Vasa

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Vascular Medicine

18. Unionstagung der Schweizerischen
Gesellschaften für Gefässkrankheiten gemeinsam
mit der Schweizerischen Gesellschaft
für Ultraschall in der Medizin Sektion Gefässe

18^e Congrès de l'Union des Sociétés Suisses des
Maladies Vasculaires en collaboration avec la
Société Suisse d'Ultrasons en Médecine Section
Vaisseaux

1. – 3. November 2017 / 1 – 3 novembre 2017
Music & Convention Centre 2m2c, Montreux

Union of Vascular Societies of Switzerland
Union Schweizerischer Gesellschaften für Gefässkrankheiten
Union des Sociétés Suisses des Maladies Vasculaires
Unione delle Società Svizzere di malattie vascolari
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PD Dr. med. Jos C. van den Berg
Servizio di Radiologia Interventistica
CENTRO VASCOLARE TICINO
Ospedale Regionale di Lugano, sede Civico
Via Tesserete 46 I 6903 Lugano
jos.vandenberg@eoc.ch

Organisation

Meister ConCept GmbH
Bahnhofstrasse 55
5001 Aarau
T +41 62 836 20 90
F +41 62 836 20 97
unionstagung@meister-concept.ch

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Congress Organisation
Bahnhofstrasse 55
5001 Aarau
T +41 62 836 20 90
F +41 62 836 20 97
unionstagung@meister-concept.ch

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Freie Mitteilungen / Communications libres

FM 1.1

Limb salvage in patients with acute ischemia due to thrombosed popliteal artery aneurysm

P. Kissling, S. Jungi, C. Kümmerli, D. Becker, T. R. Wyss, J. Schmidli (Bern)

Objective: Acute ischemia due to thrombosed popliteal artery aneurysm (PAA) is associated with high incidence of limb loss. The aim of this study was to analyze the rate of limb salvage in patients with acute ischemia due to thrombosed popliteal artery aneurysm.

Methods: Retrospective analysis of all consecutive patients who underwent immediate surgery for acute limb ischemia due to thrombosed popliteal artery aneurysm between January 2007 and December 2016 at a tertiary referral centre. Perioperative and long-term outcomes were analyzed.

Results: Fifty-one consecutive 51 patients (48 males, median age 75 years, range 46–97) were included. The median size of the PAA was 33mm (range 13–80mm). According to the Rutherford classification of acute limb ischemia, 20 (39%) patients presented with a category 2a, 20 (39%) with a category 2b and 11 (22%) with a category 3. Four patients (8%) underwent primary major amputation. Forty-three (84%) patients underwent great saphenous vein bypass. A 1-vessel runoff was present in 27/47 (57%) patients. Intraarterial thrombolysis was used in 2/51 (4%) patients preoperatively and 17/51 (33%) patients intraoperatively.

Compartment syndrome occurred in 14/47 (30%) patients. Thirty-day major amputation rate after revascularization was 8% (four patients). Overall, 30-day major amputation rate was 16% (eight patients). Thirty-day mortality was 4% (two patients).

Mean clinical follow-up was 37 months. No major amputation was necessary. Estimated four-year cumulative survival was 62%. One-year primary and secondary patency rate was 85% and 91%, respectively. Estimated 4-year primary and secondary patency rate was 77% and 88%, respectively. Seven patients underwent eight interventions to salvage a failing graft and three patients underwent five redo bypass procedures due to bypass occlusion.

Conclusion: Successful surgical revascularization in acute limb ischemia in patients with thrombosed popliteal artery aneurysm leads to high rate of long-term limb salvage, despite poor runoff. Even in severe ischemia, a revascularization attempt can be limb saving.

FM 1.2

Erfahrungen mit der perkutanen AngioVac®-Thrombektomie bei ilio-kavaler und atrialer Thrombose

T. Pfammatter, N. G. Nagaraj, G. Puippe, B. Amann-Vesti, M. Lachat (Zürich)

Objective: Das AngioVac®-System (Angiodynamics, USA) besteht aus einer Aspirations- (22 Fr) und einer Infusionskanüle (18 Fr.), die extrakorporell mit einer Pumpe (mini-ECC, Sorin, I) verbunden sind. Letztere generiert den Sog zur Thrombenaspiration. Die Thromben werden durch Filterung aus diesem veno-venösen Bypass entfernt. Ziel der Studie ist über unsere erste AngioVac®-Thrombektomien zu berichten.

Methods: Zwischen März 2015 und Dezember 2017 wurden 7 PatientInnen (5 Frauen, 2 Männer; 27 bis 71 jährig, Durchschnittsalter = 53 J.) thrombektomiert. 5 Pat. hatten ilio-kavale und 2 eine rechts-atriale Thromben, die sich innerhalb 6 Wochen manifestiert hatten. Ursache für die Thrombose waren Cavafilter (n = 2), zentrale Infusions- oder Oxygenations-Katheter (n = 2), vorangegangene Cava-Operationen (n = 2) und Thrombophilien (n = 2). 4/7 Pat hatten einen positiven präinterventionellen Lungenembolie-Nachweis. Eine Lysetherapie war bei 5/7 Pat kontraindiziert. Die Thrombektomien erfolgten in Intubationsnarkose (n = 6) oder moderater Sedation (n = 1) durchleuchtung (n = 5) – oder echokardiographie (= 2) – gesteuert.

Results: Eine komplette Thrombektomie gelang bei 4/5 der ilio-kavalen Thrombosen. Bei 1 Pat. mit Thrombophilie und anamnestisch wiederholten thrombo-embolischen Ereignissen mussten zusätzlich Venen-stents platziert werden. Nur bei einer der beiden Pat mit flotierenden atrialen Thromben gelang die komplette Thrombektomie. Die andere wurde am Folgetag offen thrombektomiert. Alle Thrombektomien verliefen komplikationslos, insbesondere gab es keine de-novo Lungenembolien. Eine ilio-kavale Früh-rethrombosierung wurde bei 2/5 Pat beobachtet, wobei bei beiden eine Thrombophilie vorlag (HIT, F8 erhöht).

Conclusion: Bei Pat. mit frischen ilio-kavalen Okklusionen und Kontraindikation zur medikamentösen Thrombolyse stellt die AngioVac-Thrombektomie eine wirksame therapeutische Neuerung dar. Nach unserer Erfahrung muss die Indikation bei Pat. mit einer Thromboseneigung eng gestellt werden.

FM 1.3

Results of primary stenting for the treatment of de novo long lesions of the superficial femoral artery

K. Villat, C. Dubuis, L. Briner, F. Saucy, J.-M. Corpataux, S. Déglise (Lausanne)

Objective: Endovascular therapies are increasingly used as first choice for the treatment of long lesions of the superficial femoral artery (SFA), classified as TASC C and D. Many studies confirmed this strategy with excellent outcomes at short-term. However, due to heterogeneity in the studies regarding the type of lesions and the material used, no strong guidelines exist. The aim of this study is to report our experience in the treatment of long lesions (>15 cm) of the SFA with primary stenting.

Methods: Retrospective analysis of data retrieved from our Department between January 2012 and December 2014 was done. All consecutive patients with primary stenting of long (> 15 cm) de novo lesions of the SFA were included. Endpoints were patency rates, postoperative complications and re-interventions.

Results: During the study period, 70 limbs in 66 patients have been treated. There were 36 men and 30 women, with a mean age of 74 years old (range 51–94). Indications were critical limb ischemia in 59% of patients and claudication in 49%. The majority (73%) of the lesions were occlusions. The mean length of the lesions was 173 mm ± 25. A total of 123 stents have been implanted, with a majority of self-expanding stents (93.5%). During the mean follow-up of 590 days (range 1–1512), 19 occlusions occurred (27%) and 38 vascular reinterventions have been performed. Moreover, 5 major amputations were required. The estimates of primary and secondary patency rates at 6, 12, 24 and 36 months were 78%, 71%, 59%, 41% and 86%, 82%, 80%, 68%, respectively. Limb salvage rates at 12, 24 and 36 months were 93%, 90% and 90%. Survival rates were 98%, 92% and 85%.

Conclusion: In long lesions of the SFA, endovascular therapy with primary stenting seems to offer good results especially in the short-term. After the first year, re-interventions are required to reach acceptable secondary patency rate. Stenting remains the endovascular therapy of choice, while waiting for more results about eluting technology.

FM 1.4

Late rupture after endovascular aortic aneurysm repair: analysis of cause, treatment and outcome

V. Makaloski¹, L. Meuli², P. Kissling¹, D. Becker¹, T. R. Wyss¹, J. Schmidli¹ (Bern, ²St. Gallen)

Objective: Endovascular aneurysm repair (EVAR) is being used to treat abdominal aortic aneurysm (AAA) to prevent rupture. Late rupture after EVAR has a low incidence but entails severe complications. We describe our single-center experience with late aneurysm rupture after EVAR.

Methods: In this single-center retrospective observational study, we analyzed all consecutive patients diagnosed with AAA rupture

occurring > 30 days secondary to elective EVAR performed between January 2001 and December 2012. Cause, treatment and outcome were assessed.

Results: A total of 251 elective EVARs were performed. Eleven (4.4%) patients (10 males) with a median age of 82 years (range 58–91) experienced late rupture. Median time interval between initial EVAR and rupture was 63 months (range 32–119) and between last follow-up and rupture was 33 months (range 2–78). Four type Ia, five type Ib and two type III endoleaks were the causes of rupture. Retrospectively, four patients had a known endoleak at the last follow-up before rupture, two type Ia and two type II.

Six patients underwent urgent open repair, two endovascular repair and three were treated conservatively. Thirty-day mortality was 27% (3/11): two conservatively treated and one patient after open repair. Median follow-up after rupture was 12 months (range 1–21 months). During follow-up three patients died, two after three months and one after 20 months, all of them due to cardiopulmonary failure. No aortic related re-intervention was observed during follow-up. Seven patients had poor surveillance compliance.

Conclusion: Endoleaks type I and III appear to be main causes of late aneurysm rupture after previous endovascular repair. Therefore, intervention is recommended once an endoleak type I or III is detected. Time to rupture is unpredictable and adherence to long-term post-EVAR surveillance seems to be essential.

FM 1.5

Innovation: Darstellung von Mikroaggregaten in der Hochfrequenzsonographie als Indikatoren der venösen Insuffizienz

J. C. Ragg (Zürich)

Objective: Während die Spätstadien der „chronisch“ venösen Insuffizienz gut bekannt sind, bestehen noch Lücken der Erklärung zwischen den Faktoren der hereditären oder erworbenen Rezeptormodifikationen, der Wandbelastung durch Druckanstieg, Dehnung und Scherstress sowie den histologisch nachgewiesenen entzündlichen Infiltraten. Mittels hochauflösendem Ultraschall können heute nicht nur Klappenstrukturen, sondern auch Mikroaggregate dargestellt werden, die im Gegensatz zum temporären „Sludge“ nicht bewegungs- bzw. flussvariant sind.

Methods: 45 Patienten (21 f, 11 m; 32–58 J.), darunter 22 Sitz- und 12 Stehberufler mit unauffälligem Routinebefund einer V. saphena magna am Oberschenkel wurden der Analyse ausgewählter Venenklappen (n = 120) mit hochauflösenden Ultraschallgeräten (HRU, 8–16 MHz, peak bis 40 MHz, B-Flow) unterzogen. Kriterien waren neben Erkennbarkeit, Form und Dicke der Segel insbesondere das Vorhandensein von Mikroaggregaten und deren Resistenz gegenüber Flusserhöhungen durch Bewegung oder externe Kompression. Im Falle positiver Befunde wurden in Teilkollektiven Veränderungen nach A) Erstversorgung mit Kompressionsstrümpfen (MKS; 3 Monate KKL 1, n = 12) oder B) Flavonoiden (Daflon 500, 2 x 500 mg/d, 3 Monate, n = 6) untersucht.

Results: Nichtmobilisierbare („persistierende“) Mikroaggregate wurden im Sinusbereich von 47/120 „gesunden“ Venenklappen (39,1%) gefunden, dabei signifikant häufiger bei Klappen von Steh- und Sitzberuflern (87/96; 90,6%). Nach Erstanwendung von MKS fanden sich in 21/26 kontrollierten Klappen (80,8%) sichtbare Verän-

derungen im Sinn reduzierter Aggregatmengen. Nach Daflon wurde eine Reduktion der Aggregate in 9/13 kontrollierten Klappenregionen (69,2%) gesehen.

Conclusion: Die Beobachtungen von Klappenregionen im B-Flow-Modus legt nahe, dass es in der Addition von Phasen mit unzureichendem Fluss zur Bildung zellulärer Aggregate im Sinusbereich kommt, die Ursache entzündlicher Veränderungen sein können. Ein potentieller präventiver Nutzen konnte in ersten Pilotserien sowohl für Kompressionsstrümpfe als auch für Flavonoide nachgewiesen werden. Dies nährt die Hoffnung, mit dem Kriterium der Mikroaggregate in der HRU ein Instrument zur Leistungsbeurteilung therapeutischer Maßnahmen entwickeln zu können. Die nächsten Studien sehen zytologische und histologische Untersuchungen der Aggregate und Klappen vor.

FM 1.6

Evaluierung eines neuartigen Folienkompressionsverbandes bei großen oberflächlichen Varizen – Bericht über die zweite Pilotstudie

J. C. Ragg (Zürich)

Objective: Große oberflächliche Varizen werden bei qualitätsorientierter Strategie meist mittels Phlebektomie behandelt, da die Schaumverödung zwar einfach und weniger invasiv ist, jedoch oft trotz leitliniengerechter Kompression mit nachteiligen Symptomen (Verödungsreaktionen) und Verfärbungen einhergeht. Ein neuartiger Folienkompressionsverband (FKV), wurde nun in einer erweiterten Pilotstudie hinsichtlich seiner Wirksamkeit nach Schaumverödungen großer Varizen untersucht

Methods: 354 sukzessive Patienten (23 – 74 J.) mit 450 Beinen mit oberflächlichen Varizen, 5–16 mm Ø (MW: 7.9 mm Ø) und Eignung für eine Schaumverödung (Aethoxysklerol 1%) wurden in die Studie eingeschlossen. Es wurden Prototypen eines FKV (Venartis Inc./3M) eingesetzt, mit einem selbstklebenden, transparenten und dampfdurchlässigen Polymerfilm aus elastischem Polyurethan von 18m Dicke (Venartis Inc./3M). Die Beine wurden in 6 Gruppen mit ähnlicher Durchmesser-Verteilung ($\pm 0,3$ mm) randomisiert und erhielten FKV für 14 oder 28 Tage, oder FKV mit zusätzlichem medizinischen MKS KKL. 2 für 14 bzw. 28 Tage, oder MKS allein für 14 oder 28 Tage. Klinische, sonographische und fotografische Verlaufskontrollen erfolgten nach 2, 4 und 8 Wochen.

Results: Während der 8-wöchigen Kontrollphase wurden symptomatische Entzündungsreaktionen sowie Verfärbungen der MKS-Gruppe in 62,5% bei 14 Tagen Tragezeit gesehen und in 51,3% bei MKS für 28 Tage. Unter FKV reduzierten sich die Symptome auf 9,3% bzw. 4,7% d.F. (statistisch hochsignifikant, $p < 0.01$). Der Tragekomfort, beurteilt durch die Patienten auf einer subjektiven Skala von 0–10, war am höchsten mit 9.1 für den FKV (14 d) und am niedrigsten mit 4.6 für alleinigen MKS (28 d). Es wurden keine relevanten folienbezogenen Komplikationen beobachtet.

Conclusion: Der untersuchte Folienverband stellt eine effektive und sichere Kompressionsmodalität dar, die die Regression von schaumbehandelten oberflächlichen Varizen signifikant verbessert. Die Wirkung ist günstiger als die eines MKS KKL. 2. Kombinationen von MKS und Folienverband weisen eine maximale Effektivität bezüglich der Venenregression auf.

FM 1

Venous distension in patients with aneurysmatic arterial disease compared to the venous distension in patients with arterial occlusive disease and to healthy controls

C. Jeanneret-Gris, J. Bartelt (Bruderholz)

Objective: The aim of the study was, to assess venous distension in patients with aneurysmatic arteriopathy and in patients with peripheral arterial occlusive disease (PAOD) compared to venous distension in healthy subjects.

Methods: Measurements were carried out in 150 legs in 79 patients, 27 with an arterial aneurysm disease, 26 with peripheral arterial occlusive disease (PAOD) and 26 subjects without AAD or PAOD. The aortic diameter in Patient with AAD had to be > 3 cm, for the popliteal artery aneurysm a diameter of > 1.5 cm was mandatory. Patients with arterial occlusive disease (PAOD) were included if their ankle brachial index (ABI) was < 0.9 and if they fulfilled the criteria of PAOD using the Edinburgh questionnaire. In the healthy control (HC) group age and gender matched persons without PAOD (ABI > 0.9) and without AAD were included. Venous diameter while normal breathing and during a standardized Valsalva Maneuver was assessed. The common femoral vein (CVF), the femoral vein (FV) and the great saphenous vein (GSV) were investigated in a longitudinal view in M-mode. The absolute and relative venous diameter differences (VD diff and VD diff %) were measured. Relative venous diameter difference in % was the quotient of venous diameter difference and maximal venous diameter.

Results: Absolute and relative venous diameter differences were significantly larger in the common femoral vein (CFV), great saphenous vein (GSV) and femoral vein (FV) in patients with AAD compared to patients with PAOD and also compared to healthy subjects. For example, the absolute median (IQR) venous diameters in cm measured in the right CFV of patients with AAD, PAOD and HC showed a p for AAD versus (vs) HC = 0.0016, p for AAD vs PAOD = < 0.0001 , p for PAOD vs HC = 0.14. Significant results were found all right and left veins investigated.

Conclusion: Venous diameter differences measured with a standardized Valsalva manoeuvre as a parameter of venous distensibility are significantly larger in patients with AAD compared to patients with PAOD and compared to healthy controls, The venous distension does not differ between HC and patients with PAOD. We assume a vessel - wall weakness in patients with AAD affecting not only the arterial but also the venous system. Future studies should address the issue of pathological ultrastructural changes of the arterial and venous wall explaining the increased wall distensibility in patients with AAD.

AAA

Descriptive Statistics

Inclusion criteria: Criteria 1 from AAA Distensibility

	age	Height	Weight	BMI
Mean	72.091	176.741	81.296	25.923
Std. Dev.	8.237	8.032	13.861	3.431
Count	27	27	27	27
Minimum	55.350	162.000	55.000	18.500
Maximum	92.470	192.000	114.000	33.310
# Missing	0	0	0	0
Median	73.930	178.000	80.000	25.860
IQR	11.298	13.500	17.500	3.040

PAVK

Descriptive Statistics

Inclusion criteria: Criteria 2 from AAA Distensibility

	age	Height	Weight	BMI
Mean	68.652	168.115	71.346	25.171
Std. Dev.	10.501	8.613	12.201	3.621
Count	26	26	26	26
Minimum	50.580	149.000	48.000	19.230
Maximum	86.530	186.000	90.000	33.120
# Missing	0	0	0	0
Median	68.115	168.500	73.000	24.590
IQR	17.880	9.000	14.000	5.310

Gesund

Descriptive Statistics

Inclusion criteria: Criteria 3 from AAA Distensibility

	age	Height	Weight	BMI
Mean	66.342	174.462	78.192	25.520
Std. Dev.	8.725	8.714	14.732	3.397
Count	26	26	26	26
Minimum	54.310	161.000	50.000	18.370
Maximum	88.600	193.000	106.000	31.070
# Missing	0	0	0	0
Median	65.075	173.000	79.500	25.780
IQR	7.730	10.000	23.000	5.040

AAA

Descriptive Statistics

Inclusion criteria: Criteria 1 from AAA Distensibility

	CFV re VD Diff means	CFV re VD diff %	CFV li Diff	CFV li Diff %
Mean	.504	32.164	.589	35.110
Std. Dev.	.204	11.618	.223	10.804
Count	27	27	27	27
Minimum	.190	11.830	.240	13.470
Maximum	1.060	58.940	1.060	54.300
# Missing	0	0	0	0
Median	.480	30.500	.590	37.820
IQR	.265	16.563	.317	17.590

PAVK

Descriptive Statistics

Inclusion criteria: Criteria 2 from AAA Distensibility

	CFV re VD Diff means	CFV re VD diff %	CFV li Diff	CFV li Diff %
Mean	.257	18.870	.343	22.760
Std. Dev.	.132	9.939	.159	9.872
Count	26	26	26	26
Minimum	.050	3.010	.080	4.330
Maximum	.610	41.180	.750	40.340
# Missing	0	0	0	0
Median	.240	19.170	.345	21.190
IQR	.190	13.430	.170	14.220

Gesund

Descriptive Statistics

Inclusion criteria: Criteria 3 from AAA Distensibility

	CFV re VD Diff means	CFV re VD diff %	CFV li Diff	CFV li Diff %
Mean	.324	19.952	.342	21.941
Std. Dev.	.188	9.334	.219	13.758
Count	26	26	26	26
Minimum	.050	3.660	.050	3.550
Maximum	.940	42.310	1.050	61.320
# Missing	0	0	0	0
Median	.290	19.790	.300	20.685
IQR	.170	9.980	.240	14.440

Unpaired Means Comparison for CFV re VD Diff means

Grouping Variable: AAA PAVK Gesund

Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value	95% Lower	95% Upper
AAA, GESUND	.179	51	3.328	.0016	.071	.288
AAA, PAVK	.247	51	5.211	<.0001	.152	.342
GESUND, PAVK	.067	50	1.496	.1410	-.023	.158

Group Info for CFV re VD Diff means

Grouping Variable: AAA PAVK Gesund

	Count	Mean	Variance	Std. Dev.	Std. Err
AAA	27	.504	.042	.204	.039
GESUND	26	.324	.035	.188	.037
PAVK	26	.257	.017	.132	.026

Unpaired Means Comparison for CFV re VD diff %

Grouping Variable: AAA PAVK Gesund

Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value	95% Lower	95% Upper
AAA, GESUND	12.212	51	4.209	.0001	6.387	18.038
AAA, PAVK	13.294	51	4.468	<.0001	7.321	19.267
GESUND, PAVK	1.082	50	.405	.6875	-4.289	6.453

Group Info for CFV re VD diff %

Grouping Variable: AAA PAVK Gesund

	Count	Mean	Variance	Std. Dev.	Std. Err
AAA	27	32.164	134.975	11.618	2.236
GESUND	26	19.952	87.132	9.334	1.831
PAVK	26	18.870	98.787	9.939	1.949

Unpaired Means Comparison for CFV li Diff

Grouping Variable: AAA PAVK Gesund

Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value	95% Lower	95% Upper
AAA, GESUND	.247	51	4.067	.0002	.125	.369
AAA, PAVK	.246	51	4.606	<.0001	.139	.353
GESUND, PAVK	-.001	50	-.022	.9828	-.108	.106

Group Info for CFV li Diff

Grouping Variable: AAA PAVK Gesund

	Count	Mean	Variance	Std. Dev.	Std. Err
AAA	27	.589	.050	.223	.043
GESUND	26	.342	.048	.219	.043
PAVK	26	.343	.025	.159	.031

Unpaired Means Comparison for CFV li Diff %

Grouping Variable: AAA PAVK Gesund

Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value	95% Lower	95% Upper
AAA, GESUND	13.168	51	3.884	.0003	6.361	19.976
AAA, PAVK	12.349	51	4.339	<.0001	6.636	18.063
GESUND, PAVK	-.819	50	-.247	.8062	-7.489	5.851

Group Info for CFV li Diff %

Grouping Variable: AAA PAVK Gesund

	Count	Mean	Variance	Std. Dev.	Std. Err
AAA	27	35.110	116.719	10.804	2.079
GESUND	26	21.941	189.275	13.758	2.698
PAVK	26	22.760	97.458	9.872	1.936

AAA

Descriptive Statistics

Inclusion criteria: Criteria 1 from AAA Distensibility

	FV re VD diff	FV re VD diff %	FV li VD diff	FV li VD diff %
Mean	.269	27.835	.227	24.734
Std. Dev.	.113	9.231	.120	9.111
Count	27	27	27	27
Minimum	.110	10.560	.050	7.460
Maximum	.540	51.330	.550	45.440
# Missing	0	0	0	0
Median	.250	27.490	.190	22.570
IQR	.152	9.655	.125	12.277

PAVK

Descriptive Statistics

Inclusion criteria: Criteria 2 from AAA Distensibility

	FV re VD diff	FV re VD diff %	FV li VD diff	FV li VD diff %
Mean	.124	15.113	.118	14.727
Std. Dev.	.075	8.220	.095	10.571
Count	26	26	26	26
Minimum	.010	1.000	0.000	0.000
Maximum	.270	32.730	.390	39.080
# Missing	0	0	0	0
Median	.115	13.805	.105	13.225
IQR	.110	11.140	.110	14.380

Gesund

Descriptive Statistics

Inclusion criteria: Criteria 3 from AAA Distensibility

	FV re VD diff	FV re VD diff %	FV li VD diff	FV li VD diff %
Mean	.113	13.657	.128	15.855
Std. Dev.	.070	7.796	.087	9.223
Count	26	26	26	26
Minimum	.030	4.910	.010	1.190
Maximum	.350	35.740	.410	41.950
# Missing	0	0	0	0
Median	.105	12.295	.115	14.360
IQR	.090	11.960	.090	10.580

Unpaired Means Comparison for FV re VD diff

Grouping Variable: AAA PAVK Gesund

Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value	95% Lower	95% Upper
AAA, GESUND	.156	51	6.016	<.0001	.104	.208
AAA, PAVK	.145	51	5.509	<.0001	.092	.198
GESUND, PAVK	-.011	50	-.536	.5946	-.051	.030

Group Info for FV re VD diff

Grouping Variable: AAA PAVK Gesund

	Count	Mean	Variance	Std. Dev.	Std. Err
AAA	27	.269	.013	.113	.022
GESUND	26	.113	.005	.070	.014
PAVK	26	.124	.006	.075	.015

Unpaired Means Comparison for FV re VD diff %

Grouping Variable: AAA PAVK Gesund

Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value	95% Lower	95% Upper
AAA, GESUND	14.178	51	6.030	<.0001	9.458	18.899
AAA, PAVK	12.722	51	5.291	<.0001	7.895	17.549
GESUND, PAVK	-1.456	50	-.655	.5152	-5.919	3.007

Group Info for FV re VD diff %

Grouping Variable: AAA PAVK Gesund

	Count	Mean	Variance	Std. Dev.	Std. Err
AAA	27	27.835	85.215	9.231	1.777
GESUND	26	13.657	60.782	7.796	1.529
PAVK	26	15.113	67.575	8.220	1.612

Unpaired Means Comparison for FV li VD diff

Grouping Variable: AAA PAVK Gesund

Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value	95% Lower	95% Upper
AAA, GESUND	.099	51	3.436	.0012	.041	.157
AAA, PAVK	.109	51	3.645	.0006	.049	.168
GESUND, PAVK	.010	50	.380	.7054	-.041	.060

Group Info for FV li VD diff

Grouping Variable: AAA PAVK Gesund

	Count	Mean	Variance	Std. Dev.	Std. Err
AAA	27	.227	.014	.120	.023
GESUND	26	.128	.008	.087	.017
PAVK	26	.118	.009	.095	.019

Unpaired Means Comparison for FV li VD diff %

Grouping Variable: AAA PAVK Gesund

Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value	95% Lower	95% Upper
AAA, GESUND	8.879	51	3.526	.0009	3.823	13.936
AAA, PAVK	10.008	51	3.696	.0005	4.572	15.443
GESUND, PAVK	1.128	50	.410	.6834	-4.398	6.655

Group Info for FV li VD diff %

Grouping Variable: AAA PAVK Gesund

	Count	Mean	Variance	Std. Dev.	Std. Err
AAA	27	24.734	83.004	9.111	1.753
GESUND	26	15.855	85.060	9.223	1.809
PAVK	26	14.727	111.752	10.571	2.073

GSV
AAA

Descriptive Statistics

Inclusion criteria: Criteria 1 AAA from AAA Distensibility 20042017

	GSV re VD diff	GSV re VD diff %	GSV li VD Diff	GSV li VD Diff %
Mean	.124	21.342	.165	26.305
Std. Dev.	.060	7.576	.091	10.383
Count	25	25	21	21
Minimum	.040	8.120	.030	7.000
Maximum	.240	34.680	.360	51.480
Median	.130	22.300	.140	24.630
IQR	.112	11.680	.108	12.905

PAVK

Descriptive Statistics

Inclusion criteria: Criteria 2 PAVK from AAA Distensibility 20042017

	GSV re VD diff	GSV re VD diff %	GSV li VD Diff	GSV li VD Diff %
Mean	.052	11.662	.052	11.231
Std. Dev.	.031	5.971	.033	6.206
Count	26	26	26	26
Minimum	.010	1.780	0.000	0.000
Maximum	.120	24.130	.140	26.190
Median	.050	11.615	.045	9.835
IQR	.040	7.610	.030	7.950

Gesund

Descriptive Statistics

Inclusion criteria: Criteria 3 Gesund from AAA Distensibility 20042017

	GSV re VD diff	GSV re VD diff %	GSV li VD Diff	GSV li VD Diff %
Mean	.053	10.916	.057	12.156
Std. Dev.	.034	6.336	.029	6.278
Count	26	26	26	26
Minimum	0.000	1.490	0.000	0.000
Maximum	.130	23.770	.120	27.290
Median	.055	12.520	.050	10.815
IQR	.060	10.950	.040	8.650

Unpaired Means Comparison for GSV re VD diff

Grouping Variable: AAA PAVK Gesund

Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value	95% Lower	95% Upper
AAA, GESUND	.071	49	5.232	<.0001	.044	.098
AAA, PAVK	.072	49	5.395	<.0001	.045	.098
GESUND, PAVK	.001	50	.086	.9319	-.017	.019

Group Info for GSV re VD diff

Grouping Variable: AAA PAVK Gesund

	Count	Mean	Variance	Std. Dev.	Std. Err
AAA	25	.124	.004	.060	.012
GESUND	26	.053	.001	.034	.007
PAVK	26	.052	.001	.031	.006

Unpaired Means Comparison for GSV re VD diff %

Grouping Variable: AAA PAVK Gesund

Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value	95% Lower	95% Upper
AAA, GESUND	10.426	49	5.339	<.0001	6.502	14.350
AAA, PAVK	9.680	49	5.078	<.0001	5.849	13.510
GESUND, PAVK	-.746	50	-.437	.6640	-4.175	2.683

Group Info for GSV re VD diff %

Grouping Variable: AAA PAVK Gesund

	Count	Mean	Variance	Std. Dev.	Std. Err
AAA	25	21.342	57.403	7.576	1.515
GESUND	26	10.916	40.142	6.336	1.243
PAVK	26	11.662	35.648	5.971	1.171

Unpaired Means Comparison for GSV li VD Diff

Grouping Variable: AAA PAVK Gesund

Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value	95% Lower	95% Upper
AAA, GESUND	.108	45	5.694	<.0001	.070	.146
AAA, PAVK	.112	45	5.844	<.0001	.074	.151
GESUND, PAVK	.005	50	.542	.5905	-.013	.022

Group Info for GSV li VD Diff

Grouping Variable: AAA PAVK Gesund

	Count	Mean	Variance	Std. Dev.	Std. Err
AAA	21	.165	.008	.091	.020
GESUND	26	.057	.001	.029	.006
PAVK	26	.052	.001	.033	.006

Unpaired Means Comparison for GSV li VD Diff %

Grouping Variable: AAA PAVK Gesund

Hypothesized Difference = 0

	Mean Diff.	DF	t-Value	P-Value	95% Lower	95% Upper
AAA, GESUND	14.149	45	5.772	<.0001	9.212	19.087
AAA, PAVK	15.074	45	6.171	<.0001	10.155	19.994
GESUND, PAVK	.925	50	.534	.5956	-2.553	4.402

Group Info for GSV li VD Diff %

Grouping Variable: AAA PAVK Gesund

	Count	Mean	Variance	Std. Dev.	Std. Err
AAA	21	26.305	107.801	10.383	2.266
GESUND	26	12.156	39.408	6.278	1.231
PAVK	26	11.231	38.514	6.206	1.217

FM 2

Endovascular treatment for long steno-occlusive disease of femoro-popliteal arteries: a retrospective study

K. Oung, D. Imsand, R. Wutschert, A. Chouiter (Neuchâtel)

Objective: The aim of this study was to evaluate efficacy, safety, and midterm patency of long femoro-popliteal steno-occlusive disease (≥ 15 cm) treated by endovascular treatment in patients with intermittent claudication or chronic critical limb ischemia.

Methods: From January 2012 to March 2014, twenty patients (22 legs) were treated for TASC C (57%) and D (43%) femoro-popliteal lesions by angioplasty with provisional stenting (bare-metal self-expandable stent). The patients were followed for up to 12 months by Doppler ultrasound examinations, ankle-brachial index and assessments of Leriche and Fontaine class.

Results: Technical success was achieved in 100% of procedures. The one-year primary patency rate was 54%. Ten out of 22 legs underwent successful drug eluting balloon angioplasty because of endofibrotic in-stent restenosis. At twelve months, the primary assisted patency rate was 100%.

Conclusion: Percutaneous endovascular treatment of TASC C and D atherosclerotic disease of the femoro-popliteal arteries is a safe and clinically effective procedure. It offers a durable patency provided that patients obtain a close angiologic follow-up.

FM 3

Thrombophlebitis and thromboembolic events in a patient cohort undergoing small saphenous vein surgery

G. S. Heil, N. Steinmueller, K. Mouton, W. Mouton (Thun)

Objective: In our study the primary aim was to retrospectively assess the incidence of thrombophlebitis in a patient cohort that had undergone small saphenous vein (SSV) surgery due to chronic venous disease (CVD). The secondary aim was to assess the incidence of thromboembolic events (deep venous thrombosis and pulmonary embolism) within the patient cohort. The tertiary aim was to assess if the incidence of thrombophlebitis of SSV is influenced by age, gender, cardiovascular risk factors or malignant disease within this patient cohort.

Methods: Retrospectively, all patients who had undergone primary SSV surgery for symptomatic varicose veins and other forms of chronic venous disease (CVD) over a four year time span were included in this study. Diagnosis of SSV thrombophlebitis was made by means of patient history and preoperative duplex ultrasonography findings. Information about thromboembolic complications were taken from the patient history and radiological results. Preoperatively, the CEAP class was assessed for each limb. Cardiovascular risk factors, a history of malignant disease and a family history for CVD were recorded for all patients.

Results: 76 consecutive, unselected patients (91 legs) were included in this study. Thrombophlebitis was diagnosed in 28 patients (36.8%) (36 legs). Thromboembolic complications such as deep venous thrombosis and pulmonary embolism occurred in 11 of 76 patients (14.4%). All of these patients suffered from thrombophlebitis. It was found that the valve disease class correlated statistically significantly with the increasing C-class of CEAP (< 0.01). There was no statistically significant influence of age, gender, any of the cardiovascular risk factors or malignant diseases on the incidence of thrombophlebitis.

Conclusion: We conclude that studies on thrombophlebitis of the SSV and possible thromboembolic complications are rarely found in the literature. The morbidity associated with SSV insufficiency may be underestimated. Patients with known chronic SSV insufficiency should be carefully informed about thrombophlebitis and thromboembolic complications in order to avoid or early detect them and and its thromboembolic complications.

FM 4

Isolated mesenteric artery dissection – a case series

S. Jungi, S. Weiss, D. Becker, T. Wyss, R. Bühlmann, J. Schmidli (Bern)

Objective: Isolated mesenteric artery dissection is rare entity and treatment consensus guidelines do not exist. We aim to evaluate clinical presentation, management and outcome of patients with isolated mesenteric artery dissection.

Methods: All patients with either isolated celiac trunk (CT) and/or superior mesenteric artery (SMA) dissection treated at our department between January 2006 and December 2016 were analyzed retrospectively.

Results: We identified 11 isolated mesenteric artery dissections in nine patients. Four patients had isolated SMA and three had isolated CT dissection while one patient had concurrent SMA and CT dissection. One patient suffered from isolated SMA dissection followed by CT dissection two years later. Seven patients presented with abdominal pain. In the remaining patients, it was an incidental finding. Three patients had progressive abdominal pain with signs of intestinal ischemia leading to one open fenestration and patch plasty, one aorto-mesenteric bypass and one CT stenting. No bowel resection was necessary and all operated patients were asymptomatic thereafter and developed no postoperative complications. The remaining patients were rapidly asymptomatic under medical treatment with acetylsalicylic acid and oral anticoagulation for 3 months. Median follow-up was 20 months (range 3 – 125) and was performed by computed tomography or duplex sonography. Five patients had post-dissection aneurysms of the affected mesenteric artery but diameter was stable over time with no indication for treatment. No ruptures occurred.

Conclusion: Isolated mesenteric artery dissection is a rare entity and the natural course is mostly benign. Endovascular options should be considered in patients with progressive symptoms. Open surgical options remain second line treatment. Surveillance by ultrasonography is recommended in order to detect post-dissection aneurysm.

FM3. Figure I – Flow-chart of thromboembolic events (* one patient had both DVT and PE).

FM5

Association of serum hydrogen sulfide production with post-operative mortality in patients undergoing surgical revascularization

A. Longchamp, C. Dubuis, J. Longchamp, G. Sharma, C. Hine, W. King, M. Tao, F. Allagnat, S. Deglise, J.-M. Corpataux, C.-K. Ozaki, J.-R. Mitchell (Lausanne)

Objective: Hydrogen Sulfide (H₂S) is an endogenously produced gas with broad protective effects on the vascular system. Activities of enzymes that produce H₂S can also be measured in blood serum. Here, we aimed to determine the predictive value of circulating H₂S production with regard to survival following vascular surgery.

Methods: We measured serum H₂S production capacity using the

lead acetate method in 115 patients (mean age 69 years, male 67%) prior to undergoing carotid endarterectomy (n = 49), open lower extremity arterial revascularization (n = 44) or major leg amputation (n = 22) as well as in 20 control patients (mean age 68.4 years, male 65%). Given the Gaussian distribution of serum H₂S, we divided high (n = 57) versus low (n = 58) H₂S producing patients using the median as the cut-off. For comparison of continuous clinical, demographic variables, and H₂S, either Pearson or Spearman correlation testing was used depending upon the normality of distribution.

Results: Control patients that did not require cardiovascular surgery had the highest serum H₂S production capacity [mean ± SD (81 ± 13)]. Among patients that underwent surgery for vascular disease, preoperative serum H₂S production capacity was significantly lower in patients with mortality (Fig. 1A), [mean ± SD (53 ± 7); n = 20 all-cause mortality events during a 2 year follow up] than those alive [mean ± SD (57 ± 8)]. Furthermore, the percentage of survival in the low H₂S (defined as < median) was lower [6 months, 2 years (78 and 74)] com-

pared to high H₂S (defined as >median, Fig. 1B), 6 months, 2 years.

Conclusion: Serum H₂S production capacity was linearly correlated with mortality following surgical revascularization and may serve as an easily quantified measure with biological significance with regards to vascular health.

FM 6

Postoperative low on-treatment aspirin response in patients undergoing major aorta and peripheral open vascular surgery

C. Dubuis, F. Hadorn, F. Gronchi, J. F. Iglesias, L. Alberio, J.-M. Corpataux, C. Kern, C. Marcucci (Lausanne)

Objective: Patients undergoing vascular surgery are at the highest risk of postoperative cardiovascular complications. Most of these patients are chronically treated with daily low-dose aspirin for secondary prevention. Low on-treatment response to aspirin is associated with increased cardiovascular morbidity.

We hypothesized that the postoperative inflammatory reaction and thrombocytosis would reduce aspirin response.

Methods: 26 patients chronically treated with low-dose aspirin undergoing open vascular surgery were enrolled. Platelet count and platelet aggregation were measured daily from the day of surgery until the fifth postoperative day. Aggregation was measured by impedance aggregometry after activation with arachidonic acid (ASPI-test) on the Multiplate® analyzer.

Results: Platelet count and IA at baseline were 240 ± 78 G/L and 19 ± 3 AU respectively. Platelet count dropped significantly on postoperative days 1, 2 and 3 and returned to baseline on postoperative day 4. ASPI-test results were similar to baseline for the first 3 postoperative days and increased to 33 ± 4 on postoperative day 4. The number of aspirin

low responders increased from 11% on the day of surgery to 30% on day 4.

Conclusion: The increased platelet turnover between postoperative days 3 and 4 coincides with reduced response to aspirin. Aspirin insufficiently inhibits new platelets entering into circulation during postoperative thrombocytosis.

FM 7

Ten-years experience using cryopreserved allografts for distal bypass

S. Masmejan¹, C. Dubuis¹, C. Haller², F. Saucy¹, J.-M. Corpataux¹, S. Déglise¹ (¹Lausanne, ²Sion)

Objective: Nowadays, the prevalence of peripheral arterial disease reaches 20 %, especially in our ageing population. In long occlusions, the treatment of choice remains the venous distal bypass. However, the number of patients who have already been operated and/or in whom no veins are available is continuously growing. Is has been shown that distal prosthetic bypass is associated with bad outcomes in term of patency but also limb salvage and others solutions have to be proposed in this situation. The aim of this study is to report our 10-years experience of distal bypass using arterial cryopreserved allografts.

Methods: Retrospective analysis of data retrieved from our Department between January 2006 and December 2015 was done. All consecutive patients with distal bypass with arterial cryopreserved allografts coming from the European Bank in Brussels, Belgium were included. Endpoints were patency rates, postoperative complications and survival rate.

Results: During the study period, 47 bypasses have been performed in 43 patients. There were 16 men and 27 women, with a mean age of

FM 5. Figure.

77 years old (range 43–94). Indications were critical limb ischemia in 83% of patients, acute ischemia in 15% and popliteal aneurysm in the remaining 2% and 86% (37/43) of patients have already been operated on the same leg. Half of the distal anastomoses were performed on one of the tibial vessels. The mean length of operation was 172 minutes (range 74–407). In the post-operative period, 16 complications occurred (6 occlusion, 4 bleeding and 6 wound dehiscences) and required 14 re-interventions. Among them, there were 4 thrombectomies, 1 overbypass and 2 major amputations. During the mean follow-up of 844 days (range 98–2568), estimates of primary and secondary patency rates at 6, 12, 24 and 48 months were 64%, 50%, 46%, 28% and 84%, 73%, 65 and 45%, respectively. Limb salvage rates at 12, 24 and 60 months were 88%, 88% and 78%. Survival rates at 12, 24 and 60 months were 97%, 78% and 45%.

Conclusion: Despite a low rate of primary patency at 2 years, the secondary patency is acceptable and the limb salvage reached almost 90%. This is good considering the complex treated population, whom only 50% survived at 5 years. Considering these results, cryopreserved arterial allografts seem to be a suitable alternative for distal bypass in the absence of venous material.

FM8

Periaortitis de novo after Endovascular Aneurysm Repair and simultaneous obstructive pyelonephritis

D. Jaeger¹, D. Reitnauer¹, R. Tunesi¹, M. Krause², C. Medugno¹

(¹Frauenfeld, ²Münsterlingen)

Objective: Periaortic inflammation is a rare pathogenesis and has a number of possible causes, including trauma, infections and certain immune disorders or connective tissue diseases. The appearance of periaortic inflammation after EVAR is rarely described. We report on a case of a simultaneous (or following) appearance of a periaortic inflammation and an obstructive pyelonephritis caused by ureteral strictures.

Methods: Case Report.

Results: We report the case of a 74-year-old man who underwent EVAR for an asymptomatic, infrarenal abdominal aortic aneurysm and made an uncomplicated recovery. Routine follow-up CT scanning showed satisfactory positioning of the graft and no evidence of periaortitis. 6 Month after operation he subsequently presented in emergency department with fever, cough and fatigue. Routine blood tests revealed newly elevated serum creatinine level of 2.0mg/dL (estimated glomerular filtration rate, 32 mL/min per meter squared) as well inflammatory parameters. Sonography showed urinary retention caused by ureteral strictures on the left hand side. Bacterial invasion was detectable (e. coli). An ureteric stent was placed and in addition IV antibiotic therapy with meronem was started. Repeat CT Scan demonstrated significant periaortic fibrosis and sclerosis and gives reasons for obstruction of the left ureter, same to Morbus Ormond (3). We decided to perform a PET CT. It demonstrated a relevant 18F-FDG evidence of metabolic activity in the aortic wall. The patient was commenced on a reducing dose of oral steroids (initial prednisolon 50mg daily). He recovered from his symptoms but still continues the steroid therapy after 7 weeks' treatment because of persistently increased inflammatory parameters and missing evidence of bacterial invasion.

Conclusion: Inflammation of the abdominal aorta can occur many reasons. Primary inflammatory abdominal aortic aneurysms present in 3% to 10% of all abdominal aortic aneurysms. (1) (2) The development of a secondary periaortic inflammation after Endovascular Aneurysm Repair seems to be a rare complication and late manifestation for which recognition and immune modulating therapy, as for example prednisone and or tamoxifene (5), is needed. Differential diagnosis between infection and (sterile) de novo (6) periaortitis is important for the choice of treatment (4–7).

FM9

Implantable pump for lymphedema treatment: technological feasibility study and implant test in sheep

V. Triacca, M. Pisano, C. Lessert, L. Mazzolai (Lausanne)

Objective: Lymphedema is a frequent chronic, yet under-recognized, disease characterized by accumulation of interstitial fluid and macromolecules in the subcutis, leading to tissue swelling. The standard of care for lymphedema is complete decongestion therapy, a treatment that alleviates symptoms and side effects, but necessitates a lifelong treatment plan for the patient.

We previously proposed an innovative approach to restore continuous lymph flow and we showed, in a rat model of lower limb lymphedema, that excess volume can be reduced by drainage of accumulated fluid with an implanted peristaltic pump. Here we moved onto the assessment of the technological feasibility of an implantable pump suited for human use. The objective of the study was to finalize the design of the device and test its functionality, via both bench testing and implantation in sheep.

Methods: The pump was designed following state of the art engineering principles, aiming to minimize the size of the implantable component. Materials were chosen according to their biocompatibility and mechanical properties. The device was produced by CNC machining and pump characterization curve was obtained with bench performance testing.

Final devices were implanted subcutaneously in the posterior limb of 6 Swifter sheep, and connected to an outlet catheter inserted in the peritoneal cavity. Feasibility of the surgical implantation, device functionality (verified via lymphofluoroscopy) and device removal procedure were tested.

Results: We verified the technological feasibility of the implantable pump for the treatment of lymphedema and characterized pump flow rate and pressure head. We produced 12 fully functional prototypes, 6 of which were implanted in sheep. The implant procedure was minimally invasive and no post-surgical complications were observed. Device functionality was confirmed via lymphofluoroscopy, upon subcutaneous injection of indocyanine green on the distal side of the pump, and visualization of the drained dye in the outlet catheter of the device draining to the peritoneal space. The implanted devices were easily removed two weeks after implantation.

Conclusion: We designed and developed a fully functional prototype of the implantable pump for lymphedema treatment. Results from the implantation study in sheep demonstrated the feasibility of the surgical procedure and safety of the device.

FM 2.1

Endovascular iliac aneurysm repair preserving the internal iliac artery

S. Hofer, G. Heller, U. Derungs, P. Knüsel, M. Furrer (Chur)

Objective: Management of common (CIAA) and internal iliac artery aneurysm (IIAA) is difficult and heterogeneous. Therefore, we wanted to analyse our experience with an endovascular approach preserving the internal iliac artery.

Methods: Data from patients with a CIAA and IIAA and a diameter larger than 3 cm treated endovascularly between August 2014 and March 2017 were retrospectively analysed. We evaluated the strategies of repair, the technical success rate and the 3 and 12 month follow-up. From the outset we included applications outside the instructions for use (IFU).

Results: 23 patients were included, three patients had ruptured aneurysms. 18 patients were treated with an iliac branch device, five patients with a tube stentgraft. Only 6 procedures were according to IFU. Two patients required a reintervention because of technical failure. The technical failures were both observed in patients undergoing procedures outside the IFU. A further endovascular reintervention was performed because of dislocation of the aortobiiliac stentgraft. In two of the ruptured aneurysms we were constrained to close the internal iliac artery to avoid an endoleak Type II and further bleeding. The mean hospital stay was 5.2 (2–15) days. The 3 and when available 12 months follow-up showed a stable sac or even sac shrinking with a patent internal iliac artery in all cases preserved. In one patient a reintervention because of an endoleak type I B was necessary. The buttock claudication rate was 0%.

Conclusion: The technical success rate in this endovascular cohort was 91%, including procedures outside the IFU. An endovascular solution preserving internal iliac artery was possible in all elective repairs, but procedures outside the IFU have to be used.

FM 2.2

Endovascular treatment in ruptured abdominal aortic or iliac aneurysm with arteriovenous fistula

S. Hofer, M. Furrer (Chur)

Objective: Aortocaval or iliac arteriovenous fistula are rare and endovascular treatment strategies are focused on sealing the arteriovenous shunt. We investigated the efficiency of an arterial stentgrafting strategy only.

Methods: We treated two patients with acute arteriovenous fistula with aortobiiliac and iliac branch stentgrafts. The clinical and technical success as well as the follow-up with the focus on the arteriovenous fistula and the changes in sac size were evaluated.

Results: The first patient was referred with suspected myocardial infarction. The subsequent workup revealed a ruptured aortic aneurysm with an aortocaval fistula. We performed a percutaneous endovascular aortic repair (EVAR), with landing zones in the right external iliac artery and left common iliac artery. Postoperatively an endoleak type II (EL II) with flow from inferior mesenteric, lumbar

and the right hypogastric artery through the open fistula into the inferior vena cava was observed. All previous symptoms caused by the high flow fistula such as cardiac insufficiency, renal failure and edema regressed immediately after aortic sealing. In the follow up we observed a fast shrinkage of the aneurysm sac from 99mm to 87mm in 10 months even with a persistent EL. Pathophysiologically the fistula seems to function as a EL drainage and therefore a decompression of the aneurysm could be achieved.

The second patient was referred with dyspnea and severe edema of the legs. The CT scan showed an aneurysm of the common and internal iliac arteries on both sides, additionally a rupture with a fistula between the left common iliac artery and vein could be diagnosed. We could exclude this aneurysm by an emergency iliac branch stentgraft implantation. In a staged manner we completed the procedure with an iliac branch stentgraft on the right side and a bifurcated extension to the aorta. Postoperatively we diagnosed an EL II of a lumbar artery without a persistent arteriovenous flow. The 3 months follow-up showed a sac shrinkage from 69mm to 64mm.

Conclusion: EVAR seems to be a good treatment option in arterio-venous fistula caused by a ruptured aortic or iliac aneurysm. Simultaneous venous sealing is not necessary, the high flow draining of the EL II into the vein may lead to depressurization of the sac and fast shrinkage can occur.

FM 2.3

Outcome after surgical reconstruction for traumatic popliteal vessel injury

V. Makaloski, P. G. Fairhurst, M. K. Widmer, R. Buehlmann, T. R. Wyss, J. Schmidli (Bern)

Objective: Injury of the popliteal vessels has the highest amputation rate of all vascular injuries to the lower extremity. Management remains a challenge for both vascular and trauma surgeons, especially the initial order of intervention. Aim was to evaluate the outcome of trauma patients treated for popliteal vessel injury.

Methods: Consecutive patients suffering from popliteal vascular trauma between March 2005 and December 2016 were identified. The vessel lesion was preoperatively confirmed by computed tomography angiography and/or duplex ultrasound. Vessel repair was aimed prior to bone/joint stabilization. Reconstruction was performed via medial, posterior and lateral approach depending on the location/extent of the vascular injury. Early and long-term outcomes were analyzed assessing survival, limb salvage and claudication.

Results: Twenty-five patients (14 male; median age 46 years, range 21–88) with popliteal vessel injury were identified. In 22 patients (88%) vessel reconstruction was performed prior to bone/joint stabilization. Median ischemic time prior to revascularization was 6h30m (range 2h25m–19h55m). Twelve patients (48%) had a posterior, 12 (48%) a medial and one (4%) a lateral approach to the injured vessel. Sixteen patients (64%) had a complete transection, eight (32%) suffered from local intimal disruption and one patient (4%) had a pseudoaneurysm of the popliteal artery. Five patients (20%) underwent direct re-anastomosis, four patients (16%) arteriotomy with patch plasty and an interposition or bypass graft (vein n = 15; xenograft n = 1) was used in 16 patients (64%). Seven patients (28%) had an additional transection of the popliteal vein; three were reconstructed directly, three with interposition of a vein graft and one was ligated.

No patient died and two above-knee amputations were necessary due to severe limb infection. All other arterial reconstructions were patent at discharge. One patient had asymptomatic early postoperative occlusion of the vein graft used for popliteal vein repair. After a median follow-up of 61 months (range 12–143) no death, a limb salvage rate of 92% and no claudication were observed.

Conclusion: Early surgical reconstruction of the popliteal vessel injury after lower extremity trauma shows a very high limb salvage rate. The vessel first strategy promises an excellent outcome independent of the surgical approach needed to repair the popliteal vessels.

FM 2.4

Outcome after endovascular repair for blunt thoracic

V. Makaloski, H. Widenka, R. Ausraite, F. Schoenhoff, T. R. Wyss, J. Schmidli (Bern)

Objective: To analyse long-term follow-up after thoracic endovascular aortic repair in patients with blunt injury of the descending aorta.

Methods: Consecutive patients referred with blunt traumatic injury of the descending aorta between 1st of January 2005 and 15th of January 2017. Early outcome included technical success, neurologic deterioration with or without coverage of the left subclavian artery (LSA) and 30-day mortality. During follow-up stent graft related events (migration/thrombosis/infolding), freedom from re-intervention, left-sided subclavian territory pathologies and overall survival were analysed. Follow-up was completed for all patients per 15th of January 2017.

Results: Thirty-four patients (30 males, 88%) with a median age of 46 years (range 19–70) were identified. Twenty-seven patients (79%) were treated within 24 hours, six patients (18%) within one week and one patient (3%) after one year. Intraoperative technical success was 88% (30 patients). Three patients had partial unintentional coverage of the left common carotid artery (LCCA) and one patient died on-table before the stent graft could be implanted. Another patient died on the 5th postoperative day from trauma associated brain injury, resulting in a 30-day mortality of 6%. In 19 patients (56%) the LSA was intentionally covered, in 16 completely and in three partially. Simultaneous LSA-revascularization was performed in three patients. Initial median injury severity score was 42 points (range 9–75). None of the patients suffered from stroke or spinal cord ischemia during 30-days. Median follow-up was 42 months (range 1–125). One patient was lost to follow-up. Two patients died during follow-up of non aortic-related causes. One stent graft had to be explanted due to infolding and collapse, resulting with chronic leg ischemia. He underwent open replacement via thoracotomy. Two delayed LSA-revascularizations were performed: one patient with LCCA-LSA bypass due to subclavian steal syndrome and one with LSA-transposition and stenting of the LCCA origin due to subclavian steal syndrome and left-sided amaurosis fugax.

Conclusion: Endovascular treatment of blunt thoracic aortic injury is safe treatment option in severely injured patients. Even if the LSA must be covered to create a suitable landing zone for the stent graft, functional long-term results are good.

FM 2.5

Mid-term results of chimney and periscope grafts in supraaortic branches in high-risk patients

M. Lachat, T. Pfammatter, G. Puippe, Z. Rancic, F. Pecoraro (Zürich)

Objective: To report mid-term outcomes of the chimney and periscope graft (CPG) technique to address supraaortic branches (SAB) during thoracic endovascular aneurysm repair (TEVAR).

Methods: In our centre, a retrospective analysis, of patients presenting aortic aneurysms where TEVAR with zone in zone 0, 1 or 2 proximal landing was associated to CPG in SAB was performed. Were included patients treated from 2009 to 2014. The measured outcomes were perioperative mortality and morbidity, aneurysm diameter evolution, endoleak incidence, survival freedom from reinterventions and freedom from occlusion. The median follow-up of 21.2 (mean:22; range:0–65; SD:18) months.

Results: Forty-one patients were included in the study. Aortic disease was a thoraco-abdominal aortic aneurysm in 7 (17%) patients, arch aneurysm in 16 (39%), descending aneurysm in 14 (34%) and aneurysm extending from arch to the visceral aorta in 4 (10%). Fifteen (37%) patients were treated non-electively.

The CPG technique was used to address 59 SABs: 1,2,3 and 4 CPG were employed in 71%; 19%; 5%; and 5% of patients respectively. In 49% of patients had proximal landing was in zone 0; 17% in zone 1; and 34% in zone 2. Technical success was 95%. Perioperatively 5 (12%) deaths occurred. Both complications and neurological events were registered in 3 (7%) patients respectively. A type I/III endoleaks were registered in 3 (7%) cases and reintervention in 6 (15%) patients. A significant aneurysm sac shrinkage ($P < .001$) was reported at mean follow-up and no significant aneurysm sac increase ($>5\text{mm}$). The estimated 2-years' survival, freedom from reintervention, freedom from endoleak and freedom from branch occlusion was 75%; 77%, 86% and 96% respectively.

Conclusion: The chimney and periscope grafts technique showed to be safe in aortic aneurysmal disease involving supra aortic branches, even in emergent setting using off-the shelf devices. Mid-term follow-up results in this high-risk population are good, but longer follow-up is mandatory before this technique may be used in intermediate risk patients.

FM 2.6

Mid and longer-term follow-up of chimney and / or periscope grafts

M. Lachat, T. Pfammatter, G. Puippe, Z. Rancic, F. Pecoraro (Zürich)

Objective: To report mid-term results results with the chimney and periscope grafts (CPGs) technique in renovisceral arteries (RVA) to treat endovascularly pararenal (PRAAs) or thoracoabdominal aortic aneurysm (TAAAs).

Methods: Retrospective analysis of 100 patients with PRAA (69) or TAAA (31) treated by CPG and endovascular aneurysm repair. In this cohort, 224 (mean:2.24 per-patient) RVA were preserved with 136 (61%) chimney and 88 (39%) periscope grafts. Patients were follo-

wed by clinical examination, CTA (82%) and/or duplex (18%). The mean follow-up was 29 months (range:0–65;SD:17); 59% patients were followed >2 years, 30% >3 years and 16% > 4 years.

Results: The CPG immediate technical success was 99% (222/224 branches). A CPG occlusion was observed perioperatively (≤ 30 days) in 3 (1.3%) branches and during follow-up in 10 (4.5%). Estimated primary patency at 36 and 48 months was 93% and 93%. After corrective percutaneous (10) or surgical (3) re-interventions, estimated secondary patency was 96% and 96%. 3The perioperative mortality was 2%; 36 and 48 months estimated patient survival is 79%. A significant shrinkage [72 (SD:23) vs. 62 (SD:24) mm; $P < .001$] was observed.

Conclusion: Self-expandable CPGs proved to be highly successful and durable treatment for RVA preservation up-to 5 years. These mid and longer-term results support CPG use to treat PRAAs or TAAAs in patients unfit for open surgery or fenestrated/branched stent-grafts.

FM 3.1

Assessing clinical probability of pulmonary embolism: Prospective validation of the simplified Geneva score

H. Robert-Ebadi¹, K. Mostaguir¹, M. Hovens², M. Kare³, F. Verschuren⁴, P. Girard⁵, M. Huisman², F. Mustafa⁶, P. Kamphuisen⁷, H. Büller⁸, M. Righini¹, G. Le Gal⁹ (¹Geneva, ²Leiden NL, ³Agen F, ⁴Bruxelles B, ⁵Paris F, ⁶Clermont-Ferrand F, ⁷Groningen NL, ⁸Amsterdam NL, ⁹Ottawa CAN)

Objective: Background: Pretest probability assessment by a clinical prediction rule (CPR) is an important step in the management of patients with suspected pulmonary embolism (PE). A limitation to the use of CPR is that their constitutive variables and corresponding number of points are difficult to memorize. A simplified version of the Geneva score (i.e. attributing one point to each variable) has been proposed but never been prospectively validated.

Aims: Prospective validation of the simplified Geneva score (SGS) and comparison with the previous version of the Geneva score (GS).

Methods: In the ADJUST-PE study, whose primary aim was to validate the age-adjusted D-dimer cut-off, the SGS was prospectively used to determine the pretest probability in a subsample of 1,621 study patients.

Results: Overall, PE was confirmed in 294 (18.1%) patients. Using the SGS, 608 (37.5%), 980 (60.5%), and 33 (2%) were classified as having a low, intermediate and high clinical probability. Corresponding PE prevalences were 9.7%, 22.4% and 45.5%; 490 (30.1%) of patients

Simplified Geneva score (SGS)				
	Low	Intermediate	High	Total
Patients, n (%)	608 (38)	980 (61)	33 (2)	1621
Confirmed PE, n (%)	59 (10)	220 (22)	15 (46)	294 (18)
Geneva score (GS)				
Patients, n (%)	625 (39)	934 (58)	62 (4)	1621
Confirmed PE, n (%)	62 (10)	202 (22)	30 (48)	294 (18)

FM 3.1. Table – Pretest probability assessment using the simplified Geneva Score compared to the original Geneva score.

with low or intermediate probability had a D-dimer level below 500 µg/L and 653 (41.1%) had a negative D-dimer test according to the age-adjusted cut-off. Using the GS, the figures were: 491 (30.9%) and 650 (40.9%). None of the patients considered as not having PE based on a low or intermediate SGS and negative D-dimer had a recurrent thromboembolic event during the 3-month follow-up.

Conclusion: The use of SGS results in a similar yield and safety than the GS to exclude PE in association with the D-dimer test.

FM 3.2

Early results after endovascular repair of iliac aneurysm with bifurcated stent-graft

V. Makaloski, R. Frey, P. Kissling, D. Becker, T. R. Wyss, J. Schmidli (Bern)

Objective: The use of iliac branch device in treatment of isolated iliac aneurysms is a common technique. Alternatively it can be used for creating a save distal landing zone during endovascular aortic aneurysm repair. Aim was to evaluate the early results after endovascular repair of iliac aneurysm with bifurcated iliac stent-graft.

Methods: Consecutive case series (2008–2016) of patients with an aneurysm of the common and/or internal iliac artery undergoing endovascular repair with branched iliac stent-graft. In the presence of an associated abdominal aortic aneurysm/ectasia, or if a safe proximal landing zone was missing an additional endovascular aortic repair (EVAR) was performed. All patients were assessed preoperatively with contrast-enhanced computed tomography (CT) and postoperatively after 30 days with contrast enhanced ultrasound and CT angiography. Technical success, 30-day mortality and morbidity as well as early stent-graft occlusion were analysed.

Results: A total of 44 iliac branch devices were implanted in 39 patients (34 men) with a median age of 74 years (range 57–84). Repair of common iliac artery aneurysm was the indication in 35 patients (88%) and of an isolated internal iliac artery aneurysm in five patients (12%). Additional EVAR was needed in 22 (56%) patients. All grafts were deployed successfully via common femoral artery. Twelve patients (30%) needed an additional brachial access. One (3%) patient died on the 18th postoperative day after experiencing acute hemorrhagic pancreatitis. One patient needed revision for a wound complication. Another patient had peripheral embolisation, which was treated by percutaneous aspiration thromboembolectomy. All patients completed the follow-up at 30 days. One internal iliac artery branch occluded after simultaneous bilateral implantation of iliac branch device prior to hospital discharge, resulting in early primary patency rate of 98%.

Conclusion: Bifurcated iliac stentgrafts can be deployed safely and with high technical success. Despite the complexity of these procedures, this approach remains a valuable alternative to the open management of iliac aneurysmatic disease.

FM 3.3

Transluminar (intussusceptive) pillars and their role in plexus remodeling

H. Handrkova, M. Vladymyrov, V. Djonov (Bern)

Objective: Intussusceptive angiogenesis (IA) or “growth within itself” is a mechanism of capillary network expansion, blood vessel splitting, and remodeling of branches. Hallmarks of IA are numerous thin transluminar pillars that may grow and merge together and thus shape the vascular bed. These pillars were documented in a variety of organs and species including tumor vasculature, and IA is of high clinical relevance since it may present an escape mechanism to anti-VEGF therapy. However, the dynamics of IA and its regulation remain poorly understood. Our aim was to 1) document pillar formation and behavior in high resolution, 2) explain how this process is regulated.

Methods: Intussusceptive pillars have also been observed in caudal vein plexus of zebrafish embryos between 1–2dpf (days post fertilization). To document formation of these pillars, we used transgenic zebrafish Tg(Fli1:eGFP//Gata1:dsRed) (to label endothelium and erythrocytes) and time-lapse confocal microscopy. Pillars were tracked using custom-made software. The ultrastructure was analyzed using TEM and whole-mount immunostaining. Molecular mechanism is being studied using highly specific inhibitors of signaling pathways.

Results: Transluminar pillars were hypothesized to form by contact of opposing capillary walls followed by subsequent perfusion of the contact zone and infiltration by collagen fibers and perivascular cells. Our data indicate that most pillars form by alternative mechanisms (often by sprouting), and that not all pillars eventually participate in blood vessel splitting. Our data also didn't support the original hypothesis of infiltration of thin pillars by perivascular cells and collagen fibers: pillars seem to either contain collagen core from the beginning, or not at all. Pillar formation and behavior does not seem to be dependent on a single signaling pathway, but the data are still pending.

Conclusion: We've documented for the first time the formation of transluminar pillars in high spatiotemporal resolution in vivo and conclude that at least in zebrafish model, plexus remodeling may occur differently than the original hypothesis of intussusception suggested. Instead of different stages of intussusceptive pillars, we propose that there are several ‘classes’ of transluminar pillars that differ by mechanism of origin, ultrastructure, and their behavior.

present study, we used a PAD mouse model to investigate cholesterol-independent effect of atorvastatin on ischemic hindlimb function.

Methods: Hypercholesterolemic/atherosclerotic ApoE^{-/-} mice with hindlimb ischemia were treated orally with (ATOR) or without (CON) atorvastatin (20 mg/kg/day) for 1 week or 4 weeks. Walking capacity was assessed on a running wheel for 24h. Arteriogenic response was evaluated using laser Doppler perfusion imaging as well as alpha-smooth muscle actin immunostaining in ischemic gastrocnemius muscle. Real-time RT-PCR analysis was performed both in ischemic gastrocnemius and spleen tissues. Proportion of circulating monocytes and of monocyte subsets was analyzed by flow cytometry.

Results: Walking capacity was improved in ATOR-treated mice in comparison with CON (5.0 ± 2.1 km vs. 2.0 ± 1.5 km at end of the study, $p < 0.05$). Compared to CON, ATOR-treated mice showed increased hindlimb perfusion recovery as well as VEGFA and HIF-1 α mRNA expression, higher arteriolar density, and higher number of regenerating muscle fibers ($p < 0.05$). ATOR significantly increased ischemic gastrocnemius mRNA expression of CD11c, iNOS, TNF- α , IL-18 and IL-1 β (pro-inflammatory M1-macrophage marker) ($p < 0.05$), but did not modulate mRNA expression of CD206, Arg1, IL-10, IL-1 α and TGF- β (anti-inflammatory M2-macrophage marker) at 2 weeks post-hindlimb ischemia. No significant difference in IFN- γ , IL-4, IL-17, and IL-10 (signature cytokines for Th1, Th2, Th17, and Treg) mRNA expression in spleen tissue was observed between the 2 groups. The proportion of total monocytes, pro-inflammatory, intermediate, and resident anti-inflammatory monocytes did not significantly differ among the 2 groups.

Conclusion: Atorvastatin improves ischemic limb function by skewing ischemic muscle resident macrophages toward a M1-like pro-inflammatory phenotype in the early stage of disease. Our data provide rational for the use of statin in PAD patients for improving functional status.

FM 3.5

Low discriminating power of the modified Ottawa risk score in a cohort of patients with active cancer and acute venous thromboembolism

A. Alatri¹, L. Mazzolai¹, C. Font², A. Tafur³, R. Valle⁴, P. J. Marchena², A. Ballaz⁵, E. Tiraferri⁶, L. Font⁷, M. Monreal² (¹Lausanne, ²Barcelona ES, ³Evanston USA, ⁴Santander ES, ⁵Vizcaya ES, ⁶Rimini I, ⁷Tarragona ES)

Objective: Treatment of patients with cancer-associated venous thromboembolism (VTE) remains a major challenge. The modified Ottawa score is a clinical prediction rule evaluating the risk of VTE recurrences during the first six months of anticoagulant treatment in patients with cancer-related VTE. We aimed to validate the Ottawa score using data from the RIETE registry.

Methods: RIETE is an ongoing multicenter, prospective registry of consecutive patients presenting with symptomatic acute VTE confirmed by objective testing. Consecutive patients with acute VTE and concomitant active cancer were included in the analysis. According to the modified Ottawa score, patients were stratified in three risk categories: low, intermediate, and high risk. We calculated the incidence of the following variables: recurrent deep vein thrombosis,

FM 3.4

Atorvastatin enhances hindlimb regeneration and arteriogenesis by modulating muscular macrophage phenotype in a lower limb peripheral artery disease mouse model

M. Pellegrin, K. Bouzourène, M. Sipion, J.-F. Aubert, L. Mazzolai (Lausanne)

Objective: The benefits of statins in limb outcome remain uncertain in patients with lower limb peripheral artery disease (PAD). In the

recurrent pulmonary embolism, recurrent VTE, overall mortality, and fatal PE, during the first six months of anticoagulant treatment. We assessed accuracy and discriminating power of the score to predict VTE recurrence by calculating sensitivity, specificity, positive and negative predictive values, likelihood ratios and the area under the receiver operating characteristic curve.

Results: A total of 11,123 cancer patients with VTE were included in the analysis. According to modified Ottawa score, 2,343 (21%) were categorized at low risk for VTE recurrences, 4,525 (41%) at intermediate risk, and 4,255 (38%) at high risk. Overall, 477 episodes of VTE recurrences were recorded during the course of anticoagulant therapy, with an incidence rate for low, intermediate, and high risk groups of 6.88% (95% CI 5.31–8.77), 11.8% (95% CI 10.1–13.6), and 21.3% (95% CI 18.8–24.1) patient-years, respectively. Overall mortality had an incidence rate of 21.1% (95% CI 18.2–24.3), 79.4% (95% CI: 74.9–84.1), and 134.7% (95% CI: 128.3–141.4) patient-years, respectively. The accuracy and discriminating power of the modified Ottawa score for VTE recurrence was modest, with low sensitivity, specificity and positive predictive value, and a C-statistics of 0.58 (95% CI: 0.56–0.61).

Conclusion: In our analysis, the modified Ottawa score did not accurately predict VTE recurrence among patients with cancer-associated thrombosis, thus hindering its use in clinical practice. It is time to define a new score including other clinical predictors

FM 3.6

Duplication of the inferior vena cava

F. Oularé, R. Clemens, T. Pfammatter, B. Amann-Vesti, T. Meier (Zurich)

Objective: Objective: The duplication of the inferior vena cava (D-IVC) is a rare finding with a frequency of 0.3% (CT-Study) up to 1.2% (surgical study). This anomaly leads to a decrease of circulatory speed in iliac veins and can be a risk factor for deep vein thrombosis

Methods: Case report

Results: A 37y male patient with a liver transplantation 3 years ago due to a sclerosing cholangitis was referred because of a painful right groin and a swollen right leg. Prograf was his only medication. No previous episodes of thromboembolism. No dyspnoea.

Initial duplex ultrasound (DU) revealed a DVT of the right iliac and femoral vein. The orthotopic IVC was occluded. An open left IVC could be seen. The review of old CT scans confirmed the diagnosis of a D-IVC. Heparin and catheter directed thrombolysis was started. Symptoms did not improve. A recanalization with stenting of the left IVC and iliac veins eventually was successful. Phlebography 5 month later showed a physiological flow in the iliac veins and both IVC's. Anticoagulation could be stopped

Conclusion: The diagnosis of DVT of iliac veins in a younger patient should lead to the search for an underlying anomaly of the IVC by DU or CT. This anomaly might be a duplication of the IVC. In case of persistent symptoms under therapeutic anticoagulation and after thrombolysis, stenting of the anomalous IVC might be successful.

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FC 1.1

MicroangioCT: new horizons in microvascular imaging

R. Hlushchuk, D. Haberthür, V. Djonov (Bern)

Objective: In angiogenesis research there are a few modalities available for the visualization of the vasculature. But none of them provides 3D-visualization of the vasculature down to the capillary level with the possibility for quantitative analysis.

Therefore, we aimed to develop a contrast agent appropriate for ex vivo microangioCT with superior perfusion features in order to visualize microvasculature, including capillaries. Moreover, it should be suitable for the successive morphological analysis using light or transmission electron microscopy.

Methods: After washing blood out the mice or rats were perfused with the novel contrast agent developed in cooperation with Fumeda AG (Switzerland). The organs of interest (kidney, skeletal muscles, brain, eye, heart etc.) were then harvested and fixated in PFA-solution. The samples were scanned (SkyScan 1172 or 1272) at different resolution levels: overview scans followed by detailed scan of the organ/site of interest. The volumes of interest were, if needed, excised, and processed for paraffin/epon embedding.

Results: Besides the developed contrast agent we have developed an ex vivo microangioCT approach that swiftly provides 3D-microCT datasets of superior quality, which are sufficient for qualitative and quantitative analysis of the vasculature down to the capillary level.

Conclusion: The developed ex vivo microangioCT-approach provides microvascular imaging at unprecedented level and enables correlative microscopy. The aforementioned features as well as high reproducibility make it a reliable partner in a very broad spectrum of basic research studies and clinically-oriented research where the microvasculature is of significant importance.

FC 1.2

Role of Foxc2 in organ-specific lymphatic vessel maintenance and function

E. Bovay, A. Sabine, S. Luther, T. V. Petrova (Lausanne)

Objective: The lymphatic vasculature is present in virtually every organ, where it plays a number of vital functions. Capillaries uptake interstitial fluid, proteins, antigens and cells, whereas collecting vessels, interconnected by intraluminal valves, transport the lymph through lymph nodes and back to the blood vascular system. Recent studies have shed light on the complexity of this system and organ-specific structural organization of lymphatic vessels, however our knowledge of molecular mechanisms ensuring development and stability of tissue-specific lymphatic vessels, such as in the lymph node (LN) is still fragmentary.

Heterozygous loss-of-function of the forkhead transcription factor Foxc2 leads to lymphedema-distichiasis (LD), a debilitating

disease with impaired capillary and collecting vessel specification and lymphatic vessel dysfunction. Recently, we have described the role of Foxc2 as a critical transcription factor necessary for postnatal lymphatic vascular function. Foxc2 deletion after birth in lymphatic endothelial cells leads to chylothorax and rapid 100% lethality, as a result of degeneration of intraluminal valves, loss of lymphatic endothelium integrity and overall aberrant lymph transport.

Methods: Here we investigated the role of lymphatic vessels in lymph node development. We analysed wildtype and Foxc2f/f; Prox1-CreERT2 mice, in which inactivation of Foxc2 in lymphatic endothelial cells is achieved by administration of tamoxifen from the age of E13.5 and E14.5.

Results: Loss of Foxc2 during embryonic development led to the absence of intraluminal valves and impaired vessel specification. These events, in turn, effected the LN development of the animals.

Conclusion: We demonstrate here the importance of a close interaction and interdependency between embryonic LN anlagen and lymphatic collecting vessel remodeling to form a functional LN.

FC 1.3

Comparing the migration of Th1 versus Th17 cells across cervical spinal cord microvessels during neuroinflammation by two-photon imaging

N. Haghighy Jahromi, H. Tardent, G. Enzmann, U. Deutsch, J. V. Stein, B. Engelhardt (Bern)

Objective: Extravasation of autoaggressive T cells across the blood-brain barrier (BBB) is a crucial step in the pathogenesis of multiple sclerosis (MS) and can be studied in its animal model, experimental autoimmune encephalomyelitis (EAE). EAE can be induced by two subsets of CD4+ T cells, namely Th1 or Th17 cells differing in their cytokine profile and trafficking properties. It has been proposed that Th1 cells preferentially invade the spinal cord while Th17 rather home to the brain.

Moreover, our previous in vitro data showed the essential role of endothelial intercellular adhesion molecule-1 (ICAM-1) and ICAM-2 in T cell crawling on an in vitro model of the BBB. Here we compared the cellular and molecular mechanisms mediating Th1 versus Th17 cell migration across cervical spinal cord microvessels during EAE in vivo.

Methods: We observed side-by-side the migration of fluorescently labeled Th1 and Th17 cells across cervical spinal cord microvessels in mice suffering from EAE by employing a cervical spinal cord window model and two-photon intravital microscopy.

Results: We observed higher numbers of Th1 versus Th17 cells arresting on the inflamed spinal cord microvessels in mice suffering from EAE. While lack of ICAM-1 and ICAM-2 on T cells failed to affect T cell crawling on the inflamed cervical spinal cord microvessels of WT mice suffering from EAE, absence of ICAM-1 and ICAM-2 on the endothelium abrogated crawling of both, Th1 and Th17 cells on the inflamed BBB.

Conclusion: Supporting the notion that Th1 cells preferentially home to the spinal cord they more efficiently arrested in inflamed spinal cord microvessels compared to Th17 cells. However, endothelial ICAM-1 and ICAM-2 are essential for post-arrest crawling of both, Th1 and Th17 cells on inflamed spinal cord microvessels.

FC 1.4

Vascular JNK2 inhibition improves obesity-induced endothelial dysfunction and oxidative stress after Roux-en-Y gastric bypass

E. Osto^{1,2}, P. Doytcheva², T. Baechler², E. Tarasco², G. Pellegrini², S. Stivala², L. Rohrer², C. Matter², T. A. Lutz², T. F. Lüscher² (Schwerzenbach, ²Zurich)

Objective: Roux-en-Y gastric bypass (RYGB) reduces obesity-associated comorbidities and cardiovascular mortality. We showed in diet-induced obese (DIO) rats that RYGB improves endothelial vasodilatation 8 days after surgery independently from weight loss. The effect was associated with decreased aortic phosphorylation of c-jun N-terminal kinase (JNK), which is a crucial player linking obesity with endothelial dysfunction. Here we examined if JNK1 or JNK2 mediates obesity-induced endothelial dysfunction and if this beneficial effect after RYGB can be mimicked by pharmacological JNK inhibition.

Methods: After 7 weeks of high-fat high-cholesterol diet, DIO rats underwent RYGB or sham surgery. Sham-operated rats received either control peptide D-TAT or the JNK peptide inhibitor D-JNKi-1 (D-JNK; 20mg/kg/day s.c.) for 8 days after surgery. Cumulative concentration-relaxation curves were obtained in rings of thoracic aorta in response to glucagon like peptide-1 (GLP-1 7-36) amide (10-12 to 10-6 mol/L) or insulin (10-12 to 10-5 mol/L). Western blot of aortic lysates was performed for JNK, Akt, endothelial nitric oxide (NO) synthase (eNOS) protein phosphorylation. NADPH Oxidase Activity was measured.

Results: In vivo D-JNK treatment mimicked the improvement in endothelial function seen after RYGB. Obesity increased JNK2 but not JNK1 phosphorylation in the aorta. After RYGB or D-JNK treatment, aortic JNK2 phosphorylation was blunted, as was the inhibitory phosphorylation of insulin receptor substrate-1 (IRS-1), while Akt/eNOS activation was increased. Oxidative stress decreased as shown by decreased aortic NADPH oxidase activity comparably after RYGB and D-JNK treatment, resulting in improved NO bioavailability.

Conclusion: In obese rats, decreased aortic JNK2 phosphorylation after RYGB rapidly improves obesity-induced endothelial dysfunction. Pharmacological JNK inhibition mimics the endothelial protective effects of RYGB. These findings highlight a novel JNK2-dependent mechanism for the cardiovascular benefits of RYGB surgery.

FC 2.1

EphrinB2/EphB4 signaling controls the switch between normal and aberrant angiogenesis by VEGF

A. Banfi¹, E. Groppa¹, S. Brkic¹, G. Wirth², P. Korpisalo-Pirinen², V. Sacchi¹, M. G. Muraro¹, M. Trani¹, S. Reginato¹, R. Gianni-Barrera¹, S. Ylä-Herttuala² (Basel, ²Kuopio FIN)

Objective: Vascular Endothelial Growth Factor-A (VEGF) is the master regulator of angiogenesis. We previously found that: 1) exogenous VEGF induces either normal or aberrant vessels depending on its dose in the microenvironment around each producing cell in vivo; and 2)

VEGF delivery to skeletal muscle induces angiogenesis by circumferential enlargement followed by longitudinal splitting (intussusception) rather than sprouting. Further, stimulation of pericyte recruitment by Platelet Derived Growth Factor-BB co-expression prevents VEGF-induced aberrant angiogenesis. Here, we investigated the role of specific pericyte-mediated signaling pathways in regulating this switch.

Methods: Monoclonal populations of genetically modified myoblasts, homogeneously expressing either a low or high VEGF dose, were implanted in skeletal muscle of mice to induce normal vascular growth or aberrant angiogenesis, respectively. Cells were further transduced to co-express blockers of the TGF β -1/TGF β -R, Tie2/Angiopoietin or EphrinB2/EphB4 pathways. EphB4 signaling in vivo was stimulated by systemic treatment with recombinant EphrinB2-Fc protein. VEGF-expressing adenoviral vectors were delivered i.m. in a mouse hindlimb ischemia model.

Results: Only EphrinB2/EphB4 inhibition switched the normal angiogenesis induced by low VEGF to aberrant angioma-like structures. Conversely, EphB4 stimulation by systemic EphrinB2-Fc treatment replaced aberrant angiogenesis by high VEGF with normal capillary networks. EphrinB2/EphB4 signaling did not affect pericyte recruitment, but regulated the degree of endothelial proliferation induced by specific VEGF doses, limiting the size of vascular enlargements and enabling successful splitting despite high VEGF. Mechanistically, EphB4 did not directly affect VEGF-R2 activation by VEGF, but it specifically regulated VEGF-R2 downstream signaling through phospho-ERK1/2. Lastly, after clinically relevant VEGF gene delivery with adenoviral vectors, systemic treatment with EphrinB2-Fc normalized vascular growth in both normoxic and ischemic muscle, leading to flow normalization and improved tissue regeneration.

Conclusion: EphrinB2/EphB4 signaling controls the switch between normal and aberrant angiogenesis by VEGF independently of pericyte recruitment, and is a promising molecular target to improve both safety and efficacy of therapeutic VEGF gene delivery.

fbret/ret) develop brain calcifications similar to PFBC patients and possess a strong pericyte-deficiency in the brain, as PDGFB/PDGFRB signaling pathway is crucial for pericyte recruitment to developing vessels. In this study, we have investigated the pathomechanism of cerebral microvascular calcification using Pdgfbret/ret mice, to understand if ectopic mineralization of tissue in this mouse model occurs either by precipitation of calcium phosphate on a permissive extracellular matrix, or by active deposition due to the presence of a bone forming cell.

Methods: In this study, we performed immunohistochemistry (IHC) and RNAseq to investigate the presence of bone cell markers. Lineage tracing to understand the cellular contribution and MRI and brain clearing to monitor calcifications.

Results: We detected the presence of bone forming and absorbing cell markers around calcifications in Pdgfbret/ret animals and characterized the environment surrounding calcifications using IHC and RNAseq. We also performed lineage tracing studies to understand the cellular origin contributing to ossification. Additionally, we present different approaches to monitor and quantify brain calcifications ex vivo and in vivo using MRI and brain clearing.

Conclusion: We find evidence that the microvascular mineralisation in Pdgfbret/ret mice is a result of osteogenic calcification. We also propose different methodologies to monitor calcifications in longitudinal studies.

FC 2.3

Endothelium as a determining factor for organ-specific metastasis

E. Biglieri, L. Borsig (Zürich)

Objective: Metastasis is the main reason of cancer-related death and accumulating evidence suggest that the tumor cell microenvironment, including endothelial cells and leukocytes, significantly modulate the invasiveness and metastatic capacity of tumor cells. Our hypothesis is that the metastatic spread of tumor cells is not random and rather reveal an organ specificity. Thus, the physiology of blood vessels in different organs and the degree of endothelial activation determine the efficiency of tumor seeding and metastasis. Overall, the aim of the project is study the capacity of the microvascular endothelium to contribute metastasis.

Methods: We use three different spontaneously metastatic mouse models of metastasis for the analysis of lung, liver and brain metastasis. The analysis of endothelial cells from in vivo models is complemented with an in vitro analysis of primary endothelial cells isolated from respective target organs co-cultured with tumor cells.

Results: In previous studies we recently demonstrated how CCL2 facilitate the metastatic initiation through the recruitment of inflammatory monocytes and the activation of endothelial cells at lung metastatic site [1]. In addition, endothelial activation associated with induced expression of E-selectin, was shown to be required for lung metastasis [2]. Initial data in breast and lung cancer models indicate that endothelial activation during metastasis to the lung and liver show different state of endothelial activation and the composition of the metastasis microenvironment.

Conclusion: Our initial data indicate that metastasis induces different endothelial activation in different metastatic sites, while its contribution to this process remains under investigation.

FC 2.2

Cerebral microvascular calcification in the mouse model for primary familial brain calcification is caused by ossification of capillaries

Y. Zarb, D. Kirschenbaum, D. Kindler, J. Klohs, A. Aguzzi, A. Keller (Zurich)

Objective: Primary familial brain calcification (PFBC) is a neurodegenerative disease, which exhibits an autosomal dominant inheritance. Clinical manifestations are variable (e.g. parkinsonism, dementia, psychosis), however, all patients present with bilateral brain calcifications in the basal ganglia. The pathogenic mechanism of PFBC is unknown, but several autopsy studies point to microvascular insufficiency. Although PFBC is a rare disease, brain calcifications are a common CT finding, and vascular dysfunction is the second cause of dementia after Alzheimer's disease. Thus insights into PFBC will aid in better understanding vessel-associated calcification in the brain. Loss of function of platelet-derived growth factor-B (PDGFB) and its receptor, PDGFRB, are associated with PFBC, nonetheless the pathomechanism of vessel calcification due to their haploinsufficiency is not known. Mouse PDGFB hypomorphs (Pdg-

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FC2.4

Wnt-high colorectal cancer stem cells promote resistance to anti-angiogenic therapy

J. Bernier-Latmani, C. Cisarovsky, S. Ragusa, F. Renevey, S. Siegert, S. Davature, P. Anderle, N. Zangger, P. Yan, F. T. Bosman, C. Sempoux, S. A. Luther, M. Delorenzi, T. V. Petrova (Lausanne)

Objective: Chemotherapy combined with the anti-angiogenic, VEGF-blocking antibody bevacizumab is the first-line treatment for metastatic colorectal cancer (CRC), however it provides only a modest survival benefit. In this work, we examine potential mechanisms of bevacizumab resistance in tumors with high levels of Wnt signaling, which make up 70 % of CRC cases.

Methods: Blood vessels in Wnt-high CRC genetic mouse models and implanted tumors treated with control or blocking antibodies to VEGFR2 were analyzed by both whole-mount immunostaining and immunohistochemistry. Furthermore, Wnt-high and Wnt-low tumors from CRC patients were analyzed by immunohistochemistry.

Results: We show both in animal models and human samples that, unlike other stem cell niches, both normal and transformed intestinal stem cells are associated with a normoxic environment and VEGF-independent vasculature, while differentiated intestinal epithelial cells are hypoxic and associated with actively sprouting, VEGF-dependent vessels. Furthermore, while anti-VEGF treatment efficiently prunes sprouting blood vessels in Wnt-high tumors, stem cell-associated vessels are highly resistant to VEGF deprivation. Analysis of Wnt-high human CRC tumors revealed a similar distribution of vessels with active VEGF signaling near differentiated epithelial cells.

Conclusion: Our work suggests that CRC stem/progenitor cells actively promote VEGF-independent angiogenesis to remain in normoxic conditions. This may represent one of the mechanisms for acquired or intrinsic resistance to anti-VEGF therapies in CRC, which should be explored for the development of novel treatments and diagnostic tools.

Anzeige

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Poster

P1

Early Experience and Outcome with the Fenestrated Anaconda Custom AAA Stent Graft System

S. Ockert, R. Seelos (Luzern)

Objective: Beneath several developments in Endovascular Device Design treatment of perirenal aortic aneurysms is still challenging. Limited flexibility, conformability and a single access side for branch cannulation from the bottom of the graft presents major concerns on contemporary devices. The aim of this study is to present the experience and the early results using the Anaconda-FEVAR System in a single center.

Methods: All consecutive patients treated with the Anaconda-FEVAR System at our institution were included in the study. Prior implantation a 3D aortic model has been produced based on 1 mm sliced CTA to guarantee right position of the fenestrations for successful cannulation of the aortic branches. All implantations have been performed by two experienced vascular surgeons in a Standard Operating Theatre equipped with a mobile C-Arm System. After implantation all Patients received postoperative control CTA to prove sufficient branch perfusion, exclusion of the aneurysm from the blood flow and for detection of endoleak occurrence.

Results: From July 2015–Jan 2017 (16 months) 10 patients underwent Anaconda-FEVAR. All patients were male and the average age was 65 (range 54–81 yrs). The median diameter of the aneurysms was 58 mm (range 51–64mm). The majority of patients suffered of juxtarenal aneurysm (7/10), two patients suffered of TAAA and one patient presented CEAD.

The whole amount of aortic branches treated with fenestrations in our series was 32 (range 1–4 fenestrations/case). Technical success was 100%. All fenestrations could be cannulated during procedure and have been documented to be open via postoperative CTA. The average time of procedure was 232 min (172–347 min).

There was no death, no stroke or spinal ischemia in our group of patients during hospitalization (and follow-up). We could detect no Type I or Type III Endoleak in our series, the rate of Typ II Endoleak was 4/10. No patient needed postoperative dialysis. The median time of hospitalization was 7 days, the median time of ICU stay was 1 day. There was no Redo-procedure necessary during hospitalization and also not during Follow-up period.

Conclusion: The Anaconda FEVAR-System is a feasible and safe device in treatment of complex aortic anatomies on a CMD basis. In a limited early series we could show the absence of early mortality without relevant procedure specific complications.

P2

Oral antiplatelet therapy and platelet inhibition after venous stenting of chronic total occlusion of the caval vein and iliac veins: a case report

C. Kohler, T. Fuss, N. Kucher, I. Baumgartner, M. Schindewolf (Bern)

Objective: Endovascular stent reconstruction of chronic pelvic and caval vein occlusion can improve quality of life in patients with PTS [1]. The antiplatelet/anticoagulatory therapy to prevent rethrombosis is still not standardized. This becomes more complex when thrombotic complications occur as presented in this case report.

Methods: A 46 y/o man with severe PTS due to idiopathic thrombosis of the inferior caval (ICV) and both pelvic veins (PV) in 2006 presented for elective interventional vein recanalization [Fig.1]. He was on oral anticoagulation with rivaroxaban 1 x 20mg q.d.

Results: Under bridging with unfractionated heparin (UFH), the ICV, the PV and profunda femoral veins (PFV) were recanalized with 8 nitinol stents. Clopidogrel loading-dose (600mg) followed by a maintenance dose 1 x 75mg q.d. was given. On the second postinterventional day (PI2) a complete thrombotic occlusion of the stents was seen, so an angiojet-thrombectomy and local thrombolysis with alteplase was performed. Clopidogrel and UFH were continued. On PI3 a thrombotic reocclusion of the stents was seen, so an aspirin-thrombectomy, angioplasty and local thrombolysis was done. Anticoagulation was changed to dabigatran 150mg po q.d. combined with clopidogrel. Testing for heparin-induced thrombocytopenia and antiphospholipid syndrome were negative. On PI4 there were still residual thrombi, so an angiojet-thrombectomy, angioplasty and stent extension of the left PFV was performed. Dabigatran level was < 30. ng/ml. On PI8 an instant-occlusion of the right PV was seen. Local thrombolysis was performed. Antiplatelet therapy was changed to prasugrel 1x 10mg q.d. due to clopidogrel-resistance (Verify-Now® P2Y12 inhibition 11%). Anticoagulation was continued with phenprocoumon (bridged with fondaparinux 1 x 10mg sc q.d. until INR was >2) [2]. Duplexsonography finally showed recanalized veins without rethrombosis. The further hospital stay was uneventful.

Conclusion: Antiplatelet/anticoagulation therapy after venous stenting is still not standardized, data from randomized-controlled trials are missing. Rare prothrombotic disorders and drug non-responsiveness must be taken into account. This case shows successful complication management in a patient with a very rare combination of clopidogrel resistance and supposedly subtherapeutic dabigatran levels. However, therapeutic dabigatran levels are not clinically validated yet.

P2. Figures.

P3

Axillary artery lesion and thrombosis after humeral head fracture-dislocation: a case report

S. Pozza, G. Prouse, F. Marbach, J. Müller, L. Giovannacci (Lugano)

Objective: Lesions of the axillary artery in case of blunt trauma are rare and generally associated with a mechanism of hyperabduction of the arm. The goal of this abstract is to present a peculiar case with review of the literature.

Methods: A 50-years-old woman comes to the Emergency Department after a ground-level fall with blunt right shoulder trauma. The physical examination showed soft tissue swelling and tenderness. The skin was pink and warm. Radial and ulnar pulses were palpable. Capillary refilling time ≤ 2 s. No neurological deficit was present. Radiographs showed anterior dislocation and fracture of the humeral head into 4 big parts requiring open reduction and osteosynthesis. A deltopectoral approach was used but suddenly massive bleeding from a branch of the axillary artery. Ligation was performed. By checking the integrity of the rest of the axillary artery, an occlusion was found, caused by intimal tear leading to secondary thrombosis. The operative choice was to proceed with the osteosynthesis: osteotomy of the coracoid process was performed to better expose the vascular structures. Fracture is reduced and fixed. At this point the vascular procedure started: thrombectomy of the subclavian artery was performed and a good blood flow restored. The artery is washed and clamped. The axillary stump is prepared, but dissection propagated proximally to the subclavian artery: a new thrombectomy at this level is performed and the artery is clamped. A termino-terminal anastomosis with reversed greater saphenous vein graft from distal subclavian to distal axillary artery is done. The Doppler examination showed a good distal flow. Coracoid process is fixed with a cannulated screw.

Results: The analysis of the literature underlines that this vascular complication rarely occurs but it also points out that the anterior dislocation of the humeral head is the main mechanism and is followed by signs of vascular impairment. There is no consensus concerning the vascular approach to this kind of lesion, which is generally based on the vascular surgeon's choice.

Conclusion: The main message of this case report after review of the literature is that, with a fracture-dislocation of the proximal humerus, although no anamnestic, clinical or imaging sign indicated any vascular impairment, we should always be ready for such complications and if they occur, a vascular surgeon is needed.

P4

The use of BeGraft® balloon-expandable covered stent in the treatment of infra-renal aortic occlusive disease

A. Longchamp, C. Dubuis, J. Longchamp, F. Saucy, J.-M. Corpataux, S. Deglise (Lausanne)

Objective: Peripheral arterial disease (PAD) affects more than 20 % of the population above 70 years old. Nowadays, the treatment of

Figure 1

Figure 2

Figure 3

occlusive aorto-iliac disease has moved to an endovascular-first approach in many centers, even for complex TASC C and D lesions. In this situation, balloon-expandable covered stents have demonstrated superior results. However, few options exist when dealing with aortic lesions requiring large diameter covered stents.

Methods: To report a case of the use of a large diameter BeGraft® balloon-expandable covered stent in the treatment of an isolated infra-renal aortic stenosis.

Results: A 71-year-old man was referred to our Department for pelvic and thigh claudication and impotence worsening over the last 2 months. He underwent an angio-CT scan, which demonstrated a significant tight stenosis of the infra-renal aorta, starting 3 cm below the renal arteries and extending to the iliac bifurcation (Figure 1). Flows were monophasic at the femoral level on both sides. The patient was offered percutaneous endovascular treatment through the right common femoral artery. After pre-dilatation, two 18x48mm BeGraft balloon-expandable covered stents (Bentley, Hechingen, Germany) were successfully implanted. Completion angiography demonstrated a patent aorta, no residual stenosis and a rapid flow down to the limbs (Figure 2B). Patient was discharged on the following day.

At 1 month follow up, the patient was free from pain during exercise and described normal sexual function. Vascular examination revealed palpable pedal pulses. An angio CT-scan confirmed a patent aortic stent, without any complications. (Figure 3).

Conclusion: To our knowledge, this is the first report of the implantation of a large diameter BeGraft covered stent at the level of the abdominal aorta to treat occlusive disease. Aortic lesions are often highly calcified, partially thrombosed and thus difficult to cross. Due to the risk of flow limiting dissection, perforation or embolization, the use of covered stent allows to immediately treat these complications. BeGraft stent appears to be a safe and valid in the treatment of isolated aortic stenosis. Further cases and studies are required to confirm this preliminary excellent result.

P5

Treatment of abdominal aortic aneurysms with the Bolton Treo stentgraft: preliminary single center experience

R. Seelos, S. Ockert (Luzern)

Objective: Despite the growing utilisation of endovascular aortic repair (EVAR) in abdominal aortic aneurysm (AAA) treatment over the last 25 years, there is still a demand to improve stentgraft behaviour in challenging anatomies of the aorta and access vessels, and to reduce complications and reinterventions. Therefore newer generation grafts and delivery systems are designed to meet these requirements, based on the experience with older stentgrafts. Our goal is to present our preliminary experience with a new generation trimodular stent graft (Bolton Treo, Bolton, Barcelona, Spain) for AAA repair.

Methods: Endovascular treatment of all patients with AAA using the Bolton Treo endograft according to manufacturers instruction for use in the period from 03/2015 to 01/2017. Redo procedures and exclusive iliac aneurysms were excluded. The analysis was based on a prospective database.

Results: In the time period 22 patients (1 female) with a mean age of 73.8 years were treated. Mean AAA diameter was 57 ± 8.8 mm, including one penetrating aortic ulcer. Primary technical success

was 100 %. No mortality occurred. Within 30 days six (27.3%) type II endoleaks were detected. One type Ib endoleak (4.5%) and two limb kinkings, due to severe iliac tortuosity, resulted in 3 reinterventions (one limb extension, two scaffolds).

12 of 22 patients had a CT and clinical follow up > 30 days (mean 9.4 ± 5.7 months). All patients were alive with no type I or III endoleak, further reintervention, limb occlusion, conversion, migration or rupture. Type II endoleaks persisted in two patients (16.6 %). At follow up no AAA sac increase was detected, in 4/12 patients diameter remained unchanged and 8/12 patients had sac shrinkage (mean diameter regression -8.3 ± 6.4 mm).

Conclusion: Our preliminary single EVAR center experience with the Bolton Treo endograft is encouraging with a high technical success even in challenging anatomies. The two encountered limb kinkings reflected the severe angulation in iliac anatomy. In the short term follow up, the graft performs well with respect to endoleaks, sac regression and complication rate.

P6

Impact of the Prevena™ aspiration wound system therapy on groin wound complication following vascular surgery

J. Longchamp, C. Dubuis, A. Longchamp, F. Saucy, J.-M. Corpataux, S. Déglise (Lausanne)

Objective: To evaluate the impact of the Prevena™, a preventive negative pressure aspiration wound system, on the incidence of groin complications.

Methods: In this single-center, prospective, non-randomized cohort study of 159 consecutive patients and 183 limbs, with a mean age of 69.7 year, the control group (C) included 107 cases and 76 in the Prevena group (P). The Prevena™ was placed from the time of surgery, until post-operative day 5. Antibiotrophylaxis was given to all patients. The primary endpoint was the reintervention rate due to groin complications within the first 3 months.

Results: There were no significant differences in the major comorbidities between both groups except for hypertension (72% C vs 88% P, $p = 0.01$). Indication for surgery was chronic arterial disease with Rutherford stages II-VI, (67% vs 87%, $p = 0.009$), acute ischemia (15% vs 11.8%, $p = \text{ns}$) and aneurysmal disease (11.2 vs 1.3%, $p = \text{ns}$). There were no differences regarding the number of redo in each group (26% vs 24%, $p = \text{ns}$). The overall rate of wound complications was 13.1%. No statistical difference was observed between both groups (10.3% vs 17.1%, $p = \text{ns}$). When considering only the redo vascular procedures, the rate of complications tends to be higher in the Prevena group (33.3% vs 10.7%) but this difference didn't reach statistical significance.

Conclusion: This study shows no benefit in the systematic use of the Prevena system on the incidence of groin complications after vascular surgery, especially after redo surgery. Further studies are required to find some specific indications where this therapy could bring an advantage.

P7

Unusual fate of residual popliteal artery aneurysm perfusion

C. J. Geppert, R. Bühlmann, J. Schmidli (Bern)

Objective: Popliteal artery aneurysms (PAAs) are treated by bypass reconstruction and inflow and outflow occlusion or endovascularly. Patent collaterals can continuously pressurize the aneurysm leading to growth and rarely to rupture.

Methods: We present two patients with giant, repetitively rupturing PAAs caused by retrograde perfused arteries.

Results: Case 1: A 68 year old patient presented with a critically ischaemic left foot due to chronic arterial embolization from a partially thrombosed PAA. This was treated by femoropopliteal venous interposition. In- and outflow arteries were ligated. Nine years after surgery, the patient was referred with intermittent painful swelling of the left thigh. A giant PAA (22x9x12 cm) was diagnosed by computed tomography angiography. Treatment included, ligation of a backbleeding artery and partial resection of the opened aneurysmal sac.

Case 2: A 77 year old patient had suffered the past two years from progressive and intermittent painful swelling of the right thigh. Several investigations including MRI, lymphatic and musculoskeletal scintigraphy scans and incision biopsy were inconclusive. Superficial femoral artery and below-knee popliteal artery were chronically occluded. Finally, a completely thrombosed, giant PAA (39x11x10cm) extending from the popliteal fossa to the ischial tuberosity was diagnosed. Resection of the aneurysm was performed (dorsal approach). Simultaneous revascularisation was not done due to the absence of symptoms and sufficient collateral blood flow. In both patients, retrograde bleeding arteries were the cause for the continuously expanding and consequently repetitively rupturing aneurysms.

Conclusion: Despite in- and outflow occlusion, PAA perfusion via collaterals can still lead to aneurysm growth and intermittent oligo-symptomatic ruptures without being diagnosed as such. After bypass surgery, follow-up imaging should include not only the bypass itself, but also the size of the excluded PAA.

P8

Extensive embolization of splanchnic artery aneurysms due to segmental arterial mediolysis

A. Najafi, C. Binkert (Winterthur)

Objective: Segmental arterial mediolysis is a rare non-inflammatory, non-infectious arteriopathy in middle-aged patients that tends to affect medium-size splanchnic arteries. The hallmark findings are dissecting aneurysms, which in case of rupture have a mortality rate up to 25%. Due to the nature of the disease vast vessel areas might be affected, which in case of rapid disease progression or even rupture pose a challenge in treatment. These include watchful waiting and endovascular or surgical intervention. No official treatment guidelines have been proposed. The goal of this study is to assess the outcome of SAM after extensive endovascular embolization.

Methods: We performed a retrospective search for all patients refer-

red to our institute with splanchnic manifestation of SAM who were treated with endovascular embolization.

Results: Four patients were treated with coil embolization. One of them had presented with rupture of multiple aneurysms, one had presented with abdominal pain due to dissection, and two displayed rapidly progressing disease during short-term follow-up. All patients were treated with complete exclusion of the diseased segments by coiling all branches to and from the diseased segment. In three cases there was complete exclusion of the main hepatic arteries. There were no immediate complications. In addition, there was no bleeding, hepatic failure, liver abscess, or biliary duct necrosis. Patients were followed up to six years. During follow up, there was no development of a new diseased segments.

Conclusion: Endovascular exclusion of the entire diseased arterial segment with coils is a safe and effective treatment option in patients with SAM who present with rapidly growing or ruptured aneurysms. Provided that patients have a normal liver function and proper portal venous flow, there seems to be a low risk of hepatobiliary complications even after massive embolization.

P9

In-stent restenosis of the superficial femoral artery and popliteal artery segment: long-term results after combined treatment with excimer laser debulking and drug coated balloon angioplasty

S. Engelberger, G. Prouse, P. Nicotera, J. Van Den Berg, L. Giovannacci (Lugano)

Objective: Long term results of most stand-alone treatments of in-stent restenosis after superficial femoral artery (SFA) stenting, remain suboptimal. Short-term results after treatment with drug coated balloons (DCB) or with excimer laser debulking (ELA) alone were positive, but trials have shown that their efficacy fades in the mid-to long-term. The aim of this study is to evaluate the long term outcome of combined treatment of SFA and popliteal artery in-stent restenosis with ELA and DCB.

Methods: A cohort of 25 patients with in-stent restenosis or occlusion of the SFA and popliteal artery was followed-up prospectively after combined treatment with excimer laser debulking and drug coated balloons. The procedures were all performed at the same center. Classification of the treated lesions followed the angiographic patterns described by Tosaka. Primary patency and freedom from target lesion revascularization were calculated as Kaplan-Meier estimates at 1, 2, 3, 4 and 5 years from treatment of in-stent restenosis. Mean Duplex follow-up was 35.1 months (range 4-77) and clinical follow-up was 37.3 months (range 10-78).

Results: Mean age of the treated patients was 71.8 years, 15 of them suffered from critical limb ischemia and 10 from intermittent claudication. Of the treated lesions 20 were in-stent occlusions (Tosaka class III) and 6 were focal lesions $\leq$ 50 mm (Tosaka class I). The average lesion length was 105.6 mm (range 10-380 mm). Technical success was achieved in all cases. In 2 cases distal embolization was observed and both were treated successfully by endovascular means. The calculated primary patency rates were 88.0%, 78.2%, 71.7%, 71.7%, 62.7%, whereas freedom from target lesion revascularization was 89.7%, 85.9%, 76.4%, 76.4% and 70% at 1, 2, 3, 4

and 5 years respectively. No amputations were needed during follow-up.

Conclusion: Treatment with excimer laser debulking combined with drug coated balloon angioplasty of in-stent restenosis in the SFA and popliteal segments seems to offer significantly better long-term outcomes than most stand-alone treatments. Encouraging mid-term results have been described with the use of drug-eluting stents, whereas results after covered stenting are still uncertain.

P 10

Vascular parameters as predictors of walking performances prior and following supervised exercise training in lower extremity artery disease

S. Lanzi, L. Calanca, B. Ney, A. Berchtold, L. Mazzolai (Lausanne)

Objective: To evaluate the effect of supervised exercise training (SET) on vascular parameters [ankle-brachial index (ABI), toe-brachial index (TBI), and transcutaneous oxygen pressure (TcPO₂)] and whether these parameters are predictors of walking performances at baseline and following SET, in symptomatic patients with lower extremity artery disease (LEAD).

Methods: ABI, TBI, and TcPO₂ were measured in each patient at beginning and end of 3-month SET (3 weekly sessions: twice Nordic walking and once lower limbs strengthening). Pain-free walking distance (PFWD) and maximal walking distance (MWD) were assessed.

Results: Eighty-five LEAD patients (65.3 ± 1.0 yr, 72% men) were analyzed. Following SET, PFWD (95.3 ± 8.4 m prior- vs. 230.2 ± 31.2 m post-SET; $P \leq 0.001$), and MWD (289.7 ± 25.6 m vs. 561.6 ± 50.9 m; $P \leq 0.001$) significantly increased. ABI (0.79 ± 0.02 vs. 0.82 ± 0.02 ; $P = 0.12$), and TcPO₂ (49.3 ± 1.8 mmHg vs. 50.6 ± 1.4 mmHg; $P = 0.55$) did not change significantly. TBI (0.59 ± 0.02 vs. 0.63 ± 0.02 ; $P = 0.02$) significantly increased following SET. Patients with higher baseline TBI had significantly higher baseline PFWD ($\beta = 0.25$; $P = 0.01$). Patients with higher baseline TcPO₂ had significantly higher baseline PFWD and MWD ($\beta = 0.30$; $P = 0.005$, and $\beta = 0.22$; $P = 0.04$, respectively). No significant relationship existed between ABI and walking performances at baseline and between baseline ABI, TBI, and TcPO₂ and changes in walking performance following SET. Following SET, PFWD increased significantly (time effect: $P \leq 0.001$) in both patients with ($n = 31$; +85%) and without ($n = 54$; +175%) type II diabetes mellitus (T2DM). There was no group x time interaction effect ($P = 0.12$). MWD significantly increased (time effect: $P \leq 0.001$) in both groups (+59% and +112%, respectively). A significant group x time interaction effect ($P = 0.03$) was found; MWD significantly increased only in patients without T2DM ($P \leq 0.001$, t-test with Bonferroni adjustment). Both women and men significantly increased PFWD (time effect: $P \leq 0.001$), but more substantially women (+230% vs. +101%, respectively; group x time interaction effect: $P = 0.02$). MWD also significantly increased (+120% and +82%, respectively; time effect: $P \leq 0.001$) with no group x time interaction effect ($P = 0.33$).

Conclusion: TBI and TcPO₂ predict baseline walking performances. Women and non diabetic patients may particularly benefit from SET with a substantial increase in walking performances.

P 11

Innovative Therapie eines flottierenden VSM-Thrombus. Falldiskussion

J. C. Ragg (Zürich)

Objective: Bei einem 75-jährigen Patienten (Arztkollege), wurde als Zufallsbefund ein flottierender Thrombus ($14 \times 7 \times 6$ mm) in der Mündung der rechten, auf 9 bis 18 mm dilatierten und bis zum Unterschenkel refluxiven V. saphena magna gefunden. Zur therapeutischen Wahl standen: 1) Chirurgische Extraduktion des Thrombus mit oder ohne gleichzeitiger Entfernung der kranken Stammvene, 2) der interventionelle Versuch einer Thrombusaspiration und späterer Thermookklusion, oder 3) der interventionelle Sofortverschluss als One-Step-Lösung. Nach interdisziplinären Beratungen wurde für die letztere Lösung entschieden.

Methods: Zunächst Verengung der Mündung der VSM mittels Feinnadel-Tumeszenz unter sonographischer Sicht, so dass eine Passage des Thrombus nicht mehr möglich war. Danach Sondierung der VSM mit hydrophilem Führungsdraht (0.035", Terumo, weich, J-Tip), Positionieren eines Führungskatheters (PhleboCath 2,3 mm) vor der Thrombusregion. Mittels einer sphärischen 600 micron Faser und 810 nm Laser (12 W) Fixierung des Thrombus durch fokale Koagulation. VSM-Okklusion mit 80–120 J/cm bis Höhe der Body-Perforans. Entlassung unter Clexane 2 x 20 mg s.c. für 3 Tage sowie Kompressionsstrumpf KKL 2 für 14 Tage.

Results: Die Kontrolle nach 2 Stunden zeigte einen glatten Verschluss der VSM zur V. femoralis mit laminarem Fluß. Beschwerdefreier Verlauf. In den Kontrollen nach 2 und 8 Wochen konnte der stabile Verschluss der rechten VSM bestätigt werden. Spätere Laboruntersuchungen ergaben keinen Hinweis auf eine Thrombophilie.

Conclusion: Eine chirurgische Thrombusextraktion wäre die übliche Wahl gewesen, da bei vorsichtigem Vorgehen die VSM sicher abgeklemmt und eine Embolisierung ausgeschlossen werden kann. Eine interventionelle Thrombusaspiration ohne weiteren Embolisationschutz wäre unsicherer gewesen, mit Filterimplantation weitaus aufwändiger. Thrombosierte und stark dilatierte Venen stellen eher eine Indikation zur chirurgischen Sanierung als zur Thermookklusion dar. Das gewählte Verfahren der Thrombusfixierung und Thermookklusion mit zwingender Wahl von 810 nm zur optimalen Koagulation zeigt jedoch eine sichere Alternative auf, die mit minimaler Invasivität, dem Entfall einer Narkose und der sofortigen Mobilisierung ohne langfristige Antikoagulation einige Vorteile bietet.

P 12

Mycotic pseudoaneurysm in the groin due to injection drug abuse

D. Becker, M. Münchow, M. Bégiun, P. Kissling, V. Makaloski, T. Wyss, J. Schmidli (Bern)

Objective: Mycotic pseudoaneurysm in the groin due to repetitive injection drug abuse is a common severe problem in drug addicted patients. Complications like haemorrhage, distal embolization with ischemia, need for amputation and death are well known. The aim of

this study was to evaluate management and outcome of this challenging surgical situation.

Methods: This is a retrospective analysis of consecutive patients with femoral mycotic pseudoaneurysm in drug addicted patients presenting at a tertiary referral centre between January 2000 and December 2016. Surgical management, predominant microorganisms, complications, mortality and re-infection were assessed.

Results: Twenty-two patients (14 male, 8 female) with a median age of 39 years (range 27–49) were treated. All patients underwent emergency surgery with radical debridement and in situ revascularisation with biological grafts. In 16 patients (73%) subcutaneous vacuum-assisted wound closure (VAC) was performed. In five patients (23%) secondary wound closure was possible. Four patients (18%) were treated with continued VAC therapy until secondary healing. Primary wound closure was achieved in three patients (14%). Muscular flaps to protect the vascular sheath were used in seven patients (32%). Predominant microorganism was *Staphylococcus aureus* (73%), followed by *Streptococcus* (18%) and *Enterococcus* (14%). Main postoperative complications were wound healing disorders (23%). One patient needed an above knee amputation due to repetitive drug injection and embolism. No peri- and postoperative death occurred. Graft re-infection occurred in three patients after a median duration of six months (range 1–14).

Conclusion: Radical debridement and in-situ reconstruction using biological grafts is an effective treatment with a low rate of re-infection in this difficult cohort of patients. Wound healing disorders remain a major postoperative issue. Follow up is difficult due to poor patient compliance.

anlagung und individuelle Stressmuster, die Progression. Falls sich diese Daten in größeren Kollektiven bestätigen, sollte über die Sinnhaftigkeit einer Frühdiagnostik und die Entwicklung kindgerechter Therapien nachgedacht werden

P 14

Innovatives Konzept eines Verödungsschaumes mit einer autologen Biomatrix

J. C. Ragg (Zürich)

Objective: Herkömmliche Verödungsschäume (Aethoxysklerol, STS; Varithena) sind instabil und sehr gashaltig, sie schwimmen bei der Injektion rasch der Blutsäule auf und hinterlassen somit Zonen mit unsicherer oder fehlender Wirkung. Mit zunehmenden Venendurchmessern sind daher in der Regel mehrere Sitzungen erforderlich, Rezidive sind häufig. Eine Biomatrix aus autologem Blut könnte dazu beitragen, stabilere und visköse Verödungsschäume (Projekt „Biomatrix Sclerofoam“, BSF) herzustellen.

Methods: 85 Patienten (56 f, 29 m, 31–78 J.) wurden in Bail-out-Situationen (Kontraindikationen zu OP, Narkose, thermischen Verfahren sowie herkömmlichem Schaum) für BSF ausgewählt. Ziele waren 1. VSM – Insuffizienz 6–14 mm Ø, MW: 8,7, n = 65; 2. VSP – Insuffizienz 6–11 mm Ø, MW: 7,2, n = 20; 3. Perforansdefekte, 4–11 mm Ø, MW: 6,9 mm, n = 43; 4. Seitenastvarizen 5–13 mm Ø, n = 64; 5. Rezidivvarizen 5–15 mm Ø, n = 38. Es wurde ein Schaum aus 40% Aethoxysklerol 2%, 20% Biomatrix und 40% Gasanteil eingesetzt. Die Injektion erfolgte über PTFE-Katheter (PhleboCath, 2.0–2.3 mm Ø), im Fall der selektiver Perforansokklusion über Mikrokatheter. Klinische und sonographische Kontrollen erfolgten nach 2 Wochen, 2 Monaten und einem Jahr.

Results: Eine primäre und vollständige Okklusion aller behandelten Venensegmente wurde in 213/220 Fällen (96,9%) erreicht. 7 Ziele (3,2%) benötigten eine ergänzende Schaumdosis in zweiter Sitzung (VSM: n = 1, Seitenäste: n = 2, Perforantes n = 2, Rezidivvarizen n = 2). Es wurden keine unerwünschten Nebenwirkungen beobachtet, insbesondere keine Thrombosen der tiefen Beinvenen. Nach einem Jahr wurden Reperfusionen gesehen in der VSM-Krosse in 3/65 Fällen (4,3%), im VSM-Verlauf: 4/65 (6,2%), VSP-Krosse: 1/20 (5,0%), Seitenäste: 6/64 (9,4%), Perforantes: 4/43 (9,3%), Rezidivvarizen 4/38 (10,5%).

Conclusion: Der neuartige Schaum ist in den beschriebenen Anwendungen sicher und effektiv. Die guten Ergebnisse nach einem Jahr, angesichts der geringen Fallzahlen noch innerhalb der Lernkurve, geben Anlass zu weiteren Untersuchungen und direkten Vergleichen mit den chirurgischen und endovenösen Standardverfahren.

P 15

The role of brain pericytes in the regulation of leukocyte trafficking under homeostatic and pathological conditions

O. Török, B. Schreiner, A. Keller (Zürich)

Objective: Under homeostasis lymphocyte trafficking into the central nervous system (CNS) is tightly controlled by the blood-brain bar-

HR – Ultraschall: Neue Erkenntnisse zur kongenitalen venösen Insuffizienz

J. C. Ragg (Zürich)

Objective: Die venöse Insuffizienz wird bisher überwiegend für ein genetisch beeinflusstes, erworbenes Geschehen erachtet. Kinder wurden wenig untersucht. Ältere Arbeiten schätzen die Inzidenz kongenitaler Insuffizienzen der unteren Extremitäten auf unter 1%.

Methods: In einer laufenden Studie an Angehörigen von Venenpatienten wurden bisher 26 Kinder zwischen 6 und 16 Jahren (13 m, 13 w) mittels hochauflösendem Ultraschall (HRU, u.a. Vevo MD, 16–32 MHz) systematisch im Bereich der Venen der unteren Extremität untersucht.

Results: Bei 9/22 Kindern (34,6%) wurden venöse Pathologien gefunden: Klappendefekte der V. saphena magna mit Reflux (n = 3), Klappendefekte der VSM ohne makroskopischen Reflux (n = 3), Reflux der VSM ohne erkennbaren Klappendefekt (n = 1), Klappendefekt der VSP (n = 1), Perforansinsuffizienz (n = 1). 4/9 Fälle (44,4%) zeigten eine Betonung regionaler oberflächlicher Venen (Durchmesser, Färbung, Erkennbarkeit).

Conclusion: Setzt man voraus, dass zum Erwerb einer Klappeninsuffizienz durch Faktoren wie Überdruck und Stase Jahrzehnte erforderlich sind, dann handelt es sich bei den gefundenen Pathologien in diesem Alter mit hoher Wahrscheinlichkeit um angeborene Klappendefekte. Unbehandelt droht der bekannte Circulus vitiosus der Flussmodifikation mit Überlastung und konsekutiver Schädigung benachbarter Klappen und somit, modifiziert durch genetische Ver-

rier (BBB). In multiple sclerosis (MS) autoreactive leukocytes enter the CNS and cause demyelinating pathology. Although vast effort is made to understand the pathophysiology of autoimmunity in MS, knowledge about pathological changes of the CNS vasculature that permit the extravasation of autoimmune leukocytes is still limited. Though it was demonstrated that pericytes play an important role in the development of the BBB, further studies are needed to better define the role of pericytes in regulating immune cell trafficking in the CNS.

Methods: We use genetically modified, pericyte-deficient (Pdgfr^{ret/ret}) mice. These animals show approximately 85% reduction of pericyte coverage in the CNS vasculature. We use an animal model of MS-experimental autoimmune encephalomyelitis (EAE) to investigate the role of pericytes in neuroinflammation. In this model, active immunization with myelin oligodendrocyte glycoprotein (MOG 35–55) peptide or an adoptive transfer with MOG 35–55 activated T-cell blasts is performed. The following techniques are used: immunohistochemistry, histochemistry, confocal microscopy, electron microscopy and flow cytometry.

Results: The analysis of brains of adult Pdgfr^{ret/ret} mice has shown increased extravasation of leukocytes into the CNS. These infiltrates were found mainly in the corpus callosum and in periventricular regions. Flow cytometry analysis demonstrated that, the number of CD45^{high}CD11b⁺ myeloid cells was increased in pericyte-deficient CNS compared to control. Immunization of Pdgfr^{ret/ret} mice with MOG peptide led to an early and strong atypical EAE phenotype.

Conclusion: Our data suggest that pericytes regulate several BBB characteristics and inhibit leukocyte extravasation into the CNS by contributing to the non-permissive properties of the endothelium during homeostasis, and restrict immune cell migration. Pericyte-deficiency changes the clinical phenotype in EAE. However, further characterization is needed to better define the role of pericytes in immune cell trafficking in the CNS.

P 16

Brain endothelial mechanisms directing the cellular pathway of T cell migration across the blood brain barrier

L. Marchetti, N. Haghayegh, D. Francisco, I. Gruber, R. Lyck, R. Bruggmann, B. Engelhardt (Bern)

Objective: The endothelial blood-brain barrier maintains central nervous system (CNS) homeostasis and strictly controls lymphocyte trafficking into the CNS. During multiple sclerosis or its animal model experimental autoimmune encephalomyelitis (EAE) autoaggressive CD4⁺ T cells cross the BBB and cause neuroinflammation. Diapedesis of T cells across the BBB can occur via a paracellular or transcellular route. Using an in vitro BBB model of primary mouse brain microvascular endothelial cells (pMBMECs), we found that endothelial ICAM-1 influences the cellular pathway of CD4⁺ T-cell diapedesis across the BBB. Here we search the molecules downstream of ICAM-1 involved in this process and include investigation of encephalitogenic Th1 and Th17 subsets which differ in their trafficking molecules profiles.

Methods: Multi-step extravasation of Th1 and Th17 cells across pMBMECs expressing high or low levels of ICAM-1 is investigated under physiological flow by means of in vitro live cell imaging. Novel

molecular candidates involved in the cellular pathway of T cell diapedesis are investigated by comparing transcriptome profiles obtained by RNAseq analysis of pMBMECs stimulated to express different levels of ICAM-1.

Results: We observed differences between Th1 versus Th17 cells in their ability to arrest to pMBMECs under physiological flow. Their post-arrest behaviour, e.g. probing the endothelial cells, crawling and diapedesis is presently analysed. RNAseq analysis identified 56 candidate genes potentially involved in directing the cellular pathway of T cell diapedesis.

Conclusion: Th1 and Th17 cells differ in their ability to interact with the BBB under physiological flow suggesting that these CD4⁺ T cell subsets use different molecular mechanism to cross the BBB. Ongoing experiments address if Th1 and Th17 cells choose different cellular pathways to cross the BBB and if the candidate genes identified are involved in this process.

P 17

Determining the protein atlas of normal human blood-brain barrier and glioblastoma blood-brain barrier – towards understanding glioblastoma biology and improved therapies

J. B. Schaffnerath, A. Keller (Zürich)

Objective: Glioblastoma multiforme (GBM) is the most common primary brain tumor with high severity and low therapeutic success. Currently available therapies are not effective and the life expectancy is in average 12–15 month after diagnosis.

One important aspect in successful treatment of GBM is to achieve entrance into brain parenchyma. This is difficult since the brain endothelium presents low permeability to blood molecules due to the blood-brain barrier (BBB). The BBB allows free passage of small lipid soluble molecules or molecules with appropriate receptor binding sites. Until now, the development and homeostatic regulation of human BBB is poorly understood. It is known that GBM vasculature has different features compared to the normal brain vasculature. There are areas within the GBM showing BBB leakage, yet no increased drug transport into the tumor site. Extending the knowledge about the molecular composition of the GBM BBB will hopefully bring insights into biology of GBM vasculature, and help to design better treatment strategies.

Methods: In this study, we aim to characterize the transcriptome and proteome of the human BBB in health and GBM. Human endothelial cells (EC) are isolated from GBM and normal human brain tissue. As a control, we use autopsy material with a maximum PMI of 20 hours. For both tissues, normal and GBM, the isolation of EC includes tissue homogenization and a first step of negative selection with anti-CD15 and anti-CD45 antibodies coupled to magnetic beads to exclude leukocytes and circulating progenitor cells. ECs are isolated using anti-hCD31 antibody conjugated magnetic beads. Isolated cell fractions are lysed for RNA and protein isolation. In addition to characterization of RNA and protein profile of the EC fraction, we will perform RNA sequencing and proteome analysis on tumor tissue depleted for EC, in order to molecularly profile GBM and to identify neo-epitopes expressed by GBM.

Results: We have successfully isolated RNA with a high integrity number from autopsy and GBM ECs. In addition, we obtained a suf-

ficient amount of proteins for mass-spectrometry analysis from EC fractions. We will present first analysis of transcriptome and proteome of human normal and GBM BBB.

P 18

Organ-specific regulation of lymphatic vessel function by the autonomic nervous system

S. Bachmann, S. Proulx, J. Montoya, M. Scheider, M. Rudin, M. Detmar (Zurich)

Objective: The neural regulation of lymphatic vessel function has been a rather neglected topic. We aimed to establish new imaging methods to better understand regulatory influences from the nervous system on lymphatic vessel (LV) activity.

Methods: In order to get a general impression of possible influences of the autonomic nervous system on LVs, we first examined the expression of neurotransmitter receptors on LVs at different organ sites using whole mount stainings. The same method was used to identify different nerve types running along LVs.

To quantitatively characterize the effects of the autonomic nervous system in vivo, we developed a new imaging method where the flank lymphatic collector is exposed in the living mouse and a small amount of a pegylated near-infrared dye is infused into the inguinal lymph node by an infusion pump to perfuse the efferent collecting vessel. This set-up allows quantification of the frequency of contractions and the end-systolic and end-diastolic diameters.

Results: The stainings show that skin-associated collecting LVs express muscarinic receptors as well as beta-adrenergic receptors on their endothelial cells. The associated smooth muscle cells express muscarinic receptors in combination with alpha-adrenergic receptors. In contrast to these findings, intestinal lacteals express beta-adrenergic receptors only. Furthermore, the smooth muscle cells present in the villi express muscarinic receptors only. These findings indicate an ingenious regulation of the lymphatic system by the autonomic nervous system and can explain some contradictory results published. In line with these findings, we also identified differences in the types of nerves running along collecting LVs in different organs. Using the in vivo imaging technique we were able to characterize the direct effects of neurotransmitters on the pumping behavior of lymphatic collectors.

Conclusion: We could show for the first time that murine LVs are innervated and express different neurotransmitter receptors in an organ-dependent way. We also could characterize the regulatory influence of the autonomic nervous system on LV pumping, which opens up potential new therapeutic approaches for lymphedema and other diseases with lymphatic vessel involvement.

P 19

ACKR4 is expressed by afferent lymphatic collectors and affects T cell migration to draining lymph nodes

M. Friess¹, S. Proulx¹, A. Rot², C. Halin Winter¹ (¹Zürich, ²York GB)

Objective: Atypical chemokine receptors (ACKRs) are chemokine receptors that are uncoupled from G-proteins. ACKRs function as scavengers, internalizing and degrading the chemokines they bind. Additionally, they can also present these chemokines which has been shown so far for ACKR1 (Pruenster et al., Nat Immunol 2009). ACKR4, which binds the chemokines CCL19, CCL21 and CCL25, was recently shown to be expressed by lymphatic endothelial cells (LECs) lining the subcapsular sinus (SCS) ceiling of lymph nodes (LNs). As such, ACKR4 is important for the formation of a CCL21 gradient across the SCS and for enabling DC migration into LNs (Ulvmar et al., Nat. Immunol 2014). In this project, we set out to investigate ACKR4 expression by LECs in other parts of the lymphatic vasculature and to further study its function in the lymphatic system.

Methods: We performed experiments using ACKR4-GFP knock-in mice (ACKR4-GFP/GFP and ACKR4-GFP/+) expressing GFP instead of ACKR4, in order to investigate the role of ACKR4 expression on leukocyte trafficking within lymphatic vessels and on lymphatic vessel biology.

Results: Wholmount-stainings in ACKR4-GFP knock-in mice (ACKR4-GFP/GFP and ACKR4-GFP/+) revealed strong expression of ACKR4 in large lymphatic collectors, while only some of the smaller pre-collectors and no capillaries in the dermis displayed a GFP signal. These findings prompted us to investigate the functionality of ACKR4 in collector LECs and to study its effect on leukocyte trafficking. Performing an in vivo chemokine uptake assay with fluorescently labelled CCL19 injected into footpad we found that ACKR4 expressed in LECs of the large afferent collectors is functional; i.e. it bound CCL19 in ACKR4-GFP/+ mice while no CCL19 signal was detected in ACKR4-GFP/GFP mice. Moreover, adoptive transfer experiments revealed an impairment of T cell migration in ACKR4-GFP/GFP mice: Upon injection into the footpad, fewer T cells were found in the draining popliteal LN of ACKR4-GFP/GFP as compared to wild type mice. In a next step, we plan to further investigate the impact of ACKR4 expression on T cell migration through lymphatic collectors, by wholmount stainings and intravital microscopy.

Conclusion: Overall, we could show so far that ACKR4 is expressed by lymphatic collectors and affects T cell migration through lymphatics into the draining LN.

P 20

Claudin 3-deficient C57BL/6 mice display intact brain barriers

M. Dias¹, C. Coisne¹, P. Baden¹, I. Lazarevic¹, D. Francisco¹, R. Lyck¹, G. Enzmann¹, U. Deutsch¹, R. Bruggmann¹, C. Betsholtz^{2,3}, M. Furuse⁴, B. Engelhardt¹ (¹Bern, ²Uppsala S, ³Stockholm S, ⁴Okazaki J)

Objective: In multiple sclerosis and its animal model experimental autoimmune encephalomyelitis (EAE), loss of blood-brain bar-

rier (BBB) integrity is a disease's hallmark. Claudin-3 was reported to localize to tight junctions (TJs) of the BBB endothelium and the blood-cerebrospinal fluid barrier (BCSFB) epithelium. Claudin-3's contribution to brain barriers' integrity was supported by selective loss of claudin-3 immunostaining from leaky CNS microvessels surrounded by inflammatory cuffs in EAE. Additionally, claudin-3^{-/-} mice on a mixed genetic background developed aggravated EAE due to increased BCSFB leakiness. Thus, our main aim was to study EAE pathogenesis in claudin-3^{-/-} C57BL/6 mice and compare the role of claudin-3 in BBB vs BCSFB integrity in vitro and in vivo.

Methods: Claudin-3^{-/-} mice were backcrossed to the C57BL/6J background for 12 generations. Expression of claudin-3 and other TJ molecules at the BBB and BCSFB ex vivo and in vitro was investigated by qPCR and immunostainings. Primary mouse brain microvascular endothelial cells and primary mouse choroid plexus epithelial cells from WT and claudin-3^{-/-} mice were used as in vitro models for the BBB and BCSFB, respectively. TJ immunofluorescence staining, transelectrical resistance (TEER) measurement and permeability assays were performed to assess barrier functionality in vitro. Brain barriers' integrity in vivo was assessed for exogenous and endogenous tracers in CNS tissue sections. Development of EAE was compared in WT and claudin-3^{-/-} animals.

Results: We found no difference in the development and progression of EAE in claudin-3^{-/-} C57BL/6 mice compared to WT littermates. In addition, absence of claudin-3 did not increase leakage of exogenous or endogenous tracers across both barriers in vivo. Similarly, in vitro investigations failed to demonstrate any role for claudin-3 in maintaining barrier's properties, as determined by TEER, TJs immunostainings and permeability assays in vitro. Compensatory upregulation of other TJs proteins (such as occludin, claudin-2 and claudin-11) in claudin-3^{-/-} mice that might mask the absence of claudin-3 was excluded by expression analysis of the mRNA.

Conclusion: We demonstrate that absence of claudin-3 in C57BL/6 mice does not impair brain barrier properties during health and neuroinflammation.

successful adaptation of this in vitro BBB model to a flow chamber allowing for live cell imaging of T-cell migration across the BBB under physiological flow.

Methods: The CD34⁺ ECs were cultured in the custom made flow chambers on nanoporous pnc-Si membranes with high optical characteristics. Pericyte co-culture was replaced by a pericyte conditioned medium and barrier characteristics were confirmed by immunostaining for tight junction molecules (claudin-5, ZO-1) and evaluation of permeability of the EC monolayer for Lucifer Yellow. Physiological flow was established using a pump system. Placing the flow chamber under an inverted microscope allows for real time imaging of cell-cell interactions.

Results: The CD34⁺ ECs formed tight monolayers on the nanoporous pnc-Si. Employment of pericyte conditioned medium induced BBB characteristics in CD34⁺ ECs comparable to those observed under standard pericyte co-culture. Employing this novel in vitro model of the human BBB we could observe the multi-step extravasation of human T cell subsets across the BBB under physiological flow.

Conclusion: This novel in vitro fluidics model of the human BBB is a powerful tool to study the multi-step extravasation of precious human T-cell subsets across the human BBB under flow by means of live cell imaging.

P22

Absence of the junctional adhesion molecule (JAM)-B ameliorates experimental autoimmune encephalomyelitis

S. Tietz¹, T. Périnat¹, U. Deutsch¹, B. Imhof², M. Aurrand-Lions³, B. Engelhardt¹ (¹Bern, ²Geneva, ³Marseille F)

Objective: Unique intercellular junctional complexes between the central nervous system (CNS) microvascular endothelial cells establish the paracellular diffusion barrier of the blood-brain barrier (BBB). In addition to occludin and the claudins, the junctional adhesion molecules (JAM-A, JAM-B, and JAM-C) are localized in BBB tight junctions. In multiple sclerosis (MS) and its animal model experimental autoimmune encephalomyelitis (EAE) autoaggressive CD4⁺ T-cells cross the BBB and cause BBB breakdown and neuroinflammation. Therapeutic targeting of CD4⁺ T-cell trafficking into the CNS using the humanized anti- α 4-integrin antibody has proven beneficial for the treatment of MS, however comes with the risk of progressive multifocal leukoencephalopathy, probably caused by inhibition of CD8⁺ T cell entry into the CNS. We have recently shown that CD8⁺ T-cells require α 4b1-integrin to cross the BBB in neuroinflammation. Besides vascular cell adhesion molecule - 1 (VCAM-1) we identified junctional adhesion molecule -B (JAM-B) as alternative vascular α 4b1-integrin ligand mediating CD8 T-cell trafficking across the BBB.

Methods: Using a novel transgenic mouse model with constitutive lack of JAM-B we here investigated the role of JAM-B in mediating T-cell trafficking into the CNS during EAE.

Results: Although JAM-B^{-/-} C57BL/6 mice developed ameliorated EAE when compared to wild-type littermates, we found higher numbers of infiltrating immune cells in the CNS of JAM-B^{-/-} C57BL/6 mice suffering from EAE. The majority of inflammatory cells were trapped behind the BBB in leptomeningeal and perivascular spaces. To investigate a possible role for JAM-B in T-cell proliferation and

P21

Modelling the multi-step migration of human T cells across the human blood-brain barrier under physiological flow in vitro: Introduction of a novel nanomembrane based flow chamber system

A. Mossu¹, M. Rosito¹, H.-L. Chung², T. Khire², F. Gosselet³, J. McGrath², B. Engelhardt¹ (¹Bern, ²New York USA, ³Leuven F)

Objective: The endothelial blood-brain barrier (BBB) in central nervous system (CNS) microvessels establishes an important interface between the immune system and the CNS. In multiple sclerosis (MS) BBB properties change and promote the migration of pathogenic T cells into the CNS. To this end molecular mechanisms mediating T-cell entry into the CNS has largely been studied in animal models, but translation of these findings to humans is still incomplete. Recently a new human BBB model has been established by coculturing endothelial cells (ECs) differentiated from human CD34⁺ cord blood cells with bovine pericytes. This model exhibits strong BBB characteristics with low permeability and junctional localization of tight junction molecules like ZO-1 and claudin-5. Here we introduce

polarization we adoptively transferred encephalitogenic polyclonal CD4 T-cells generated in either wildtype or JAM-B-/-C57BL/6 donor mice into wildtype or JAM-B-/-C57BL/6 recipient mice. Irrespective of their origin, adoptively transferred T-cells induced EAE with similar severity in wildtype and JAM-B-/-C57BL/6 mice.

Conclusion: Our findings suggest that although JAM-B is not required for T-cell diapedesis across the BBB its absence limits the inflammatory cell entry into the CNS parenchyma. The signalling events downstream of vascular JAM-B leading to amelioration of EAE are presently investigated.

P23

Vascular characterization of pericyte deficient Pdgfrb ret/ret mice

E. Erlebach¹, J. Stobart¹, C. Glück¹, M. Barrett¹, M. Li¹, V. Efremov^{1,2}, A. Keller¹, B. Weber¹ (¹Zurich, ²Munich D)

Objective: A special feature of the microvascular capillaries is their coverage with pericytes, mural cells embedded within the basement membrane of the vascular wall. The close contact to the bloodstream and their contribution to the neurovascular unit make them to promising candidates for blood flow regulation and blood-brain barrier built-up. Mice lacking part of the pericyte gene, normally used for their recruitment to the vessel wall, present with a reduced number (80% less), decreased vessel wall coverage and detachment of these cells.

With help of these pericyte deficient Pdgfrb ret/ret mice we aim to identify and verify the functional role of pericytes in the vascular network.

Methods: Two-photon imaging of Pdgfrb ret/ret mice allows us to investigate the morphological differences of the brain vasculature as well as alterations in oxygen distribution in an animal over time. Absolute oxygen levels are measured using an intravenously injected phosphorescent probe (PtTCHP-C3071), enabling the detection of vascular pO₂ while imaging with the two-photon microscope.

Results: The angioarchitecture of Pdgfrb ret/ret mice shows balloon like evaginations of the vessel wall in combination with an overall increase of vessel diameter. Beyond that visual analysis suggests an increased vessel branching and therefore a decreased segmental length between branching points.

Concerning blood flow behavior we detected a diminished flux and velocity of red blood cells as well as turbulent blood flow, presented by an increased pulsatility index.

Unlike the blood flow data we were not able to detect any striking differences in oxygen pressure levels of Pdgfrb ret/ret mice.

Conclusion: So far our results suggests that a loss or dysfunction of pericytes during the development leads to alterations in vessel architecture and subsequently to a change in blood flow behavior, including a pulsatile and irregular blood flow.

P24

Vasodilatory actions of GLP-1, GLP-2 and Glucagon

V. Marzolla¹, A. Taheri¹, T. A. Lutz², T. F. Lüscher¹, C. Wolfrum³, E. Osto^{1,3} (¹Schlieren, ²Zurich, ³Schwerzenbach)

Objective: Roux-en-Y gastric bypass (RYGB) reduces weight and cardiovascular mortality. In obese rats, increased glucagon-like peptide-1 (GLP-1) levels after RYGB are associated to improved aortic endothelial function through PKA/endothelial nitric oxide synthase (eNOS) activation. Glucagon (Gluc), GLP-1 and Glucagon-like peptide-2 (GLP-2) are three hormones derived by cleavage from the common precursor pre-proglucagon, and the levels of all three increase after RYGB. This study aims to investigate the vasodilatory role of GLP-1, GLP-2 and GLC in mice deleted for the pre-proglucagon gene (PPG-/-).

Methods: Thoracic aortic rings isolated from 25 weeks old male PPG-/- (n = 8) and PPG+/+ (WT, n = 8) fed a chow diet were subjected to ex vivo isometric tension recordings. After submaximal contraction with phenylephrine (PE, 3*10⁻⁷mol/L), cumulative relaxation responses were performed with acetylcholine (Ach, 10⁻⁹ to 10⁻⁶mol/L), GLP-1 (10⁻¹² to 10⁻⁶mol/L), GLP-2 (10⁻¹² to 10⁻⁶mol/L), Gluc (10⁻¹² to 10⁻⁶mol/L) or insulin (10⁻¹¹ to 10⁻⁶mol/L) with or without the eNOS inhibitor L-NAME (10⁻⁴mol/L). Gluc/GLP-1/GLP-2- and insulin- dependent pathways were evaluated in aortas by western blot.

Results: PPG-/- and WT mice showed overall no differences in contraction and relaxation in response to PE, Ach and insulin. In PPG-/- mice, GLP-1, GLP-2 and Gluc induced a greater vasorelaxation compared to WT indicating a greater sensitivity to the vasodilatory effect of these three hormones upon PPG deletion. This was associated to enhanced aortic expression of the GLP-1 receptor and PKA in PPG-/- versus WT mice. In all groups, the response to GLP-1 and GLP-2 was blocked by preincubation with L-NAME, suggesting an eNOS-dependent mechanism. Instead, L-NAME did not modify the vasodilatation in response to Gluc, which likely acts via eNOS-independent mechanisms.

Conclusion: Lack of endogenous PPG hormones in PPG-/- mice is associated with increased responses to GLP-1, GLP-2 and Gluc compared to WT. GLP-1 and GLP-2 induce NO-dependent effects, likely mediated by GLP-1R and PKA activation; instead further investigations are needed to examine the GLC-dependent vasodilatation in PPG-/- mice.

P25

Calcium signaling in CNS cortical pericytes

C. Gluck, J. Stobart, A. Keller, B. Weber (Zurich)

Objective: Central nervous system (CNS) pericytes are mural cells, embedded within the vascular basement membrane. They are important for structural support to the microvasculature and for the maintenance of the blood brain barrier. Together with astrocytes, neurons and endothelial cells they form the neurovascular unit (NVU) and are involved in brain hyperaemia, i.e. a fundamental mechanism for CNS homeostasis. Pericyte deficiency is linked to

several diseases like diabetic retinopathy and blood brain barrier breakdown. However, little is known about intracellular signaling mechanisms in pericytes and their role in the regulation of blood flow. We seek to understand the calcium transients in pericytes and their involvement in signal transduction pathways.

Methods: We utilized a novel mouse model expressing a genetically encoded calcium indicator (GCaMP6s) specifically in pericytes to visualize intracellular calcium signals by two photon-laser scanning microscopy (2PLSM) in vivo and in brain slices where we are able to modulate calcium transients pharmacologically.

Results: We observed fast, spontaneous calcium transients in pericyte fine processes and cell bodies. We have also used several pharmacological interventions to identify the underlying cause of these basal pericyte calcium dynamics.

Conclusion: Pericytes have high frequent calcium transients not only in their cellbodies but also along their processes, covering large parts of the microvascular endothelium.

Further understanding of pericyte calcium signaling pathways will shed light on the communication and interaction between the cells of the NVU and their impact on proper brain functioning.

P26

Role of endothelial calcineurin signaling in tumor progression

S. Hendriks¹, S. Coso¹, B. Prat Luri¹, A. Sabine¹, C. Franco², T. V. Petrova¹ (¹Epalinges, ²Lisboa P)

Objective: Suppression of calcineurin/NFAT pathway has been linked to increased non-viral related cancer incidence in organ transplant patients receiving cyclosporin A. To date, disruption of immune function via inhibition of calcineurin in immune cells is considered to be the primary reason. However, calcineurin/NFAT signaling is also activated in endothelial cells in response to the main angiogenic factor VEGF-A and previous studies suggested that activation of this pathway is an essential component of the angiogenic response of endothelial cells in vitro.

Methods: Here we investigated the role of calcineurin/NFAT signaling in physiological and pathological angiogenesis as well as metastatic dissemination. Using mouse models with inducible inactivation of calcineurin in endothelial cells, we have studied postnatal retinal vascularization as well as B16F10 (melanoma) primary tumor formation and lung metastasis.

Results: We show that this pathway is dispensable for angiogenic responses during retinal and tumor angiogenesis, and it is mostly implicated in stabilization of vascular anastomoses. Interestingly, while the growth of primary tumors and tumor cell extravasation was not affected, the metastatic outgrowth was potentiated in animals without endothelial calcineurin signaling.

Conclusion: Our data show that endothelial calcineurin/NFAT signaling is principally implicated in vascular stabilization, in contrast to a broader angiogenic role of VEGF-A. Furthermore, they suggest that post-transplantation immunosuppressive therapy also directly targets the endothelium, potentially contributing to aggressive cancer development in organ transplant recipients. Further knowledge of the exact molecular mechanisms will be important for understanding the role of blood vessels in metastatic outgrowth.

P27

Pannexin1 links lymphatic function to lipid metabolism and atherosclerosis

F. Molica¹, M. Meens¹, J. Dubrot¹, S. Morel¹, G. Pelli¹, A. Ehrlich¹, V. Braunersreuther¹, M. Chanson¹, S. Hugues¹, E. Scemes², B. Kwak¹ (¹Geneva, ²New York USA)

Objective: Atherosclerosis is a progressive disease of the arterial wall arising from an unbalanced lipid metabolism and a maladaptive inflammatory response. Extracellular ATP is a central signaling molecule in the inflammatory cascade. Pannexin1 (Panx1) channels release ATP in a controlled manner and are implicated in a plethora of inflammatory pathologies. Here, we investigated the role of Panx1 in atherogenesis.

Methods: We used atherosclerosis-prone mice with ubiquitous deletion of Panx1 (Panx1^{-/-}-Apoe^{-/-}) or with Cre recombinase-mediated deletion of Panx1 in endothelial cells (EC) and monocytic cells (Tie2-CreTgPanx1fl/flApoe^{-/-}; Panx1del) to study atherogenesis in thoraco-abdominal aortas and aortic roots after 5 or 10 weeks high-cholesterol diet. Panx1 expression in atherosclerotic plaques was assessed by immunofluorescence. Total cholesterol and triglyceride (TG) levels were measured in the serum. Cryosections from aortic roots were immunostained for specific cell markers (CD68, CD3, CD31, alphaSMA). Footpad injections of Evans Blue and oral lipid tolerance tests were performed to determine the drainage of interstitial fluids and dietary fat absorption, respectively.

Results: Atherosclerosis was enhanced in Panx1del vs. Panx1fl/fl mice (14.2 ± 3.6% vs. 6.9 ± 0.9, N = 10, P < 0.05), pointing to an atheroprotective role for Panx1 in EC and/or monocytes. Unexpectedly, atherogenesis was not affected in mice with the ubiquitous deletion of Panx1, but Panx1^{-/-}-Apoe^{-/-} mice displayed reduced body weight (24.8 ± 0.5 vs. 29.2 ± 0.6 g, N = 10, P < 0.0001), serum cholesterol (727.3 ± 36.3 vs. 921.5 ± 67.4 mg/dL, N = 10, P < 0.05) and TG (133.3 ± 16.2 vs. 284.2 ± 47.6 mg/dL, N = 10, P < 0.01) as compared to Apoe^{-/-} controls, suggesting altered lipid metabolism in these mice. Mechanistically, Panx1^{-/-}-Apoe^{-/-} mice showed impaired lymphatic function with decreased drainage of interstitial fluids (P < 0.05) and reduced dietary fat absorption compared to control (P < 0.05).

Conclusion: The deleterious effect of Panx1 deletion in EC and/or monocytic cells during atherogenesis is counterbalanced by an opposite effect, which results from impaired lymphatic function in ubiquitous Panx1-deficient mice. Our findings unveil a pivotal role of Panx1 in linking lymphatic function to lipid metabolism and atherosclerotic plaque development.

P28

Bile acid-mediated vasodilatation in TGR5-deleted mice

A. Taheri¹, M. Engeli¹, P. Doytcheva¹, R. Urbanet¹, M. Lannoo², L. Rohrer¹, C. Wolfrum³, T. F. Lüscher¹, T. A. Lutz¹, E. Osto^{1,3} (¹Zurich, ²Leuven B, ³Schwerzenbach)

Objective: Bile acids (BA) may mediate many beneficial cardiovascular effects after Roux en-Y gastric bypass (RYGB). BA can exert

vasoactive actions via membrane (TGR5) and nuclear (farnesoid-X receptor (FXR)) receptors at the aortic level. Here, the vasodilatory action of tauro lithocholic acid (TLCA), a potent TGR5 activator, and chenodeoxycholic acid (CDCA), a potent FXR activator, was investigated in TGR5-deleted mice (TGR5^{-/-}).

Methods: Thoracic aortic rings of TGR5^{-/-} and controls (WT) male mice aged 20 weeks and fed on normal chow were collected and suspended for isometric tension recording. Cumulative concentration-relaxation curves were obtained in response to TLCA (10⁻⁷ to 10⁻⁴ mol/L), CDCA (10⁻⁷ to 10⁻⁴ mol/L), norepinephrine, (NE, 10⁻¹¹ to 10⁻⁵ mol/L), acetylcholine (ACh, 10⁻⁹ to 10⁻⁵ mol/L), and sodium nitroprusside, a nitric oxide donor (SNP, 10⁻¹⁰ to 10⁻⁶ mol/L), and after incubation with the H₂O₂ scavenger, catalase (1200 U), indomethacin (10⁻⁴ mol/L), a COX1/2 inhibitor; propylargylglycine (PAG, 3 mM), a cystathionine γ-lyase inhibitor; and L-NAME (10⁻⁴ mol/L), the endothelial nitric oxide synthase (eNOS) inhibitor, respectively. Removal of the endothelium with Triton X-100 0.05% was used to assess endothelium-independent responses. Plasma concentrations of total bile acid species in TGR5^{-/-} and controls were measured using spectrophotometry.

Results: There was no difference in vasorelaxation induced by TLCA and CDCA as well as by ACh, and SNP in TGR5^{-/-} vs WT. The vasodilatation in response to TLCA and CDCA was significantly reduced by L-NAME and endothelium removal. This supports the presence of endothelial and NO-dependent vasodilatation in these mice. Preincubation with catalase, indomethacin, and PAG had no effect on vasoactive properties of TLCA and CDCA in TGR5^{-/-} vs WT, suggesting a vasorelaxatory mechanism exists independent from hydrogen peroxide, prostacyclin production, and hydrogen sulfide. There was no significant difference in baseline levels of total plasma bile acids between TGR5^{-/-} (n = 9) and controls (n = 7) (35.19 ± 13.71 nmol/L vs 36.96 ± 16.58 nmol/L), likely due to the regulation of bile acid synthesis by FXR.

Conclusion: TLCA and CDCA induce endothelium-dependent vasorelaxation, likely through the production of NO. TGR5^{-/-} mice may compensate for the absence of the receptor through a yet unclear pathway at the endothelial level.

P29

IL-7 receptor signaling affects vascular function and the progression of chronic skin inflammation

M. Vranova, O. Hagedorn, D. Andina, D. Impellizzieri, J.-C. Leroux, O. Boyman, S.-T. Proulx, C. Halin Winter (Zurich)

Objective: The lymphatic and blood vasculature play an active role in the progression of chronic skin inflammation. The vessels expand, increased vascular permeability leads to edema, and the vessels mediate leucocyte trafficking. Interleukin-7 (IL-7) and thymic stromal lymphopoietin (TSLP) are cytokines that signal through the IL-7 receptor alpha (IL-7Ra). IL-7 is a cytokine important for T cell development and homeostasis, while TSLP induces Th2 T cell responses. IL-7 and TSLP levels are elevated in psoriasis, but their role in diseases progression has not been addressed.

Our lab has shown that IL-7Ra is expressed on lymphatic endothelial cells and activates these cells in vitro (Iolyeva et al., Blood, 2013). Furthermore, the lymphatic vessel network and drainage function

are altered in IL-7Ra knockout (KO) mice in a stromal cell-dependent manner. Currently, we are investigating the role of IL-7 and TSLP in blood vascular function. Additionally, we are investigating the role of these cytokines in psoriasis progression. In this context, we are dissecting the effect of IL-7 and TSLP on both the vasculature and immune compartments and how this affects disease progression.

Methods: To study the role of IL-7Ra signaling in blood vascular function we conduct in vivo experiments in IL-7Ra KO mice and in mice with a ve-cadherin-driven endothelial specific KO of the IL-7Ra. These experiments comprise of immunofluorescence analysis of the vascular network and functional assays to assess blood vascular leakage. In addition, we perform in vitro assays on blood endothelial cells (BECs). To study the role of IL-7 and TSLP in psoriasis, we employ the K14-VEGF-A and imiquimod inflammation models.

Results: We show that IL-7 and TSLP activated BECs in vitro and that the blood vessel network was altered in IL-7Ra KO mice. Furthermore, blood vascular leakage was reduced in global IL-7Ra KO mice, as well as in endothelial-specific IL-7Ra KO mice. Blocking IL-7Ra with an antibody ameliorated inflammation in two psoriasis models, showing reduced edema and immune cell infiltration.

Conclusion: IL-7Ra signaling affects blood vascular leakage and is important in the pathogenesis of psoriasis. Currently, we are dissecting the protective mechanisms of the anti-IL7Ra treatment on the vascular and immune compartments in the endothelial specific IL-7Ra KO mice.

P30

The role of PSGL-1 in neutrophil accumulation after ischemic stroke

P. Kargaran, G. Enzmann, B. Engelhardt (Bern)

Objective: Neutrophils are considered to be involved in neuronal cell death and reperfusion injury following ischemic stroke. We have recently shown that despite the upregulation of P-selectin, ICAM-1 and VCAM-1 on the blood-brain barrier (BBB) in the ischemic brain, neutrophils fail to infiltrate the infarcted brain parenchyma and rather accumulate within the neurovascular unit (NVU). This suggests that the molecular mechanisms involved in neutrophil interaction with the ischemic BBB are unique. The aim of the present study was to investigate the role of P-selectin glycoprotein ligand-1 (PSGL-1) which constitutes the first step of neutrophil extravasation across inflamed vascular beds by mediating neutrophil rolling on endothelial P-selectin.

Methods: We investigated ischemic stroke in a model of transient middle cerebral artery occlusion (tMCAO) in PSGL-1^{-/-} C57BL/6 mice and their wild-type littermates. Lesion size, upregulation of adhesion molecules and accumulation of leukocytes were studied by immunohistochemistry and immunofluorescence staining of tissue sections of ischemic brains at 24 hours reperfusion following 30, 45 and 60 min occlusion.

Results: Already after 30 min tMCAO/24h reperfusion we observed positive immunostaining for P-selectin on cerebral blood vessels of wild-type C57BL/6 mice. This was accompanied by accumulation of Ly6G⁺ neutrophils in the leptomeninges and to a low degree in the ischemic hemisphere of wild-type C57BL/6 mice. Interestingly, although PSGL-1^{-/-} C57BL/6 mice displayed similar levels of endothelial P-selectin in meningeal blood vessels, Ly6G⁺neutrophil

accumulation in the leptomeninges was abrogated. In contrast, leptomeningeal accumulation of CD45⁺/CD11b⁺/Ly6G⁺ myeloid cells was observed in both PSGL-1^{-/-} and wild-type C57BL/6 mice.

Surprisingly, PSGL-1^{-/-} C57BL/6 mice subjected to 60 min tMCAO succumbed to the injury within 20 hours of reperfusion suggesting an additional protective role of PSGL-1 in ischemic stroke.

Conclusion: Our findings point to an essential role for PSGL-1 in leptomeningeal neutrophil accumulation after ischemic stroke. Therapeutic targeting of PSGL-1 might however be prohibited by a not yet appreciated protective role of PSGL-1 after ischemic stroke.

P31

T cell migration from inflamed skin to draining lymph nodes requires intralymphatic crawling supported by ICAM-1/LFA1 interactions

M. Hunter¹, A. Teixeira², E. Russo¹, S. T. Proulx¹, T. Frei¹, G. F. Debes³, M. Coles⁴, I. Melero², M. Detmar¹, A. Rouzaut², C. Halin Winter¹
(¹Zurich, ²Pamplona E, ³Philadelphia USA, ⁴York GB)

Objective: T cells are the most abundant cell type found in afferent lymph, but the mechanisms of their migration through afferent lymphatic vessels are poorly understood. We aimed to image T cell migration through afferent lymphatic vessels in vivo and further elucidate the mechanisms involved in intralymphatic T cell migration.

Methods: We performed intravital microscopy in the ear skin of a dual lymphatic vessel and T cell fluorescent reporter mouse model. Further in vitro T cell adhesion, crawling and transmigration experiments, as well as in vivo adoptive transfer experiments, complemented our imaging approach.

Results: T cells entered into and actively migrated within lymphatic capillaries but were passively transported in contractile collecting vessels. Contact hypersensitivity-induced inflammation increased lymphatic endothelial expressed ICAM-1 and, correspondingly, intralymphatic T cell motility. Antibody-mediated blockade of ICAM-1 or its integrin ligand LFA-1 equally reduced intralymphatic T cell motility. In vitro, blockade of lymphatic endothelial cell-expressed ICAM-1 significantly reduced Th1 cell adhesion, crawling and transmigration across lymphatic endothelium and decreased T cell advancement from lymphatic capillaries into collectors in skin explants. In vivo, antibody-mediated blockade of ICAM-1 or LFA-1 significantly reduced the migration of adoptively transferred T cells from the skin to draining lymph node.

Conclusion: Overall, our findings demonstrate that T cell migration through afferent lymphatic vessels occurs in distinct steps and reveal a key role for ICAM-1-LFA-1 interactions in this process.

P32

Generation of an inducible knock-out in the VE-cadherin / Cdh5 gene to study endothelial cell-cell interactions during sprouting angiogenesis

N. Schellinx, H. G. Belting, M. Affolter (Basel)

Objective: VE-cadherin/Cdh5 is a prominent adhesion protein located in endothelial adherens junctions. Amongst its many functions, VE-cadherin is important for cell shape changes to generate multicellular vascular tubes. Analysis of cytoskeletal organisation and dynamics has led us to a model, in which bipolar actin polymerisation drives junctional elongation between endothelial cells via VE-cadherin. We now want to analyse the VE-cadherin based cell interactions, which drive tube formation, more closely, by generating mosaic angiogenic sprouts in zebrafish that contain cells with different VE-cadherin levels.

Methods: To achieve this, I am generating an inducible VE-cadherin loss of function allele, using Bacterial Artificial Chromosome (BAC) recombineering technology. Hereto, the exon 2 of a BAC containing the VE-cadherin gene will be replaced by the VE-cadherin open reading frame flanked by LoxP sites, coupled to mCherry (see graph) to visualise its expression and will subsequently be introduced into the zebrafish genome. Via expression of tamoxifen-inducible Cre-recombinase, this line will enable us to examine VE-cadherin function at different time points during vascular development.

Results: At the moment, the modification in the VE-cadherin BAC's backbone by BAC recombineering are done. In addition, the recombination plasmid has been cloned and generated as the current design (see graph). The recombination plasmid is being replaced by VE-cadherin's exon 2 in the BAC, whereupon the final BAC construct will be introduced into the zebrafish' genome.

Conclusion: This line will enable us to examine VE-cadherin function at different time points during vascular development and therefore will help us to elucidate more about the dynamic endothelial cell behaviours underlying sprouting angiogenesis.

P33

ICAM-1null C57BL/6 mice are not protected from experimental ischemic stroke

G. Enzmann¹, S. Pavlidou¹, M. Vaas², J. Klohs², B. Engelhardt¹
(¹Bern, ²Zurich)

Objective: Accumulation of neutrophils in the brain is a hallmark of cerebral ischemia and considered central in exacerbating tissue injury. Intercellular adhesion molecule (ICAM)-1 is upregulated on brain endothelial cells after ischemic stroke and suggested to be involved in neutrophil recruitment as ICAM-1-deficient mouse lines were found protected from experimental stroke.

Translation of therapeutic inhibition of ICAM-1 into the clinic however failed. This prompted us to investigate stroke pathogenesis in *Icam1*^{tm1Alb} C57BL/6 mutants, a true ICAM-1null mouse line.

Methods: Performing transient middle cerebral artery occlusion (tMCAO) we found that absence of ICAM-1 did not ameliorate stroke pathology at acute time points after reperfusion.

VE-Cadherin/Cdh5 gene containing BAC (with modified backbone)

P32. Figure.

Results: Near infrared imaging showed comparable accumulation of neutrophils in the ischemic hemispheres of ICAM-1null and wild type C57BL/6 mice. We also isolated equal numbers of neutrophils from the ischemic brains of ICAM-1null and wild type C57BL/6 mice. Immunostaining of the brains showed neutrophils to equally accumulate in the leptomeninges and brain parenchymal vessels of ICAM-1null and wild type C57BL/6 mice. In addition the lesion size was comparable in ICAM-1null and wild type mice. Extensive blood-brain barrier permeability was observed in both genotypes. Finally, we observed a higher incidence of hemorrhagic transformation in blood vessels of ICAM-1null mutants with extravasation of individual neutrophils into the brain parenchyma.

Conclusion: Thus absence of ICAM-1 neither inhibits cerebral ischemia induced accumulation of neutrophils within cerebral vessels nor provides protection from ischemic stroke. In conclusion, our results demonstrate that in contrast to peripheral tissues, in the brain, endothelial ICAM-1 does not regulate neutrophil accumulation after ischemia-reperfusion. This assigns a unique role of the BBB in the regulation of post-ischemic vascular events.

into the CNS. This prompted us to study if brain endothelial cells can present Ag and if this contributes to CD8+ T-cell trafficking across the BBB.

Methods: We used primary mouse brain microvascular endothelial cells (pMBMECs) as in vitro model for the BBB. Endothelial expression of MHC-class I and the co-stimulatory/co-inhibitory molecules were shown by immunofluorescent (IF) staining of pMBMECs. The role of Ag presentation by pMBMECs in the interaction with T-cell receptor transgenic OT-I CD8+ T-cells that recognize the immunodominant MHC class I (H-2Kb) epitope of chicken ovalbumin (SIINFEKL) was studied by flow-cytometry. The mechanisms mediating the multi-step migration of OT-I cells across the pMBMECs under physiological flow were studied by in vitro live cell imaging.

Results: We localized MHC class I expression on luminal and abluminal sides of TNF-α/IFN-γ stimulated pMBMECs. SIINFEKL pulsed, stimulated pMBMEC co-cultures with naïve OT-I cells prompted the proliferation and activation of these cells both, in wild type (WT) and in MHC class I restricted β2 microglobulin deficient (β2M^{-/-}) mice. An intriguing observation was that OT-I cells killed WT pMBMECs but not the β2M^{-/-} ones. Post-arrest OT-I interactions with stimulated pMBMECs under physiological flow showed that the presence of SIINFEKL peptide had no effect on arrested cell number. However, it reduced OT-I cell crawling and increased stalling on pMBMECs monolayer. The pMBMECs destruction was also observed under physiological flow with the presence of SIINFEKL peptide.

Conclusion: Our observations suggest that endothelial Ag-presentation may trigger rapid CD8+ T-cell mediated killing of BBB endothelial cells under physiological flow in vitro. CD8+ T-cell initiated focal BBB breakdown may significantly contribute to the pathogenesis of MS.

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The role of endothelial antigen-presentation in the migration of CD8+ T-cells across the blood-brain barrier in neuroinflammation

S. Aydin, B. Engelhardt, A. Klopstein (Bern)

Objective: Multiple sclerosis (MS) is the most common inflammatory disease of the central nervous system (CNS) with unknown aetiology to this date. Accumulating evidence points to a critical role of CD8+ T-cells in MS pathogenesis. Immune cell recruitment into the CNS is controlled by the highly specialized endothelial cells forming the blood-brain barrier (BBB). Unfortunately, our current understanding of the molecular mechanisms used by CD8+ T cells to cross the BBB is rudimentary. It has been suggested that antigen (Ag) presentation by brain endothelial cells contributes to CD8+ T-cell migration

P35

Functional glycomics of lymphatic and blood vascular endothelia: The role of glycosylation in vascular biology

M. D'Addio¹, R. D. Cummings², M. Detmar¹, V. I. Otto¹
(¹Zurich, ²Boston USA)

Objective: To date only very little is known about the functional role of glycans in vascular biology. We hypothesized that glycosylation of lymphatic and blood vascular endothelial cells (LECs and BECs) differs and that the differences lead to differential interactions with immune cells and circulating tumor cells.

Methods: To investigate vascular glycosylation, we used primary matched LECs and BECs isolated from human neonatal foreskins. RNA sequencing data from these cells were analyzed to determine differences in the transcript levels of glycosyltransferases. We also determined the N-glycan profiles of LECs and BECs by MALDI-TOF-MS and assessed the "glycophenotype" of both cell types by FACS, using biotinylated plant lectins with known glycan specificities.

Results: The transcriptomic profiling of LECs and BECs unveiled subtle differences in the expression of glycosyltransferases involved in the biosynthesis of N- and O-glycans. The levels of sialyltransferase transcripts were higher in LECs than in BECs. In contrast, higher expression of a glycosyltransferase involved in the synthesis of poly-N-acetylglucosamine chains was observed in BECs. In LECs and BECs, T-synthase and Cosmc-1 were prominently expressed, indicating that the predominant O-glycans were core-1 O-glycans.

In accordance with the RNA sequencing data, sialylated N-glycans appeared to be more abundant in LECs than in BECs, as assessed by MALDI-TOF-MS. In contrast, large elongated N-glycans were more abundant in BECs than in LECs.

FACS analysis of cultured cells revealed that the plant lectin MAL-II bound more strongly to LECs, showing that more alpha-2,3 linked sialic acid glycans were present. In contrast, there was no difference in binding of SNA, which specifically recognizes alpha-2,6 linked sialic acids. BECs showed higher LEL binding, indicating that there were more poly-N-acetylglucosamine chains compared to LECs.

Conclusion: We present a thorough analysis and comparison of the glycosylation of LECs and BECs. LECs carry more heavily sialylated N- and O-glycans than BECs. In contrast, BECs have longer, non-sialylated antennae. These glycosylation differences lead to clearly distinct binding of plant lectins, which strongly suggests that there may also be differential interactions with glycan-binding proteins as present on immune cells and circulating tumor cells.

P36

Elucidating the role of ACKR3 for lymphatic vessel function and immune cell migration towards draining lymph nodes

E. Sigmund¹, J. Arasa¹, M. Thelen², R. Stahl³, C. Halin Winter¹ (¹Zurich, ²Bellinzona E, ³Hamburg D)

Objective: Atypical chemokine receptor 3 (ACKR3, CXCR7), belongs to a group of chemokine receptors that do not signal via G proteins but instead act as decoy and scavenger receptors. Known ligands of ACKR3 are CXCL12, CXCL11 and likely the vascular hormone adrenomedullin. During mouse embryonic development, ACKR3 deficiency causes lymphatic hyperplasia and lymphedema in addition to aberrant cardiac development, leading to postnatal death.

A previous report showed that this phenotype could be caused by an overabundance of adrenomedullin. The role of ACKR3 in adult stage lymphatic vessels (LVs), however, is unknown. The aim of this study is to determine the importance of ACKR3 for LV function during adulthood i.e. for tissue fluid drainage and immune cell migration.

Methods: To investigate expression of ACKR3 in LVs, we performed whole mount stainings using ACKR3-GFP/+ reporter mice. For RNA sequencing we FACS-sorted lymphatic and blood endothelial cells from wild type C57BL/6 mice. In order to determine the activity of ACKR3 in lymphatic endothelial cells (LECs), we used a fluorescently labeled, ACKR3 specific chimeric chemokine CXCL11/12 in an in vitro uptake assay with human LECs.

Results: First results obtained by whole mount immunostainings and RNA sequencing showed expression of ACKR3 in adult murine lymphatic capillary and collector type vessels but not in lymph node LECs. In addition, we found that CXCL12 and adrenomedullin are also highly expressed in collecting and capillary type lymphatic vessels. In an in vitro uptake assay using an ACKR3- specific chimeric chemokine CXCL11/12, we demonstrate ACKR3 mediated chemokine scavenging in human LECs. To further study the function of ACKR3 in adult LVs in vivo, we have recently generated a conditional tamoxifen-inducible ACKR3 knockout model (Prox-1CreERT2 ACKR3 fl/fl Redstop fl/fl) which is currently undergoing characterization.

Conclusion: In summary, we show that ACKR3 is expressed in murine adult LVs and plan to elucidate its contribution to LV biology and function.

P37

Interplay of FOXC2 and TAZ regulates shear stress responses of lymphatic endothelial cells

C. Saygili-Demir, A. Sabine, T. V. Petrova (Lausanne)

Objective: Shear stress induced by lymph flow plays an important role in lymphatic vessel development and maturation. The valve region in collecting lymphatic vessels is exposed to recirculating flow and FOXC2 is induced in those areas. Our aim is to decipher the mechanisms of endothelial cell maintenance and renewal in collecting lymphatic vessels.

Methods: Primary lymphatic endothelial cells (LECs) were subjected to oscillatory (4 dynes/cm², 0.25Hz) or laminar (4 dynes/cm²) flow shear stress for 48 hours by using parallel plate flow chamber system (ibidi). Wild type LECs and FOXC2 knockdown LECs were used for shear stress experiments. Shear stress exposed cells were analysed for cell death and cell proliferation by immunofluorescence stainings or live cell imaging.

Results: We have showed that LECs become quiescent upon recirculating flow by analyzing stainings of proliferative markers (i.e Ki67 and EdU). On the other hand, in the absence of FOXC2, cells enter into cell cycle and eventually go into cell death most probably due to abnormal cell division. Our further analysis demonstrated that cell proliferation is regulated strictly in these mechanically challenging environments due to teamwork of FOXC2 and TAZ. TAZ, a transcriptional coactivator of Hippo pathway, is accumulated in nucleus upon recirculating flow. FOXC2 masks the proliferative effect of TAZ, whereas in the absence of FOXC2, TAZ is liberated and induce proliferation.

Conclusion: Our work reveals the importance of FOXC2 in maintenance of lymphatic vasculature where flow shear stress dominates. Moreover, our results show that FOXC2 and TAZ are in crosstalk in the regulation of LEC quiescence and maintenance. We are currently investigating the role of TAZ in adult lymphatic vasculature maintenance and how TAZ coordinate with FOXC2.

efficient mice, possibly due to compensatory mechanisms: In fact, we found that CD112^{-/-} mice displayed higher expression of the junctional molecule VE-cadherin in lymphatic vessels, but not in BVs. Interestingly however, preliminary data indicated significant differences in the blood vascular network in CD112^{-/-} in comparison to WT mice: Specifically, absence of CD112 appeared to enhance blood vascular density in various tissues, such as skin and retina.

Conclusion: Collectively, our data reveal a novel role for CD112 in stabilizing endothelial cell interactions and in modulating BV function.

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CD155 (PVR) is expressed in afferent lymphatic vessels and modulates lymphatic endothelial cell biology in vitro

P. Schineis, A. Arasa Aparici, J. Montoya, P. Runge, M. Hertwig, C. Halin Winter (Zürich)

Objective: CD155, formerly known as Poliovirus Receptor (PVR) or nectin-5, is a cell adhesion molecule of the nectin family, which is expressed on fibroblasts and certain endothelial cell types, but also on dendritic cells (DCs). CD155 reportedly engages in heterophilic interactions with Nectin-3 and alpha-V-beta-3 integrin. Physiologically, its role in fibroblast biology has been investigated and these studies could identify CD155 as a regulator of cell proliferation and cell-cell contact inhibition. In addition, DC-expressed CD155 lately has emerged as a key regulator of a novel T cell regulatory pathway through its interaction with TIGIT and CD226.

The aim of this project is to validate the expression of CD155 in the lymphatic system and to investigate the role of CD155 in lymphatic vessel (LV) function and its impact on lymphatic endothelial cell (LEC) biology.

Methods: In the course of our studies we performed transcriptional analysis of mouse ear skin LECs and validated our results at the protein level with FACS. In addition, we conducted immunofluorescence (IF) stainings of human skin sections and of human LECs. Finally, we performed functional in vitro assays with human LECs, such as tube formation, cell adhesion and cell proliferation assays.

Results: Transcriptional analysis of LECs isolated from murine ear skin, recently indicated to us that CD155 is expressed in the lymphatic vasculature. Performing FACS based stainings of mouse ear skin we confirmed CD155 expression at the protein level on capillary and collecting LECs of afferent LVs in vivo and on cultured human and murine LECs in vitro. In addition, IF-staining of human skin sections showed a vessel-like expression pattern of CD155.

In functional in vitro assays, a ligation of CD155 with monoclonal antibodies (clone D171 and SKII.4), exhibiting agonistic and blocking functions, increased human LEC proliferation and adhesion to fibronectin and collagen coated plates. Moreover, in tube formation assays, CD155 ligation enhanced tube network complexity and tube persistence.

Conclusion: Collectively, our results for the first time show the expression of CD155 on LVs, and our in vitro results indicate a potential contribution of CD155 to lymphangiogenesis.

P38

Investigating the role of CD112 in vascular biology

E. Russo¹, P. Runge¹, H. Naboth¹, A. Landtwig¹, M. Vranova¹, Y. Takai², C. Halin Winter¹ (¹Zurich, ²Kobe J)

Objective: Endothelial junctional proteins play important roles in vascular permeability and tissue leukocyte transmigration. From a microarray gene expression analysis (Vigl et al., 2011b), we have identified CD112 (nectin-2), an adherent junction molecule, to be highly expressed in lymphatic and blood vessels. CD112 belongs to the immunoglobulin superfamily which can interact homophilically or heterophilically with other nectin family members to mediate cell-cell adhesion. Moreover, CD112 was shown to interact with immune receptors (e.g. TIGIT, DNAM-1) on specialized immune cells to modulate immune function. In this project, we investigated the role of CD112 in regulating lymphatic vessel (LVs) and blood vessel (BVs) biology.

Methods: Protein expression of CD112 on LECs and BECs was investigated in vitro and in vivo by FACS and immunofluorescent stainings. To investigate a functional role of CD112 (lymph)angiogenesis, in vitro experiments, such as adhesion, scratch wound healing, permeability and cord formation assays were performed. A potential lymphatic and/or blood vasculature phenotype in vivo was investigated in CD112-deficient (CD112^{-/-}) mice. Furthermore, lymphatic drainage experiments were performed in those mice.

Results: We found that CD112 is expressed at protein level by human and murine cultured lymphatic endothelial cells (LECs) in vitro and by murine tissue in lymphatic and blood vasculature in vivo. In functional in vitro studies, CD112 blockade resulted in a reduction of LEC migration and enhanced permeability of LEC monolayers. Surprisingly, no lymphatic drainage defect was observed in CD112-de-

P40

Automatic computational-analysis of in vitro lymphatic endothelial cell tube formation

J. Montoya, P. Runge, P. Schineis, S. Stoma, S. Noerrelykke, M. Detmar, C. Halin Winter (Zürich)

Objective: The study of the lymphatic endothelial cell (LEC) tube formation assay plays an important role for revealing new information that can be used for treating diseases such as cancer or autoimmune disorders. To do so, images at specific timepoints during the process of tube formation are acquired from a 2D microscope. Those images reveal how the lymphatic vascular network changes over time, i.e. from tube-formation to tube-reduction. Traditionally, at each timepoint a set of measurements are manually extracted from the images, such as the skeleton of the network and the number of branching points. This process is however tedious and time-consuming. In addition, since the annotation is person-subjective, different results can be obtained based on which person performed the manual analysis. To cope with these issues, we have developed a new tool to facilitate the automatic analysis of in vitro LEC tube formation over time. Our software is able to specifically recognize and detect tubes formed by fluorescently labelled LECs in a 2D-image and to quantify tube length, branching points, and tube area.

Methods: To validate our software, an in vitro tube formation endpoint experiment using human LECs was performed. Cells were fluorescently labeled after tube formation into a collagen-based matrix was achieved at 14 hours. To visualize the overall tube formation process, time-lapse an in vitro tube formation experiment was performed. LEC monolayers were fluorescently labeled and tube formation was monitored at a 2D-fluorescent microscope over time.

Results: Our software is able to specifically recognize and detect tubes formed by fluorescently labelled LECs in a 2D-image and to quantify tube length, branching points, and tube area. By extracting these measurements over time, statistical evidence can be obtained on how the tube formation is done. Combining this tool with time-lapse imaging (hourly image acquisition and analysis), we found that in comparison to control-treated conditions, VEGF-A not only enhanced tube formation but also stabilized the maintenance of the tube-like network over longer time periods.

Conclusion: Overall, our software allows for a fast, reliable and more complex, longitudinal investigation of the in vitro LEC tube formation process.

P41

Hydrogen sulfide limits the development of intimal hyperplasia in a mouse model of femoral wire injury

F. Allagnat, A. Longchamp, C. Dubuis, N. Yamagushi, M. Lambelet, J.-M. Corpataux, S. Déglise (Lausanne)

Objective: Arterial occlusive disease is the leading cause of death in Western countries. Mainstays of contemporary therapies for this disease include angioplasties, stents, endarterectomies and bypass surgery. However, these treatments suffer from high failure rates due to re-occlusive vascular wall adaptations, namely intimal hyperplasia (IH). IH develops in response to endothelium injury, leading to inflammation, vascular smooth muscle cells (VSMC) dedifferentiation, migration and proliferation at the site of injury. Hydrogen Sulfide (H₂S) is a gazotransmitter with important vaso-relaxant, cytoprotective and anti-inflammatory properties.

Methods: Here, we combined in vivo and in vitro approaches to test the therapeutic potential of H₂S in limiting the development of IH. WT C57BL/6/J male mice treated with NaHS (a H₂S donor) (1mM in the drinking water) were submitted to femoral wire injury surgery and IH was measured 28 days post-surgery by histology. Human great saphenous vein segments obtained from patients undergoing bypass surgery were maintained in culture ex-vivo for 7days in presence of various H₂S donors (NaHS, GYY4137, diacetyltrisulfide). Primary human umbilical vein endothelial cells (HUVEC) and primary VSMC derived from human vein segments were treated with the various H₂S donors and cell migration and proliferation were assessed by wound healing assay and BrDU incorporation, respectively.

Results: NaHS treatment strongly attenuated IH in the mouse model of femoral wire injury. Similarly, the various H₂S donors prevented the development of IH in vein segments ex-vivo. In vitro, the same H₂S donors stimulated human endothelial cells (HUVEC) migration and proliferation, while inhibiting migration and proliferation of primary VSMC derived from human vein segments.

Conclusion: Current strategies based on the use of drug-eluting angioplasty balloons and stents limit VSMC proliferation to reduce IH, but they also impact re-endothelization, limiting their long-term efficacy and prolonging the need for anti-thrombotics. Our data suggest that exogenous H₂S supply may provide new therapeutic strategies to limit VSMC proliferation while promoting re-endothelization.

Software pipeline

Results at specific timepoints

FITC: Processed image with detected skeleton

PC: image with detected skeleton

Mit dem Unbewussten das Rauchen vergessen

Maja Storch

Rauchpause

Wie das Unbewusste dabei hilft, das Rauchen zu vergessen

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Auch als eBook erhältlich

Warum raucht man eigentlich? Warum kann man nicht einfach wieder aufhören? Und warum ist es so qualvoll, mit dem Rauchen aufzuhören? Was hat die Psyche mit dem Rauchen zu tun?

Die Erfolgsautorin und Psychologin Maja Storch zeigt in ihrem Buch, dass beim Wunsch, mit dem Rauchen aufzuhören, nicht nur der körperliche Entzug bedacht werden muss. Auch das psychische System, vor allem das Unbewusste, muss damit einverstanden sein, denn die Zigarette hat meistens auch mit persönlicher Identität zu tun. Storch zeigt, dass das Rauchen durch unbewusste Lernvorgänge mit positiven Erinnerungen verknüpft ist, die – oft unbe-

merkt – zu einem Bestandteil der eigenen Identität werden. Daher ist nicht nur der körperliche Entzug ein Thema sondern auch die Neuorganisation des gesamten psychischen Systems: Es braucht eine neue Identität, die sich auch ohne das Rauchen gut und „komplett“ anfühlt.

In „Rauchpause“ werden anschaulich die theoretischen Grundlagen, die zum Verständnis dieser Zusammenhänge benötigt werden, erläutert. Anschließend wird anhand des amüsanten Beispiels der Autorin selbst und weiterer Fallbeispiele gezeigt, mit welchen Schritten ein qualfreier, identitätsgerechter Neubeginn in die lebenslange Rauchpause eingeleitet werden kann.

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Das Buch ist ein Nachschlagewerk für alle, die sich für das Gesundheitssystem und die Gesundheitspolitik interessieren: Fachleute aus dem Gesundheitswesen und den Sozialversicherungen, für Politik, Medien und Wissenschaft und selbstverständlich auch für interessierte Versicherte und Patientinnen/Patienten. Besonders geeignet ist es auch als Lehrmittel in den verschiedenen Aus-, Weiter- und Fortbildungsgängen im Gesundheits-, Sozial- und Versicherungswesen.