Conclusions: The AVF-model, which resembles the AVF configuration most frequently used in humans, shows that despite substantial outward remodeling, progressive stenotic lesions develop as a result of rapid neointimal hyperplasia in the venous outflow tract. Similar to failed human AVFs, the neointimal hyperplasia is mainly composed of α -sma positive cells. These lesions make this model suitable for intervention studies using e.g. genetically modified mice. We conclude that this murine AVF-model is a good addition to the AVF animal model arsenal.

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The Effect of Temporal Variation in Wall Shear Stress on the Remodeling of Arteriovenous Fistulae

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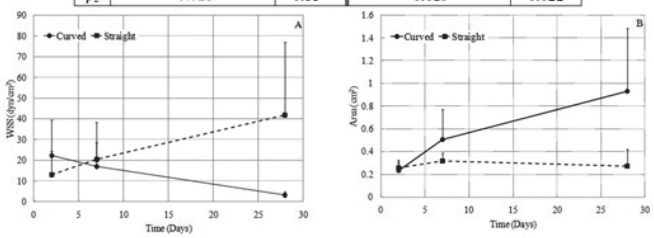
Background: Non-maturation of arteriovenous fistulae (AVF) is in many ways the "Achilles Heel" of hemodialysis. The surgical configuration of the AVF and the subsequent wall shear stress (WSS) are key players in the remodeling of the AVF. This study aimed to investigate the temporal effect of WSS on the maturation of AVFs created in two different configurations.

Methods: AVFs were created between the femoral artery and vein of three pigs in a curved (n=3) and straight (n=3) configuration. Reconstructed geometry of the AVF obtained from CT-scans and flow data from Doppler ultrasound were utilized to numerically evaluate WSS at 2D (D: days), 7D, and 28D post-surgery. Time dependent WSS-area data was regressed using a random effects model: Area = β0 + β1time + β2ΔWSS/Δtime, where βi and Δ were the regression coefficients and the gradient, respectively. A p-value < 0.05 indicated statistical significance.

Results: For the curved AVF, the slope of temporal gradient of WSS (-0.019) had a statistically significant effect (p = 0.022) on the dilation of the vein, while it was not significant for the maturation of the straight AVF (p = 0.53). Also, time had a positive effect (β1 = 0.337) on the maturation of the curved AVF (p < 0.05), while it had a negative effect (β1 = -0.071) for the straight AVF (p < 0.05).

Conclusions: Our results document a temporal linkage between an increase in diameter and a decrease in WSS in the curved AVF, with an opposite interaction in the straight AVF. Creation of an AVF in a surgical configuration which results in a favorable linkage between WSS and diameter could result in a significant improvement in AVF patency rates.

	Straight Fistula		Curved Fistula	
	regression coefficients	p-value	regression coefficients	p-value
β_0	0.498	0.041	-0.166	0.041
β_1	**-0.071**	<.0001	**0.337**	<.0001
β_2	-0.025	**0.53^a**	**-0.019**	**0.022**



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FR-PO1932

Treatment with Recombinant Human Type 1 Pancreatic Elastase (PRT-201) Does Not Alter the Safety of Angioplasty in a Porcine Arteriovenous Graft Model

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Background: PRT-201 is being developed as a treatment for newly created arteriovenous grafts (AVGs) and fistulas to promote access patency. It is not known if degrading elastin fibers in the access outflow vein impacts the safety of subsequent angioplasty procedures.

Methods: Eleven male Yorkshire swine underwent bilateral femoral artery to vein ePTFE grafts insertion (Bard Carboflo 4-6 mm taper) followed by application of PRT-201 6 mg (n=11) or vehicle (n=11) to the external surface of the venous anastomosis and outflow vein. Acute effects were measured using digital photography. At 28 days, AVGs underwent angiography, measurement of graft blood flow (Transonic ReoCath), and angioplasty (Bard Conquest 8mm x 4cm). The animals were euthanized and anastomoses/veins were excised for histology.

Results: Two animals were euthanized early: one due to intestinal torsion, the other due to bilateral AVG occlusion. PRT-201 treated vessels (n=11) increased in diameter by 12 ±14% (p=0.01). In the nine animals surviving to Day 28, 17 of the 18 AVGs had some anastomotic and venous stenosis, one was occluded. Stenosis was > 50% for 5 of 8 PRT-201 and 6 of 9 of vehicle. In this study there were no significant differences in average and minimum lumen diameters and blood flow. Angioplasty was successful in all cases resulting in significant increases in lumen diameter and blood flow. The pressures required to efface stenoses were similar between PRT-201 (10.5±2.6 atm) and vehicle (10.2±3.1 atm). No venous ruptures were documented even after a final inflation of 20atm held for 30sec. Histopathology of the excised veins/anastomoses demonstrated elastin degradation by PRT-201 and a trend to increased mean vein (+18%) and lumen (+26%) areas and decreased mean neointimal area (-25%) for PRT-201 vs. vehicle. There was no apparent adverse effect of PRT-201 with respect to fibrosis, endothelialization, inflammation, and wound healing.

Conclusions: In comparison to vehicle, PRT-201 applied to the venous anastomosis and outflow vein immediately following AVG creation did not impair the safety of subsequent angioplasty.

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FR-PO1933

Prospective Clinical Investigation of Vascular Structural and Functional Changes Following Hemodialysis Vascular Access Surgery

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Background: Vascular access (VA) complications represent a major cause of morbidity and hospitalization in hemodialysis (HD) patients and are the major limitation of HD treatment. The ARCH project (EU FP7-ICT) aims to computational modelling tools for surgical planning of VA. These tools are developed using ultrasound (US) measurements and multi-scale computational model of blood flow (BF). Given the high inter-subject variability, the modelling tools must be patient-specific and need calibration and validation using clinical data.

Methods: To this purpose, a prospective observational clinical study has been conducted to collect anatomic, physiologic and clinical data to quantify structural-functional relation between patient vasculature and and its changes after surgery. 93 consecutive patients with ESRD awaiting VA creation have been enrolled in the study (63/30 M/F, age 62Y [18-85]). Pre- and post-operative clinical data and US measurements have been collected for a two years period.

Results: Mean artery diameter in distal (radial artery, RA) and proximal (brachial artery BA) VA and BF before (V0) and after surgery (V1-V4) are as follows.

Visit	time	N	RA Diam mm	RA BF ml/min	N	BA Diam mm	BA BF ml/min
V0	0	52	2.7±0.6	39±33	37	4.2±0.8	89±45
V1	1d	42	3.6±0.9	549±418	22	4.6±0.8	890±554
V2	1w	41	4.0±1.0	676±430	32	4.7±0.7	1288±606
V3	6w	41	4.4±1.1	933±472	28	5.0±0.8	1760±629
V4	>8w	32	4.5±1.1	1057±437	23	5.4±1.0	2229±985

Data are mean+SD. All patients in V4 were on HD treatment.

A large variability in both arterial size and BF was observed during VA maturation. As expected, larger changes in artery diameter were observed in distal than in proximal VA while BF increase was higher in proximal as compared to distal VA.

Conclusions: The clinical data set obtained is currently used to calibrate the model and to simulate BF before and after surgery to investigate major determinants of BF in VA and to predict flow related VA complications.

FR-PO1934

Computational Model for Simulation of Vascular Adaptation Following Hemodialysis Vascular Access Surgery

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Background: Up to 50% of surgical procedures for autologous vascular access (VA) in hemodialysis (HD) patients result in inadequate increase in blood flow volume (BFV). The required increase in BFV after arteriovenous anastomosis of native vessels depends on the ability of the vasculature to dilate and remodel. These changes ultimately determine VA maturation and subsequent use for HD treatment. We have previously reported changes in radial artery (RA) diameter and BFV over time after end-to-end distal fistula creation in 28 ESRD patients. The aim of the present study was to use these data to develop and validate a 1-D computational model of arterial and venous circulation able to simulate changes in vessel diameter in response to surgically induced increase in BFV.

Methods: Blood vessel dimensions and elastic properties have been assumed according to a set of rules defined for generation of patient-specific vascular network models that are dependent on gender, age and body surface area. Arterial and venous diameters, as well as BFV, have been calculated before and after VA creation by assuming constant peak wall shear stress in the arm vasculature.

Results: The best comparison between experimental measurements and computed results of RA diameter and BFV during VA maturation was obtained for a reference arterial peak wall shear stress of 40 dynes/cm2. These results are as follows.

	Time (days)	t=0	t=10	t=40	t=100
RA diameter (mm)	Measurements	2.4	3.7	4.1	4.4
	Computed results	2.5	3.1	4.0	4.3
RA blood flow (ml/min)	Measurements	18	329	476	584
	Computed results	18	380	480	578

t = 0, before surgery. Values are mean of 28 patients.