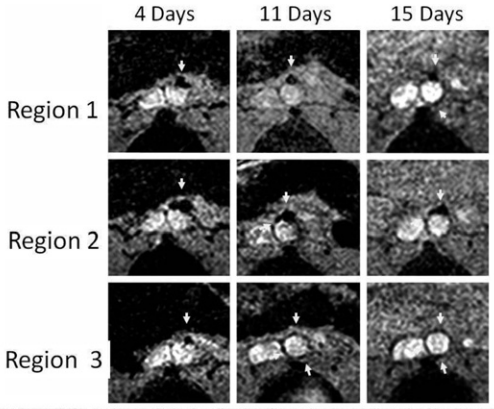

Figure 1: Representative MRI images obtained as a function of time. The arrows indicate signal loss due to the presence of iron. Images from three separate porcine aneurysm regions are shown (1,2,3). All slices were matched based upon the unique vertebrae anatomy. Migration of the iron was observed in all slices at the time interval studied.

Fig.

Conclusions: Ferex can be used as an in-vivo tracking agent of MSCs in PAAA models.

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PS198.

Vascular Endothelial Growth Factor-C Derived from CD11b Positive Macrophages Induces Therapeutic Improvements in a Murine Model of Hind Limb Ischemia

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Objectives: Bone marrow cells(BMCs) that include stem and progenitor cells are widely accepted to apply to patients suffering with peripheral arterial disease(PAD) as a therapeutic approach to induce neo- vascularization. However, the critical paracrine effects are still unclear to administrate BMCs. We focused macrophages that regulate VEGF, especially in VEGF-C.

Methods: Male C57BL/6 mice were administered intramuscular injections of PBS control, unselected BMCs, CD11b+, CD11b- cells from BMCs, and recombinant VEGF-C to ischemic model of hind limb. As the evaluations, perfusion was measured with a laser Doppler scanning that were collected on days 0,1, 3, 7, 14, 21, and 28 including a functional assay such as catwalk in parallel. Capillary density was determined by direct counting vessels positive with Von Willebrand factor at individual time points. Moreover, lymphangiogenesis was assessed as LYVE-1 positive cells.

Results: Post-ischemic recovery of hind limb perfusion was significantly improved in BMCs, CD11b+ and VEGF-C group to compare with control group as the result of laser Doppler scanning. In the functional assay, VEGF-C group dramatically recovered compared to control group. The capillary/myofiber ratio in the thigh muscle was higher in BMCs and VEGF-C group than in control group same as LYVE-1 positive cells. Furthermore, the expression of VEGF, VEGF-C, their receptors of mRNA and Protein were involved predominately in CD11b+ cells.

Conclusions: CD11b+ macrophages play the critical role for angiogenesis and lymphangiogenesis in the murine model of hind limb ischemia. Consequently, recombinant VEGF-C accelerates the recovery and may be a promising therapeutic strategy for PAD patients.

Author Disclosures: S. Kodama: Nothing to disclose; **G. Kuwahara**: Nothing to disclose; **H. Nishinakamura**: Nothing to disclose; **T. Tashiro**: Nothing to disclose.

C9l: Poster Session - Research (2)

PS200.

Performance of a Nanocomposite Polymer Small Diameter Bypass Graft in a Log-term Sheep Model

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Objectives: To evaluate in vivo performance of small diameter grafts (5 mm) made from a compliant, thromboresistant, bio-durable POSS-PCU polymer in a challenging ovine model.

Methods: POSS-PCU grafts were implanted in 12 sheep as interposition grafts in left common carotid artery (LCA) (GLP Regulations; all had daily 75 mg aspirin). Duplex imaging was performed on days 1, 7, 14 and then monthly. Comparison was made with 5mm ePTFE grafts as control (n=6 sheep) and in all animals with the unoperated right common carotid artery (RCA). Flow rates and graft compliance were measured in all target vessels/grafts. Patent grafts were explanted after 9 months. Following explantation, all grafts were assessed independently by histological analysis.

Results: Animal 8 did not survive the anaesthetic and grafts 1 and 9 thrombosed immediately; these two carotids exhibited irreversible spasm during surgery. Animal 7 had tortuous LCA with gross diameter mismatch and thrombosed on day 14. Graft 4 blocked on day 15 and Graft 3 on day 59. Six grafts were patent for 9 months. Patency rates were 67% at 9 months and 78% at 6 weeks. The ePTFE grafts in comparison had all occluded by 1

month. On explantation patent POSS-PCU grafts showed no significant difference in diameters, dimensions, biostability, flow or compliance as compared to native LCA or RCA. On histology, graft wall was free of any significant degenerative change, or cellular ingrowth; only very minimal intimal hyperplasia at distal anastomosis was found in 3 grafts.

Conclusions: The POSS-PCU small diameter bypass graft had an impressive 9-month patency rate of 67% in this sheep carotid model recognised as having high occlusion and intimal hyperplasia rates in PTFE and Dacron. These results confirm that small diameter POSS-PCU grafts should now be investigated as a realistic alternative to current grafts in patients who do not have suitable autologous conduits.

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PS202.

Biomarkers for Subclinical Renal Injury following Endovascular Aneurysm Repair in Human Subjects

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Objectives: Endovascular aneurysm repair (EVAR) is less invasive and has fewer complications than open surgery but introduces the risk of peri-operative renal injury due to a combination of guidewire manipulation within the aorta and contrast induced nephropathy (CIN). In this setting of pre-clinical renal failure traditional measures of renal function are relatively insensitive. Newer markers of subclinical renal injury exist, but are mostly used within the research setting. We aim to establish the sensitivity of a range of biomarkers for renal injury in an in-vivo human clinical study.

Methods: Using elective EVAR as a model, sixteen patients were recruited into the study between December 2009 and April 2010. Urine was collected pre-operatively then at 6, 12, 24 and 48 hours and tested for biomarkers of renal damage (N-GAL, Interleukin-18, retinol binding protein and albumin creatinine ratio). Serum creatinine and eGFR were calculated at all time points.

Results: Sixteen patients (12 male), median age 80 years (range 69-87) underwent EVAR. The novel biomarkers for subclinical renal damage were raised within the initial 12 hour period post-operatively, however no markers showed significant elevation at subsequent time points. At 12 hours post-operatively there was a significant rise in urinary NGAL ($P = .0029$) and IL-18 levels ($P = .0305$). Urinary creatinine was significantly raised at 6 hours ($P = .0345$) but at no other time points. Serum creatinine was no different at 24 hours but elevated with borderline significance ($P = .062$) at 48 hours.

Conclusions: N-GAL and IL-18 appear to be sensitive markers for renal injury in the initial 12 hours following EVAR. Traditional measures of renal damage did not become elevated before 48 hours post-operatively. These urinary biomarkers are potential useful predictors of renal injury and may be used to assess the effectiveness of therapeutic strategies aimed at ameliorating CIN during EVAR.

Author Disclosures: J. Boyke: Nothing to disclose; **K. Burling**: Nothing to disclose; **A. Noorani**: Nothing to disclose; **K. E. Rollins**: Nothing to disclose.

PS204.

Mechanical (or "Gravitational") Unloading Reduces Inflammatory and Cell Adhesion Molecule Gene Expression in Human Endothelial Cells

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Objectives: Mechanical forces including gravity affect mechanotransduction and cell function. The goal of this study was to investigate the impact of mechanical unloading (MU) and loading (ML) of endothelial cells (ECs) with microgravity and hypergravity respectively, with the hypothesis that MU alters expression of inflammatory and adhesion molecule gene expression and these changes are reversed by ML.

Methods: Human umbilical vascular ECs grown to confluency were studied. A desktop random positioning machine and a gravitational cell-loading apparatus provided MU and ML. The experimental conditions included: 1) controls exposed to 1-gravity environment for 24 h (CL), 2) MU for 24 hours, 3) MU for 24 hours with three 30-minutes periods of ML of 12-gravity (MU/ML). Gene expression was studied with reverse transcription followed by real-time quantitative polymerase chain reaction (qRTPCR).

Results: MU led to a significant decrease in gene expression of the adhesion molecules ICAM-1, VCAM-1, E-Selectin, as well as TNF-α, IL-6 and VEGF. In contrast, NOS-3, Caveolin-1 and −2 were significantly increased with MU. The changes observed in gene expression with MU were reversed by gravitational mechanical loading (MU/ML).

Conclusions: Gravitational MU decreases inflammatory and adhesion molecule gene expression and these changes are reversed by short periods of ML. This points towards the importance of gravitational loading in ECs function and cellular interactions.

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