Drug Eluting Stents

Angioplasty is the mechanical widening of a narrowed or totally-obstructed blood vessel. These obstructions are often caused by atherosclerosis. At first, angioplastic balloons were used to widen coronary arteries. Unfortunately, a small percentage of arteries collapsed immediately after the balloon was deflated. Secondly, a substantial portion of arteries began to close up again, a process called restenosis. Restenosis proved to be the body's response to the 'controlled injury' of angioplasty, similar to a scar forming over an injury, rather than a recurrence of coronary artery disease.

In the 1980's and 90s, metal devices called 'stents' were developed to assist cardiologists to overcome the balloon angioplasty related issues. These metal mesh-like tubes eliminated many of the complications of abrupt artery collapse, but restenosis persisted. Although the restenosis occurrence improved to about 25% of the cases, bare metal stents still experienced reblocking, necessitating a new surgical procedure typically at six-months.

In order to further reduce the process of restenosis after angioplasty, the next generation stents consist of a regular metal stent that is coated with a drug that is known to interrupt the biological processes that cause restenosis. In the clinical data gathered so far, these so called drug-eluting stents appear to reduce restenosis to the single digits. There are three major components to a drug-eluting stent:

- Type of stent that carries the drug coating
- Method by which the drug is delivered/eluted by the coating to the arterial wall
- The drug itself – how does it act in the human body to prevent restenosis?

Representative Publications:

1. Ikonen TS, Gummert JF, Serkova N, Hayase M, Honda Y, Kobayase Y, Hausen B, Yock PG, Christians U, Morris RE. Efficacies of sirolimus (rapamycin) and cyclosporine in allograft vascular disease in non-human primates: trough levels of sirolimus correlate with inhibition of progression of arterial intimal thickening. Transpl Int 2000; 13 Suppl 1: S314-20.
2. Zhang YL, Bendrick-Peart J, Strom T, Haschke M, Christians U. Development and validation of a high-throughput assay for quantification of the proliferation inhibitor ABT-578 using LC/LC-MS/MS in blood and tissue samples. Ther Drug Monit 2005; 27: 770-778.
3. Ostojic M, Sagic D, Jung R, Zhang YL, Nedeljkovic M, Mangovski L, Stojkovic S, Debeljacki D, Colic M, Beleslin B, Milosavljevic B, Orlic D, Topic D, Karanovic N, Paunovic D, Christians U; NOBORI PK Investigators. The pharmacokinetics of Biolimus A9 after elution from the Nobori stent in patients with coronary artery disease: the NOBORI PK study. Catheter Cardiovasc Interv. 2008; 72: 901-908.
4. Clavijo C, Storm T , Moll V , Betts R, Zhang YL, Christians U, Bendrick-Peart J. Development and validation of a semi-automated assay for the highly sensitive quantification of Biolimus A9 in human whole blood using high performance liquid

chromatography-tandem mass spectrometry. J Chromatogr B Analyt Technol Biomed Life Sci. 2009; 877: 3506-3514.

5. Steudel W, Dingmann C, Zhang YL, Bendrick-Peart J, Clavijo C, Shulze J, Betts R, Christians, U. A randomized, double-blind, placebo-controlled, single intravenous dose escalation study to evaluate the safety, tolerability and pharmacokinetics of the novel coronary smooth muscle cell proliferation inhibitor Biolimus A9 in healthy individuals. J Clin Pharmacol 2011; 51: 29-39.
6. Tada N, Virmani R, Grant G, Bartlett L, Black A, Clavijo C, Christians U, Betts R, Savage D, Su S, Shulze J, Kar S. Polymer-free biolimus A9 coated stent demonstrates more sustained intimal inhibition, improved healing and reduced inflammation in comparison to a polymer-coated sirolimus eluting Cypher stent in a porcine model. Circulation Cardiovasc Interv 2010; 3:174-183.
7. Ostojic MC, Perisic Z, Sagic D, Jung R, Zhang YL, Bendrick-Peart J, Betts R, Christians U. The pharmacokinetics of Biolimus A9 after elution from the BioMatrix II stent in patients with coronary artery disease: The Stealth PK study. Eur J Clin Pharmacol 2011; 67: 389-398.