Background: Cypher stent reduces restenosis in stable pts with simple lesions. Our aim was to assess the safety and efficacy of cypher stent in AMI pts. Methods: AMI pts admitted for PCI during the 6 mths period (16th Apr. 15th Oct 02) were screened for eligibility for cypher stent. AMI pts who underwent PCI during the prior 6 mths (16th Oct 01 - 15th Apr 02) were recruited as historic control. Results: Up to 27th Aug 02, totally 92 AMI pts (presented within 6 hrs) were screened and 66 (72%) were recruited (cypher gp). These 66 accounted for 17% of the 384 pts who were recruited in the RESEARCH study during the same period. Reasons for exclusion (n=8). Among pts (70% male) in the cypher gp, the average age was 66+/-4 yrs. Risk factors were smoking (24%), DM (7.6%), HT (52%) and adverse family history (33%). Peak CK was 3367+/-2239 IU/L. Anterior MI accounted for 50% of infarction. Average 1.5 stents (1-5) were implanted per pt. Majority (80%) received 3-mm diameter stent. Results: Procedural success rate was 92% were 8% failed to achieve TIMI 3 flow. Average follow-up period was 2.2 mths (2.0-4.5). There was no stent thrombosis. The cypher gp showed a positive trend towards reduction in repeat revascularization rate (figure). Conclusion: Cypher stent is safe and effective in reducing the repeat revascularization rate in pts presented with AMI.

1053-174 Effective Stent-Based Delivery of Tissue Inhibitor of Metalloproteinase 3 to Porcine Coronary Arteries Using a Novel Biosynthetic Stent Coating

Thomas W. Johnson, Yin Xiong Wu, Christian Herdeg, Andreas Baumbach, Andrew C. Newby, Karl R. Karsch, Martin Oehmert, Bristol Heart Institute, Bristol, United Kingdom, University of Tubingen, Tubingen, Germany

Background: In-stent restenosis continues to pose a problem for the long-term success rate of percutaneous coronary intervention. We aimed to develop a suitable vehicle for the local delivery of a therapeutic adenovirus to coronary arteries, resulting in overexpression of Tissue Inhibitor of Metalloproteinase 3 (TIMP3). TIMP3 is known to induce apoptosis of vascular smooth muscle cells, thus reducing neointima formation.

Method: We used a Matrix III phospholipid coated (PC) stent (Biocompatibility, Farnham, U.K.), with enhanced castronic charge to increase viral transduction efficiency to porcine coronaries.

Preliminary studies to evaluate the coating & optimal viral dosing were performed with uncoated and PC stainless steel coupons. Subsequently, stents pre-treated with β-Galactosidase adenovirus, were implanted, in vivo, in porcine coronary arteries & flushed with 1 of 5 solutions - no flush, 0.9% saline, contrast media, blood, or culture medium (n=1 per each group). The stented arteries were cultured for 48h, fixed & stained with X-Gal to confirm viral transduction. Transduction was quantified 'en-face' using Image Pro. In vivo transduction was first assessed with β-Gal PC-stents in porcine coronary arteries & following this, TIMP3 stents were implanted for up to 7 days. Harvested tissues were analyzed for presence of virus & gene product using PCR & immuno-histochemical methods.

Results: PC-stainless steel coupons showed superior β-Gal transduction rates compared to uncoated controls. In vivo transduction rates were; No Flush 9.5±3.7%, 0.9% Saline 0.2±1%, 0.9% contrast media 6.9±3.7%, Culture medium 7.2±1.2%, Culture medium (post flush) 16.2±9.3%. In vivo, we demonstrated localized transduction of β-Gal, & more importantly, TIMP3 without systematic distribution of the virus, up to 7 days after implantation.

Conclusion: Our results demonstrate effective, in vivo, delivery of transgene via adenovirus from a stent using a novel biosynthetic coating, already licensed in humans. Additionally, we demonstrated effective & localised production of TIMP3 in stented coronaries. The combination of TIMP3 & a PC stent is a potentially attractive candidate for the prevention of in-stent restenosis.

1053-176 Endovascular Cryotherapy Increases Luminal Area in the Focally Atherosclerotic Hypercholesterolemic Rabbit

Christopher J. Davis, Joshua J. Flasher, John M. Damore, Daniel K. Bennett, Mike Uriot, Patrick Chauvet, Ian J. Sarembock, University of Virginia Health System, Charlottesville, VA, CryoCath Technologies, Montreal, PQ, Canada

Background: There is recent interest in the use of cryotherapy to treat atherosclerotic lesions. The objective of this study was to characterize the effects of endovascular cryotherapy on vessel wall components in the hypercholesterolemic, focally atherosclerotic rabbit.

Methods: Bilateral focal femoral atherosclerosis was induced by air desiccation in twenty New Zealand White rabbits. Animals were then placed on a 0.5% cholesterol diet for 28 days. Utilizing a cryo-balloon system, vessels underwent a sham procedure (n=10) or cryotherapy at 4 temperatures: -20°C(n= 4), -10°C(n=8), 0°C(n=8), and +10°C(n=10). Animals were placed on a chow diet for 28 days post cryotherapy at which time animals were euthanized and arteries harvested for analysis.

Results: Vessels treated at +10°C had significantly larger external elastic lamina (EEL) and luminal area (2.13±0.12 mm² vs. 1.23±0.16 mm², p<0.0004; 0.85±0.10 mm² vs. 0.51±0.12 mm², p<0.0004) together with a higher macrophage content and lower total collagen content compared with sham controls (26±4% vs. 20±7%±9%, p<0.01; 52±3% vs. 46±3%, p<0.01). Vessels in the other groups were not different from sham controls although a trend for larger EEL area (1.78±0.25 vs. 1.23±0.16 mm², p=.37) and a trend for increased wall thickness/collagen content (4,7% vs. 10±4%, p= .15) were seen at -10°C. The cross sectional area of narrowing by plaque (CSAN-P) and smooth muscle cell content were similar among groups.

Conclusion: Endovascular cryotherapy at +10°C significantly increases luminal and EEL area of focally atherosclerotic arteries without a change in CSAN-P, consistent with a positive remodeling effect. Furthermore, there were more macrophages and less collagen deposition in these vessels, which may have facilitated positive remodeling. A trend for increased CSAN-P area was also seen at -10°C as well as increased collagen content in the neointima and media, which may enhance plaque stability. Further studies of this novel technique utilizing various treatment temperatures and regimens are currently in progress.