Stents: an overview

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Over the last 10 years the development of stent technology has had a major effect on the treatment of patients with cardiac vascular and non-vascular disease. However, no two abnormalities are ever alike and stents differ hugely in their properties.

The concept of a device to support structures in the human body has been around since the late 19th century when Charles Stent, a dentist, invented a material to support skin grafts. Visionaries such as Andreas Gruntzig and Charles Dotter recognized their potential in the 1960s and 1970s and, using home-made metal coils and springs, experimented widely in animal models. Crude materials and production techniques limited their human use to plastic tubes delivered via large bore devices.

The development of stainless steel manufacturing technologies and new metal alloys, such as Nitinol, allowed the production in the early 1990s of balloon expandable and self-expandable stents that were biocompatible and which could be delivered via small delivery systems.

The ideal stent should be easy to introduce and trackable, i.e. easy to deliver to its final site. The stent should be easy to place accurately and therefore should be radio-opaque and mounted on a delivery system that allows accurate deployment. Once deployed the stent should take up the normal contour of the tube it is inserted into and should be flexible enough to allow normal movement, but have a radial strength which allows it to resist elastic recoil and external deforming forces.

Vascular stents should be non-thrombogenic and should become rapidly endothelialized without promoting significant intimal hypoplasia. Non-vascular stents should resist bacterial colonization and tumour or hyperplastic epithelium ingrowth.

At present there is no stent on the market that meets all the above criteria. The first mistake doctors make when considering stenting is to assume that all stents do meet all criteria and that they are all similar in their properties. Stent choice has to be based on compromise. This means assessing the nature of the lesion to be stented, in terms of its histology, anatomy and morphological characteristics, and selecting the most appropriate stent for that lesion.

MATERIALS FOR STENTS

The commonest metals used for stent manufacture are stainless steel 316L, Nitinol and tantalum. The choice of metal depends on its 'biofunctionality' and 'biocompatibility'. Biofunctionality is the degree to which the metal is resistant to corrosion, metal fatigue and deformity. Biocompatibility is the degree to which the metal remains inert once implanted, without promoting a foreign body reaction or toxic ion release.

The three metals mentioned above, along with several others, have proven adequate biofunctionality, so the limiting factor as to which metal is suitable is more dependent on biocompatibility. The body provides a hostile environment which is intolerant to foreign bodies and produces corrosion in a metal stent. Once corrosion begins, a toxic local reaction can be triggered by ion release.

In practice stainless steel 316L (an alloy of iron, nickel and chromium plus trace elements), Nitinol (nickel, titanium alloy), chromium cobalt alloys and tantalum are the only metals which have the necessary biofunctionality and biocompatibility required in stent manufacture. All implantable metals rely on an oxidized layer forming on the metal surface to render them passive in situ. In the case of stainless steel 316L, it is provided by a thin layer of chromium oxide.

Nitinol, named after 'the Nickel Titanium Naval Ordinance Laboratory' where it was developed, is an alloy of nickel and titanium containing trace elements of cobalt, chromium, magnesium and iron. The oxide layer that protects the device from corrosion is titanium oxide. Nickel forms 54–60% composition by weight,

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although changes in this range can be used to affect the metal's characteristics.

Nitinol has two very distinct properties that make it particularly suitable for stent manufacture: its 'thermal memory' and 'super elasticity'. When Nitinol is cooled its crystalline structure changes, and the metal can be deformed to allow it to be loaded on to a delivery system. On release at body temperature, it regains its original shape and stiffness. Super-elasticity allows the metal to deform in a stressed state, but to regain its original shape and strength when that stress is removed. Although nickel is famed for causing allergic reactions, there have to date been no reports of nickel hypersensitivity in conjunction with Nitinol implants.

The nature of the stent metal contributes towards the thrombogenicity of the stent. The intraluminal surface of blood vessels has an electronegative potential and is thromboresistant. Therefore the ideal stent metal should also have an electronegative surface potential. Unfortunately stainless steel 316L and Nitinol have an electropositive charge in saline solution.

Polished tantalum has an electronegative potential but on exposure to saline will become electropositive very quickly. Experimentally, however, this electropositivity encourages the deposition of plasma protein with subsequent deposition of a thin fibrinogen layer that then counteracts the electropositive charge. Unfortunately, at the present time the more electronegative a metal is, the higher is its susceptibility to corrosion, following which it will become thrombogenic. Electropolishing of stents also provides a smoother surface than mechanical polishing and this also makes the stents less thrombogenic. For non-vascular stents, non-corrosion and smooth surfaces prevent the release of toxic ions, the ingrowth of tumour and colonization by bacteria.

STENT PLACEMENT

It is extremely important to ensure maximum stent apposition against the wall of the target tube during deployment. In the vascular system, if craters and ulcers are left under the stent struts this will lead to the development of thrombus, which can propagate and cause intra-stent thrombosis. Good stent apposition will also lead to rapid stent endothelialization. For both vascular and non-vascular stents a firmly embedded stent will provide the maximum luminal diameter, reducing sheer stress in blood vessels and stasis elsewhere.

STENT CONSTRUCTION

Stent construction confers many of the basic properties that can be adapted to meet different situations and environments. The original Palmaz stent (Johnson and Johnson, Cordis, Berkshire) was a stainless steel tube with eight rows of staggered offset slots cut into it. Balloon expansion of the slotted tube produced a stent with a diamond-shaped configuration. This produced extremely good radial force but a lack of flexibility. It was not possible to produce stents longer than 4 cm using this design, making them impractical in procedures such as trans-jugular intra-hepatic porto-systemic shunt (TIPSS), partly because of the expense of inserting up to five stents. It also made them rather rigid and thus impractical to deliver in tortuous structures. Nevertheless, where they were deployed these first generation stents have stood the test of time and are still very much in use.

The flexibility problem was improved by linking one or more short stents with a single filament bridge, for example the Palmaz–Shatz stent (Johnson and Johnson, Cordis, Berkshire) and the Z-Stent (Cook, Letchworth). This had the desired effect but when flexed left a gap between the stent bodies through which tissue could protrude. As laser technology and computer design has improved, stents have become more flexible, with less shortening on deployment while still maintaining good radial force. Self-expanding stents rely either on their construction (Wallstent, Boston Scientific, St. Albans, Herts), or on the metal from which they are constructed (Nitinol stents).

It is the method of weaving monofilaments and the crossing angles of those filaments which give the Wallstent its self-expanding capabilities and radial strength. Because the crossing points in the Wallstent are not welded or fixed, the stent can be elongated in order to reduce its diameter and secure it to small delivery systems. This absence of welding also makes the stent extremely flexible. The Memotherm (Bard, Crawley, West Sussex) stent is manufactured from a tube of Nitinol, with slots cut by laser in a similar manner to the Palmaz stent. Flexibility is obtained by selectively cutting the joints of the diamond.

USE OF DIFFERENT TYPES OF STENTS

Stress analyses of the various stents available suggest that balloon expandable stents are of most value in situations where there may be a constant and high deforming force. However, they should not be placed where there is repeated high deformation force, i.e. in a blood vessel over a joint or in the gastrointestinal tract.

Self-expanding stents are ideally suited to situations where moderate and repeated deforming forces may be expected. However, even self-expanding stents vary in their degree of flexibility. Stents based on the Wallstent design or the Instent Vascucoil/Oesophacoil can be flexed

180°, but not all are as flexible as this. Continued flexing can lead to metal fatigue and there are many instances of stent fracture described in both the vascular and non-vascular systems.

Radio-opacity of stents is vital as they are most easily positioned fluoroscopically. Radio-opacity is a product of the metal used, the thickness of the struts and how close the struts or wires lie together. As a rule stainless steel stents are more radio-opaque than Nitinol, although manufacturers often get round the problem by placing small dots of highly radio-opaque metal, such as gold, at the two ends of the stent. Generally stents are far more difficult to see when being placed into structures where there is overlying bone.

STENT DELIVERY

Even the most perfect stent would be of little use unless it could be mounted on a suitable delivery system. Ideally, delivery systems should be flexible but have good pushability and low crossing profiles. Balloon expandable stents are positioned between markers on the balloon shaft and can be accurately placed to within 1 mm. Self-expanding stents have markers indicating the position of the stent within a coaxial system, but stent movement on release is a common cause of malpositioning, particularly where there is shortening of the stent. In the vascular system a great degree of experience is necessary to accurately place a self-expanding stent, but in the non-vascular system stents should generally be chosen to provide maximum proximal and distal cover of normal mucosa, i.e. the longest stent to fit the available space.

COVERED *VS* NON-COVERED STENTS

In theory, covered stents should offer considerable advantages over non-covered stents in both the vascular and non-vascular system. However, the choice of covering material is limited to polyester (PET/Dacron), polytetrafluoroethylene (PTFE) and polyurethane (PU). These materials enhance thrombogenicity, reduce elasticity, are subject to kinking and degeneration, induce an inflammatory response and increase surface area for bacterial overgrowth and new intimal hyperplasia. As a consequence, covered stents have yet to be shown to have long-term patency in peripheral vascular disease where their use has been limited to the exclusion of aneurysms in large vessels such as the thoracic and abdominal aorta and to emergency situations where smaller arteries are bleeding.

Patency of covered stents in the biliary system has so far been poor. However, covered stents are of value in the palliation of malignant gastrointestinal tumours. The covering material can be placed inside or outside the stent. This affects the stent's ability to grip the tube into which it is inserted when dealing with lesions at the gastro-oesophageal junction. It makes sense to use a stent with covering on the inside so that the struts of the stent can produce better purchase.

BIOLOGICAL SURFACES

Developments in bioengineering allow the creation of biological surfaces on non-biological medical implants, e.g. covered and non-covered stents, which may enhance the long-term efficacy of devices. Inherent in this is the potential for local drug delivery. The properties of metal bonding make it difficult to bind a drug directly to the metal surface. However, a polymer coating, which may be non-biodegradable or biodegradable, may serve as an interface for bonding bioactive agents.

Homogeneity of the polymer coating is essential and clearly the polymers have to be non-toxic and strong, but they also must be elastic. Non-biodegradable polymers must also be chemically resistant and the thickness of any polymer layer should be as small as possible. Drugs can be bound to the polymer, either directly through chemical functional groups such as amino, carboxy or hydroxyl groups, or via a molecule which links the polymer and the bioactive agent. Such molecules are known as spacers.

At the present time there are a number of drugs which are considered or are being evaluated as suitable for stent coating. These include heparin, hirudin, glycoprotein IIb/IIIa receptor antibodies and nitric oxide donors. Antiproliferative agents such as angiopeptin, corticosteroids and taxanes which inhibit neointima and local tumour proliferation, and endothelial growth factors, e.g. vascular endothelial growth factor (VEGF), are also undergoing evaluation.

CONCLUSIONS

There is no ideal stent available at present and there is certainly no one stent that will suit all lesions in either vascular or non-vascular systems. Because of this, any department involved in vascular or non-vascular stenting procedures should keep a range of different stents so that all types of lesions can be treated in different locations. HM

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KEY POINTS

- All stents are different and all lesions requiring stents are different.
- Stents should match the morphological characteristics of the lesion to be treated.
- Stent delivery is as important as the stent itself.
- The future for stents may lie in better coverings and biological surfaces.