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.

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 immunochemistry. 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.

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 ($n = 3$ / 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 blot 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

known to stabilize the vascular wall highlighting the important role pericytes play in vascular homeostasis. In addition we show for the first time that pericytes do not only react to stretch but are sensitive to direct shear-stress.

Effect of Intensified Decellularization of Equine Carotid Arteries on Scaffold Biomechanics and Cytotoxicity

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Introduction: Decellularized equine carotid arteries (dEAC) are suggested to represent an alternative for alloplastic vascular grafts in haemodialysis patients to achieve vascular access. Recently it was shown that intensified detergent treatment completely removed cellular components from dEAC and thereby significantly reduced matrix immunogenicity. However, detergents may also affect matrix composition and stability and render scaffolds cytotoxic.
Methods: Intensively decellularized carotids (int-dEAC) were evaluated for their biomechanical characteristics (suture retention strength, burst pressure and circumferential compliance at arterial and venous systolic and diastolic pressure), matrix components (collagen and glycosaminoglycan content) and indirect cytotoxicity (WST-8 assay) and compared with native (n-EAC) and conventionally decellularized carotids (con-dEAC).
Results: Both decellularization protocols led to comparable reduction of matrix compliance (venous: 32.2% and 27.4% of n-EAC; $p < 0.01$ and arterial: 26.8% and 23.7% of n-EAC, $p < 0.01$) but had no effect on suture retention strength and burst pressure. Matrix characterization revealed unchanged collagen contents but a 39.0% (con-dEAC) and 26.4% (int-dEAC, $p < 0.01$) reduction of glycosaminoglycans, respectively. Elastine fibres were scattered and less wavy in both dEAC. Cytotoxicity was not observed in either dEAC matrix.
Conclusion: Thus, even intensified decellularization generates matrix scaffolds highly suitable for vascular tissue engineering purposes, e.g. the generation of haemodialysis shunts.

Impact of Thoracic Endovascular Aortic Repair on Pulsatile Aortic Changes

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Introduction: The thoracic aorta experiences high hemodynamic forces and shows significant aortic pulsatile changes during the cardiac cycle. Thoracic endovascular aortic repair (TEVAR) may cause modifications to this dynamic condition, which may vary based on the aortic disease. Analysis before and after TEVAR, may help to evaluate the impact of stent-grafts on aortic pulsatile changes and its implications on post-TEVAR thoracic aortic behaviour.
Methods: Custom developed software and dynamic CT imaging were used to quantify aortic radial expansion and elongation during the cardiac cycle, together defined as aortic pulsatile changes. Through the assessment of the aortic vessel centreline, diameter and area changes were measured at the level of the sinotubular junction (level A), 1 cm proximal to the brachiocephalic trunk (level B), left subclavian artery (LSA, level C), 10 cm distal to LSA (level D), 20 cm distal to LSA (level E), and celiac bifurcation (level F) (Figure 1). Two patients treated with TEVAR for type B aortic dissection, of whom one affected by Marfan syndrome, one with thoracic aortic aneurysm and one healthy control subject were analysed. Aortic elongation changes, including length ascending aorta (L1), length aortic arch (L2), length descending aorta (L3), and total length (L) (Figure 1), were measured pre- and post TEVAR.
Results: In all patients two stent-grafts were implanted. Pre- and post-operative radial expansion and elongation changes were visualised during the cardiac cycle. Pre-operative aortic pulsatile changes were more evident in the patient with Marfan syndrome, in particular in the ascending aorta. After stent-graft placement, a trend of overall increased aortic pulsatile changes was observed, with aortic elongation marked proximally to the stent-graft (Figure 2).
Conclusion: The aortic pulsatile changes were overall increased after TEVAR, in particular aortic elongation proximally to the stent-graft. This study represents an initial investigation for understanding the impact of TEVAR on both aortic elongation and radial expansion. Further studies are warranted to understand if these observations may have implications for patient selection, stent-graft sizing, design, durability, and prevention of TEVAR related complications.

CCL5-dependent Mediation of Transplant-induced Atherosclerotic Lesion Formation in the Aorta

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Introduction: The CCL5 chemokine plays an active role in the initiation of inflammation, and by recruiting monocytes to sites of atherosclerotic lesion growth is critically involved in atherosclerosis. A function of CCL5 in circulating cells versus resident vessel wall cells in atherosclerosis within transplanted aortic segments has not yet been examined.
Methods: We have orthotopically transplanted infrarenal abdominal CCL5−/− Apoe−/− aortic segments into Apoe−/− mice and Apoe−/− aortas in CCL5−/− Apoe−/− mice ($n = 4$-6 mice) (anastomosis time 22 min). After 4 weeks, the intimal plaque size in the region of the transplanted aorta was analyzed in serial sections, and the plaque macrophage assessed by immunohistochemical staining.
Results: Deficiency of CCL5 in vascular cells of the transplanted segment (transplantation of CCL5 Apoe−/− aortas into Apoe−/− mice) entailed a reduction in the formation of atherosclerotic plaques and the accumulation of macrophages, compared to the deficiency of CCL5 in circulating