Drug-eluting stents (DES) became available for the treatment of atherosclerotic coronary heart disease about five years ago. The polymer coatings used in the first-generation DES (Cypher™ and Taxus™) were non-biodegradable. Virmani et al. studied autopsy patients and suggested that late stent thrombosis post-DES implantation might be caused by the polymer.1 Recently, using a hierarchical classification of stent thrombosis, Mauri et al. reported a significantly higher incidence of definite or probable stent thrombosis events in the DES group than in the bare-metal stent (BMS) group during a four-year follow-up.2 Nowadays, the consensus is to extend clopidogrel usage for a minimum of 12 months (perhaps longer in patients post-DES implantation) to prevent stent thrombosis. However, the 2005 updated American College of Cardiologists (ACC)/American Heart Association (AHA) Percutaneous Coronary Intervention (PCI) Guidelines recommend that clopidogrel 75mg/day should be given for at least one month after BMS implantation, for three months after sirolimus-eluting stent placement and for six months after paclitaxel-eluting stent implantation.

Besides biocompatibility, there are now concerns about polymer layer integrity. Otsuk et al. assessed discontinuities and other irregularities in the polymer layer by scanning electron microscopy.3 Several types of defects in the polymer layer have been found after balloon expansion on several commercially available first-generation DES (Cypher, Taxus and BiodivYsio™), and these defects may be responsible for thrombosis, coronary microembolism and late inflammatory or neointimal reactions post-DES placement.

There are two ways to resolve the problems associated with the biocompatibility of polymers. One method uses a permanent but completely biocompatible polymer such as phosphocholine. Another method is to use a bioabsorbable polymer. A DES with a bioabsorbable polymer is defined as a second-generation DES. This may have potential advantages regarding the long-term result, as the new stent has no sustained stimulation to the local tissue. This article will focus on the newly available DES with bioabsorbable polymers.

Many biodegradable materials have been investigated in pre-clinical studies. Polyglycolic acid/polyactic acid, polycaprolactone, polyhydroxybutyrate valerate, polyorthoester and polyethyleneoxide/polybutylene terephthalate were tested in a porcine model, and all induced significant inflammation reactions.4 Minimal inflammation reactions were seen after poly-L-lactic acid (PLA) stent implantation in a dog model.5 Therefore, research is focusing on the PLA stent. PLA can be hydrolysed slowly and broken down into lactic acid molecules. The molecules are ultimately metabolised into natural products (carbon dioxide and water) and are released from the body without any harmful side effects. The PLA polymer is now used in the coronary DES by many manufacturers. Besides PLA sirolimus stents, a number of analogues (limus family) are also being investigated: everolimus by Guidant, tacrolimus by Sorin, biolimus-A9 by Biosensors and Terumo and zotarolimus (ABT-578) by Medtronic and Abbott.

Everolimus
In the prospective, randomised First Use to Underscore Re-stenosis Reduction with Everolimus (FUTURE)-I and -II trials,6 106 patients were randomised to Champion™ everolimus-eluting stents with PLA coating or BMS. After analysis of the pooled FUTURE-I and -II trials, both in-stent and in-segment angiographic re-stenosis and late loss were significantly reduced with the everolimus-eluting stent compared with the control BMS. There was no stent thrombosis or aneurysm formation. Effective everolimus delivery was also achieved with PLA coating. FUTURE-III and -IV will be conducted to further validate the efficacy and safety of an everolimus-eluting stent with a PLA polymer.

Sirolimus
The pre-clinical research on a sirolimus-eluting stent coated with PLA polymer (Excel™, JW Medical systems, China) demonstrated that it takes about four weeks for sirolimus to be completely released from the coating and about six months for the polymer to fully degrade. We were the first group to observe the safety and efficacy of the Excel stent in the treatment of human coronary artery disease.7 Thirty-one patients with 34 lesions were treated successfully with 48 Excel stents. Twenty patients with 30 stents completed six months of angiographic follow-up. In-stent late loss was 0.07mm. There were no major adverse cardiac events and no malapposition post-Excel implantation. This promising result was supported by other research groups. The ability to reduce the incidence of major adverse cardiac events and the risk of re-stenosis was similar with the Excel, Firebird® or Cypher® durable polymer sirolimus-eluting stent.

Biolimus A9
Biolimus A9 possesses anti-inflammatory and antiproliferative activity with an improved pharmacokinetic profile. Both the Nobori™
Drug-loaded polymer stents have also been tested in porcine coronary arteries and were shown to reduce the degree of stent-induced re-stenosis.

Reduced inflammatory reaction secondary to both tissue injury after stent implantation and acidic intermediate products associated with polymer degradation may be responsible for the aforementioned excellent results of limus-eluting stents with a PLA coating. The time taken for the drug to be completely released from the PLA polymer is designed to be four weeks in order to obtain the optimal overlap; this may further suppress the migration and proliferation of smooth muscle cells over a long period post-DES with PLA coating implantation.

Second-generation limus-eluting stents are not perfect, as the speed of drug release from the polymer is faster than the speed of polymer degradation. There may be a period during which the inflammation reaction induced by acidic intermediate products is not inhibited by limus. Another fact is that the polymer degradation speed was not constant due to a varied microenvironment around the stent, and suboptimal results may be expected in the vessels that suffered remarkable stimulation. Moreover, the amount of polymer is correlated with the dosage of the drug being used. Potent drugs need less polymer and may have better outcomes. Besides the factors already mentioned, as with the first-generation DES, the defects of polymer integrity after stent implantation may never be thoroughly avoided, although there are no data available yet.

PLA polymer can be used not only as a stent coating but also as a stent strut. The first fully bioabsorbable polymer coronary stent is the Igaki-Tamai stent, which is composed of high-molecular-weight (321kDa) PLA with a novel zigzag helical coiled design. Drug-loaded polymer stents have also been tested in porcine coronary arteries and were shown to reduce the degree of stent-induced re-stenosis. The ABSORB trial is a prospective, non-randomised, open-label study designed to evaluate the overall safety and performance of a fully bioabsorbable DES platform for the treatment of coronary artery disease.