Results: Compared to Group 1, Group 2 had a reduced LVSV, 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 (73.2±13% vs 42.1±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 dependent 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 chandelier 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±0.8%) 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 denaturation and similarly striking reductions in thrombus formation. (p<0.001).

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, Tarvezan Inc.) on circulating NO levels and coronary vascular function in a clinically relevant model of metabolic syndrome (MetS).

Methods: MetS was generated in Osawab miniswine fed an atherogenic 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 acquisition. Following pre-constriction with PGF2α, vascular relaxation to sodium nitroprusside was assessed.

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 μM; p=0.03) after 3 weeks of treatment compared to placebo. SR-Nitrite treatment resulted in significant improve ment in vasoreactivity to SNAP 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 everolimus-eluting stents (SynergyTM [Boston Scientific]), thick-strut bioerodable polymer biolimus-circulation stents (BioMatrix(TM) [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 RAM1-positive monocytes.

Results: Endothelial coverage was greatest in Synergy (14-days, 27%; 28days, 66%) 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<0.001, 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 RAM1 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 scaffolds 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 bioreabsorable 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 A porcine ex vivo carotid to jugular arteriovenous shunt model involving a

Conclusions: shunt arteriovenous shunt model involving a
least in XIENCE with significant difference compared to BioMatrix Flex (p < 0.001) and Synergy (p < 0.001).

Conclusions: The current ex vivo swine shunt model demonstrated the least thrombogenicity in permanent polymer XIENCE as compared to 4 biodegradable polymer DES, which emphasizes its acute protective effect against thrombus formation.

TCT-437
Transcatheter vs surgical mitral annuloplasty: computational analysis of the biomechanical impact
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Background: Transcatheter mitral annuloplasty (TMA) has been introduced as an alternative to open-heart surgery. The Cardioband TMA (Valtech Cardio, Israel) is a flexible band delivered over the posterior annulus by multiple anchors. The implant size is adjusted to reduce the annulus dimension. The aim of the study is to compare the biomechanical impact of the Cardioband TMA vs. a surgical annuloplasty procedure (SAP) with a rigid-complete ring.

Methods: A computational model of pathological functional mitral valve (MV) was derived from cardiac MRI, to analyse effects during systolic closure following TMA and SAP. The TMA was simulated by placing 14 anchors (8mm spacing) in the posterior annulus, as per device specifications. An homogeneous 33% shortening of the device was imposed, as from clinical data. The SAP was simulated modelling the annulus into the surgical ring shape. Closure dynamics, leaflets and annular configuration and stresses were compared.

Results: MV area was reduced from 16.0 to 7.8 and 6.5cm2 with TMA and SAP, respectively. Coaptation length (CL) increased from 0 to 3.5 and 4.3mm respectively. MV area was reduced from 16.0 to 7.8 and 6.5cm2 with TMA and SAP.

Conclusions: SAP was associated with slightly higher CL and reduced MV area, but induced higher stresses on the mitral annulus. TMA resulted in an effective improvement of valve competence while avoiding mechanical overloads. These promising outcomes are under further clinical evaluation.

TCT-438
Acute and chronic effects of cryotherapy on atherosclerotic plaque composition in the thoracic aorta of cholesterol-fed rabbits: a potential solution for treatment of plaques
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Background: Atherosclerotic plaque rupture remains the leading cause of acute cardiovascular syndromes and the need for plaque stabilizing interventions is high. In the last 10 years, cryotherapy was investigated as a new treatment technology to control vessel disease. Previous studies focused mainly on treatment and prevention of restenosis in peripheral arterial disease. The efficiency of cryotherapy on stabilizing atherosclerotic plaques has never been described. The purpose of the present study was to evaluate the effect of catheter-based cryotherapy on atherosclerotic plaque composition in a rabbit model of atherosclerosis.

Methods: Twenty-four New-Zealand White rabbits were fed a 0.3%-cholesterol supplemented diet for 24 weeks. At three predefined sites of the atherosclerotic thoracic aorta, balloon angioplasty applying either single dose, double dose cryotherapy or control inflation was performed. Rabbits were continued on cholesterol-supplemented diet for 1 day (acute) or 4 weeks (chronic). After euthanasia and preparation for histology, sections were analyzed for apoptosis, content of smooth muscle cells (SMC), collagen, and macrophages, endothelium and calcifications.

Results: One day after cryotherapy, apoptotic cell death of SMCs and endothelial cells (ECs) was observed, whereas macrophages were unaffected. Four weeks after cryo-treatment, the amount of SMCs was restored and the EC layer was regenerated.

Conclusions: For the first time in atherosclerotic lesions, this present study demonstrated that cryotherapy is safe and appears to stabilize atherosclerotic plaques in a rabbit model. This warrants further investigation.

TCT-439
Assessment of Biocompatibility of the Multilayer Flow Modulator with Varying Thread Numbers
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Background: The Multilayer Flow Modulator (MFM) (Cardiatis, Isnes, Belgium) is a self-expandable mesh of cobalt alloy wires used for the treatment of aortic aneurysms. We assessed the impact of design thread count and duration of implantation on the biocompatibility of the MFM in porcine animal models.

Methods: Eight mini-piglets received 26 MFM (12 with 56 thread design, 14 with 80 or 96 threads) in iliac, carotid, and renal arteries. Animals were sacrificed/examined at 1, 3, and 6 months, when histological and ultrastructural analyses were conducted.

Results: The MFM was successfully deployed in 25 of 26 cases. Percentage stenosis was 16.9% ± 5.1% for the 56 thread devices versus 33.4% ± 10.2% for the 80-96 thread devices (p = 0.001) at 3 months, and 21.7% ± 9.9% for the 56 thread devices versus 33.6% ± 12.4% for the 80-96 thread devices (p = 0.004) at 6 months. The 5 devices selected for SEM examination were well deployed, integrated into the vessel wall and endothelialized (Figure 1), and had patent side branches.

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