The Crown stent, an innovation of Dean Kamen’s DEKA Group, introduced a sinusoidal wave strut configuration that looked interesting, but did little to improve flexibility and was not very well received. The NIR stent was also a closed cell, peak-to-peak stent, but this design first introduced the flex connector. This V-shaped element did improve flexibility, and the stent became quite successful. The MultiLink stent introduced peak-to-valley connectors and open cell design. The peak-to-valley connections and open cell structure of this stent made it quite flexible; its successors continue to lead the market five years after its introduction.

1997: NITINOL STENTS

The above mentioned devices were all coronary stents, fabricated from 316L Stainless Steel. While the coronary market is the largest in terms of dollars, the peripheral vascular and nonvascular systems present a far greater variety of potential stent applications. For these applications, the clinical

requirements are quite diverse, but often necessitate stents of larger diameters that can recover from dynamic motions or outside forces. The carotid arteries of the neck, and superficial femoral arteries of the legs are both examples of vascular beds where plastically deformable stainless steel stents could become crushed and compromise blood flow. These indications demanded self-expanding, crush recoverable stents, and thus a different material. The Wallstent is a braided mesh type stent constructed from filaments of a cobalt based alloy [5]. It had been available since the early 1990s and developed a loyal following in spite of drawbacks including substantial length differences between its expanded and constrained states that made accurate placement difficult. It was clear that the unique superelastic properties of nickel-titanium (Nitinol) would be a benefit for many peripheral vascular indications, but the only Nitinol stents available were wire based, and were not particularly successful. In the mid 1990s, as laser cut stainless steel tube coronary stent became the standard, it became apparent that the same technology could be applied to Nitinol tubing.

Bard released the Memotherm in 1997 (Figures 2J), and Cordis released the SMART stent in 1998 (Figures 2I); both are examples of open cell, peak-to-peak constructions. The SMART stent became the dominant design in the endovascular marketplace, and remains the leader today. The success of the SMART stent design was largely due to its very fine mesh structure that offered exceptional contouring, flexibility, and apposition characteristics.

It is estimated that Nitinol stents now comprise 60% of the endovascular stent market. Nitinol stents also dominate nonvascular markets including urologic, upper and lower gastrointestinal, and trachea-bronchial applications.

DESIGN CHARACTERISTICS

Flexibility

Flexibility is often cited as the most important characteristic of any stent design. Flexibility usually implies deliverability, or the capacity for the unexpanded stent to navigate tortuous anatomy en route to its destination. Flexibility is also often associated with contourability, or the capacity for an expanded stent to assume the natural curve of a vessel without unnatural straightening. Both of these characteristics are fairly easy to observe, measure, and understand for physicians and stent designers alike. Some of the design characteristics impacting flexibility are as follows:

Cell Structure: Open cell structures are often substantially more flexible than closed cell structures, but require some compromises. First, when the unexpanded stent is placed in a tight bend, unconnected inflection points can lift up and present an irregular edge to the surrounding lumen—this is often described as fish scaling (Figures 2K). Second, when the expanded stent structure is placed in a bend, the unconnected inflection points can spread apart from each other, thus compromising scaffolding (Figures 2L).

Flex Connectors: Flex connectors add flexibility, but do so at the expense of scaffolding. The addition of flex connectors between expandable rings increases cell size, thus compromising scaffolding. More flexible flex connectors require increased spacing between expandable rings, and consequently decreased strength of the full structure.

Dimensions: Stent dimensions also play an important role in flexibility. Flexibility is inversely related to stent diameter, wall thickness, and the width of flex connectors.

Strength

Strength is arguably the single most important characteristic of stent design, and is perhaps the least understood. The FDA guidance document [6] defines radial strength as, “change in stent diameter as a function of circumferential pressure ... noting the point at which deformation is no longer reversible.” Stent designers have interpreted this in many ways: the external hydraulic pressure required to collapse a stented tube; the force required to crush a stent between flat plates; or the tension in a collar used to reduce the diameter of an expanded stent. Physicians, however, most commonly interpret the strength of a stent as the amount of *recoil* the vessel experiences after the stent is expanded. This creates another point of confusion, because the FDA guidance document (and stent designers) define stent recoil as the amount of elastic recoil experienced by a stent in the absence of any external loading. Superelastic self-expanding stents create further confusion in this area, as the concepts of nonrecoverable deformation and elastic recoil are meaningless. It is proposed that stiffness is a more appropriate and universal measure of the strength of a stent. In the stiffness interpretation, an expanded stent is constrained by a contracting collar and the tension in the collar is measured as a function of stent diameter. This tension can then be normalized by the length of the stent, and plotted against diameter. The slope of the resulting line relates to the stiffness of the structure, and corresponds with the physician’s observation of stent “recoil” when loaded by a diseased vessel. The choice of materials and dimensions are the main factors that influence stent strength.

Material: The choice of material, its elastic modulus, and its stress-strain curve are key drivers of stent strength. Plastically deformed balloon expandable stents offer rigidity that cannot be matched by self-expanding Nitinol stents, for example. However, superelastic Nitinol provides a constant and gentle outward force over time, and can recover from crushing or other large deformations. Bioabsorbable polymer stents are compelling in theory, but have found limited success to date because of the fundamentally limited strength of these polymeric materials.

Dimensions: Once the material has been chosen, the strength of the design is dictated by the dimensions of the struts comprising the expandable ring segments of the stent. In most general terms, each strut has a length L , a width W , and a thickness T . These factors do not contribute equally to the strength of the stent. Strut width has the most substantial impact by far, followed by length, and finally wall thickness.

Scaffolding

Scaffolding is the third key design characteristic of stent design, and it is inexorably linked with strength and flexibility. Improving flexibility demands the ability for expandable ring segments to pull apart from each other on the outer radius of a bend and push together on the inner radius. Allowing this freedom requires disconnecting some inflection points, or connecting them with spring-like flex connectors. Both actions compromise scaffolding to some degree. Alternatively, scaffolding can be improved by decreasing the length of struts and placing more of them around the circumference. This creates more expandable ring segments along the length of the stent, and therefore decreases the amount of separation required between any two expandable rings to assume a given bend radius. This improves scaffolding and flexibility, but decreases strength.

A SURVEY OF STENT DESIGNS

The stent marketplace evolved in a Darwinian model, as innovators and opportunists bred the geometries of weak with the strong, peaks with valleys, and open with closed cells. A recent survey

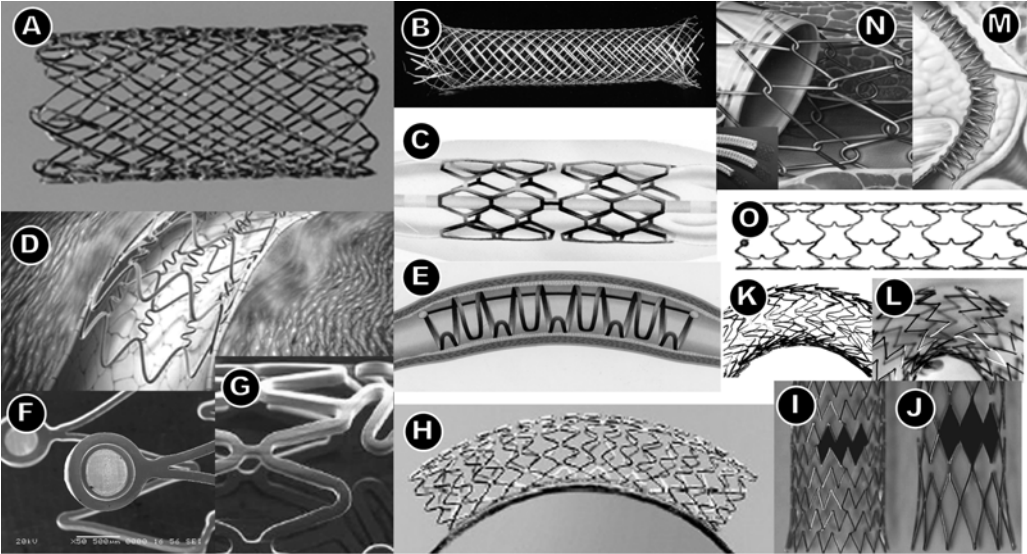


Figure 2 A variety of stent designs: (A) An early prototype of Dr. Julio Palmaz, (B) Braided Wall-stent, (C) Palmaz-Schatz Coronary Stent, (D) Cypher drug-eluting stent, (E) Gianturco-Roubin Flex-Stent II, (F) Radiopaque markers, (G) Combination of flex and non-flex connectors, (H) Welded ring AVE stent, (I) Nitinol SMART stent, (J) Nitinol Memotherm stent, (K) Dynalink peak-valley construction, (L) Open cell design with poor bend scaffolding, (M) Intracoil coil stent, (N) Nitinol wire stent-graft, and (O) Midstrut connection.

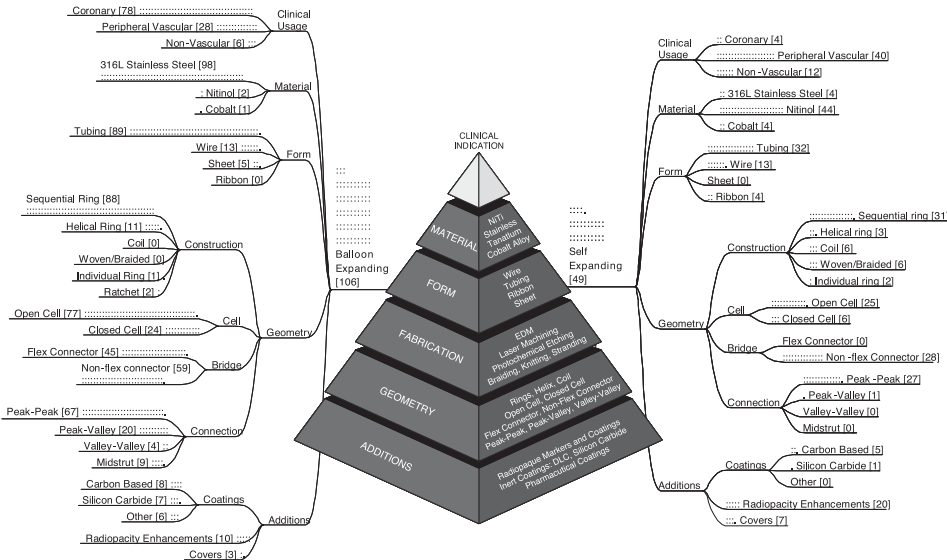


Figure 3 A survey of stent designs. Layers of the pyramid summarize the major design options faced by stent designers. Bracketed numbers depict the numbers of stent designs which fall in each of the described categories. These numbers are also graphically represented by dots on each branch. (::::: = [9])

has revealed at least 157 stent designs that have been commercialized or are in development. Virtually every combination of peak, valley, and midstrut connection has been commercialized in the pursuit of the ultimate design. Hybrid designs even pack multiple design strategies within a single stent. These designs can be divided into balloon-expanding (BX) and self-expanding (SX) categories, then further classified by clinical indication. These categories are depicted graphically in Figures 3 and described in greater detail below.

Clinical Use: Coronary stent applications are overwhelmingly dominated by balloon expanding stents, while a majority of peripheral vascular and nonvascular designs are self-expanding.

Material: 316L stainless steel has been the material of choice for plastically deformed BX stents since the success of the Palmaz-Schatz stent in 1994, but there is a trend away from this material. Cobalt-based alloys are becoming increasingly popular for next generation BX stent designs, because they offer higher strength with less material. Nitinol dominates the SX stent designs, and its unique properties assure that it will remain the material of choice for these applications for some time.

Form: Seamless tubing has been the most popular choice of material form since the success of the first slotted tube stents because of its profile advantages and continuous structure. This is true of both SX and BX designs, though in both cases several wire-based designs have proven viable and successful.

Fabrication: Laser micromachining dominates the current practice of stent manufacture of tube-based stents, though photochemical etching has been proven viable on tubes as well. The most intriguing development on the horizon is nanomanufacturing, which uses high vacuum sputtering techniques to build metallic vascular implants atom-by-atom in an additive fashion.

Geometry: Stent geometries have been very thoroughly explored in the past decade. Briefly describing each category:

Construction: The sequential ring type of construction has proven most functional and popular for both plastically deforming and self-expanding stents. They offer the best combination of strength, flexibility, and small diameter for most vascular applications. Coil designs are quite popular for nonvascular applications—such as prostate and urethral stenting—because these designs are typically fully retrievable weeks or months after implantation. These coil type designs were never particularly successful in vascular applications because they are much larger in their constrained state than ring type designs.

Cell: Despite the early success of closed cell geometries, open cell structures have proven successful and now dominate the BX stent designs 3 to 1. SX stents use open cell constructions almost exclusively. It is interesting to consider why this is the case. When designing with Nitinol tube, maximizing strength while minimizing diameter is often of paramount importance. Consequently, the designer must use as much material as possible in the expanding rings, leaving little if any room for effective flex connectors between the expanding rings. Since flex connectors are often not practical, Nitinol tube designs most often derive their flexibility from open cell construction and not from flex connectors.

Bridges–Connector Type: The survey shows a nearly even split between balloon expandable with flex and with nonflex connectors; several featured a combination of both (Figures 3G). Flex connectors have been constructed in the shape of almost every letter of

the alphabet: “S”, “N”, “V”, and so on. In self-expanding designs, flex connectors are virtually nonexistent for reasons noted above.

Connector Location: Peak-to-peak connection is the original and most common form of bridge connection, though alternatives are not uncommon. Different connection strategies can serve to improve flexibility and influence the foreshortening characteristics of a stent. Generally, peak-to-peak bridge connection will tend to draw adjacent expanding rings apart from each other as strut angles increase during expansion. This often results in foreshortening, or a reduction in length as the stent is expanded. Some designs feature flex connectors that are designed to stretch during expansion to reduce the tendency of the stent to shorten. Theoretically, valley-to-valley connection causes the opposite effect: adjacent rings will tend to push apart from each other, causing the stent to lengthen during expansion. Peak-to-valley connection counters these effects, and effectively eliminates the tendency for the stent to shrink or grow in length as it is expanded. It should be noted that the choice of bridge connection strategy could greatly impact the strength of a stent. A stent’s strength is derived in large measure from the width of its constituent struts. The width of the struts is a function of the circumference of the tube and the utilization of the material around that circumference. Peak-to-valley, valley-to-valley, and midstrut connections require some circumferential material to be sacrificed from the struts—forcing a compromise in strength or profile. With peak-to-peak connections, however, no circumferential material is sacrificed. In Nitinol design, it is usually imperative to maximize the strength of the design, which explains the near exclusive use of this connection strategy in self-expanding stents in the survey.

Additions: This is the final frontier of stent design differentiation. Grafts or related covers may transform a simple stent into a device that performs some specialized function: exclude an aneurysm, repair a damaged vessel, or protect a lumen from tumor ingrowth. Such covered stents are more common among self-expanding stent designs. A variety of different types of coatings may be applied to stents. Usually, these claim to improve biocompatibility in some way, often purporting to decrease thrombogenicity or protect the body from metal ion release. Common coatings include diamond-like-carbon (DLC) and silicon carbide. These coatings are found on a handful of BX and SX stents. It is quite clear, however, that pharmaceutical coatings will play a profound role in the future evolution of stent designs. Heparin was the first commercially successful drug coated onto a stent. Similar to aspirin, heparin is generally administered systemically to reduce the risk of thrombus formation when the stent is first placed. A heparin coated stent effectively provides a biological non-stick surface, protecting the stent from attracting or collecting clot. The most recent developments in stent pharmaceutical combinations are antirestenosis drugs such as Sirolimus or Paclitaxel that are combined with a polymer on the stent surface and designed to elute from the implant during the healing process. These drugs have been proven to dramatically reduce restenosis (relogging of the vessel), and promise to make stenting an even more effective therapy in the treatment of coronary and peripheral vascular disease.

CONCLUSION

The history of stent design has demonstrated that each new device innovation is preceded by an enabling technology. Stenting itself was enabled by balloon angioplasty; EDM slotted tube technology brought us the first successful stent; laser micromachining enabled more flexible and easy to

use stents. Advances in the application of Nitinol opened the peripheral vascular world to the benefits of stenting. Incredible new pharmaceutical technologies now are being combined with implantable stents as we enter yet another dimension in successful minimally invasive interventional therapy. The next decade is certain to bring more sophisticated drugs in combination with more sophisticated devices, and likely new and transformational technologies as well.

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