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CORONARY PERFORATIONS AND GENERATION OF STENTS: AN UPDATE AND REVIEW

***Supriya Shidhaye[1], Nikhita Prabhu[2], Farheen Badshah[2], Priyank Parikh[3]**

[1]Principal of Vivekanand Education Society's College of Pharmacy, Mumbai, INDIA.

[2] M.Pharm Scholar , Department of Pharmaceutics, Vivekanand Education Society's College of Pharmacy, Mumbai, INDIA

[3] M.Pharm Scholar , Department of Quality Assurance, Vivekanand Education Society's College of Pharmacy, Mumbai, INDIA.

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***Correspondence for Author**
Dr. Supriya Shidhaye
Principal of Vivekanand Education Society's College of Pharmacy, Mumbai, INDIA.

ABSTRACT

Percutaneous transluminal coronary angioplasty (PTCA) is a standard treatment for coronary arterial disease. Use of this 'noninvasive' treatment has rapidly expanded, since its introduction in 1977, to more than 500 000 cases per year in the United States alone. There has been a high restenosis rate of the treated segment following PTCA, up to 30%. Metallic intracoronary stents were introduced to prevent arterial dissection, elastic recoil, and intimal hyperplasia associated with PTCA treatment. However, metal stents themselves induce an inflammatory response which can contribute to intimal hyperplasia [2, 3]. This problem has led to the intensive development of drug eluting stents and bioabsorbable stents that can be loaded with various drugs for the treatment of coronary arterial disease. This review article not only highlights various problems on coronary arterial disease but also gives an updated review of various stents which are currently used for its treatment.

Key words: PTCA, metal stents, drug eluting stents, bioabsorbable stents.

INTRODUCTION

Coronary artery disease (CAD) occurs when the major blood vessels that supply the heart with blood become damaged or diseased usually due to a build-up of fatty deposits of plaque. Over time, diminished blood flow may cause chest pain (angina), shortness of breath, or other symptoms. Because coronary artery disease often develops over decades, it can go unnoticed until it manifests as a heart attack. While studies have shown that stents improve longevity

and quality of life, and reduce the chance of heart attack, a question still remains as to which patients most benefit from a stent rather than coronary bypass surgery. While bypass surgeries in the U.S. have dropped by about a third in the past decade, the number of patients receiving stents has grown to nearly a million a year, in part because patients may be averse to major surgery

Disease

CAD is a condition caused by narrowing or occlusion of the coronary arteries that supply blood to the heart muscle. The disease may be silent or may lead to symptoms such as angina. Continued curtailment of the blood supply leads to heart muscle damage in the form of a myocardial infarction (MI) or death. Manifestation of symptoms of CAD may be acute or chronic. Recently the term acute coronary syndrome (ACS) has been defined as an operational term that includes acute myocardial infarction (AMI) (ST segment elevation and depression, Q-wave and non-Q-wave) and unstable angina. Previous research reports have not necessarily utilized this definition and have differentiated between AMI and sub acute manifestations of CAD that include angina and unstable angina.[2]

Characteristics of the disease

Blockage of the coronary arteries is a process that evolves over time. It is caused through the deposition of material inside the artery, eventually leading to a decrease in blood flow or a total obstruction. One reported measure of the extent of the disease includes a description of the blockage or lesion. Standardized criteria have been developed to describe the various lesion types and these are presented in *Table 1*. Other characteristics of the disease process are also important and of specific interest in this review. These include not only the lesion type but also the extent of the disease process (e.g. single versus multiple-vessel disease; total versus partial occlusion of vessels) and the size of the diseased vessel.

Table 1: Characteristics of the lesions[4]

Lesion A	Discrete, Less than 10 mm ,Concentric readily accessible in a non-angulated segment, Less than 45° with a smooth contour ,Little or no calcium, Less than totally occlusive not ostial in location ,No major side-branch involvement, Absence of thrombus
Lesion B	10–20 mm length, Eccentric, Moderate tortuousity of proximal Segment, Moderately angulated segment between 45 and 90°, May have an irregular contour, Moderate to heavy calcification, Total occlusion less than 3 months old, Can be ostial in location, Can be a bifurcation lesion

Lesion C	Lesions have a combination of being diffuse, Greater than 20 mm in length, Excessive tortuousity of the proximal segment before lesion, Extremely angulated segments with 90°,May be total occlusion

Current treatments

Treatment protocols may include:

1) medical management
2) surgical intervention (CABG).
3) percutaneous treatment (PTCA with or without stent)

Medical management

Medical management is designed to assist in the modification of risk factors, reduction of symptoms and prevention of disease progression and adverse events. The treatment may include the use of medications such as beta-blockers, nitrates, calcium channel blockers, antiplatelet agents or anticoagulants. [3, 7, 8]

CABG

The development of surgical treatment such as CABG began in the late 1960s. The treatment involves bypassing the area of arterial blockage using either the internal mammary artery or a graft from another vessel [e.g. saphenous vein graft (SVG) from the leg]. Use of CABG may be elective or used in emergency circumstances (e.g. failed PTCA).[3, 9, 10]

PTCA

Research in the late 1970s focused on the development of less invasive treatments. The first PTCA was performed in Switzerland in 1977.[11] A coronary angioplasty in its simplest form involves the inflation of a balloon within a coronary artery at the site of an atherosclerotic lesion. This balloon inflation will compress the atherosclerotic matter and stretch the vessel to accommodate the compressed plaque material. On deflation, the vessel has a wider lumen to allow increased blood flow. Adjunct techniques evolved as a part of what has come to be classified as percutaneous coronary intervention (PCI). The term PCI may be used to include balloon angioplasty, artherectomy and stenting.[4] Initial success of elective PTCA ranges between 96 and 99%.[12]

Drawbacks to the use of PTCA

1. The first is acute closure of the target vessel during treatment. This is considered an emergency and in the past has required emergency CABG. Acute closure is reported in 2–

10% of cases of PTCA and has been the basis for recommendations that PTCA only be carried out with the backup of emergency CABG facilities. A later advance in PTCA was the use of 'bailout stenting'.

2. The second drawback of PTCA is restenosis. The cause of restenosis is probably multi-factorial and may include the development of scar tissue, vessel re-coil or vessel remodelling. Restenosis of the treated vessel requires repeat procedures in approximately 20–50% of patients.[2] Reports also indicate lower treatment success rates in patients with small arteries, long lesions, previous CABG and diabetes.[13]

These problems prompted the research into methods to decrease or eliminate restenosis. This included the development of coronary artery stents. The technology was developed to address the two key issues faced during PTCA, acute closure and restenosis. A number of different stent types are available/licensed for use. There also exist a number of different stent platforms or devices that may be used during the insertion of the stent. An illustration of the process of PTCA and stent insertion is presented in ***Figure 1.***

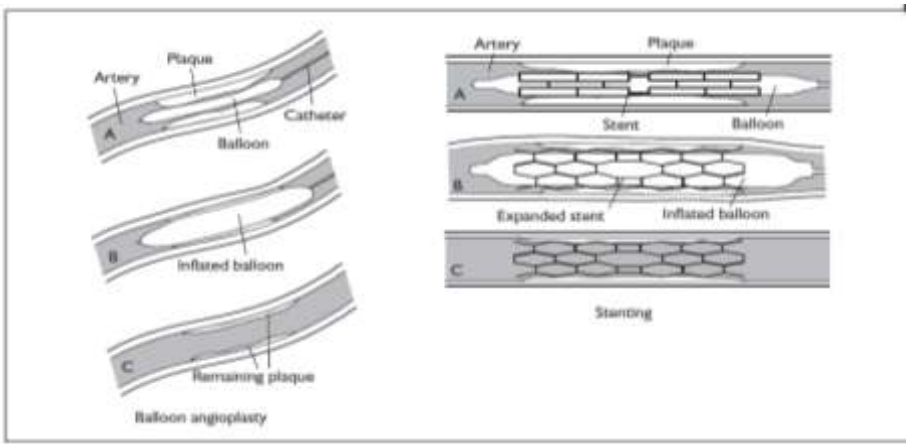

Figure1: llustration of the process of PTCA and stent insertion. Representation of (left) PTCA (balloon angioplasty) and (right) stenting.

PTCA including stents

Stent

A stent is a small, expandable tube. It is a tiny tube placed into an artery, blood vessel, or other hollow structure (such as one that carries urine) to hold it open. A stent is placed in an artery as part of a procedure called angioplasty. Angioplasty restores blood flow through narrow or blocked arteries. A stent helps support the inner wall of the artery in the months or years after angioplasty. Doctors also may place stents in weak arteries to improve blood flow

and help prevent the arteries from bursting. Stents usually are made of metal mesh, but sometimes they're made of fabric. Fabric stents, also called stent grafts, are used in larger arteries. Some stents are coated with medicine that is slowly and continuously released into the artery. These stents are called drug-eluting stents. [1]

A stent is designed to:

- Press the plaque against the artery walls and open up the artery, thereby improving blood flow.
- Keep the artery open after the balloon is deflated and removed.
- Seal any tears in the artery wall.
- Prevent the artery wall from collapsing or closing off again (restenosis).
- Prevent small pieces of plaque from breaking off, which might cause a heart attack.[6]

Stents are commonly used to treat the following conditions that result from blocked or damaged blood vessels:

- Coronary heart disease (CHD) (angioplasty and stent placement - heart)
- Peripheral artery disease (angioplasty and stent replacement - peripheral arteries)
- Renal artery stenosis
- Abdominal aortic aneurysm (aortic aneurysm repair - endovascular)
- Carotid artery disease (carotid artery surgery)[6]

Stent design

There are six major stent-related factors which should be considered while designing a stent:

1. Mechanism of expansion (self-expanding or balloon-expandable);

2. Materials (stainless steel, cobalt-based alloy, tantalum, nitinol, inert coating, active coating, or biodegradable);

3. Forms (sheet, wire or tube)

4. Manufacturing methods (laser cut, water-jet cutting, photo-etching, etc.)

5. Geometrical configurations/design (mesh structure, coil, slotted tube, ring, multi-design, or custom design)

6. Addition to stent (grafts, radio-opaque markers, coatings, etc.)[31, 33]

Mechanism of expansion

In general stents can be divided on the basis of the mechanism of expansion into two major types: self-expanding stents and balloon-expandable stents. Balloon-expandable stents are made from materials that can be plastically deformed through the inflation of a balloon. After

the balloon is deflated, the stent remains in its expanded shape, except for slight recoil caused by the elastic portion of the deformation. Self-expanding stents, on the other hand, are manufactured in the expanded shape, then compressed and constrained in a delivery system. Upon release from the delivery system they spring back , *i.e.* self-expand, to the preset diameter.

Materials used in stents

Table 2: Properties and examples of materials used in stents

Type of stent	Properties	Examples
Balloon expandable stents	low yield stress (to make it deformable at manageable balloon pressures),high elastic modulus (for minimal recoil),small diameter,	Stainless steel 316L, tantalum, platinum alloys , niobium alloys and cobalt alloys
Self expanding stents	expanded shape then compressed and constrained in a delivery system ,low elastic modulus and a high yield stress	Stainless steel 316L, Nitinol

Raw material form

Stents can be made from sheet, wire (round or flat) or tubing. By far most of the balloon expandable and self-expanding stents are made from wire or tubing. A few exceptions are the ones, which are made from sheet. Stents made from sheet have to be rolled up to a tubular configuration after the pattern has been created. .

Figure 2:Cook GRII. Formed from stainless steel sheet, featuring an axial backbone with integral gold markers.

Fabrication

The choice of fabrication method depends mainly on the raw material form used. Wires can be formed into stents in various ways using conventional wire forming techniques, like

coiling, braiding, or knitting. The simplest shape of a wire stent is a coil. All coil stents marketed today are made from Nitinol and are self-expanding. Welding at specific locations after wire forming produces closed-cell wire stent or increase longitudinal stability. The most common wire based self-expanding stent is the Wall stent (BSC), a braided design using multiple Elgiloy (a cobalt based alloy) wires. Knitting allows the production of flexible balloon-expandable and self-expanding wire stent.

Examples:

Figure 3: stent fabricated by photochemical etching

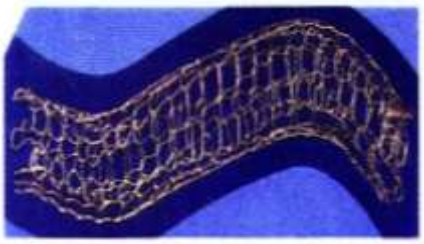

Figure 4: Strecker stent, Knitted

Geometry

Stent geometries are classified into one of five categories: Coil, Helical Spiral, Woven, Individual Rings, or Sequential Rings.

Table 3: Geometry of stent[33]

Geometry of stents	Properties
Coil	Common in non-vascular applications, allows for retrievablity after implantation, extremely flexible, but their strength is limited and their low expansion ratio results in high profile devices
Helical Spiral	Very flexible, but lacks longitudinal support. With internal connection points, some flexibility is sacrificed in exchange for longitudinal stability and additional control over cell size
Woven	Constructed from one or more strands of wire, offer excellent coverage, shorten substantially during expansion. The radial strength of such a braided structure is also highly dependant on axial fixation of its ends.
Individual Rings	Single “z” shaped rings are commonly used to support grafts or similar prostheses, as they can be individually sutured or otherwise attached to the graft material during manufacture. These structures are not typically used alone as vascular stents.
Sequential Rings	This category describes stents comprised of a series of expandable z shaped structural elements (known as "struts" joined by connecting elements (known as "bridges", "hinges", or "nodes"). It is further refined according to the manner in which the structural elements are connected, and the nature of the resulting cells as regular connection ,periodic connection, peak-peak connection or peak-valley connection.

Additions

Table 4:add-ons used in stents[31]

Sr.no	Additions	Property
1	**Radio-opacity enhancements**	To improve X-ray visibility, markers are often attached to the stents. These additions are typically made from gold, platinum or tantalum, and can either be sleeves crimped around a strut, rivets coined into tabs at the end of the stent or integrated in a strut, or welded-on tabs. Electroplating(with gold) is also being used to enhance X-ray visibility.
2	**Coating**	Stent coatings can be applied as passive and active coatings. Whereas passive coatings serve just as barriers having good biocompatibility, active coatings should directly influence intimal proliferation. These compounds are either chemically bonded onto the surface of the stent or the drug is trapped in three-dimensional polymers which acts like a sponge. **Biodegradable polymers:** Several biodegradable polymers like polyglycolic acid/polylacticacid (PGLA), polycaprolactone (PCL),were found to be suitable carriers for anti-proliferative drugs **Non-biodegradable polymers**: polyurethane, silicone , polyethylene terephthalate, Polyethylene terephthalate (Dacron) provide no restenosis and antithrombotic property in stent coating **Metallic Surface Coating:** Coating 316L stainless steel with gold metal not only ameliorates the biocompatibility of stents ,but also gives favourable results with respect to thrombogenicity. At the same time it also increases risk of restenosis **Carbon Coating:** In its pure form, carbon exists in two different crystallographic modifications, as diamond and graphite. graphite enhances thrombogenicity, whereas diamond like carbon reduces metal ion release. Biocompatibility is ameliorated in carbostent, and preliminary clinical results report an angiographic restenosis rate of 11 % after implantation of the Carbostent. **Membrane Covered Stents** Using this technique, a polytetrafluoroethylene (PTFE) membrane is mounted between two stents in order to diminish peri-interventional thrombus embolization
3	**Drug**	Stent-based drug delivery has been accomplished by 3 distinct mechanisms: - bio-absorbable polymeric stents can be loaded with a drug that is eluted slowly over time; -metal stents can have a drug bound to their surface or embedded within macroscopic fenestrations or microscopic nano-pores, thus providing more rapid drug delivery; -metal stents coated with an outer layer of polymer(bio-absorbable or non-bio-absorbable) can be drug-loaded, thus providing more controlled and sustained drug delivery, which might allow more effective drug-tissue interactions.

Generation of stents

Table 5: Generation of stents

Generation of stent	Stent type	Description	Examples
First generation stent	Drug eluting stent	BMS, that had been sprayed with polymer and drug. In the first-generation DES, 316L stainless steel was used as the platform and the strut thickness ranged from 130 to 140μm	CYPHER, TAXUS
Second generation stent	Drug eluting stent	Use cobalt–chromium, which has greater radial strength per thickness , radio-opaque, has thin stent struts (80–90μm)	Endeavour and Xience prime
Next generation stent	Bioabsorbable stent	Completely biodegradable, bioabsorbable stent, typically polymer or magnesium, sometimes coated with anti-restenotic agent	BVS,REVA,Igaki-tamai,Magnesium metallic stent

Drug eluting stents

First generation DES stents

First-generation DES was considered to be essentially BMS that had been sprayed with polymer and drug. Since drug-eluting stents (DES) received the CE mark in 2002 and the US Food and Drug Administration (FDA) approved the first DES in 2003, there has been a significant increase in the use of these devices. The advent of DES has not only revolutionized the field of interventional cardiology but also have a major impact on patient care through their efficacy in reducing the need for repeat revascularisation.[19]

Drugs used in first generation stents

Rapamycin (Sirolimus)

Rapamycin modulates immune function and acts on T-lymphocyte activation and cell proliferation. It enters cells easily because of its lipophilic property and then binds to an intracellular receptor called FKBP12. This complex then increases cellular cyclin dependent kinase inhibitor (CDKI) p27 and inhibits the action of retinoblastoma protein (pRb), which regulates vascular smooth muscle cell proliferation. Inhibition of vascular smooth muscle cell proliferation and migration occurs as a result of growth arrest between G1 and S phases of the cell cycle. Rapamycin also inhibits inflammation after injury by inhibiting T-lymphocyte proliferation and activation. The biological effects of rapamycin lead to overall inhibition of neointimal formation thereby reducing restenosis[19]

Paclitaxel

Paclitaxel belongs to a group of drugs called taxanes which are antiproliferatives used in cancer treatment. It inhibits cell prolifeation and migration by promoting polymerisation of tubulin dimers and subsequently stabilising microtubules into an assembled state Microtubule disassembly is required for transition between G2 and M phase of the cell cycle. Therefore cell proliferation (such as in smooth muscle cells) is inhibited by this drug. It is also lipophilic and therefore rapidly taken up by cells. However, by altering the cytoskeletal structure, Paclitaxel exerts long-lasting effects in vascular smooth muscle cells[14-16]

Marketed products

Figure 5:CYPHER™ Sirolimus eluting stent

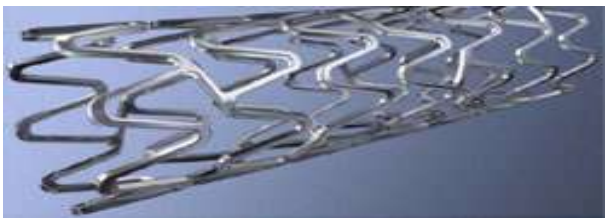

Figure 6: ION™ Paclitaxel-Eluting Stent

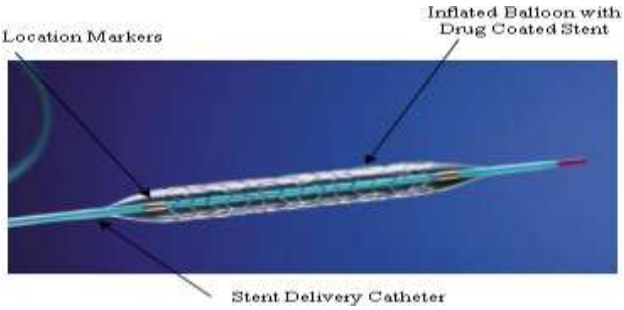

Figure 7: TAXUS™ Paclitaxel eluting stent

These first-generation stents – the SES and PES – were based on a combination of a metallic platform, a durable biocompatible polymer and an antiproliferative drug.While these first generation DES are a major step forward in that they have the need for repeat revascularisation without an increase in death or myocardial infarction (MI), there is an increased risk of late stent thrombosis (LST), which is of particular concern after discontinuation of dual antiplatelet therapy.

Second generation DES stents

In the first-generation DES (Taxus and Cypher), 316L stainless steel was used as the platform and the strut thickness ranged from 130 to 140μm. With 316L stainless steel, the radial strength is dependent on the thickness of the stent's struts. Newer stent designs use cobalt–chromium, which has greater radial strength per thickness and is radio-opaque, allowing

thinner struts. The second generation DES includes the Endeavor (Medtronic, Minneapolis, MN, USA), Resolute (Medtronic), Xience V (Abbot Vascular, Santa Clara, CA, USA) and Promus (Boston Scientific, USA) stents and utilizes a more biocompatible, non-erodible polymer.[6]

The Endeavor, second generation stents utilize cobalt - chromium (CoCr) platform and a permanent phorylcholine polymer that facilitates the release of the sirolimus analogue, zotarolimus. Although not biodegradable, this biocompatible polymer releases 95 per cent of zotarolimus within 14 days. Both animal and in vivo studies have demonstrated less inflammation and greater endothelial stent strut coverage with zotarolimus eluting stents (ZES) compared with SES and PES29-31.

Xience V and Promus stents elute everolimus, an antiproliferative agent in the same family as sirolimus. Attached to a CoCr or platinum-chromium (PtCr) stent platform, is a biocompatible polymer that assists in the release of approximately 80 per cent of everolimus within 30 days and almost 100 per cent within 4 months.[5]

Marketed products

Figure 8: Endeavor, Zotarolimus-eluting stent

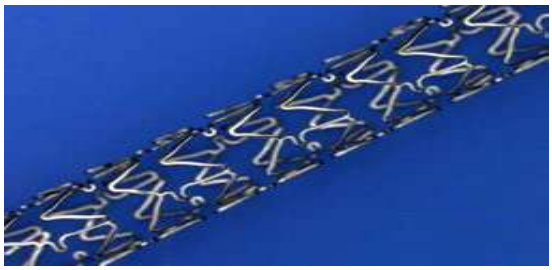

Figure 9: Xience prime technology

Working of DES stents

- The Stent, mounted on a balloon catheter (stent delivery catheter), is inserted into a blood vessel in the arm or groin. It is advanced within the vessel to the narrowed section of the coronary artery. When the Stent is correctly positioned within the coronary artery the balloon is inflated, causing the stent to expand.
- Expansion of the stent pushes the plaque aside, opening the narrowed section of the artery. This restores normal blood flow to the heart. The balloon on the stent delivery catheter is then deflated and the delivery catheter is removed from the patient.

- The Stent remains permanently implanted within the coronary artery, acting as a support (scaffold) of the newly opened section of the vessel, while the drug (sirolimus/paclitaxel) is slowly released into the artery wall around the stent.
- Expansion of the Stent within the narrowed section of a coronary artery opens the narrowing, allowing more blood flow to the heart. If the narrowing is not treated, it can lead to a heart attack (myocardial infarction) or even death.
- Sometimes, after a coronary artery stent procedure, re-narrowing of the artery occurs, due to overgrowth of normal tissue that occurs during the healing process. The action of the drug (sirolimus/paclitaxel) is intended to limit this overgrowth of normal tissue.[20]

Next generation stents

In addition to the improvements that have been made in second generation DES, there are currently newer approaches being tested such as biodegradable polymers and stents, polymer-free drug delivery and the pro-healing approach. The next major breakthrough could be bioabsorbable polymers and stents as a potential solution to avert the risks such as thrombosis and delayed vessel healing associated with currently available Drug eluting stents. Compared with metallic stents, there are several potential advantages, including complete absorption of stent material, a phenomenon that may facilitate repeat treatments to the same site and allow restoration of vasomotion with enhanced potential for vessel remodelling.

Bio-absorbable stents

The permanence of metallic stents is not ideal as these, for a variety of reasons, can lead to blood clots (thrombosis) in the stented vessel later (sometimes after a year or more). The development of bioresorbable stents is an attempt to prevent this risk of clotting. Bioresorbable stents are designed to slowly disappear over time, leaving patients with a treated vessel free of a permanent implant. With no material left behind, the vessel has the potential to return to a more natural state and function reducing the risk of late thrombosis.

Igaki- Tamai Bioabsorbable Stent

The expanded Igaki-Tamai bioabsorbable stent. It is constructed from poly-L-lactic acid and is a zig-zag helical coil design with straight bridges. Strut thickness is 170m, and coverage of the artery by stent is 24%. It does not have a drug coating. Self-expansion is hastened by balloon inflation with heated contrast. It has gold radio-opaque markers at its ends. The Igaki-Tamai stent (Igaki Medical Planning Company,Kyoto, Japan), the first absorbable stent

implanted in humans,is constructed from poly-L-lactic acid (PLLA). In the absorption process, hydrolysis of bonds between repeating lactide units produces lactic acid that enters the Krebs cycle and is metabolized to carbon dioxide and water. The stent design is a zig-zag helical coil with straight bridges (Figure1). [21-23]

The REVA stent

The REVA (Reva Medical Inc, San Diego, Calif) stent is constructed from an absorbable tyrosine-derived polycarbonate polymer that metabolizes to amino acids, ethanol, andcarbon dioxide. The absorption time can be modified. It is balloon expandable with a slide and lock (ratchet) design that allows stent expansion without material deformation .Whenexpanded, the stent to artery ratio is 55%. It is radio-opaque by inclusion of iodine atoms to the polymer, has high radial strength and uses standard balloons for deployment.

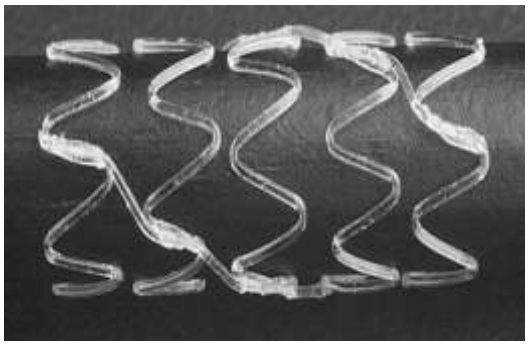

Figure10 : Igaki-tamai technology[22]

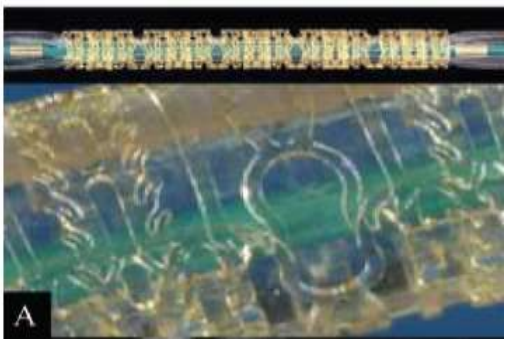

Figure 11:REVA technology[22]

A Bioabsorbable Magnesium Stent

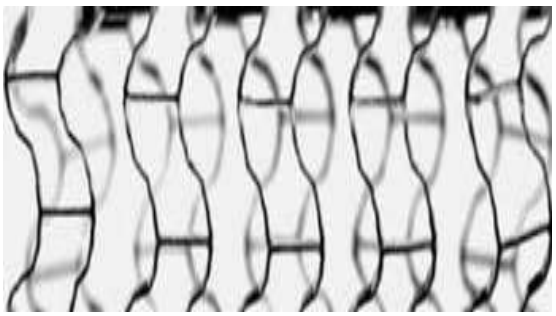

Figure 12: Bioabsorbable Magnesium Stent

This stent is a tubular, slotted, balloon-expandable bare-metal stent sculpted by laser from a tube of a biodegradable magnesium alloy and rare earth elements with two radio-opaque markers at either end, as the metal itself is not visible on fluoroscopy.4 It has low elastic recoil (<8%), like stainless steel stents, with minimum shortening after inflation (<5%).The

cells are large, with an open mesh design ideal for side-branch access (see *Figure 4*). Degradation rates range from 60 to 90 days, with overall integrity remaining at 28 days.[22]

BVS Everolimus-Eluting Bioabsorbable PLLA Stent

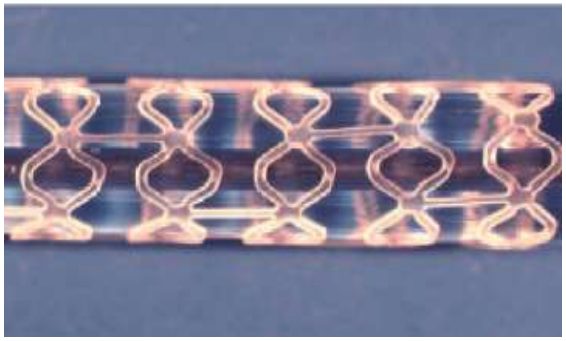

Figure 13:BVS Everolimus technology

The BVS everolimus-eluting stent (Abbott Vascular, Santa Clara, Calif) is the first bioabsorbable stent to have clinical and imaging outcomes similar to those following metallic drug-eluting stent (DES) implantation for 2 years but with the potential advantages of full-stent absorption. This stent has a bioabsorbable polymer backbone of PLLA with a polymer coating of poly-D,L-lactide that contains and controls the release of the anti-proliferative drug, everolimus.[21-28]

Table 6: Comparative-technical specifications of bioabsorbable stent[29,30,32]

Company	Stent name	Stent material	Drug	Strut thickness	Absorption time (months)	Design
kyoto medical	Igaki tamai	PLLA	None	170	24	zig-zag helical coils with straight bridges
biotronik	AMS	Magnesium alloy	None	165	<4	sinusoidal in-phase hoops linked by straight bridges
REVA medical	REVA DES	tyrosine derived polycarbonate	paclitaxel/sirolimus	200	36	slide and lock
BTI	IDEAL	polyanhydride ester	sirolimus/salicylic acid	200	6	tube with laser cut voids
Abbott	BVS	PLLA	Everolimus	156	24	hoops with straight and direct links

CONCLUSION

Stents play an increasingly important role in percutaneous coronary interventions. Various metal stents have been shown to reduce the restenosis rate compared with angioplasty alone. This success has prompted the expansion of stent usage to peripheral arteries, the urethra, trachea, esophagus and GI tract. Stents do not eliminate the problem of coronary arterial restenosis and may contribute to it by inducing neointimal hyperplasia. Several bioresorbable stent designs are in development for temporary mechanical support combined, in some cases, with drug and/or gene therapy delivery. Such temporary, bioresorbable stents that match the expandability and recoil resistance of metal stents in the coronary arterial setting have been reported. These stents are theoretically superior for arterial wall healing, but face challenges in their application to smaller, more tortuous channels. Radioisotope-loaded metal or polymeric stents are also appealing for the local treatment of tumors and for the prevention of excessive granulation tissue formation in non-coronary settings. Stent design and development is currently a very active area of bioengineering practice. The expanding range of applications and new designs, materials, and surface treatments suggest that more effective, less invasive therapies may be anticipated in the near future.

ACKNOWLEDGEMENT

CAD=Coronary Artery Disease, AMI= Acute Myocardial Infarction, ACS= Acute Coronary Syndrome, PCI= Percutaneous Coronary Intervention, PTCA = Percutaneous Transluminal Coronary Angioplasty, CABG=Coronary Artery Bypass And Grafting , DES=Drug Eluting Stent, BMS =Bare Metal Stents, PLLA=Poly d-l Lactide.

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