flow in the popliteal artery of patients with peripheral vascular disease (PVD). IPC promotes local vasodilatation and arteriogenesis.

Methods: The aim is to investigate whether it has a systemic remote effect on distant arteries and this effect is mediated through circulating nitric oxide. Fifteen patients with PVD, mean age 73.8 with range (61-84), ABI <0.9, superficial femoral artery stenosis >50%, and 15 healthy volunteers, mean age 57 range (37-75) were randomised for forearm hyperaemia IPC for an hour and sublingual glyceryl trinitrate (S/L GTN). 15 healthy volunteers were controls. Using duplex ultrasound, the BA diameter was measured at 1-minute post-hyperaemia, 30 and 60 minutes during pump use. At 16 minutes post-pump cessation, 2 puffs S/L GTN were administered. Venous blood sample collected at baseline, 5 minutes and 30 minutes of the pump use to be analysed for nitric oxide.

Results: The percentage change of BA diameter among 30 candidates at 1 min post-hyperaemia was 3.3% (p < 0.05) (Wilcoxon), and at 30 and 60 minutes of IPC was 1.5% (p < 0.05) and 3% (p < 0.05) respectively. The response to GTN was 17.1% (p < 0.05). The difference between the controls and other groups was statistically significant. The nitric oxide level in patients group did increase significantly at 30 minutes p = 0.028 while healthy volunteers the level remained steady.

Conclusion: IPC produces a significant dilatation of the BA and has thus a systemic effect on the arterial system. This is a novel finding. This effect is mediated via nitric oxide released from lower extremity vessels as a result of their exposure to the increased shear stress generated through the IPC.

Radio Protective RP105 Protects against Vein Graft Disease and Lesion Stability Via DAMPening of Inflammatory Responses

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Introduction: Vein grafts are often used to bypass atherosclerotic lesions; however, patency rates are troublesome due to the development of vein graft disease. Deficiency of toll like receptor (TLR4), a key initiator of inflammatory signalling, results in reduced vein graft disease. As TLR4 signalling is regulated by the accessory molecule Radio Protective 105 (RP105), we aimed to investigate the effects of RP105 on vein graft disease.

Methods: Vein graft surgery was performed on Rp105−/− mice (n = 13) and C57BL/6 mice (n = 11), as well as on Ldlr−/−/Rp105−/− mice (n = 11) and Ldlr−/− mice (n = 11) fed a western type diet, 28 days later lesion size and composition was analysed. Furthermore, in vitro experiments on smooth muscle cells and mast cells were performed.

Results: A 90% increase in vein graft lesion size was observed in Rp105−/− mice. Lesion size did not differ between Ldlr−/−/Rp105−/− mice and Ldlr−/− mice, but interestingly, we detected a significant increase in the number of unstable lesions and intraplaque haemorrhage upon RP105 deficiency. In both experimental setups, an increase in lesonal macrophages was seen. Peritoneal Rp105−/− mice showed an increase in proliferation. Rp105−/− smooth muscle cells and bone marrow derived mast cells secreted increased levels of the monocyte chemoattractant CCL2. In both the Rp105−/− and Ldlr−/−/Rp105−/− vein grafts the amount of lesonal CCL2 was significantly increased, as well as the number of activated perivascular mast cells.

Conclusion: Together, these data indicate that RP105 has a protective role in vein graft disease by dampening the inflammatory effect, since RP105 deficiency results in an increased inflammatory response and exacerbated CCL2 production by both mast cells and smooth muscle cells.

Morphological and Stent Design Risks Factors to Prevent Migration Phenomena and Type 1a Endoleak for Thoracic Aneurysm: A Numerical Analysis

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Introduction: The primary mechanically related problems of endovascular aneurysm repair are migration and type 1a endoleaks. They occur when there is no effective seal between the proximal end of the stent-graft and the vessel. In this work, we have developed several deployment simulations of stent parameters using the finite element method (FEM) to investigate the contact stiffness of a nitinol stent in a realistic Thoracic Aortic Aneurysm (TAA).

Methods: The following factors associated with these complications were evaluated: (1) Proximal Attachment Site Length (PASL), (2) stent over-sizing value (O%), (3) different friction conditions of the stent/aorta contact, and (4) proximal neck angulation. Then, the numerical observations are used as a guide to optimize the stent design in such neck morphology to strengthen the contact and prevent migration or endoleak type 1a.

Results: The simulation results show that PASL >18 mm is a crucial factor to prevent migration at a neck angle of 60°, and the smoothest contact condition with low friction coefficient (μ = 0.05). The increase in O% ranging from 10% to 20% improved the fixation strength. However, O% ≥ 25% at 60°caused eccentric deformation and stent collapse. Higher coefficient of friction μ >0.01 considerably increased the migration risk when PASL = 18 mm. No migration was found in an idealized aorta model with a neck angle of 0°, PASL = 18 mm and μ = 0.05. The optimized stent results showed better contact stability to resist the migration. They also showed a good compromise of stent design requirements (flexibility and stiffness). Moreover, the new design can also prevent the risk of folding or collapse of stent struts by mitigating the energy of eccentric deformation caused by high angulation and oversizing.
**Conclusion:** Our results suggest carefully considering the stent length and oversizing value in this neck morphology to strengthen the contact and prevent migration. The new design can increase the overall contact stability and reduce the stress peak of circumferential stresses at the proximal attachment zone, especially when the stent length is critical. Moreover, this design could also prevent the risk of folding or collapse of stent struts by mitigating the energy of eccentric deformation caused by high angulation and oversizing.

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**Human Adipose Tissue-derived Mesenchymal Stem Cells Promote Capillary Formation of Peripheral Blood Outgrowth Endothelial Cells in Autologous Fibrin Gels**

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**Introduction:** Tissue engineered vascular grafts are promising alternatives in vascular surgery. However, adverse immune reactions to xenogeneic or allogeneic scaffolds demand for graft materials seeded with vascular cells from autologous tissue sources like blood or adipose tissue. Fibrin isolated from blood plasma can be used to form vascular prostheses which however still display insufficient stability. Integration of capillary networks in the fibrin gel could be a strategy to achieve both higher stability of the grafts and pre-vascularization of the graft wall for a rapid connection of the prosthesis to blood supply after implantation. We here demonstrate capillary network formation in fibrin gels by peripheral blood-derived outgrowth endothelial cells (PB-OEC) which was enhanced by adipose tissue-derived mesenchymal stem cells (ASC) showing pericyte-like functions.

**Methods:** Human fibrinogen was isolated from fresh frozen plasma by cryo-precipitation and polymerized with thrombin. PB-OEC were derived from magnet-sorted CD34+ blood cells after 10-14 days of cultivation and were characterized for endothelial cell markers by immunocytochemistry. ASC were isolated from donors scheduled for visceral surgery after informed consent and characterized for stem cell surface antigens, pericyte markers and their mesodermal differentiation potential. 3D tube formation assay in fibrin gels were performed with PB-OEC only or in co-culture with ASC in two different ratios (1:0.5 and 1:1). Human umbilical cord vein endothelial cells (HUVEC) served as control.

**Results:** PB-OEC expressed mature endothelial cell markers (CD31, VE-Cadherin, vWF, eNOS) and were able to take up ac-LDL. Flow cytometry and immunostaining of ASC revealed the expression of stem cell markers CD73, CD90 and CD105 as well as pericytes markers NG2 and PDGFRβ and three lineage differentiation capability was confirmed by specific stainings. PB-OEC showed tube formation in fibrin gels with significantly more branching points and increased tube length than HUVEC (2 resp. 1.3-fold, \( p < 0.01 \) and \( p < 0.05 \)). ASC-PB-OEC co-culture in both ratios further increased these parameters significantly (branching 5±2-fold, \( p < 0.001 \) to 7±3-fold, \( p < 0.0001 \) and tube length 2±0.7-fold, \( p < 0.0001 \), to 3±0.6-fold, \( p < 0.0001 \)). The number of tubes was decreased 1.3±0.7-fold to 1.7±0.5-fold (\( p < 0.05 \) and \( p < 0.01 \)) whereas the total tube area remained constant indicating less single capillaries but higher branched networks. HUVEC-ASC co-cultures displayed similar effects.

**Conclusion:** Endothelial cells and ASC from putative autologous tissue sources were able to form highly branched capillary networks and thus are promising tools for the generation of fully autologous pre-vascularized fibrin-based vascular grafts.

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**Pericytes Upregulate Vasoprotective Genes Under Shear Stress**

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**Introduction:** Atherosclerosis is the key underlying pathologies for coronary artery disease and peripheral artery disease. The initiation of an atherosclerotic lesion, is the formation of a fibrous cap directed by myofibroblasts. Pericytes residing in the media and adventitia of a vessel own the potential to differentiate into myofibroblasts. As it is known that shear stress induces atherosclerotic lesions, nothing is known about its impact on pericytes. We investigate the effect of shear stress on pericyte to myofibroblast differentiation.

**Methods:** Pericytes (HVBP), endothelial cells (HUVEC) or co-cultures were seeded into flow chambers and subjected to laminar flow (10 dyn, 30 dyn) or static conditions for 48h \((n = 3 / \text{group})\). Samples were analysed for the proteases TIMP3 and ADAMTS-1 by qPCR and western blot. In addition, IF staining of both cell types (f-actin, VE-cadherin) was performed. In a new established 3D-method pericytes and HUVECs could be seeded into different compartments resulting in a subjection to flow for HUVECs and a subjection to stretch for pericytes.

**Results:** HUVECs aligned in direction of flow, pericytes subjected to direct shear stress revealed an opposite behaviour aligning almost perpendicular. HUVECs upregulated ADAMTS-1 \((p < 0.001)\) on RNA and protein level, pericytes showed a slight ADAMTS-1 protein decrease. Pericytes upregulated TIMP3 \((p < 0.05)\) under increased shear stress, while HUVECs did not show any TIMP3 in western blots and almost undetectable expression in qpcr. When co-cultures were subjected to the same conditions TIMP3 expression was already detectable under static conditions but downregulated \((p < 0.01)\) when subjected to flow. Static co-cultures showed less ADAMTS-1 expression than each cell type alone. With shear stress ADAMTS-1 showed a retarded increase on RNA level and decreased on protein level. When both cell types were applied to the 3D-system TIMP3 resembled pericyte monocultures with a TIMP3 increase with increasing shear stress.

**Conclusion:** Shear stress induces extracellular matrix turnover in pericytes and leads to upregulation of proteases