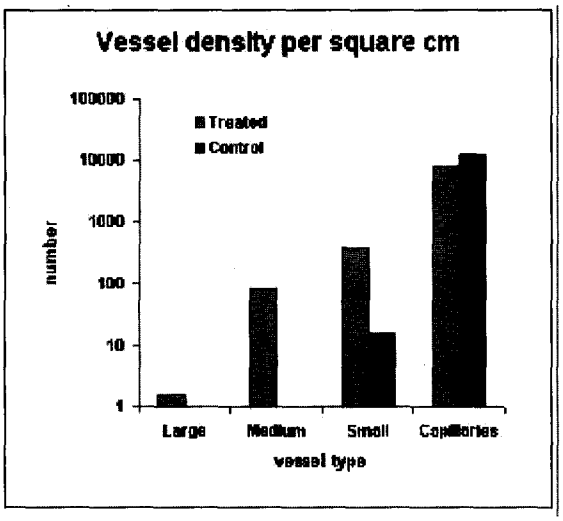
large myocardial region subtended by a DRD for 12 weeks. Histopathologic analysis of the subendocardium indicates a significant angiogenesis effect resulting from systolic perfusion.






## 1004-95 Extracellular Nucleotide Contractions in Human Coronary Bypass Vessels

Tomas Gudbjartsson, Catharina Borna, Lingwei Wang, Lena Karlsson, Sverker Jern, Malin Malmsjö, David Erlinge, Lund University Hospital, Lund, Sweden, Sahlgrenska University Hospital, Östra, Sweden

**Background:** Long term patency is worse for saphenous vein (SV) grafts compared to internal mammary artery (IMA) when used as conduits for CABG surgery (50% *vs.* 90% occlusion rate after 10 years). The reason for this difference is not known but P2 cell surface receptors could play a role. When activated by extracellular nucleotides (ATP, ADP, UTP and UDP) P2 receptors mediate both contraction and growth stimulatory effects on vascular smooth muscle cells (VSMC). This study was designed to evaluate the relative contribution of different contractile P2 receptors in endothelium-denuded human SV and IMA obtained during CABG surgery. **Methods:** Isolated vessel segments from 16 patients were stimulated with selective agonists *in vitro* and the isometric tension recorded, expressed as percentage of $K^+$ concentration. P2 receptor mRNA expression was quantified by realtime PCR. **Results:** The $P2X_1$ receptor agonist, αβ-MeATP, was the most potent vasoconstrictor with more efficacious contractions in the SV ($K_{25}$ = 5.19, $C_{max}$ = 76 ± 10) than in the IMA ($K_{25}$ = 4.15, $C_{max}$ =24 ± 13, $p < 0.05$). The selective $P2Y_6$ receptor agonist, UDPβS, was also more efficacious in the SV than IMA ($K_{25}$ =4.99, $C_{max}$ =80 ± 30 *vs.* $K_{25}$ = 4.28, $C_{max}$ =42 ± 14, $p < 0.05$). Furthermore, UDPβS induced longlasting contractions for more than 2 hours, explained by the low desensitization rate of the $P2Y_6$ receptor. The ATP-induced vasoconstriction could not be abolished by desensitization of $P2X_1$ receptors, with αβ-MeATP, or $P2Y_{2/4}$ receptors, with UDPβS, indicating the presence of yet another contractile ATP receptor. Based on quantification with realtime PCR, the $P2Y_{11}$, receptor could be responsible for this ATP contraction. **Conclusions:** $P2Y_6$ and $P2X_1$ receptors elicit more prominent contractions in the SV as compared to the IMA. Because $P2Y_6$ receptors also mediate growth stimulatory effects in VMSC they could contribute to increased restenosis in the SV. These results may present one explanation for the differences in SV and IMA graft properties. Selective antagonists of $P2X_1$ and $P2Y_6$ receptors could potentially be used to prevent vasospasm and restenosis in the SV during and after CABG surgery.

## 1004-96 Adaptive Coronary Vessel Remodeling Following Surgical Coronary Artery-to-Left Ventricle Stent (VSTENT ) Implantation

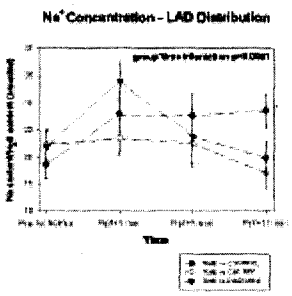
Dongming Hou, Daniel W. van Heeckeren, Matthew Josephs, Pam Rogers, Keith L. March, ICVBM, Indianapolis, IN, Case Western University, Cleveland, OH

**Background:** A left ventricle (LV)-to-left anterior descending (LAD) artery conduit (VSTENT™) has been developed as a novel approach to myocardial revascularization. Initial experiments demonstrated that upon VSTENT™ implantation distal to a total proximal LAD occlusion, significant forward flow was provided to the distal LAD, which preserved regional myocardial function. In this study, covered stent conduits were placed in the mid-LAD in the absence of proximal LAD occlusion, to evaluate the chronic response of the LAD to the flow patterns produced in the presence of the VSTENT™.
**Methods:** Eight pigs (40-60 kg) were implanted via left thoracotomy with an ePTFE-covered, balloon-expandable stent (VSTENT™). This was placed through the posterior wall of the mid-LAD artery, thus creating flow between the LAD and the LV. The LAD was not occluded proximal to the placement site. Coronary angiography was performed before VSTENT™ placement, immediately after implantation, and at 28 days post-implant. The mean diameter of proximal LAD and left circumflex (LCX) artery was measured by QCA.
**Results:** VSTENT™ was successfully implanted in all 8 pigs. A bi-directional flow pattern was seen in the LAD immediately proximal to the conduit, with retrograde systolic flow from the LV to the LAD and antegrade diastolic flow from the proximal LAD to the LV and distal LAD. Prior to the open surgical procedure, the baseline LAD diameter was 3.17±0.09 mm, and LAD/LCX diameter ratio was 1.04± 0.02 (mean±SEM, no unit). Follow-up angiograms confirmed VSTENT patency at 28 days post-implant. Quantitative evaluation then revealed an LAD diameter of 5.32±0.21 mm, and LAD/LCX diameter ratio was significantly increased to 1.43±0.05 ($p<0.0001$). **Conclusion:** Adaptive structural coronary remodeling occurs in the LAD in the presence of the LV-to-LAD conduit at 28 days post-implantation. Further studies will address the time course and persistence of this remodeling, as well as its occurrence in hte context of vessel disease.

## 1004-97 Diazoxide and Controlled Reperfusion Improve Sodium Homeostasis in Severe Ischemia-Reperfusion Injury

James E. Davies, Jr., Steven P. Goldberg, Stanley B. Digerness, Cheryl R. Killingsworth, Charles R. Katholi, William L. Holman, University of Alabama at Birmingham, Birmingham, AL

Background: Intra-myocyte $Na^+$ accumulation due to ischemia-reperfusion (IR) injury results in $Ca^{++}$ influx and myocyte damage. This study determines whether controlled reperfusion (RPF) (initial RPF with warm blood cardioplegia (CP)) and pharmacologic preconditioning with diazoxide (DZX) (a mitochondrial $K^+_{ATP}$ channel opener) improve intra-myocyte $Na^+$ homeostasis using a porcine model of severe IR injury in cardiac surgery.
Methods: Three groups (N=10 pigs/group) had 75 mins of LAD occlusion (including 30 min during 1 hour of CP arrest). Group 1 had no treatment, group 2 had controlled RPF (warm CP followed by normal blood), and group 3 had DZX (50 umol/L infused for 10 minutes prior to LAD occlusion). Transmural biopsies were taken from the LAD region prior to ischemia or DZX, and at 3, 5, and 10 mins post RPF. Intra-myocyte $Na^+$ and water contents were measured using atomic absorption spectroscopy.
Results: (see graph) By 10 mins of reperfusion intra-myocte [$Na^+$] in group 2 had decreased, and groups 2 and 3 were less than group 1 ($p=0.04$ and 0.01, respectively). Intra-myocyte [$Na^+$] during reperfusion was significantly different for group 1 vs. groups 2 and 3 due to persistence of increased [Na] concentration in group 1 (group*time effect $p=0.0001$). Conclusion: DZX and controlled RPF improve intra-myocyte $Na^+$ homeostasis in this model of severe IR injury during cardiac surgery. Our current studies will determine if improved ion homeostasis benefits contractile recovery and reduces infarct size.




## 1004-98 Surgical Implantation of Bone Marrow Cells May Reverse Perfusion and Wall Motion Abnormalities in Patients With Previous Myocardial Infarction and Dominance of Scar

Massimo Mariani, Ugo Limbruno, Claudio Favre, Paolo Marzullo, Gianmario Sambuceti, Vitoantonio Di Bello, Davide Giorgi, Rossella Di Stefano, Carmela Nardi, Anna S. Petronio, Rita Dell'Anna, Jean Grandjean, Mario Mariani, University of Pisa, Pisa, Italy

**Background:** Autologus bone marrow stem cells (SC) implantation has been suggested as a new treatment to improve blood flow distribution and regional function in infarcted myocardium.
**Methods:** To this purpose, 4 male patients (59 ± 3 yrs) underwent autologous SC intramyocardial injection in dysfunctioning myocardium concomitant with off-pump coronary artery bypass grafting. In each patient, 600 ml of bone marrow were harvested and 5 to $14x10^8$ cells obtained from the mononuclear fraction were delivered through 10 to 23 intramyocardial 0,1 ml spots. SC delivery area was chosen according to ungraftability, dominance of scar and hypo/akinesis at gated SPECT. Myocardial perfusion and function in the SC treated area were characterized by tetrofosmin gated SPECT scintigraphy and quantitative myocardial contrast echo (QMCE) performed before and 10 weeks after treatment. At gated SPECT, scar and perfusion were quantified as percent of segmental hypoperfusion (extension) and number of standard deviations below matched normals (severity) in a 20-segment model. At QMCE, myocardial perfusion was evaluated by the product slope*plateau of the filling curve of contrast-echo in the treated area. Regional