Percutaneous coronary intervention (PCI) represents an established treatment in the management of coronary disease. PCI relies on the use of a stent, a support structure delivered and expanded in situ. The evolution of stent design has reached unprecedented heights in recent years. Yet, the quest for long-term clinical stent efficacy continues. Professor Jeong Myung Ho and his team at the Korea Cardiovascular Stent Research Institute [KCSRT] are vested in innovating, evaluating, and clinically delivering novel stent solutions. The team’s work pushes the boundaries of stent design structurally and therapeutically.

Stent development and evolution has previously relied on existing stent designs, and was based on the advantages and disadvantages of their clinical safety and performance. The dawn of stent design introduced the bare metal stents, which were found to be relatively effective. However, reports of thrombosis resulting in myocardial infarction and death led to reconsidering this initial approach. Those findings led to the development of the drug eluting stents in an effort to solve the bare stent thrombosis problem. While encouraging results were reported, it was determined that the permanent presence of a “foreign body” in situ would impede the healing process by negatively impacting the process of smooth muscle formation and endothelialization. At this point, the innovation in stent design exploded through several approaches: (a) expanding drug selection beyond anti-clotting factors; (b) replacing the structural material [metal] with polymers [either biodegradable or biostable; (c) modifying the architecture of the stent with a focus on less material and improved properties; and (d) intelligently layering polymer coat + drug combinations to address the in situ neointimal hyperplasia and endothelial dysfunction.

In their current work, the KCSRT team used a porcine restenosis model to evaluate the initial efficacy of a novel poly(Lactic Acid) [PLA] sirolimus and alpha-lipoic acid [ALA] drug combination [SES]. The goal was to bring together the benefits of sirolimus in inhibiting neointimal hyperplasia with the antioxidative role of ALA, shown to improve endothelial function and prevent atherosclerosis-related disease. A rigorous evaluation was performed, with multiple control groups that included bare metal [BMS], PLA sirolimus [SAS], and ALA eluting stents with PLA [AES]. The structural stent design [base material and architecture] was identical among groups. The primary focus was investigating the correlation between drug elution kinetics and healing outcomes. The evaluation reported better restenosis outcomes at 28 days with SES compared to the controls.

The KCSRT team selected for this preliminary evaluation of the SES stent a porcine model and a critical 28 days time point, a marker of neointimal formation and inflammatory response. Careful consideration was given to drug loading. The SAS group represented the commercial stent loaded with a total of 20mg of sirolimus. The amount of ALA loaded was 20mg as well, based on the team’s preliminary in vitro and in vivo assessment of drug pharmacokinetics and pharmacodynamics. In vitro evaluation using a device mimicking circulating blood found that the ALA loaded stent released fully over 90 days compared to 120 days for the SAS stent. It is known that sirolimus in situ release requires 3-6 months. If an assumption of proportionality between in vitro experimental outcomes and in situ drug release is considered, the release of ALA in situ is expected to continue for 2-4 months. Professor Jeong and his team are currently planning long term in vivo studies to examine the in situ release profile of the ALA and SAS combination release. It will be interesting to investigate the competing kinetics between the two drugs along with their pharmacologic efficacy.

While PLA is a biodegradable polymer, the concern as to how the polymer degradation products affect the surrounding stent environment remains. Professor Jeong recognizes the potential of an artificially escalated inflammatory response as the polymer undergoes its hydrolysis. He also recognizes [based on extensive evaluations performed by his team as well as others] that PLA represents a better therapeutic choice as a drug carrier than other biodegradable polymers such as poly(Lactic – Glycolic Acid) which are characterized by a very slow degradation rate. Specifically, a slow degradation rate will impact the drug release profile and therefore its therapeutic efficacy with the complex and dynamic neointimal and inflammatory response.
The Cardiovascular Stent Research Institute is the epicenter of innovation, clinical care, and education for procedures requiring stent technology in Korea. This indigenous innovation in stent technology such as the Tiger® stent [Chonnam National University, Korea] is used in patient-care side by side with globally established technologies such as everolimus-/zotarolimus-eluting stent with biocompatible polymer, sirolimus based non-polymer stent, biolimus A9-eluting stent with biodegradable polymer, and BVS (bioabsorbable vascular scaffold). Professor Jeong and his colleagues lead the innovation and clinical care for a high-risk population, with the determined goal of extending and improving patients’ quality of life.

I would like to thank Professor Jeong and his colleagues for kindly agreeing to offer a cohesive clinical and investigational account of the ongoing work in stent design at the Korea Cardiovascular Stent Research Institute.

To our readers: I am looking forward to your comments that can be sent to gabriela.voskerician@case.edu using the heading “Editors’ Choice”. We hope to develop this feature into a dynamic forum think-tank.