**Results:** Compared to Group 1, Group 2 had a reduced LVSW, LV end-diastolic volume and end-diastolic pressure after reperfusion. Group 2 showed increased expression of myocardial and circulating levels of SDF-1, compared to Group 1. Myocardial levels of phosphorylated cardioprotective kinases: Akt, ERK, GSK3β and STAT-3 were increased in Group2, compared to Group 1. TUNEL staining demonstrated less cardiomyocyte apoptosis and levels of pro-apoptotic factors including BCL-2 and Caspase-3 were lower in Group 2, compared to Group 1. Compared to Group 1, the percent myocardial infarct size normalized to the area at risk (AAR) was reduced in Group 2 (73±13% vs 42±15%, p=0.02).
**Conclusions:** We report the potential benefit of primarily unloading the heart and delaying coronary reperfusion to salvage myocardium in AMI. This is the first report to demonstrate increased expression of SDF-1 and associated cardioprotective kinases in response to acute mechanical unloading and delayed myocardial reperfusion. This report is also the first examine the impact of the Impella CP on cardioprotective signaling in the heart.

## TCT-433

### Plasmin Immobilization for Reduced Thrombogenicity of Metallic Implants

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**Background:** Components of endovascular stents, heart valves and cardiac rhythm devices are made using metal alloys, which are inherently thrombogenic. We have developed a robust, hemocompatible plasma-activated coating (PAC) to covalently bind biomolecules in their bioactive state to metallic surfaces. We then immobilised plasmin, a major mediator of hemostasis, currently used clinically to disrupt clot formation, and investigated its blood compatibility.
**Methods:** PAC was deposited onto stainless steel (SS) substrates in a purpose built plasma polymerization chamber. Blood compatibility was assessed with heparanized whole blood in in vitro assays of clotting under rocking and flow conditions, while cell studies used human coronary artery endothelial cells.
**Results:** Increasing concentrations of plasmin, 0.1 U, 1.0 U, and 10 U, were covalently immobilized on PAC. Bioactivity was demonstrated using an established enzymatic activity assay, while 10U plasmin coating was also found to support endothelial cell proliferation, increasing 2.6-fold from day 3 to day 5 ($p< 0.001$). In a whole blood adhesion assay, these surfaces demonstrated a dramatic reduction of thrombus weight in a dose dependant manner, compared to SS controls. PAC alone reduced thrombus weight 45.4±9.1%, but further reductions were observed for 0.1U (62.3±6.4%), 1U (78.3±6.4%) and 10U (90.5±1.3%) plasmin, relative to SS ($p< 0.001$). Strikingly, the 10U plasmin surface significantly reduced clot weight 97.7±1.3% in a modified chandler loop, relative to SS and PAC alone ($p< 0.001$). Moreover, after freeze-drying and 14 weeks of storage, the reduction of thrombus was persistent (94.6±8.3%) and not significantly different from freshly prepared surfaces, indicating retention of bioactivity. These findings were successfully translated to a custom laser cut SS stent platform, demonstrating robust PAC adhesion without delamination and similarly striking reductions in thrombus formation.
**Conclusions:** Our PAC technology facilitates the covalent immobilization of plasmin, which dramatically reduced clot formation relative to SS. This has profound potential to improve the efficacy of all metallic vascular implants, and particularly endovascular stents.

## TCT-434

### Vascular Protective Actions Of A Novel Sustained Release Nitrite Formulation In Obese Swine With Metabolic Syndrome

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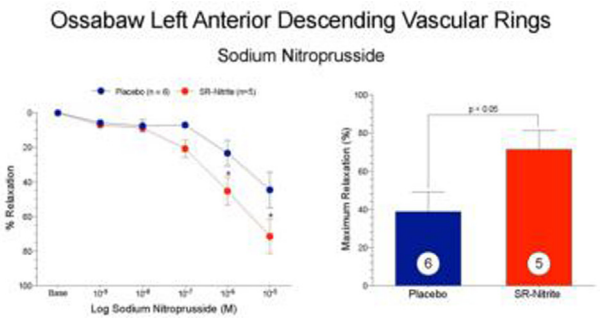
**Background:** Nitrite is a physiologically important nitric oxide (NO) storage intermediate that is reduced to NO during cardiovascular disease states and serves a cytoprotective function. We evaluated the effects of chronic administration of a novel, sustained release formulation of sodium nitrite (SR-Nitrite, Theravasc, Inc.) on circulating NO levels and coronary vascular function in a clinically relevant model of metabolic syndrome (MetS).
**Methods:** MetS was generated in Ossabaw miniswine fed an atherosclerotic high-fat diet (6 months) resulting in profound coronary vascular dysfunction. SR-Nitrite was administered orally (80 mg/kg b.i.d.) for 3 wks. Plasma levels of nitrite and nitrosothiols (RSNO) were quantified at baseline and following SR-Nitrite. Left anterior descending coronary arteries were isolated, suspended in organ chambers and isometric tension acquired. Following pre-constriction with PGF2α, vascular relaxation to sodium nitroprusside was evaluated.
**Results:** SR-Nitrite therapy increased plasma levels of nitrite (0.35 ± 0.21 vs. 1.2 ± 0.75 μM; p=0.02) and RSNO (10.7 ± 2.4 vs. 25.4 ± 5.1 nM; p=0.03) after 3 wks of treatment compared to placebo. SR-Nitrite treatment resulted in significant improvement in vasoreactivity to SNP with maximal relaxation of 39 ± 10% vs. 72 ± 10 %, ($p< 0.05$).




**Conclusions:** In a clinically relevant large animal model of MetS, treatment with SR-Nitrite increased NO bioavailability and improved ex vivo coronary artery dilation.

## TCT-435

### Comparison of endothelialization and inflammation between thin- and thick-strut contemporary bioerodable polymer drug-eluting stents and thick-strut fully resorbable scaffolds in the rabbit iliac artery at 14 and 28 days

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**Background:** Vascular healing after drug-eluting stent implantation (DES) has been shown to be an important determinant of PCI-related clinical outcomes. While lag of endothelialization and increased inflammation were reported to cause delayed arterial healing in first generation DES, it has yet to be determined if this relationship also exists for contemporary DES and fully resorbable everolimus-eluting scaffolds.
**Methods:** Twenty rabbits received thin-strut bioerodable polymer everolims-eluting stents (SynergyTM [Boston Scientific]), thick-strut bioerodable polymer biolimus-eluting stents (BioMatrixTM [Biosensors]), and thick-strut fully resorbable scaffolds (Absorb [Abbott Vascular]) in the iliac arteries for 14 and 28 days, respectively (n=6 for each stent type at 14 days, n=4 at 28days). Endothelial cell coverage was assessed using scanning electron microscopy (SEM) and confocal microscopy (CM) following staining for the endothelial marker CD31/PECAM-1 and RAM11-positive monocytes.
**Results:** Endothelial coverage was greatest in Synergy (14days, 27%; 28days, 86%) followed by BioMatrix (14days, 20%; 28days, 65%) and significantly less in Absorb (14 days, 1%; 28 days, 13%) by SEM (14days, P=0.005; 28days, P=0.0001, respectively). The percentage of CD31/PECAM-1 positive endothelial cells above struts was similar between BioMatrix (17.3%) and Synergy (13.3%), and significantly less in Absorb (0.5%) (P=0.023), while RAM11 positive macrophage area was similar between BioMatrix (0.16 mm2) and Synergy (0.17 mm2) and both were significantly less than with Absorb (2.47 mm2) at 28 days (P=0.0007).
**Conclusions:** Thin-strut bioerodable polymer everolimus-eluting stents exhibited superiority with respect to re-endothelialization as compared to thick-strut bioerodable polymer biolimus-eluting stents and fully resorbable scaffolds, while monocyte adherence was greatest in the latter. These findings confirm substantial differences in vascular healing among contemporary DES and bioresorbable scaffolds.

## TCT-436

### Ex Vivo Shunt Thrombogenicity: A Comparison of XIENCE Everolimus-Eluting Stents to Contemporary Biodegradable Polymer-Coated Drug-Eluting Stents

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**Background:** Previous preclinical experience showed that polymer-coatings of drug eluting stents (DES) lower the predisposition for stent thrombosis compared to bare metal stents. It remains unclear whether relevant differences exist in acute thrombogenicity particularly between current permanent and biodegradable polymers used in clinical practice.
**Methods:** A porcine ex vivo carotid to jugular arteriovenous shunt model involving a test circuit of three in-line stents, was used to test thrombogenicity. The permanent fluoropolymer XIENCE Xpedition™ everolimus-eluting stent (XIENCE, Abbott Vascular) (n=24 stents) was compared with 4 CE-marked DES with biodegradable polymer coatings i) BioMatrix Flex™ (Biosensors) ii) Nobori® (Terumo), iii) Orsiro (Biotronik AG), and iv) Synergy™ (Boston Scientific) (n=6 each). After 1h of circulation, platelet adherence in whole mount stents was identified by immunofluorescent staining against dual platelet markers (CD61/CD42b) and imaged and quantified under confocal microscopy.
**Results:** XIENCE showed the least area occupied by thrombus compared to the other 4 DES, with a significant difference compared to BioMatrix Flex ($p< 0.001$) and Synergy ($p< 0.001$) (Figure). The number of platelet aggregation clots was also the