Coronary stents must have excellent mechanical properties to provide strength to artery walls.

J. Lévesque, D. Dubé, M. Fiset and D. Mantovani*
Laval University
Québec City, Canada

Coronary stents are small metallic tubes implanted in heart arteries to prevent the arteries from closing up. Their principal advantage is that they do not require open-heart surgery, as they are implanted directly through the arteries. More than one million stents are implanted each year in the world, and around 60% of these are in the United States. The world market for stents in 1999 was $2.2 billion, and it is estimated that in 2006 it will reach around $3.2 billion.

Over 40 different types of stents are commercially available or in development, and they are made of stainless steel, Nitinol shape-memory alloy, cobalt-chromium alloys, platinum, tantalum, or gold. In the last decade, a large number of patents have been issued, and several papers have been published concerning stents and their properties. Most of these studies focused on material biocompatibility and the reactions between stents and tissues.

However, even though these are very important aspects to consider, mechanical properties also have to be taken into account. In fact, the main reason for stents is to provide mechanical support to the artery wall. Therefore, inappropriate mechanical properties could lead to complications such as damage to the artery wall.

This review will present the required properties for appropriate stent fabrication, and it will focus on mechanical aspects that have received little attention until a few years ago. Finally, an outlook for the future of materials and properties for stents will be discussed.

Corrosion processes

Corrosion and its associated products can affect tissues in several ways. First, corroding materials can release metallic ions into the surrounding tissues and these can be toxic to cells, or they can be mutagenic, allergenic, or even carcinogenic. For example, 316L stainless steel and Nitinol (55Ni-45Ti) contain large amounts of nickel, which is known to be potentially carcinogenic. Stainless steel contains between about 8 and 12 wt% nickel, and Nitinol contains about 55 wt%.

Nitinol owes its good corrosion resistance to a passive surface film consisting mainly of TiO₂. The chemical and mechanical stabilities of this film have still not been unambiguously established, especially after the deployment required to expand the stent after its positioning. Even though it has been demonstrated that this oxide layer remains essentially unchanged after implantation, analysis of samples from surrounding tissues from the vascular wall around a Nitinol stent has revealed tiny deposits of nickel and titanium compounds. These deposits are believed to be corrosion products that had undergone phagocytosis, meaning that they have been “captured” by some sort of white blood cells.

Even though it is probable that Nitinol does not (macroscopically) corrode substantially over the human lifetime, nickel compounds certainly diffuse through the passive layer, thus reaching the surrounding tissues. After reaching surrounding tissues, nickel tends to leave the impregnation site and to spread out, probably transported by the lymphatic system. Thus, its potential negative
Mechanical properties of stent materials

<table>
<thead>
<tr>
<th>Material</th>
<th>Composition, wt%</th>
<th>Elastic modulus, GPa (Msi)</th>
<th>Tensile strength σ\text{y} MPa (ksi)</th>
<th>Ultimate tensile strength σ\text{y} MPa (ksi)</th>
<th>Elongation, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>316L stainless steel, annealed</td>
<td>17Cr, 12Ni, 2.5 Mo, &lt;0.03C, balance Fe^a</td>
<td>193^b (28)</td>
<td>260^a (38)</td>
<td>550^b (80)</td>
<td>50^a</td>
</tr>
<tr>
<td>Nitinol^c</td>
<td>55 Ni - 45 Ti</td>
<td>Austenite 83 (12), Martensite 28 to 41 (4 to 6)</td>
<td>Austenite 195 to 690 (28 to 100), Martensite 70 to 140 (10 to 20)</td>
<td>Annealed (130), Work-hardened 1900 (276)</td>
<td>Annealed 25 to 50, Work-hardened 5 to 10</td>
</tr>
<tr>
<td>Tantalum^d</td>
<td>Commercially pure</td>
<td>185 (27)</td>
<td>165 (24)</td>
<td>205 (30)</td>
<td>40</td>
</tr>
<tr>
<td>Co-Cr-Mo alloy (Elgiloy), heat treated at 525°C for 5 hours^e</td>
<td>40Co, 20 Cr, 7Mo, 15.5Ni, 2Mn, 1Be, 0.15C, balance Fe</td>
<td>190 (28)</td>
<td>690 (100)</td>
<td>1020 (148)</td>
<td>&gt;10</td>
</tr>
<tr>
<td>Gold^d, annealed</td>
<td>≥99.99</td>
<td>79.9 (11.6)</td>
<td>nil</td>
<td>130 (19)</td>
<td>45</td>
</tr>
<tr>
<td>Gold^d, 60% reduction</td>
<td>≥99.99</td>
<td>79.3 (11.5)</td>
<td>205 (30)</td>
<td>220 (32)</td>
<td>4</td>
</tr>
<tr>
<td>Platinum, annealed</td>
<td>99.95</td>
<td>164.6^c (23.9)</td>
<td>—</td>
<td>125 to 165^d (18 to 241)</td>
<td>30 to 40^d</td>
</tr>
</tbody>
</table>

[b] www.matweb.com, as of 06/06/2003.

effects could be observed in the body, even away from the implantation site.

Leaching ions

Leaching, or releasing of metal ions, from surgical 316L stainless steel has also been investigated. It is well known that corrosion occurs to a significant degree in stainless steel implants, as it is susceptible to localized attacks in long-term applications. Nickel in the alloy can be extremely toxic in some forms, such as nickel carbonyls. Likewise chromium, also present in stainless steel, has been shown to release corrosion compounds that accumulate in tissues and red blood cells. Even if the released amounts of potentially toxic elements were very small, their long-term potential risk would have to be unequivocally evaluated prior to implantation. Because metallic stents are permanently implanted, it is very important that materials be safe on a long-term basis (at least as long as the rest of the life of the patient).

Another very interesting point about corroding materials is that corrosion is in fact an electrochemical reaction, which implies the presence of both a cathode and anode. In other words, when a metal (the anode) corrodes, a balancing reaction should take place at a cathode, causing chemical changes in the medium. Even if the metal is not corroding, anodic reactions can take place at its surface, implying a cathodic reaction somewhere else in the body.

Electrochemical tests have been carried out to investigate the relationship between biocompatibility and electrochemical behavior. It was found that the most biocompatible metals are those that form semiconductive or nonconductive oxides at their surface, preventing redox reactions between the metal and the tissues. These metals include tantalum, niobium, and titanium.

Surface properties

Surface properties are essential to stent performance. They include electrical surface charge, surface texture, and surface cleanliness.

- **Electrical charge**: Because platelets and plasma proteins are negatively charged, they should be attracted to metals that have a positively charged surface. Surprisingly, it appears from an *in vivo* study that no relationship exists between the attraction of these cells to the stent and its surface charge. The same study suggested that a higher surface charge leads to a low likelihood of hyperplasia (uncontrolled tissue proliferation).

- **Texture**: Surface texture is also important. *In vitro* tests made on flat and grooved Nitinol surfaces demonstrated that linear migration speed, alignment, and elongation of cells on the surface increase as a function of groove size (ranging from 1 to 22 microns). A grooved surface could thus enhance beneficial stent tissue ingrowth, which is always expected but rarely observed. On the other hand, because surface roughness increases specific surface areas exposed to the medium, texturing surfaces could increase the metal corrosion rate.

- **Cleanliness**: The cleanliness of stents is also an important factor. A substantial amount of foreign material has been found on handled stents, and also on untouched stents. These impurities, of unknown source, have been associated with stent-induced inflammatory response and stent failure. However,
inflammatory response was lower when stents were rinsed under a high-pressure air jet just before implantation. Manufacturers and physicians should be aware of the danger of stent contamination and try to minimize it by developing appropriate industrial methods and fabrication routines.

**Mechanical properties**

In the last decade, several studies have been carried out to improve the mechanical properties of stents. However, the function and the properties of the materials themselves have rarely been investigated. Suitable properties for a stent include easy trackability, ease of delivery, excellent radial strength, and a low recoil. The table presents the mechanical properties of the materials currently used for stent fabrication. Along with design, these properties will affect the trackability, ease of delivery, and radial strength of the stents.

- **Radial strength**: Radial strength is a very important property because the functionality of the stent, that is the ability to support the artery wall, is directly related. This is accepted as the main reason for which balloon-expandable stents are considered superior to self-expanding. When a force is applied to Nitinol, for example, the alloy assumes its martensitic (deformable) phase, and when the force is released, the alloy become austenitic (non-deformable). The high degree of deformability of martensitic Nitinol is believed to be responsible for the high acute recoil occurrence observed in the comparative study of several models of stents.

- **Elastic modulus**: Radial strength of balloon-expandable stents is also a function of the elastic modulus of the material after implantation, and of the design of the stent. The elastic modulus is an indication of the rigidity of the material.

    From a theoretical point of view, two stents made of different materials with similar elastic moduli should show similar radial strength. However, with the first generation of coil stents this was not the case. In fact, their implantation was often associated with several clinical complications even when similar materials were used to fabricate the stents. Moreover, clinical procedures had not yet been fully developed. This underlines the importance of the design of the stent, its structure, and its mechanical properties.

- **Design**: Finally, it has been observed that appropriate design enables a very elastic structure even with a very rigid material. Moreover, materials that are more rigid allow the fabrication of stents with a smaller artery coverage. This is ideal for clinical applications in which small and short side-branch arteries have to be stented.

**Conclusion and future strategies**

Stainless steel is the most common material for stent fabrication. Its physical properties are satisfactory, but not optimal. Stainless steel produces significant artifacts during magnetic resonance imaging (MRI), and its radiopacity is fair. However, tantalum exhibits excellent radiopacity and it is also MRI-compatible.

From a mechanical properties point of view, the materials for stents should possess comparable Young's moduli. Thus, the differences observed until now with different stents depend mostly on their design. Stainless steel, Nitinol, tantalum, and Co-Cr alloys apparently all possess sufficient strength to withstand stresses applied to them within the arteries. However, tensile strength of gold and platinum are low, as are their elastic moduli. Therefore, a stent entirely made of gold and platinum would exhibit poor radial strength.

Stents continue to be the source of many questions among researchers and physicians. Their long-term potential secondary effects are still unknown, and are unpredictable. It is the first time in history that metallic materials containing potentially highly toxic elements and compounds have been implanted directly in the heart, in contact with high-rate circulating blood. Furthermore, these materials are also submitted, during their implantation, to high deformations that generate significant stresses and phase changes.

**New concepts in materials**

The “perfect” stent does not exist, and it will probably never exist. However, several approaches have been or are currently under investigation to increase their clinical performance. One of these is the implanting of biodegradable stents made of nontoxic materials, either polymeric or metallic. The major clinical complication with stents is restenosis, defined as the blockage of blood flow by the coagulation of blood inside the stent. Because restenosis occurs within six months of implantation, biodegradable stents that are able to support the artery wall during this period of time may overcome problems related to the permanent nature and the potential long-term toxicity of metallic coronary stents available commercially today.

A new concept of degradable metal has been
proposed for stent fabrication, by considering magnesium-base alloys. In fact, magnesium alloys are well recognized for their high degradation rate, and magnesium stents may also address the clinical need to increase the daily intake of magnesium in the general population, by releasing magnesium into the body as they degrade.

Drug-coated stents are also under investigation and development. Polymers could be used to coat metals, or to manufacture degradable or permanent stents. Encouraging results have already been seen with polymer-based Poly-L-Lactic Acid (PLLA) coronary stents. However, one of the major drawbacks of polymers is their lack of radiopacity and weak mechanical properties.

To improve stent blood compatibility, seeding stents with endothelial cells has also been investigated, with limited success. Different metallic materials or metallic and ceramic coatings have also been studied, in order to decrease their leakage of potentially toxic compounds and therefore improve their long-term safety.

Finally, it appears evident from this work that the potential and the need for materials with targeted properties is extremely urgent in the field of coronary stents. In the coming years, as biology and material sciences evolve, we will most certainly witness a true revolution in medicine.

Challenging new concepts have only begun in the field of endovascular surgery, and minimally invasive surgery (laparoscopy) is now being combined with magnetic resonance imaging to push the science beyond the existing medical frontiers. New horizons must be opened, and clinicians, materials scientists, and manufacturers must quickly and truly work in close collaboration, as mastering such complex problems necessarily requires a multidisciplinary approach. As a result, numerous applications have been considered and many more are or will be envisaged.

This is undoubtedly the perspective by which the development of “functional materials,” which have targeted surface and volume properties, must be regarded and analyzed. However, as we deepen our knowledge, our evaluations must become more rigorous. We must learn from past experience and adopt a rational approach if we are to face and overcome tomorrow’s technological challenges without compromising the future health and welfare of patients and society.

The “perfect” stent does not exist, and it will probably never exist.

Carcinogenicity of various metallic compounds

<table>
<thead>
<tr>
<th>Trace element symbol</th>
<th>Element or compound</th>
<th>Evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Be</td>
<td>Beryllium and its compounds</td>
<td>1</td>
</tr>
<tr>
<td>Cd</td>
<td>Cadmium and its compounds</td>
<td>1</td>
</tr>
<tr>
<td>Cr</td>
<td>Hexavalent chromium compounds</td>
<td>1</td>
</tr>
<tr>
<td>Cr</td>
<td>Trivalent chromium compounds</td>
<td>3</td>
</tr>
<tr>
<td>Cr</td>
<td>Metallic chromium</td>
<td>3</td>
</tr>
<tr>
<td>Co</td>
<td>Cobalt and its compounds</td>
<td>2B</td>
</tr>
<tr>
<td>Ni</td>
<td>Nickel compounds</td>
<td>1</td>
</tr>
<tr>
<td>Ni</td>
<td>Metallic nickel</td>
<td>2B</td>
</tr>
</tbody>
</table>

1: carcinogenic in humans. 2: possibly carcinogenic in humans. 3: non-classifiable as carcinogenic in humans. Metals classified according to their carcinogenicity as established by the U.S. International Agency for Research on Cancer.