Heart disease is a common medical condition that affects hundreds of thousands of people each year in the United States alone. In response, scientists have spent decades researching technologies to treat this disease. Coronary stents are a technology developed to keep collapsing heart vessels open to promote proper blood flow and prevent further cardiovascular complications. Since the 1970s, there have been multiple generations of heart stent designs, including metal stents, drug-eluting stents, and biodegradable stents. There is an ongoing transition from drug-eluting stents, still usually composed of metals such as stainless steel or cobalt-chrome alloys, to biodegradable stents. While stents typically function properly, sometimes there are unintended consequences due to permanent placement of these stents.

Biodegradable stents are made of absorbable biomaterials and function in the same way as the aforementioned metal alloy stents, but differ from metal stents in that they entirely disappear from the body in roughly two years after they have restored the problematic arteries. Most of this particular biodegradable stent is composed of absorbable material called polylactic acid (PLA). In comparison to previous technologies, PLA stents have been praised for their incredible safety and biocompatibility. PLA coronary stents are sustainable in the sense that they are environmentally considerate and improve the quality of life of the patients who have them. In recent years, there have been many successful applications of PLA, such as in tissue engineering, targeted drug delivery systems, and implants. This paper will focus on the advantages of the application of polylactic acid as a biodegradable material for coronary stents.

Key Words—Coronary stents, Polylactic acid (PLA), Biodegradable materials, Bare metal stents, Drug-eluting stents, PCI, Bioengineering.

THE HISTORY AND PURPOSE OF CORONARY STENTS

Heart disease is a common medical condition that affects hundreds of thousands of people each year in the United States alone, and coronary artery disease (CAD) is the leading cause of morbidity and mortality in the world [1]. A major component to the development of CAD is the formation of atherosclerotic lesions, or the buildup of plaque in the artery wall causing a hardening of the walls of coronary arteries [2]. If these lesions are unstable or medically significant, they would typically be treated with percutaneous coronary intervention (PCI), which usually involves stent implementation through balloon angioplasty. Angioplasty is the medical process of surgically repairing a blood vessel. PCI is one of the most common procedures performed for treatment of CAD. The idea of coronary angioplasty was first conceptualized by Dr. Charles Dotter and his trainee Dr. Melvin Judkins in 1964, but the first procedure would not be performed until 1977 by Dr. Andreas Gruntzig [1]. While revolutionary in the development of coronary intervention, the coronary stent would not be developed until the mid-1980s, and would be first implemented through coronary angioplasty by Dr. Jacques Puel in France [3]. Coronary stents are a technology developed to keep collapsing heart vessels open to promote proper blood flow and prevent further cardiovascular complications. Dr. Ulrich Sigwart is credited with the realization of endoluminal stenting, which is stenting within organs of a tubular structure, such as blood vessels [3]. Later, coronary stenting would be used to treat acute myocardial infarction (AMI), more commonly known as a heart attack, for the first time in 1991, and this procedure would be approved one years later by the FDA to treat acute and threatened vessel collapse after failed angioplasty treatment [1]. Since the 1970s, there have been multiple generations of heart stent designs, including bare metal stents, drug-eluting stents, and biodegradable stents. There is an ongoing transition from drug-eluting stents, still usually composed of metals such as stainless steel or cobalt-chrome alloys, to biodegradable stents.

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Early generations of coronary stents were made of stainless steel, and indeed, these stents reduced early restenosis, which is a narrowing of blood vessel, leading to restricted blood flow. However, initial stents contained high metallic densities, which often resulted in stent thrombosis. Stent thrombosis is when coagulation or clotting of blood occurs at the location of the stent. Although the risk of restenosis was reduced with the bare metal stents in comparison to balloon angioplasty procedures alone, there still existed the risk of in-stent restenosis. The purpose of drug-eluting stents was to solve the problem of stent thrombosis. Drug-eluting stents release an antiplatelet drug into the blood vessel to prevent the accumulation of plaque and debris at the location of the coronary stent implantation. Unfortunately, the exposed metal components of these stents still caused platelet aggregation which would later result in thrombosis. Potential in-stent thrombosis caused by permanently placed Drug-eluting stents led to the implementation of dual antiplatelet therapy, in which the patient is prescribed an antiplatelet treatment in conjunction with the implantation of the drug-eluting stent. Recent research has altered focus to biodegradable stents that simultaneously release antiplatelet drugs while also degrading so that only the stent structure is left behind in the body of the patient.

The purpose of biodegradable stents is to resolve the possibility of in-stent thrombosis and restenosis that is still present with current drug-eluting stents, as well as to eliminate the necessity for dual antiplatelet therapy, which typically requires the patient to continue taking these anticoagulant drugs for the remainder of their life. Essentially, the purpose of biodegradable stents is to improve the quality of life of patients who need coronary stents. The standard of the quality of a patient’s life considers future inconveniences to the patient, as well as possible undesirable outcomes directly related to the stent itself. Throughout this paper, the quality of life of the patient will be mentioned referencing the goal to reduce these future inconveniences and potential undesirable outcomes.

FUNCTIONALITY AND GENERATIONS OF HEART STENTS

Percutaneous Coronary Intervention (PCI)

In our hearts, coronary arteries are like pipes that supply blood to the heart muscle. Similarly, just like a pipe, coronary arteries become clogged overtime with debris, which is called plaque. The plaque is a sticky substance made up of cholesterol, fatty deposits, calcium and other material in the body. The coronary arteries could be blocked completely as plaque accumulates over time, starving the heart of the oxygen and nutrients it needs. As a result, parts of heart muscle die because of lack of blood, which usually leads to heart attack and requires urgent treatment and intervention, often referred to as Percutaneous Coronary Intervention (PCI).

Introduction of Cardiac Catheterization and Associated Risks

One of the many intervention procedures is to reopen the artery to help the blood flow more freely to the heart muscle again. To do this, doctors will perform cardiac catheterization on the patients. During the surgery, the doctor inserts a thin flexible guide wire into the blocked artery, and pushes along the balloon catheter that is mounted with the stent over the guide wire to the area of blockage. When the balloon reaches the blockage, the doctor inflates the balloon, which pushes the plaque against the artery wall, reopening the artery, and leaves the stent behind as it is expanded by the inflated balloon, and locked in position (In figure 1, when the balloon catheter reaches the site, the doctor will expand the balloon, pushing the plaque against the artery wall as well as locking the stent in position, preventing restenosis). The placed stent acts like a scaffold to hold open the inside of the coronary artery, increasing the blood flow again. Unfortunately, there might be
potential damage to the artery receiving a cardiac catheterization surgery [5]. For example, the surgery may cause internal bleeding and myocardial infarction, which will be detailed further in this paper.

![Blood clot in artery](image)

**FIGURE 2 [6]**
Pathophysiology of Chest Pain in Myocardial Infarction

### Different Generations of Stents

The first generation of cardiac stents, bare metal stents (BMS), were put into clinical use around the 1970s. BMS are simply a stainless metal mesh stent without any drug coating. After it is locked in position, BMS will help keep the artery open, and increase the blood flow again. However, the first generation of stent tends to cause in-stent restenosis, which is the artery re-narrowing and will be specifically explained later in further detail.

To resolve in-stent restenosis, stent developers then introduced an improved stent called the drug-eluting stent (DES). Similar to the BMS, the DES is also made of stainless steel metal; in addition, DES is covered with specific drugs that can help reduce the chance of in-stent restenosis, which will be explained in detail further into this paper. Although DES will reduce the chances of in-stent restenosis, it will be placed in the artery permanently, which can cause patients many inconveniences. For example, patients who have received DES placement will not be able to receive Nuclear Magnetic Resonance Imaging (NMRI) inspection.

Therefore, there is a vital need to develop a biodegradable stent. A biodegradable stent is made of an absorbable biomaterial. Its function is similar to that of the previous metal stents, which is to dilate the arteries that suffer from serious plaque accumulation, but this kind of stent differs from previous metal stents in that it will disappear from the body in roughly two years after it has aided the restoration of the problematic arteries. Therefore, biodegradable stents can improve the quality of life of the patient by eliminating possible future complications, such as restriction from use of NMRI machines.

### Issues with Bare Metal Stents (BMS)

BMS is able to keep the artery open and increase the blood flow; however, there is a risk that the blood flow can be blocked again. One of the reasons is found in the blood itself. Inside the blood are an abundance of tiny disc-shaped fragments called platelets. These platelets are naturally sticky and easily clump together to help form clots. Most of the time, the blood clots that platelets form are helpful. For example, blood clots help prevent blood loss from a cut or wound. Blood clots can also help prevent germs from entering the body at the site of an injury. But for people with stents, blood clots can also be dangerous. Unfortunately, BMS are thrombotic, meaning that sticky substances in our blood, like platelets and fiber, will be attracted to the stent. After the stent is placed inside the patient’s artery, there is a chance that the sticky platelets can get caught on the wire mesh stent and bind together to form blood clots, blocking the artery again, which is called in-stent thrombosis (IST). To prevent the artery from clotting the coronary arteries, patients will be prescribed with certain medications. These medications help prevent the platelets from sticking together and forming blood clots and are designed to help the blood to flow more smoothly through the stent.

Generally, the medication is referred to as antiplatelet, and usually patients will need dual antiplatelet therapy to prevent IST. For example, patients will need to take different types of antiplatelet at the same time. However, after four weeks of dual antiplatelet usage, the inside of the arterial wall, which is called the endothelium, will overgrow around the stent area due to the medication and cover the metal stent. Therefore, BMS is no longer exposed in the artery, and the patients can be managed on just aspirin, which is a specific type of antiplatelet. Additionally, in about 20% [8] of cases, the endothelium will continue to overgrow, causing in-stent restenosis. Essentially, the vigorous overgrowing endothelium becomes the problem, leading to stable angina, which is a tightness in the chest. To combat this, the stent developers developed drug eluting stents.

### Progress and Challenges of Drug Eluting Stents (DES)

DES is the advanced type of BMS, consisting of a standard metallic stent, a polymer coating, and an anti-restenosis drug (eg. sirolimus and its derivative paclitaxel) that is mixed within the polymer and released over weeks after implantation, thereby reducing the chance of in-stent restenosis to 5-10% [8]. With different combinations of stent platform, polymer, and antirestenotic drug type, each stent can be unique with respect to their different performance. For example, the everolimus-eluting stent (EES) is able to resolve myocardial infarction that can be caused by cardiac catheterization. Myocardial infarction happens because of the development of a blood clot. During the cardiac catheterization, the catheter may break the arterial wall. When this happens, blood can coagulate, or clump together, at the site of the crack, forming a blood clot, which is called a thrombus. This thrombus can grow in size.
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until it completely blocks the blood flow. Compared with
BMS, DES has a lower occurrence of in-stent restenosis and a
unique performance with a different combination. However,
because of the slow growth rate of the endothelium, the metal
stent will be exposed for up to 12 months, increasing the
chances for in-stent thrombosis, unless dual antiplatelet
therapy is continued. Similar to BMS, DES also causes many
inconveniences like dual antiplatelet treatment. Even if the
metal is no longer exposed in the artery, it is still locked in
position permanently, hindering the artery from returning to its
proper function. Due to the remaining drawbacks of DES,
there is an ongoing transition from DES to biodegradable
stents (BDS).

BIODEGRADABLE STENTS (BDS) AND THE
INTRODUCTION OF POLY-LACTIC ACID
(PLA)

Biodegradable stents (BDS) serve the same purpose as
previous stents, but they are manufactured from material that
can be absorbed by the body, eventually, leaving no permanent
foreign material. Similar to DES, the BDS is developed based
on its predecessor. BDS consists of a stent platform that is
made of bio-absorbable polymer, a drug coating, and anti-
restenosis drugs. Studies have shown that the most critical
period of vessel healing is largely complete by approximately
three months [11]. Therefore, the goal of BDS is to fully
support the artery during this critical period, and then dissolve
in the body when it is no longer needed.

Generally, there are two types of stent platforms: a metal
based platform and a polymer based platform. As for metal
based platforms, popular candidates are magnesium, zinc, and
their alloys. Magnesium has shown researchers its value as a
new biomaterial, possessing a functional degradation of about
30 days in vivo, or inside the body, which is much shorter than
the artery’s recovery period. Therefore, much attention has
been given to find methods that reduce its corrosion rate.
However, a number of remaining issues limit the further
development of magnesium as a biodegradable stent, such as
metallic toxicity. On the other hand, polymer-based stents that
are made of poly-lactic acid (PLA) and its various derivatives
have been approved in some countries as a qualified stent
platform. The material, PLA, is chosen because it is able to
maintain a strong scaffold within the artery recovery period.
Also, it is a naturally occurring molecule that the body can use
for metabolism, which will be further explained in detail in the
following section.

POLY-LACTIC ACID REVIEW (PLA)

Introduction and Background

Poly-lactic acid is a biodegradable plastic material, derived
from renewable resources, such as corn and sugarcane.
Because of its mechanical and microstructural properties, PLA
and its relatives are often used in the medical field. Some
common applications are stents, sutures, soft-tissue implants
and drug delivery devices. Due to PLA’s chiral nature
(mirroring structure), there exists two stereoisomers
(compounds that differ only in the spatial arrangement of the
atom::): poly (L-lactide) acid (PLLA) and poly (D-lactide) acid
(PDLLA). These materials are common choices for many of
the applications above due to their long degradation time
(resulting from steric effects and degrees of crystallinity; both
of which will be explained in further detail), non-toxic nature,
and strong scaffold support.

Engineers have a moral responsibility to maintain the
wellbeing of the environment. One reason that the
biodegradable material PLA is significant for engineering is
that it is environmentally friendly. PLA is obtained from
renewable resources like corn and sugarcane. The utilization
of these resources to produce PLA reduces the pressure that
PLA’s production places on the environment.

Mechanical Properties

PLA has a glass transition temperature around 60-65°C, as
well as a crystallinity of approximately 37%, which is related
to a stent platform’s stiffness and degradation rate,
respectively. The Glass Transition Temperature ($T_g$) is one of
the most important properties of any polymer. $T_g$ is the
temperature region where the polymer transitions from a hard,
glassy material to a soft, rubbery material. Since PLA’s $T_g$ is
around 60°C, when it is placed in vitro environment where the
temperature is below PLA’s $T_g$, the stent becomes stiff,
providing strong support for the artery wall. However, strong
support of the stent is not enough to resolve the problem.
Additionally, it needs to have a relatively longer period to
remain in our vessel, and then dissolve after it has finished its
mission.
Degradation Behavior

The degradation behavior of PLA is the most important reason for the high interest in medical field application. PLA belongs to the group of polyesters, and has a relatively long half-life of hydrolysis, which is molecular breakdown due to a reaction with water, because of steric effects where the alkyl group hinders the attack by water [10]. For example, one of PLA’s relatives, and the most common choice for cardiac stents, PLLA, in vivo condition does not begin to degrade until after approximately 12 month [10].

Besides steric effect, degree of crystallinity is another significant factor for degradation rate. Since PLA possesses a relatively high crystallinity rate, further crystallization can take place during in vivo hydrolysis, affecting the degradation rates of PLA. Essentially, the crystalline domains are less permeable to water and hence undergo slower hydrolysis [12].

However, the main degradation mechanism of PLA is still hydrolysis, which can be an autocatalytic process when the degradation product, carboxylic acid, is trapped, causing localized increases in pH where the lactic acid from the stent helps to catalyze the hydrolysis process [10].

In summary, due to PLA’s unique properties, like steric effect, degree of crystallinity, and the triggered autocatalytic process, the material is able to dissolve in the body after a period of time. Since the stent will not exist in the vessel after it helps clean the plaque, as well as increase the blood flow, the patients who receive a BDS implant will have fewer implications compared to those who receive DES or BMS. Therefore, more and more efforts are being made to put BDS into application.

Medical Application of Poly-lactic Acid

Due to the deficiencies and drawbacks of the existing DES, stent developers have been trying to improve the functionality of the cardiac stent since the last century. Just like DES, BDS consists of the stent platform, built with degradable material (eg. PLA), and the eluting drugs. Different combinations of stent platforms and eluting drugs demonstrate different performances and results. In 2016, Japanese stent researchers published a paper; they analyzed on randomized controlled trails (RCTs), comparing BDSs built with the same material, PLA, but equipped with different eluting drugs, biolimus and everolimus (eluting drugs are used to inhibit endothelium overgrowth). In the paper, researchers analyzed 8436 patients (4654 patients randomized to the biolimus-eluting stent and 3782 patients to the everolimus-eluting stent) in 8 RCTs (of these groups, 5 RCTs were included in the analysis of mid-term follow up, 1 RCT was in long-term follow up, and 2 RCTs were included in both mid-term and long-term follow up periods) [13]. The comparison has shown similar clinical outcomes between the two. For example, the death rate for BES is 4%, and 6% for EES. However, researchers speculate that BES may be associated with higher risk of target vessel revascularization (TVR) or PCI.

Also, in 2016 in the United States, the U.S. Food and Drug Administration (FDA) approved the first BDS, called Absorb GT1 Biodegradable Vascular Scaffold (BVS) System. The BVS consists of a bioresorbable poly (L-lactide) (PLLA) scaffold, a coating polymer comprised of everolimus and biodegradable poly (D, L-lactide) (PDLLA) [14].

Benefits of PLA Coronary Stents

After the PLA stent is locked in position, the drug polymer, usually also made of biodegradable material, begins to release the contained drug over a period of time to prevent in-stent restenosis. After approximately 12 months, the stent begins the process of hydrolysis and will be absorbed completely within about 3 years. Compared with previous generations, the main advantage of BDS is that no foreign material remains in the vessel permanently, returning the artery to its proper function, and reducing the chance of late in-stent restenosis. Also, unlike metallic stents, BDS does not require dual antiplatelet therapy because the stent platform is made of biodegradable plastic instead of stainless metal or metal alloy that tend to attract adhesive substance in our blood such as platelets, causing in stent thrombosis.

Also, due to PLA’s degradable properties, it has a wide range of applications, including 3D-printing, and medical implants and devices, like cardiac stents, sutures and surgical clips. In the medical field, PLA as a bioplastic material is preferred in stent design. Except for the cardiac stent, PLA has already been used to design sutures and surgical clips. With the help of PLA, patients do not need multiple surgeries to remove the forgotten clip or implanted suture since the foreign material will dissolve itself at roughly the same time after the lesion site has healed.

ETHICS OF PLA HEART STENTS

As PLA is relatively new and still undergoing testing, there is not a large amount of information on the ethical issues that plague this material or the actual coronary stent created with this material. As with all new technological devices, though, biodegradable coronary stents are quite expensive in comparison to existing stents since they are still being researched [15]. PLA coronary stents also suffer from the common medical device issue that they have overinflated pricing in less developed countries compared to more developed countries due to the common practice of exploitation of persons in less developed countries to earn a greater amount of profit. Many companies that produce medical devices raise the price of these devices in less developed countries because there is less competition in this business field in these countries and many people are obligated to buy these devices to continue living [15]. This environment essentially forces people to pay whatever prices are set by these companies because the only other choice is death. This system of exploitation of desperate people has nurtured the growth of institutions like illegal organ trade and has caused
the occurrence of the economical ethical dilemma of the “haves” versus the “have-nots.” It is unethical that a possibly life-saving technology should exist for only a certain class of people [15].

The existence of this ethical dilemma implies that PLA coronary stents are inherently valuable and improve the quality of life of the people who need them. If this device did not improve the quality of life of the patient then the device would not be desired over existing stents, and therefore the companies which produce these biodegradable stents would have no way to exploit a population, or class of people, for profit.

On the other side, PLA coronary stents resolve many ethical dilemmas that many existing coronary stents create. A major issue of the bare metal stents and drug-eluting stents is the implantation of a foreign material in the human body that has the capability to cause medical complications in the future of the patient. For example, while drug-eluting stents were designed to prevent restenosis of the artery, in-stent thrombosis is a medical complication caused by the presence of a metallic material in the human body [16]. Current devices simply trade one medical complication for a different one. Dual platelet therapy is another ethical dilemma of many current coronary stents [1]. The implantation of nearly all bare metal stents and drug-eluting stents requires the patient to continue taking medication for the rest of their life due to medical complications that occur with the presence of these coronary stents in the body, such as in-stent thrombosis and restenosis. While often the implementation of these coronary stents saves the life of the patient, it also condemns this person to a lifetime regimen of medical treatment.

Unlike these metal materials, plastic material is not thrombogenic; when the stent is placed in the body, adhesive substances will not be attracted to the stent. Therefore, patients who receive BDS treatment do not need to take antiplatelet medication, reducing the inconvenience for the patient, which improves the quality of life of the patient.

FUTURE DIRECTION OF PLA CORONARY STENTS

While most of the biodegradable polymer stents are still presently undergoing clinical trials and approval processes, polymer-free drug-eluting stents are also being researched to optimize the biocompatibility of the stent in the human body, as well as possibly improve the durability of coronary stents and the restorative progression of the implantation site of the blood vessel [1]. As far as the future of polylactic acid, there are still necessary advances that must be made in order to optimize how biodegradable stents function. There is still a lack of understanding in how the PLA microstructure can be controlled in how it is manufactured [10].

SOURCES

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**ADDITIONAL SOURCES SECTION**


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