Heart disease is the leading cause of death in the United States. One of the most common medical interventions performed today is the percutaneous coronary intervention (PCI), which opens clogged or damaged coronary arteries. Since its development in 1977, PCI has been a widely used alternative to coronary artery bypass grafting (CABG), and it relieves patients of coronary arterial blockage 90-95% of the time.

One form of PCI, balloon angioplasty, improves necessary blood-flow by inserting a balloon into the affected artery and inflating it in order to compress any plaque present and prop open the artery. A more permanent form of PCI is coronary stenting. Stenting involves placing a tiny tube-like metal structure. Stenting can be employed following angioplasty in order to prevent restenosis, the re-narrowing of an artery, or stenting can be performed in one step, in which the artery is opened and the stent is implanted. Coronary stents have nearly eliminated the problem of abrupt occlusion (where the vessel closes), which occurs in 5% of patients when just balloon angioplasty is performed. Coronary stents have reduced the incidence of restenosis by more than 50%.

The development of drug-eluting stents (DES) has further enhanced post-operative experiences. DESs are coated in polymeric material that releases drugs locally. These polymers completely degrade by the time the drug has been released, but the metallic stent remains. DES's are used to prevent restenosis that may occur after PCI. In fact, with DES, the restenosis rate is under 10%.

The permanence of metallic stents is not necessarily ideal, however. Current metallic stents can induce late thrombosis and thickening of the inner lining of the artery as a response to arterial wall injury. The long-term effects of metallic stents in human coronary arteries are still unknown. Permanent stents may interfere with normal vessel functions and stents implanted in children must be designed to last literally a lifetime. Furthermore, metallic stents that remain in coronary arteries can present difficulties in later treatment. For example, metallic stents can hinder assessments of coronary arteries through computer tomography (CT) and magnetic resonance imaging (MRI), as well as block important side branches of the artery.

The Ideal Stent

The significant complications involved with metallic and polymer-coated stents call for further development in the treatment of clogged or damaged coronary arteries. An ideal stent would do its job and then disappear. Furthermore, the ideal stent would be made of biocompatible material to prevent vessel irritation and would have adequate radial force to prevent collapsing as a result of any injury responses that occur following implantation. With the stent gone after it does its job, late thrombosis is unlikely to occur and the stent would not interfere with CT or MRI evaluations. A bioabsorbable or biodegradable stent satisfies all the requirements for an ideal stent.

In addition to the clinical benefits of bioabsorbable stents, these stents may prove to be the patient-preferred option. Patients have expressed that they would rather have an effective temporary implant as opposed to a permanent prosthesis that may require surgical removal. Moreover, a disappearing stent would promote the restoration of the previously clogged or damaged artery to a “healthy artery,” one that can endure the pressures of a normal artery. A more speculative hypothesis about bioabsorbable stents is that they can be used to prevent further build up of plaque in arteries; instead of waiting for necessary PCI, a bioabsorbable stent could be implanted in the patient so that, by the time the stent fully degrades, the plaque would have regressed.

Thus, bioabsorbable stents seem to be a viable alternative to permanent coronary stents, but a thorough analysis of different stent models and clinical studies is necessary.

Different Bioabsorbable Stent Models: The Key Players

The development of bioabsorbable stents has become a hot topic in the medical device industry. Models of bioabsorbable stents that are currently being developed are made of either polymers or corroding metal alloys.

Polymeric Stents

There are several polymeric bioabsorbable stents that have been test-
ed. The Igaki-Tamai coronary stent and the bioabsorbable everolimus-eluting coronary stent (BVS) both use Poly-L-lactic acid (PLLA). Other bioabsorbable polymeric stents include ones developed by Bioabsorbable Therapeutics and the REVA Medical stent.

**Igaki-Tamai**

The Igaki-Tamai stent was the first bioabsorbable stent to be implanted in humans. According to the initial 6-month results of the Igaki and Tamai, 15 patients electively underwent the stent implantation; 25 stents were successfully implanted in 19 sites in the 15 patients. Their stent is made of PLLA, has a thickness of 0.17 mm, has a zigzag helical coil pattern, and is balloon-expandable (1).

The study proved PLLA to be safe in human coronary arteries. In the study, no stent thrombosis and no major cardiac event occurred within the first 6 months, meaning that there were no deaths, heart attacks, or coronary artery bypass surgeries. Full degradation took 18-24 months. Furthermore, at about 36 months, lumen size increased (12). While they had limited patients, the team viewed their initial 6-month results as promising. However, the Igaki-Tamai stent lacked a drug coating, and since focus turned to bioabsorbable stents coated with drugs, the development of the Igaki-Tamai stent halted.

**BVS stent**

The BVS everolimus-eluting bioabsorbable PLLA stent is the first bioabsorbable stent to have clinical and imaging outcomes similar to those following metallic DES implantation. The BVS stent has a polymer coating that contains and controls the release of the drug everolimus, which stops cells from reproducing by decreasing blood supply to the cells. (7)

The BVS stent was tested by Abbott in the ABSORB trial, an open-label study in which 30 patients received stent implants. In the study, 80% of the drug was released by the 30-day follow-up and the drug constrained any excessive healing response (7). The stent had a thickness of 150 μm (13). Blood vessel lumen diameter decreased and there were higher-than-expected restenosis rates. These initial results led to speculation that the absorption of the stent may have occurred too quickly (11).

After one year follow up, however, there was no stent thrombosis and only one patient experienced a heart attack (13). Full absorption of the stent took a relatively slow 18 months (8). One remarkable finding of the ABSORB trial was that, between 6 months and 2 years, there was an enlargement in lumen size (7). The increase in lumen size was due to a decrease in plaque size without a change in vessel size (14). This enlargement suggested that after stent absorption, a vessel could potentially become a healthy vessel again. The Abbott BVS stent is currently the bioabsorbable stent furthest along in clinical development and may in fact be cleared for sale in Europe (10).

**Bioabsorbable therapeutics**

The polymeric stent developed by Bioabsorbable Therapeutics (BTI) is coated with sirolimus, a drug that suppresses the body’s immune system. Both the base polymer and coating polymer of the stent are made up of bonds between salicylic acid molecules. These bonds are hydrolyzed during absorption, resulting in the release of salicylic acid, an anti-inflammatory drug that could potentially prevent restenosis. The BTI stent has a thickness of 200 μm and is balloon-expandable. In the first human clinical trial, WHISPER, the stent was implanted in 40 patients. While full absorption was expected within 6 to 12 months, significant thickening of the inner lining of the artery occurred. Thus, subsequent development of the BTI stent is necessary.

**REVA medical**

The REVA Endovascular Study of a Biodegradable Coronary Stent (RESORB) is coated with paclitaxel, a drug that inhibits cell division (11). The stent is balloon-expandable and is set into place by sliding and locking parts rather than deforming the material, which gives the stent more radial strength (8). The stent has a thickness of 150 μm (15).

The RESORB trial, which began in 2007, enrolled 27 patients. At the 30-day follow-up, two patients experienced a heart attack and one needed another PCI (7). In 2008, between 4 and 6 months after implantation, there was higher-than-anticipated occurrence of repeated PCI, driven mainly by reduced stent diameter (7). Thus, the REVA Medical model is not flawless.
Metal alloy stents

Metal alloy bioabsorbable stents perform similarly to permanent metallic stents. So far, two bioabsorbable metal alloys have been proposed for this application: iron and magnesium. However, neither of these stents is coated with drugs.

Bioabsorbable magnesium stent

Magnesium stents have potential advantages over polymeric stents in terms of higher radial strength due to their metallic nature and biocompatibility as a naturally occurring element in the body (8). The first metallic bioabsorbable stent implanted in humans was studied in the PROGRESS-AMS trial with 63 patients (8). This stent has a thickness of 165 μm and is balloon-expandable (7). In trial, absorption of a magnesium stent in humans was rapid and mechanical support lasted days or weeks, which is too short to prevent restenosis (6–7, 11). During the first four months, major adverse cardiac events were recorded in 15 of the patients (24%) and additional PCIs were needed after initial implantations (8). After one year, 45% of the patients had additional PCI. The magnesium stent can be safely degraded within 4 months, but the high restenosis rate raises concerns (7).

Bioabsorbable iron stent

Iron is an essential component of a variety of enzymes, making iron-based alloys favorable material for bioabsorbable stents. M. Peuster, et al. performed experimental studies with bioabsorbable iron stents. The experimental iron stent has a thickness of 100–120 μm and is balloon-inflatable. The researchers implanted stents made of 41 mg of pure iron, an amount equivalent to the monthly oral intake of iron for a human, into the descending aortas of New Zealand white rabbits. During the 6 to 18 months of follow-up, there was no reported thrombosis or any other significant inflammatory injury response. However, the animals experienced destruction of the internal elastic membrane of arteries and products from the degradation of the stent accumulated, resulting in significant alteration of the artery wall (9).

Conclusion

While studies of bioabsorbable stents have proven effective, small trial sizes and too many controlled variables leave many unconvinced. Currently, there are no bioabsorbable stents commercially available. The developed bioabsorbable stents are unlikely to make their way into randomized patients (11). The stents are much larger and bulkier than current permanent stents (10). This difference in size could pose a problem with jagged, calcified plaque protruding into the lumen, which many patients have. The calcium might catch on the device, preventing its proper functioning (11).

Polymeric bioabsorbable stents have demonstrated several limitations and long-term effects of polymer full-absorption products are unclear (6, 16). The polymer that both the Igaki-Tamai and BVS stents use, PLLA, holds 1,000 mmHg of crush pressure and maintains radial strength for approximately one month. Compared with metallic stents, this radial strength is lower and may result in early recoil post-implantation (8). Meanwhile, metal alloys stents do not seem biocompatible enough to use in practice.

While bioabsorbable stents may potentially be the ideal stent, further clinical studies and developments are necessary. The right balance between absorption and radial strength must be obtained, and inflammation must be prevented at the same time. Once this balance is found, though, biodegradable stents may have far-reaching implications for the treatment and/or prevention of blocked and damaged arteries.

References