Vasa

European Journal of
Vascular Medicine

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

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

24. – 26. Oktober 2018 / 24 – 26 octobre 2018
Palazzo dei Congressi, Lugano

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Freie Mitteilungen / Communications libres

FM 1.1

Perivascular perfusion on contrast-enhanced ultrasound (CEUS) is associated with inflammation in patients with acute deep vein thrombosis.

M. Kaspar^{1,2}, S. Imfeld¹, S. Partovi¹, M. Aschwanden¹, T. Baldi¹, A. Dikkes¹, D.R. Vogt¹, D.A. Tsakiris¹, D. Staub¹ (¹Basel, ²Bern)

Objective: Inflammatory processes of the venous wall in acute deep venous thrombosis (DVT) play a role in thrombus formation and resolution. However, direct evaluation of the perivascular inflammation is currently not feasible. The aim of this study is to assess perivascular perfusion in acute proximal DVT using contrast-enhanced ultrasound (CEUS) reflecting perivenous inflammation, and its association with systemic inflammatory markers in a single center, prospective observational study.

Methods: 20 patients with proximal DVT underwent CEUS imaging in the thrombosed and contralateral popliteal vein at baseline, after 2 weeks and 3 months. Perfusion was quantified by measuring peak enhancement (PE) and wash in rate (WiR) in a perivenous region after bolus injection of the contrast agent. High sensitive C-reactive protein (hsCRP) and interleukin 6 (IL 6) were determined at the time of each CEUS imaging.

Results: PE and WiR were significantly higher in the thrombosed compared to the unaffected leg at baseline (1007 vs. 34 au and 103 vs. 4 au/sec) and 2 weeks follow-up (903 vs. 35 au and 70 vs. 4 au/sec). Compared to baseline, PE and WiR in the thrombosed

leg significantly decreased to 217 au and 18 au/sec at 3 months follow-up.

At baseline hsCRP and IL 6 were elevated at 20.1 mg per ml and 8.2pg/ml and decreased significantly to 2.8 mg/ml and 2.6pg/ml at 2 weeks follow-up, remaining low after 3 months. There was a weak association between the level of inflammatory markers and the CEUS parameter at baseline on the thrombosed leg.

Conclusion: Elevated perivascular perfusion assessed by CEUS imaging is associated with the inflammatory response in acute DVT.

FM 1.2

Sclerotherapy outcome of genual and perigenual venous malformation

R. Gnannt, R. Guggenberger, D.A. Müller, M. Theiler, C. Aufdenblatten, T. Pfammatter (Zürich)

Objective: Venous Malformation (VM) adjacent to the knee are challenging with regard to interventional therapy approach and post-therapeutic outcome prognosis. The aim of the study was to analyze pre-interventional magnetic resonance imaging and correlate the findings with the outcome of percutaneous sclerotherapy treatment of VM's adjacent to the knee joint.

Methods: 24 patients with a total of 25 VMs adjacent to the knee were identified through a keyword search (one patient without a syndromal disease had a VM on each knee). Imaging findings of baseline MR of the knee were analyzed in a consensus manner by two radiologists: extent of VM, joint effusion, hemarthros, synovial thickening,

Box plots (median and IQR) for CEUS time-intensity curve (TIC) parameters (note the logarithmic scale) including peak enhancement (a) and wash-in rate (b) of the thrombosed leg (blue) and the contralateral leg (green) measured in the perivascular tissue at baseline, at 2 weeks and at 3 months after deep vein thrombosis (DVT) diagnosis. p-Values for differences in medians according to paired Wilcoxon's test are indicated.

FM 1.1. Figure.

osseocartilaginous lesions. Treatment outcome was categorized into improved, unchanged or worsening symptoms.

Results: 48 percutaneous sclerotherapy treatments were performed (mean age of patients 24yrs, range 7–55yrs; mean sclerotherapy sessions per patient 1.92, range 1–5). 11 out of 25 (44%) patients had a large VM consistent of multiple dysplastic vein without a focal lesion. The VM reached the synovium of the knee joint in 19/25 (76%) of all patients. These lesions were associated with joint effusion (3/19, 16%), hemarthros (4/19, 21%), synovial thickening (16/19, 84%), and responded poorly to direct sclerotherapy (in 7/19, 37% symptoms remained stable or became worse after mean sclerotherapy sessions per patient 2.8, range 1–5). Out of those patients who responded poorly to sclerotherapy 7/8 (88%) showed signs of arthrosis: chondral lesions in 6/8 (75%), osteophytes in 3/8 (38%), and subchondral sclerosis in 4/8 (40%) patients. However, patients without any signs of knee arthrosis and no synovial involvement on MR (6/25, 24%), 5 out of 6 patients (83%) showed improvement of symptoms after one single sclerotherapy session.

Conclusion: Symptomatic genual VMs are frequently associated with hemarthros and synovial thickening. Patients with signs of synovial involvement and/or arthrosis on pre-sclerotherapy MR deserve special consideration as these findings hamper the clinical outcome of sclerotherapy. An interdisciplinary assessment including an orthopaedist is warranted for this subgroup.

FM 1.3

BeGraft® aortic stent for the treatment of severe aortoiliac occlusive disease.

J. Longchamp, L. Bruyns, G. Verdon, B. Del Tatto, A. Longchamp, C. Dubuis, L. Briner, F. Saucy, J.-M. Corpataux, S. Déglise (Lausanne)

Objective: Peripheral arterial disease (PAD) affects more than 20 % of the population older than 70 years old. In the past 10 years, the treatment of occlusive aorto-iliac disease shifted to an endovascular-first approach, even for complex TASC C and D lesions. Recently, the COBEST trial confirmed the superiority of covered stents over bare metal stents in the treatment of occlusive aorto-iliac disease. However, the widespread use of this strategy is currently limited by the availability of large diameter covered stents.

Methods: All patients treated in our Department from October 2016 to May 2018 with an aortic BeGraft balloon-expandable covered stent (Bentley InnoMed, Hechingen, Germany) for occlusive aorto-iliac disease were included in the study. All the data were prospectively stored in our database (Secutrial) and retrospectively analysed. The primary outcome was primary patency rate and secondary outcome was the post-operative complications rate.

Results: During this period, 8 patients with a mean age of 68 years [range 54–74] were treated with aortic BeGraft covered stents. Indications were intermittent claudication in 6 patients and critical limb ischemia in 2. The majority of patients (88%) had TASC D lesions. The mean operation time was 59 ± 40 min. The procedure consisted in BeGraft aortic stents implantation in 2 cases (25%) and in a CERAB technique in 6 cases (75%). The total number of BeGraft stents implanted was 24. Regarding the 9 aortic stents, the mean diameter was 14 ± 6.6 mm and mean length was 45 ± 10 mm. For the 13 iliac stents, the mean diameter was 7.7 ± 0.9 mm and mean length was 47 ± 10 mm. Moreover, a chimney in the left renal artery was necessary

in 2 cases, with BeGraft stents of a mean diameter of 5 ± 1.4 mm and a mean length of 32 ± 8.5 mm.

The technical success was 100 %. The mean length of stay was 1.6 ± 1 days. No in-hospital or post-operative complications occurred. During the mean follow-up of 9 months (range 1–19), 1 stent occlusion occurred after interruption of the dual antiplatelet therapy, requiring an aorto-bi-iliac bypass. Overall primary patency rate was 88 %.

Conclusion: The use of BeGraft aortic covered stents seems to be a safe and efficient strategy in severe occlusive aortoiliac disease (TASC C and D). Further studies are required to define long-term patency in a larger cohort.

FM 1.4

Wasserstrahl-assistierte Liposuction zur Therapie des Lipödems

D. Münch (Bern)

Objective: Ein Lipödem ist eine chronische Erkrankung mit subkutaner Fettgewebsvermehrung an den Beinen, Schmerzen, Ödemen und Neigung zu Hämatomen. Zur operativen Behandlung dieses Leidens gewinnt die wasserstrahl-assistierte Liposuction (WAL) zunehmend an Bedeutung. Sicherheit und Effizienz der WAL sollen analysiert und mit der Tumescenz-Liposuction (TL) verglichen werden.

Methods: 141 Patientinnen mit Lipödem wurden zwischen 1. Juli 2010 und 31. Juli 2016 mittels WAL (BodyJet Evo) operiert. 71 Patientinnen konnten nach einer durchschnittlichen Beobachtungszeit von 35,9 Monaten reevaluiert werden.

Results: In jedem Fall konnten eine deutliche Reduktion der subkutanen Fettschicht und eine Verbesserung der Proportionen erzielt werden. In der Kontrolle zeigte sich eine signifikante Verbesserung aller 10 Beschwerdeparameter (Score-Reduktion auf einer 10-Punkte-Skala von 6,1 auf 3,1; Wilcoxon-Test, $p < 0,05$). Konservative Therapien waren 38,3% der Fälle nicht mehr nötig, konnten reduziert werden oder wurden als wirksamer empfunden.

Conclusion: Die Liposuction des Lipödems verspricht dauerhafte und gute Ergebnisse, wenn die Operationstechnik auf die Schonung der Lymphbahnen fokussiert ist. Im Vergleich zur TL bietet die WAL den Vorteil, dass die Adipozyten selektiv und unter maximaler Schonung der Gefässe entfernt werden. Die Anästhesielösung wird gezielt im abzusaugenden Areal appliziert, was eine optimale Analgesie und Vasokonstriktion bewirkt. Ausserdem entstehen dadurch weniger Schwellungen und die Liposuction ist intraoperativ präziser beurteilbar. Mittels WAL lassen sich sehr oft eindrucksvolle Resultate bezüglich Reduktion der Schmerzen, Verminderung der Ödemneigung, Verbesserung der Körperkontur und Steigerung der Lebensqualität erzielen.

FM 1.5

Walking performances are maintained 12 months after a supervised exercise training program in lower extremity artery disease

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

Objective: It has been largely proven that supervised exercise training (SET) is a valid and efficient way to improve claudication in

Tab. 1 Vergleich Tumescenz-Liposuction/Wasserstrahl-assistierte Liposuction

Kriterium	TL	WAL
Apparativer Aufwand	kleiner	grösser
Belastung des Körpers durch Pharmaka und Volumen	stärker, da Tumescenz grosse Volumina erfordert	minim, weil fortlaufendes simultantes Sprayen und Absaugen der Flüssigkeit exakt am Ort der Op stattfindet
Traumatisierung des Gewebes und der Lymphbahnen	vermehrt, da Flüssigkeitsdruck/Osmose potentiell zellschädigend wirken; Kanüle ohne Wasserstrahl führt eher zu Gewebeläsionen	minimal, weil Gewebe nicht aufgeschwemmt wird und Kanüle dem natürlichen Weg des Wasserstrahls folgt
Präzision der Liposuction	häufiger unregelmässige Resultate, weil Tumescenz Oberflächenstruktur aufschwemmt und Beurteilbarkeit des Arbeitsfeldes einschränkt	Korrekturingriffe seltener, da erhaltene Kontur präzise Liposuction erlaubt
Möglichkeit, empfindliche oder zuvor ungenügend anästhesierte Zonen nachträglich zu infiltrieren	umständlicher wegen zeitaufwändigem Instrumentenwechsel	einfach, da bei laufendem Sprühstrahl einzig das Vakuum vorübergehend zu deaktivieren ist
Schmerzen intraoperativ, im besonderen gegen Ende der OP	ausgeprägter, weil gegen Ende der Liposuction der Wirkspiegel der Anästhesie ungenügend wird	konstant gute Analgesie, da kontinuierliche Zufuhr von frischer Anästhesielösung am Wirkungsort bis zum Ende des Eingriffes für einen effizienten Wirkspiegel sorgt
OP-Dauer	länger, wegen erhöhtem Zeitbedarf für Infiltration/Wartephase bis zum Wirkungseintritt der Tumescenz-Anästhesie	kürzer, da Präinfiltration rascher durchgeführt und Wartezeit entfällt
Dauer des postoperativen Flüssigkeitsaustrittes	oft mehrere Tage, da grosse Volumina im Körper verbleiben	maximal 24h, weil weniger Rest-Flüssigkeit im Körper verbleibt
Rekonvaleszenzphase	länger	kürzer
Hämatome postoperativ	vermehrt	weniger ausgeprägt
Schmerzen postoperativ	ausgeprägter	geringer
Hautretraktion	oft unbefriedigend	ausgeprägter wegen Straffungseffekt durch den Wasserstrahl, abhängig von Alter und Bindegewebe
Anzahl nötiger Eingriffe für eine vollständige Liposuction	oft mehr als 2	in der Regel 2

FM 1.4. Table. **FM 1.4.** Figure.

■ vor der WAL ■ nach der WAL

PFWD, MWD performance at beginning, at the end of the program, at 6 months and at 12 months. Mean $\pm$ standard errors. * $P \leq 0.05$ for significant differences to pre-training condition (multiple comparison tests with Bonferroni adjustment)

6MWT at beginning, at the end of the program, at 6 months and at 12 months. Mean $\pm$ standard errors.

* $P \leq 0.05$ for significant differences to pre-training condition (multiple comparison tests with Bonferroni adjustment). \$ $P \leq 0.1$ for trend compared to the pre-training condition

FM 1.5. Figure.

Table 1. Characteristics of patients

Number of included patients	45	%
Age (mean ± SE)	64.8 ± 1.6	
BMI, kg m ⁻² (mean ± SE)	27.6 ± 0.7	
Women, n (%)	16	36%
Cardio-vascular risks factors		
Type 2 diabetes mellitus, n (%)	16	36%
Hypertension, n (%)	29	64%
Smoking (current), n (%)	22	49%
Smoking (former), n (%)	19	42%
Smoking (never), n (%)	5	11%
Hypercholesterolemia, n (%)	36	80%
Family history of CVD, n (%)	10	22%
Prior history of CVD		
Cardiac, n (%)	13	29%
Cerebrovascular, n (%)	2	4%
Co-morbidities		
Orthopaedic, n (%)	16	36%
Cardiac disease, n (%)	11	24%
Kidney disease, n (%)	5	11%
Lung disease, n (%)	6	13%
Other, n (%)	5	11%
Etiology of LEAD		
ATS, n (%)	35	78%
Buerger, n (%)	1	2%
Embolitic, n (%)	1	2%
Other, n (%)	8	18%
Stenosis localisation		
Aorto-iliac, n (%)	9	20%
Ilio-femoral, n (%)	0	0%
Femoro-popliteal, n (%)	32	71%
Distal, n (%)	4	9%
Proximal-distal, n (%)	0	0%
Fontaine staging		
IIa, n (%)	34	76%
IIb, n (%)	11	24%
Prior arterial revascularisation, n (%)	24	53%
Ongoing treatment		
Antiagregant (Aspirin and/or Plavix), n (%)	42	93%
Antihypertensive, n (%)	29	64%
Statine, n (%)	34	76%
Anticoagulant, n (%)	8	18%
Antidiabetic, n (%)	15	33%

*Other= 6 aneurysmal disease, 1 artery compression by a popliteal cyst and 1 unknown

FM 1.5. Table.

Table 2 Increase in PFWD, MWD and 6MWT performance at beginning, at the end of the program, at 6 months and at 12 months for men and women.

	PFWD [meters]			
	pre	post	6 months	12 months
Men	106.2±80.9	246.2±233.2	388.3±404.1	335.2±311.4
Women	126.9±113.5	328.1±358.6	433.1±438.9	496.9±578.2

	MWD [meters]			
	pre	post	6 months	12 months
Men	351.7±283.5	666.9±484.3	706.6±446.1	658.3±462.6
Women	270.0±184.6	665.6±410.1	750.6±481.4	741.9±581.5

	6MWT [meters]			
	pre	post	6 months	12 months
Men	443.9±83.9	510.8±88.7	481.8±108.4	467.6±108.7
Women	401.0±45.5	496.1±107.3	480.4±71.9	483.1±100.2

patients with lower extremity artery disease (LEAD). However, persistence of SET's benefits in time is less validated. Therefore, aim of our study was to determine long term (12 months) effect of SET in patients with LEAD.

Methods: Consecutive patients with stage IIa or b (Fontaine's classification) LEAD, undergoing a SET program were included. SET consisted in 3 months supervised training 3x/week. Two of the weekly sessions are in the form of Nordic pole walking exercise; the 3rd one consists in specific muscle reinforcement exercises.

Patients were systematically followed 6 and 12 months after SET. Pain-free walking distance (PFWD), and maximal walking distance (MWD) were assessed prior, at the end of the 3-month program, and at 6 and 12 months following the end of SET using standardized treadmill testing. Six-minute walking test (6MWT) was also performed at the same time points. Differences in PFWD, MWD performance, and 6MWT prior, at the end of the program, at 6 and at 12 months were evaluated. Comparison between groups was assessed by ANOVA and significant group interaction effect was tested using the Bonferroni test.

Results:

- Forty-five patients (36% women) with LEAD were included (characteristics of included patients are described in Table 1).
- PFWD, MWD, and 6MWT significantly improved following SET (Fig 1). Improvement remained significantly increased both at 6 and 12 months post SET (Fig 1).
- No significant difference between men and women was observed; both significantly increased walking performances at each time point (Table 2).
- PFWD was increased by 132% compared to pre-training condition in men, and by 159% in women. MWD was increased by 90% in men and 147% in women. 6MWT showed an improvement of 15% in men and 24% in women.

Conclusion: Improvement of walking parameters (PFWD, MWD, and 6 MWT) in LEAD patients is maintained up to 12 months following SET. Both men and women equally benefited. SET is a crucial first line therapy in LEAD patients with intermittent claudication. SET programs should be regularly implemented in the management of LEAD patients.

FM 1.6

Stent-assisted angioplasty (SAA) at the level of the common femoral artery bifurcation: longterm outcomes

H. Stricker¹, L. Spinedi¹, L. Giovannacci² (¹Locarno, ²Lugano)

Objective: To report the initial results and the longterm outcome after stent-assisted angioplasty of occlusive disease at the common femoral artery bifurcation.

Methods: Between 1995 and 2015, 81 consecutive patients (64 men; mean age 70±8.6 years) underwent angioplasty with self-expanding stent implantation in 94 limbs at the Regional Hospital of Locarno. Target sites included 69 common femoral arteries (CFA), 18 CFA plus superficial femoral arteries (SFA), 6 CFA plus profunda femoris arteries (PFA), and 1 CFA plus SFA and PFA. Critical limb ischemia was present in 15 limbs (16%).

Results: Cardiovascular risk factors were frequent in our patients (smoking in 82%, diabetes mellitus in 39%, arterial hypertension in 86%, and dyslipidemia in 55%). Technical success was achieved

in 93/94 limbs (99%). Complications occurred in 5/94 interventions (5.3%): 2 major puncture site hematomas, 1 av-fistula, 1 case with cholesterol embolism, and one dissection of the access site artery, treated by stenting. The intervention was outpatient-based in 98%. Patients were followed for a median of 52 months. Ankle-brachial index (ABI) rose from 0.71±0.17 to 1.0±0.2 ($p<0.001$) immediately after the intervention, and was 1.03±0.2 after one year, and 0.96±0.21 at the last follow-up visit ($p<0.001$ in all comparisons with pre-interventional ABI). During follow-up, restenosis rate was found in 23/94 limbs (25%); 15 limbs were again treated by angioplasty, 3 by surgery, and 5 conservatively. One limb with extensive crural occlusive disease was amputated below the knee 6 months after SAA. Death rate during follow-up was 39/81 patients (48%).

Conclusion: SAA of the CFA bifurcation is highly successful, and has a low complication rate. Restenosis rate during longtime follow-up is moderate, and target lesions can easily be retrated by angioplasty. The procedure compares favorably with surgical thromboendarterectomy of CFA obstruction. The main hazard for the patients was not restenosis, but death.

FM 2.1

A peptide-based hydrogen sulphide-releasing gel limits the development of intimal hyperplasia in human vein segments.

F. Allagnat¹, K. Kaur², J.-M. Corpataux¹, A. Longchamp¹, J. Matson², S. Déglise¹ (¹Lausanne, ²Blacksburg USA)

Objective: Contemporary therapies to treat arterial occlusive disease such as angioplasties, stents, endarterectomies and bypass surgery, still suffer from high failure rates due to re-occlusive vascular wall adaptations, a process called intimal hyperplasia (IH). IH develops in response to vessel injury, loss of endothelial cells (EC), leading to inflammation, dedifferentiation and proliferation of vascular smooth muscle cells (VSMC). The focal nature of IH lesions offers a therapeutic window to use local treatments. Hydrogen Sulfide (H₂S) is a very potent gazotransmitter with known anti-oxidant and anti-inflammatory properties. Here, we tested the therapeutic potential of a peptide-based H₂S-releasing gel locally at the site of injury to limit IH.

Methods: Human veins segments obtained from patients undergoing lower bypass surgery were exposed in vitro to NaHS, a H₂S-releasing gel or a control gel. IH was measured by histomorphology 7 days later. In addition, human umbilical endothelial cells (HUVEC) and primary human vascular smooth muscle cells (VSMC), prepared from human saphenous veins, were exposed in vitro to NaHS, a H₂S-releasing gel or a control gel.

Results: NaHS and the H₂S-releasing gel similarly inhibited VSMC migration, whereas they stimulated HUVEC migration. In human saphenous vein segments, NaHS or the H₂S-releasing gel, but not the control gel, similarly limited the development of IH in human vein segments.

Conclusion: Current strategies available to limit IH are based on cytotoxic molecules inhibiting VSMC proliferation (paclitaxel, sirolimus) as well as EC proliferation, thus impeding re-endothelization. Our data suggest that local perivascular H₂S release may represent a new strategy to limit VSMC proliferation while promoting re-endothelization.

FM 2.2

Influence of anastomosis angle on haemodynamics in radiocephalic arteriovenous fistulas: a computational study

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Objective: Haemodynamics has been known to play a major role in the development of intimal hyperplasia and fibrosis leading to arteriovenous fistula failure. The goal of our study is to investigate the influence of different angles of side-to-end radiocephalic anastomosis upon the haemodynamic parameters that favour the conditions that are prone to hyperplasia and fibrosis. For this purpose we used advanced computational models that include suitable tools to capture the turbulent nature of the blood flow in A-V fistulas.

Methods: Realistic 3D meshes were reconstructed using ultrasound measurements from distal side-to-end radiocephalic A-V fistulas. The velocity at the proximal and distal radial inflows and at specific locations along the anastomosis and cephalic vein was measured through single examiner duplex ultrasound. A computational parametric study virtually changing the inner angle of anastomosis was performed. The results were analyzed in terms of velocity fields, pressure distribution, wall shear stress distribution, oscillatory shear index (OSI) and derived Q-criterion at four different instants during the cardiac cycle.

Results: Preliminary results show that the regions with high OSI, that are more prone to hyperplasia formation, seem to be wider and progressively shifting from the arterial to the venous wall with the decrease of the inner angle of anastomosis. These results may be different in A-V fistulas that are subject to proximal arterial inflow only.

Conclusion: The results of this study show that inner anastomosis angles approaching 60–70 degrees seem to yield the best haemodynamic conditions for maturation and long term patency of distal radiocephalic fistulas. Inner angles greater than 90 degrees with inverted loop anastomosis did not show an improvement of haemodynamics in this kind of fistula.

FM 2.3

Risk of spinal cord ischemia after endovascular repair for juxtarenal and thoracoabdominal aortic aneurysms

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Objective: Spinal cord ischemia with paraplegia is still a relevant complication after aortic repair for extended aneurysms either by open or endovascular repair. The role of different adjuncts for prevention of spinal cord ischemia is unclear when different techniques for endovascular aortic repair are used.

Methods: Endovascular aortic repair was performed by fenestrated (FEVAR), branched (BEVAR) EVAR or using the parallel graft tech-

nique (PG-EVAR). Spinal cord ischemia was classified according to the modified Tarlow score 0–2.

Results: Between 2008 and 2016 endovascular treatment was performed in 352 patients with juxta-/pararenal (n=270) and thoracoabdominal (TAAA, n=82) aortic aneurysms by FEVAR (n=141), BEVAR (n=111) and PG-EVAR in 100 patients in two different centers. Overall risk of permanent SCI was 3.9%, with rates of 12.1% for TAAA and 1.4% for endovascular repair for juxta-/pararenal aortic repair (p<0.01) with the lowest risk for SCI in the PG-EVAR group (3% temporary SCI and 0% permanent SCI, p<0.01). Most PG-EVAR procedures were performed under local anesthesia. After introduction of a standardized protocol including staged procedures, spinal drainage, normotension, normal hemoglobin, preservation of subclavian and hypogastric perfusion, temporary aneurysm sac perfusion and early iliac perfusion risk of SCI was reduced to 4.6% (p<0.03) in the BEVAR group.

Conclusion: The risk of spinal cord ischemia during extended endovascular aortic repair can be reduced by standardized protocols with a relevant role for staged procedures, temporary aneurysm sac perfusion, early iliac Perfusion, parallel graft EVAR and interventions performed under local anesthesia.

FM 2.4

Quality of life and post-thrombotic syndrome after surgical thrombectomy of acute iliofemoral deep vein thrombosis

S. Ockert, M. Heidemann, J. Duwe (Luzern)

Objective: Patients with post-thrombotic syndrome (PTS) after deep vein thrombosis (DVT) show poorer quality of life (QOL) and more symptoms than patients without PTS. Catheter-directed or pharmaco-mechanical thrombolysis (CDT/PCDT) present the first-line recommendations for treatment of acute iliofemoral deep vein thrombosis (IFDVT). However, CDT and PCDT fail to significantly decrease the occurrence of PTS compared to anticoagulation (ATTRACT Trial). Secondary outcome for health-related QOL after catheter-directed thrombolysis also did not differ compared to standard treatment (CaVenT). As an alternative treatment option, surgical thrombectomy is recommended only in cases in which a patient is not a candidate for CDT or PCDT.

The aim of this study is to analyze long-term clinical outcome after surgical thrombectomy of acute IFDVT in terms of quality of life and the occurrence of post-thrombotic syndrome.

Methods: All patients who underwent surgical thrombectomy at our institution between April 2008 and April 2017 were included. Only patients with iliofemoral thrombosis, and only those with the first onset of symptoms <10 days, were operated and analyzed.

All patients underwent outpatient clinical investigation for PTS and duplex ultrasound to prove patency of the deep vein system. Assessment of QOL was performed using the VEINES-QOL/Sym questionnaire and the status of PTS was evaluated using the VIL-LALTA-scale.

Results: Within a 9-year period, 21 patients underwent surgical thrombectomy for acute IFDVT. Primary technical success was 100%. During follow-up (median 6 years), 19 patients (90.5%) presented patent iliofemoral veins without signs of re-thrombosis, two patients (9.5%) died of cancer without signs for recurrent

FM 2.6

Physician-modified thoracic stent-grafts for the treatment of dissecting aortic arch aneurysms

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Objective: This study evaluates the outcome of physician modified thoracic stent-grafts for the treatment of aortic arch dissecting aneurysms after complicated type B dissection or after surgical treatment of acute type A dissection.

Methods: Between May 2015 and April 2018, 33 patients underwent TEVAR using physician modified thoracic stent-grafts to treat aortic arch dissection with aneurysmal evolution after complicated type B dissection or after surgical treatment of acute type A dissection. There were 22 men and 11 women (mean age, 70.7 ± 10 years; range, 43–86 years). 8 patients (24 %) were treated in an emergent setting for a symptomatic aortic arch aneurysm. Dissection involved Zone 0 in 10 and zone 2 in 23 patients. 18 patients (57 %) were treated using an aortic arch stent-graft with a single fenestration. 11 (33 %) patients had total endovascular aortic arch repair using a double fenestrated stent graft whereas a proximal scallop was adopted in 4 cases (12 %). Stenting of at least one of the supra-aortic trunks was performed in 24 individuals (72 %). Additional planned endovascular procedures were performed in 3 patients.

Results: Median time for stent graft modifications was 18 minutes (range 14–21 minutes). Technical success was achieved in 100 % of cases. The 30-day mortality rate was 0 %. One patient had a stroke without permanent sequelae (3 %). Transcatheter aortic valve implantation via a carotid approach was performed in one case for severe pre-existing aortic regurgitation. One type 1 Endoleak was successfully treated during the same procedure with an extension cuff. No type 2 endoleaks were observed. The median length of stay was 5 days (range, 1–17 days). During follow up at 12 ± 10 months, there were no conversions to open repair, aortic rupture, paraplegia, or retrograde dissection. One patient died of myocardial infarction unrelated to aortic repair. In all patients complete thrombosis as well as stabilization or shrinkage of the false lumen in the arch and thoracic aorta were observed.

Conclusion: The use of physician modified thoracic stent-grafts for the treatment of aortic arch dissecting aneurysms after complicated type B dissection or after surgical treatment of acute type A dissection is both feasible and effective. Durability concerns will have to be addressed in further studies.

FM 3.1

Outcome of straight aorto-aortic endografts in infrarenal aneurysmal disease and penetrating aortic ulcers, a long term follow up

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Objective: We describe our experience including the long term follow up in the treatment of infrarenal abdominal aortic aneurysms

IFDVT. 13 of 19 patients (68.4 %) received analysis for QOL and PTS after surgical thrombectomy for IFDVT during FU. In our series, a modified VEINES-QOL Score (Q1–5+Q8) was 96.5 (highest QOL=107). The VILLALTA score was median 1.5 (range 0–4). No patient in our study developed ulcers (Villalta Ulcer=0) during FU (64 months).

Conclusion: For the treatment of acute IFDVT, surgical thrombectomy is not commonly given as much importance as interventional techniques. Nevertheless, the surgical approach is successful and durable with low rates of PTS and high QOL scores, and presents an alternative treatment option for acute IFDVT in selected cases.

FM 2.5

Outcome of total percutaneous endovascular aortic repair with Perclose ProGlide technique

S. Hofer, M. Furrer (Chur)

Objective: Since January 2014 the standard approach to endovascular aortic repair (EVAR) in our centre is percutaneous (pEVAR). We evaluated our single centre experience of this totally percutaneous access during abdominal and thoracic EVAR using the Perclose ProGlide device (PPD, Abbott Vascular).

Methods: Between January 2014 and December 2017 139 pEVAR were performed. Data from total 256 femoral access sites were retrospectively reviewed. For puncture the best area without calcification was assessed by CT scan previously, ultrasound controlled puncture was used in selected cases. The outer size of the access sheaths were 14 to 26 French. From 2014 to 2015 we delivered two PPD systems for each access site. After 2016 only in 16 French or more outer diameter two PPD were used. Artery calcifications and sheath size as predictive factors for failure, complications and additional PPD deployment were analyzed.

Results: We achieved adequate hemostasis in 250 of 256 (97.7 %) access sites. In six access sites bleeding required a suture of the common femoral artery. In two access sites surgical revision became necessary because of ischemia caused by plaque rupture. Further complications were two stenosis, twelve local dissections of the common femoral artery, and one arteriovenous fistula. None of these patients were symptomatic or needed further interventions. In four patients an pseudoaneurysm could be identified by CT scan and was successfully treated by compression. In 23 sites additional PPD had to be delivered. There was no correlation to access size or calcification.

Conclusion: The primary technical success rate in total percutaneous access using the PPD for endovascular aortic repair is high. In our analysis we could not identify any factors limiting the percutaneous technique.

and penetrating ulcers by placement of straight aortic endografts at our institution from 2010 to present.

Methods: We retrospectively analyzed clinical data of 31 patients treated at our institution from 2010 to present. Patients were either treated by placement of a single aortic straight endograft or by two overlapping endografts, using the so called 'double trombone' technique. Aortic diameters and length were measured in the pre-operative computed tomography-angiography using three-dimensional reconstruction (SyngoVia®, Siemens). Primary outcome was aortic re-intervention. Secondary outcomes were aortic mortality, endoleaks of any type and postoperative complications.

Results: Eight patients were treated for saccular aneurysms while 23 patients presented with penetrating aortic ulcers. Median follow up was 31 months (4–99). Twenty three patients were treated with a single straight device while 8 patients were treated using two overlapping straight devices. Aortic re-intervention occurred in 5 patients (16%), all of which treated initially with a single straight device. No aortic mortality occurred during follow up. No (late) aneurysm ruptures occurred. 4 patients died during the follow up of unrelated causes. Endoleaks occurred in 12 patients (39%). Seven endoleaks were of type I (23%), of which 4 of distal type (13%). Five endoleaks were of type II. One patient with a distal endoleak type I awaits a secondary procedure, while a second patient with a distal type I endoleak died of an unrelated cause before treatment of the endoleak. Shorter distal landing zones than 20 mm were present in two thirds of the cases with distal type I endoleaks. Postoperative complications occurred in 5 (16%) patients (1 myocardial infarction and 4 wound related complications).

Conclusion: The aortic re-intervention rate in our population was high and endoleaks of type I occurred often. The technique used is safe, showing an acceptable postoperative complication rate. Given the availability of modern bifurcated aortic endografts with possible use in low diameter aortic bifurcations, endovascular techniques using straight endografts should be limited to cases with long proximal and distal sealing zones. The double trombone technique seems preferable.

FM3.2

Hydrogen sulfide limits the development of intimal hyperplasia in human vein segments

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

Objective: Bypass surgeries and other endovascular approaches to treat arterial occlusive diseases suffer from limited long-term patency due to re-occlusive vascular adaptations, a process called intimal hyperplasia (IH). IH develops in response to vessel injury, loss of endothelial cells (EC), leading to inflammation, dedifferentiation and proliferation of vascular smooth muscle cells (VSMC). Hydrogen Sulfide (H₂S) is an endogenously produced gas, with anti-oxidant and anti-inflammatory properties. In rodent models, H₂S reduces IH, and vascular patients have reduced circulating H₂S levels. Here, we tested the therapeutic potential of various H₂S donors to limit the development of IH in human vein segments obtained from vascular patients.

Methods: Human veins segments obtained from patients undergoing lower bypass surgery cultured ex-vivo in control media or supple-

mented with various H₂S donors (NaHS, GYY4137, diacetyltrisulfide). IH was measured by histomorphology 7 days later. In addition, human umbilical endothelial cells (HUVEC) and primary human vascular smooth muscle cells (VSMC) were exposed in-vitro to the same H₂S donors. The migration and proliferation of these primary cells were measured using transmigration assay and BrDU incorporation, respectively.

Results: All the H₂S donors tested prevented the development of IH in human vein segments ex-vivo. Similarly, in vitro, the H₂S donors inhibited migration and proliferation of primary VSMC. In contrast, the H₂S donors stimulated HUVEC migration and proliferation.

Conclusion: Currently, there is no effective strategy to reduce IH in venous bypass. In addition, newer device to treat stenosis rely on coated balloon and stent with anti-proliferative drugs, limiting both VSMC proliferation and EC re-endothelization. Our data suggest that exogenous H₂S supply may provide new therapeutic strategies to limit VSMC proliferation while promoting re-endothelization.

FM3.3

EVAS versus EVAR: Endovascular aortic sealing with nellix reduces intraoperative radiation dose in a comparative analysis

S. Ockert, M. Heinrich, T. Kaufmann (Luzern)

Objective: To analyze radiation exposure during EVAS in comparison with standard EVAR in clinical practice.

Methods: From 12/2013–10/2016 (35 months), 60 patients were analyzed for intraoperative radiation exposure during endovascular aortic repair: 30 consecutive patients (mean age 73.10 ys, 28 male) received Endovascular Aortic Sealing (EVAS: Nellix Endologix); within the same time frame, 30 patients were treated with standard EVAR (mean age 71.87 ys, 30 male).

An indirect dose analysis was performed for both groups of patients, including effective dose (ED) and cumulative air kerma (CAK). Furthermore, fluoroscopy time (FT), dose area product (DAP), and time of procedure were included in the study.

Results: The effective dose (ED) was significantly reduced in the EVAS group (3.72 mSv) compared to the group treated with standard EVAR (6.8 mSv; $p < 0.001$). CAK was also lowered in EVAS (67.65 mGy vs. 139 mGy in EVAR; $p < 0.001$). Fluoroscopy time for the entire group was 13 minutes and was shorter ($p < 0.001$) for EVAS (9 minutes) in comparison to EVAR (19 minutes). DAP for the entire cohort was 16.95 Gy.cm² and was lower during EVAS (12.4 Gy.cm²) than during EVAR (22.6 Gy.cm²; $p < 0.001$). The median operating time for the entire group was 123.5 minutes and was significantly shorter ($p < 0.01$) for EVAS (119 minutes vs. EVAR at 132 minutes). The fluoroscopy time shows a significant correlation with the patient's weight ($p = 0.022$), BMI ($p = 0.004$) and time of procedure ($p = 0.005$).

Conclusion: EVAS is associated with a relevant reduction of indirect measured radiation dose and time of procedure compared to standard EVAR. A relevant reduction in dose during EVAS is highly likely to result in lower exposure to radiation for physicians and staff. Such a result would be highly advantageous and calls for further analysis.

FM 3.4

A new catheter foam sclerotherapy approach offers a valid and safe alternative for the treatment of small saphenous vein incontinence

F. Strano, H. Probst (Morges)

Objective: Endovenous thermal ablation therapy for varicose veins is nowadays a well established alternative to conventional surgery with similar short and medium term results. Catheter foam sclerotherapy (CFS) is also recommended as a safe therapy for incompetent saphenous veins (GRADE 1A). However this treatment has an higher recurrence rate compared to the other procedures. Adjuncts as intra-saphenous saline irrigation (ISI) and peri-saphenous tumescence (PST) were recently described to improve outcomes. As small saphenous vein (SSV) treatment is often altered by neurological complications, we consider this new technique in this specific indication. The purpose of this study is to assess the safety and short-term results of this procedure in the SSV incontinence.

Methods: Retrospective monocentric analysis was carried out between March 2017 and June 2018. 17 consecutive patients with SSV incompetence were enrolled and submitted to CFS, after ISI and PST. By means of peri-operative venous ultrasound (US), Lauromacrogol (400) 1% sclerosant foam was injected directly in SSV trunk through a long introducer. The surgical gesture was completed with phlebectomies. At the end of the procedure each patient worn an elastic bandage and injected subcutaneously low-molecular-weight-heparine for 10 days. Post-operative clinical and duplex US control were performed at 10 days and 6 months.

Results: 17 patients were available for follow-up at 10 days and 6 months. The occlusion rate in the respectively periods was 100%. The main complications were bruising (47%) and local pain (17%) in the areas of phlebectomies treated with NSAI and local cooling. No nervous injuries and no scar infection were observed.

Conclusion: This new CFS approach applied to small saphenous vein gives promising results as other endovenous procedures in term of safety and occlusion rate at short term. This procedure could be considered as a good alternative for SSV incompetence lowering the neurological complication rate.

FM 3.5

Patients' perception and general practitioner-based surveillance after screening detection of abdominal aortic aneurysm.

R. Trunfio, S. Engelberger, L. Uccella, L. Giovannacci (Lugano)

Objective: To assess patients' perception and efficacy of a general practitioner-based follow up in patients diagnosed with AAA in a pilot screening program performed in 2013.

Methods: Thirty-one patients, diagnosed to have an AAA in an ultrasound screening AAA study held in 2013, were reviewed to assess their disease's perception and the efficacy of a general practitioner-based FU program at 5 years from the diagnosis. Data were collected reviewing hospital files and with a phone interview to the patients (pts).

Results: Thirty-one out of 745 pts, mean age 75.5 (± 5.4), were diagnosed with an AAA in 2013. Aortic mean diameter was 35.6 (± 4.4) mm at diagnosis. There were 3 (9.7%) non-aneurysm-related death during follow-up. All 28 alive pts were phoned for an interview. Four of 28 (14%) were not reachable. Twenty-three pts (74%) had history of smoking, 7 of them (23%) were active smokers at the time of screening. Four out of this 7 pts (57%) decided to give up smoking after the diagnosis. Four out of 24 interviewed pts (17%) were not on a FU program for unknown reasons. The average aortic increase in diameter during FU was 3.9 (± 4.7) mm per year. Five pts (16%) were operated on (3 EVAR, 2 Open) at a mean time of 2.3 (± 1.4) years. The average aortic increase in diameter of operated pts was 10.6 (± 4.4) mm per year. Only one patient experienced minor anxiety after the initial diagnosis (1/24, 4.2%). All 24 interviewed pts declared that their life-style have not been negatively affected by the screening program and they believe that the program was worth doing.

Conclusion: This study shows, notwithstanding general beliefs, that most of the patients with an AAA did not experience big emotional turmoil or problems in their social life after the diagnosis. A positive finding is that 57% of them decided to give up smoking because of the diagnosis. A general practitioner-base FU is almost always effective, but a minority of patients are not on FU control. A close collaboration with a vascular department could increase the adherence of these pts to a systematized follow up program.

FM 3.6

Analysis of aortic neck dilatation after endovascular aortic repair

S. Hofer, A. Todorov, M. Furrer (Chur)

Objective: Infra-renal aortic neck dilatation after endovascular aortic repair (EVAR) can lead to late endoleak and stentgraft migration. The aim of this study was to identify predictive factors of neck dilatation.

Methods: From January 2008 to March 2017 243 EVAR were performed at our institution. Of these we analyzed only patients who had a follow-up CT scan after 12 months or later, patients with supra-renal sealing were excluded. Pre- and postoperative CT scans were reviewed. Neck diameter was measured just below the lower rim of the lower renal artery. Possible predictive factors of neck dilatation such as preoperative neck diameter, neck shape, oversizing and stentgraft type were retrospectively analyzed.

Results: 111 patients with a median follow-up time of 31.5 months (range 12 to 102 months) could be included. The types of stentgrafts were Anaconda(57), Excluder(34), Endurant(14), Aorfix(2), Incraft(2), Evita(1), and Etegra(1). Neck dilatation occurred in 83 patients (75%) during follow-up. The mean neck size growth at the latest follow-up was 2.25 mm. Upon correction for all covariates, multiple linear regression showed a highly significant effect of use of ringstent-designed stentgrafts ($p < 0.001$), use of supra-renal fixation ($p < 0.01$) and conical neck shape ($p < 0.01$) as well as a moderately significant effect of stent placement at the renal artery ($p < 0.05$), stentgraft oversizing ($p < 0.05$) and initial neck length ($p < 0.05$). The odds of neck size increase were 115:1 with the use of ring-stent-designed stentgrafts.

Conclusion: Aortic neck growth seems to occur in the majority of patients. Increased risks for neck dilatation were a conical neck

shape and stentgraft type as well as stentgraft oversizing. These factors should be considered in EVAR planning and follow-up protocols to prevent severe complications such as stentgraft migration and type I endoleak. The impact of stentgraft type on neck dilatation needs further evaluation.

FM 1

Selbstgefertigte xeno-perikardiale Grafts bei Aorteninfekten

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Objective: Die chirurgische Behandlung von Aorteninfekten und die Wahl des bestgeeigneten Materials zum in-situ Ersatz der Aorta ist eine Herausforderung. Diese Studie untersucht das Outcome nach Rekonstruktion der Aorta mit selbstgefertigten Grafts aus bovinem Perikard bei Infekten der nativen Aorta und Protheseninfekten.

Methods: Retrospektive Analyse aller Patienten, welche zwischen Januar 2008 und Dezember 2015 aufgrund eines Prothesen- oder nativen Aorteninfektes mittels in-situ Rekonstruktion mit selbstgefertigten bovinen perikardialen Grafts behandelt wurden. Das perioperative und mittelfristige Outcome inklusive Mortalität und Reinfektionsrate wurde per Ende Januar 2017 analysiert. Die verfügbaren Verlaufsbildgebungen wurden hinsichtlich Graftbeständigkeit untersucht.

Results: Bovine perikardiale Grafts wurden in 35 Patienten (86% männlich) mit einem medianen Alter von 69 Jahren (38–84) zur Rekonstruktion der Aorta ascendens oder des Aortenbogens (7), der Aorta descendens (7), der thorakoabdominalen (7) oder der abdominalen Aorta (14), verwendet. Zwölf Patienten (34%) wurden aufgrund einer Infektion der nativen Aorta und 23 (66%) aufgrund eines Protheseninfektes behandelt. Die Operation erfolgte in 22 Patienten (63%) notfallmässig. Die 30-Tagesmortalität lag bei 31% (n=11). Weitere sechs Patienten starben während des Follow-up nach median 33 Monaten (3–70). Das mittlere Follow-up der restlichen Patienten betrug 48 Monate (± 26). Es kam zu keinen Reinfektionen und zu kei-

nen Reoperationen aufgrund von Graft-assoziierten Komplikationen. Bildgebend konnten nach median 15 Monaten (3–68) keine Zeichen einer Graftdegeneration nachgewiesen werden.

Conclusion: Die chirurgische Behandlung von Aorteninfekten ist mit hohem Risiko verbunden. Die Verwendung von selbstgefertigten bovinen perikardialen Grafts ist eine vielversprechende Option. Trotz einer hohen frühen Mortalität zeigt diese Studie gute klinische Ergebnisse ohne Reinfektionen im mittelfristigen Verlauf. Frühe radiologische Resultate zeigen eine gute Graftbeständigkeit.

FM 2

Vein valve defects in children and adolescents

J.C. Ragg, S. Kreis, S. El-Chamali, K. Stoyanova (Zürich)

Objective: Venous insufficiency of the lower extremities is regarded to be a genetically determined, acquired disease. Children have rarely been examined. In earlier studies, the incidence of congenital valve defects is commonly estimated below 3%.

Methods: In an ongoing study in Germany and Switzerland, until 5/2018 a total of 170 legs in 85 children of vein patients, aged 6–18 (38 m, 47 f) could be examined with high frequency ultrasound (Siemens X 700, Mindray M9, 14–16 MHz; Vevo MD, 16–32 MHz). Investigation time was limited to 15 minutes. In case of visible vein changes (protruding, more intense colour, increased diameter), ultrasound started here. Otherwise, systematic screening of saphenous veins and medial perforators was performed

Results: In 47/85 children (55.3%), resp. 59/170 legs (34.7%) relevant venous pathology was found: Focal valvular defects of the GSV: 13/170 (7.6%), segmental GSV reflux without varices: 15/170 (8.8%, fig.2), same but with varices: 11/170 (6.5%), GSV sidebranch reflux only: 13/170 (7.6%, fig. 1), total GSV reflux 3/170 (1.8%), focal SSV valve lesion: 2/170 (1.2%), segmental SSV reflux: 1/170, 0.6%, medial perforator reflux: None. In the subgroup of 6–8 y/o kids, 9/30 legs (30.0%) already showed pathology. The rate of defects did not differ significantly from those of the whole collective. Among the cases allowing diagnosis of lesion type (n = 53), unilat-

Fig. 1: Congenital cusp mismatch temporarily by perivenous hyaluronan (HA, IntraShape)

FM 2. Figure.

eral commissural mismatch was the most frequent pattern (24/53, 45.3%). A subgroup (pilot study for treatment, informed consent also by parents) received therapy: In 5 German cases, hyaluroan valvuloplasty was successfully performed in kids > 16 years of age (fig. 1). 4 other German adolescents received a single-puncture foam sclerotherapy (POL 0.25%) for ablation of isolated GSV side branch insufficiency to potentially save the GSV. GSV reflux was not treated invasively so far.

Conclusion: As the acquisition of valvular insufficiency is supposed to take several decades, the shown pathologies should be best explained by congenital valve lesions. This thesis is supported by the high rate (30%) of lesions detected in 6–8 y/o kids. Even if taking a bias by case selection (vein patient families) into account, about one fifth of western populations could be concerned. New strategies for systematic detection and appropriate therapy (painless, cheap, vein preserving) have to be discussed and developed on an adequate ethical basis.

FM3

Klappenmorphologie und stationäre Aggregate von Blutpartikeln im Klappensinus: Eine erste Klassifizierung Stase-assoziiierter Klappenschäden.

J. C. Ragg, S. Kreis, K. Stoyanova, S. El-Chamali (Zürich)

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

Beispiel einer morphologisch unauffälligen VSM-Venenklappe (zarte, lange Segel ohne Defekte), jedoch mit permanenten Aggregaten (1–3). Diese haben folgende Effekte: Mechanische partielle Fixierung der Klappensegel (1), Einschränkung des gespülten Sinusvolumens (2), ferner potentiell inflammatorische Interaktionen (3).

FM3. Figure.

Methods: In 100 konsekutiven Patienten (68 f, 32 m; 42–64 J.) mit V.a. Stammveneninsuffizienz wurden insgesamt 180 Klappen mit SMA im VSM-Bereich ausgewählt, die einer näheren Ultraschall – Videostudie unterzogen wurden (14–18 MHz). Inhalte waren Strömungsanalyse im B-Flow-Modus, die Ausdehnung der SMA, die Segelmorphologie und mechanische Interaktionen mit den SMA.

Results: SMA korrelierten mit langsamem oder stagnierenden Fluss (<5 cm/s) in 165/180 Fällen (91,7%). Eine Änderung der Sinushämodynamik (Reduktion des gespülten Sinusvolumens) wurde in 102/180 Fällen (56,7%) gesehen. Eine Einschränkung der Klappen-segelsbewegung durch SMA mit noch gegebenem Klappenschluss war in 64 Fällen (35,6%) zu sehen. Eine völlige Fixierung der Segel ohne Reflux wurde in 6/180 Fällen (3,3%) gefunden. 8/180 Fälle (4,5%) zeigten eine totale Segelfixierung durch SMA als Quelle eines Refluxes (fig. 1). In Segmenten mit signifikantem Reflux (>1000 ms, >10 cm/s) war der partielle bzw. vollständige Verlust von Klappenstrukturen der typische Befund.

Conclusion: Die Ergebnisse legen nahe, dass SMA und der Erhaltungszustand der Klappensegel aufeinander folgende Stadien der Insuffizienz unterscheiden lassen. Diese Erkenntnisse können künftig zur Entwicklung moderner Vorsorgestrategien, venenerhaltender Therapien und objektiver Erfolgskontrollen beitragen.

FM4

Infrainguinal open surgical revascularisation in diabetic patients

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Objective: Even if endovascular-first approach is considered nowadays an adequate strategy for lower limb revascularization, open surgical revascularisation remains a good option for very long and complex lesions. Nevertheless, the proportion of open surgery is decreasing worldwide mainly related to very complex lesions frequently associated with diabetes. The purpose of this study was to evaluate the patency of infrainguinal bypasses in diabetic patients with peripheral arterial disease in a vascular tertiary center with endovascular first approach strategy.

Methods: We selected consecutive diabetic patients with infrainguinal open surgical revascularization from a prospective maintained database from May 2013 to December 2014. The design of the study was retrospective and monocentric. Duplex scan at 1, 3, 6, 12 months and every year were performed to evaluate the following outcomes. Primary outcomes are primary patency, assisted primary patency and secondary patency. Secondary outcomes included limb salvage, overall mortality and complication rate. Standard descriptive statistical analyses were performed (mean, median, standard deviation) as well as Kaplan Meier survival analyses

Results: We included 17 patients (mean age: 68.8 years, men:75%). Critical limb ischemia was diagnosed in 71.4% of the patients. We performed above the knee bypasses, below the knee and femoro distal bypasses in 49%, 40% and 11% respectively. The primary patency was 78.95%, 57.89%, 52.63% and 52.63% at 1, 6, 12, 24 months respectively. The primary assisted patency was 79%, 58%, 53% and 53% respectively. The secondary patency was 100% at 1, 6 and 12 months and 74% at 24 months. Limb salvage was 91.2%. No death occurred during the follow-up. Complication rate was 35.3%.

Conclusion: Open surgical revascularization of diabetic patients with no option of endovascular treatments has good midterm patency results but associated with a significant complication rate.

FM 5

Reality check: primary vascular access creation today

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Objective: In Switzerland, the outcome following Vascular Access (VA) creation in 4500 patients on dialysis is unknown. Mainly because there is no prospective register for patients having VA surgery for renal replacement therapy. The aim of the study was to assess the quality of vascular access creation and to compare it with the current literature and the guidelines, in order to define strategies to improve clinical outcomes.

Methods: Retrospective single-centre study in a tertiary referral centre. All consecutive patients over 18 years of age undergoing primary VA creation between January 2013 and December 2014 were included. Follow-up data for at least 12 months were collected using hospital records and by contacting external nephrologists for information.

Results: During the period, 365 patients had a surgical intervention for renal replacement therapy. A primary VA was created in 74 patients (20%), which were further analysed in our study: 63 (85%) had an arteriovenous fistula (AVF) and 11 (15%) an arteriovenous graft (AVG). The intervention-free survival (primary patency) of the primary VA at one year was 46% (95% CI 33–58) for AVF and 30% (95% CI 7–58) for AVG with a secondary patency at one year of 75% (95% CI 63–84) for AVF and 50% (95% CI 18–75) for AVG. Twenty-seven patients (36%) with primary VA underwent central venous catheter (CVC) placement (tunnelled and non-tunnelled) before the creation of the Access. Thirty-seven (50%) patients had their first dialysis through a CVC. 31 patients (42%) never received a CVC.

Conclusion: The primary patency of VA was unexpectedly low, and the number of CVC requests unexpectedly high. In light of this we consider it to be essential that centres which create VA register their activities and compare their outcomes with the upcoming medical societies' guidelines to check and improve their clinical management. To facilitate this there is an initiative starting 2018 which encourages all Swiss vascular surgeons to provide data on VA interventions, including outcomes at 12 months follow-up, in the national online registry "SwissVasc 2.0".

FM 6

Endovascular repair of thoracic aorta: analysis of the results and effects on spinal cord perfusion in elective and emergency procedures. What have we learned?

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Objective: The introduction of endograft revolutioned the treatment of patients with thoracic aortic aneurysms whether in elective or in

urgent procedures. Despite various strategies used to prevent spinal cord ischemia (SCI), it remains an important complication. Cerebrospinal fluid drainage (CSFD) is recommended as a component of a multimodal approach for prevention of neurological injury. The aim of this study was to address the SCI rates after TEVAR and to analyze potential risk factors leading to this complication.

Methods: A consecutive cohort of patients treated by TEVAR between January 2005 and September 2015 was analyzed. Neurologic examination was routinely performed by an independent neurologist before operation and at discharge. The main outcome measure was the onset of SCI (paraplegia or paraparesis).

Results: 182 patients with TAAs were included in this study. The majority of patients (n 78 [43%]) were treated for an atherosclerotic aneurysm, 49 patients (27%) were treated for a type B aortic dissection, 55 patients (30%) were treated for an aortic rupture. SCI developed in 20 patients (11%; paraplegia in 3 [15%] and paraparesis in 17 [85%]). Among them, 2 patients (43%) showed SCI directly after the procedure, 14 patients (48%) in the first 24 hours, and 4 patients (9%) after 24 hours. There was an improvement of the neurologic status in the majority of patients, with only one patient (5%) showing paraplegia at discharge. Prophylactic use of CSFD before the procedure was performed in 67 patients (37%), if MAP (Mean Arterial Pressure) was <75 mmHg and CSF pressure > 12 mmHg, and among them, 1 patient (1.5%) developed a cranial hypotension syndrome. No clinical benefit for patients with SCI receiving prophylactic placement of CSFD (CSFD, 11 of 67 patients [16.4%] vs no CSFD, 9 of 115 [7.8%]; P .623). The multivariate analysis revealed the mean measure of thoracic aortic coverage (33 cm) and the difference between MAP and CSF pressure as the significant risk factors for SCI.

Conclusion: The SCI rate after endovascular repair of TAAs was 11%. Prophylactic use of CSFD did not reduce the SCI rate and was associated with adverse events. The percentage of thoracic aortic coverage and the difference between MAP and LCR pressure were the most significant risk factors of SCI in these series.

Free Communications SSMVR

FC 1.1

Metabolic interactions between the endothelium and the muscle

K. De Bock (Zurich)

Angiogenesis, the formation of new blood vessels from existing ones, is initiated by the secretion of growth factors – the vascular endothelial growth factor VEGF is the best described one – from a hypoxic environment. To grow under low oxygen conditions, ECs rely on a special metabolic machinery. Indeed, even though they are located next to the blood stream – and therefore have access to the highest oxygen levels – ECs are highly glycolytic. However, when they need to sprout into avascular areas and form new vessels, they upregulate glycolysis even further to fuel migration and proliferation. Suppression of glycolysis via inhibition of the glycolytic regulator PFKFB3 (phosphofructokinase-2/fructose-2,6-bisphosphatase isoform 3) in endothelial cells prevents blood vessel growth in the retina of the mouse pup and also in various models of pathological angiogenesis.

While we now know that ECs are metabolically preconditioned to rapidly form new vessels, it remains an outstanding question whether this also holds true in muscle and whether endothelial metabolism can become a target for the treatment of peripheral artery disease. The Laboratory of Exercise and Health aims to investigate whether muscle endothelial cells need to reprogram their metabolism to promote optimal muscle angiogenesis. Moreover, we try to understand how muscle and the endothelium communicate to ensure optimal nutrient and oxygen delivery into the muscle.

FC 1.2

Molecular triggers to circulating tumor cells intravasation

N. Aceto (Basel)

Objective: Circulating tumor cells (CTCs) are cancer cells that detach from a primary tumor lesion and enter the bloodstream, on their way to seeding a distant metastasis. With the development of microfluidic technologies and single cell-resolution sequencing methods, the biology of CTCs is being extensively investigated. Yet, what leads to CTC intravasation from a primary tumor mass is largely unknown.

Methods: We combined microfluidic technologies, patient samples, mouse cancer models, single cell sequencing, molecular and computational biology to gain insights into those molecular features that promote the generation of CTCs from the primary tumor.

Results: We generated a lineage tracing in vivo system to dynamically observe microenvironmental stimuli on cancer cells, and identified potential triggers to CTC intravasation. We also generated new patient CTC-derived xenografts models with the ability to spontaneously shed CTCs from the primary tumor and form metastasis in organs such as the bone, liver and brain. With these tools, combined with single cell RNA sequencing of patients and mouse models, we have identified molecular signals that may promote the detachment of cancer cells from the primary tumor. Inhibition of these signals leads to the suppression of CTC generation and a remarkable reduction in metastasis formation.

Conclusion: Our work allowed us to gain important insights into the processes that govern CTC intravasation. Blocking these signaling pathways enables the reduction of CTC shedding from the primary tumor, leading to decreased metastasis formation.

FC 1.3

Perfusion characteristics of the capillary bed – homogeneities, heterogeneities and erythrocyte trajectories

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Objective: Microvascular perfusion is crucial for nutrient and oxygen supply in all tissues. Nonetheless, topological details and perfusion characteristics for many tissues are largely unknown.

Methods: We use numerical simulations in realistic microvascular networks (MVN) in combination with in vivo measurements to study flow, topology and the impact of red blood cells (RBCs) in the vasculature of the mouse brain.

Results: The RBC velocity and hematocrit distributions reveal that the perfusion of the capillary bed is highly heterogeneous (Fig.1A). However, at individual divergent bifurcations RBC velocities differ by only 27%. We conclude that velocities are balanced locally while on the network scale the velocity heterogeneity remains. Both characteristics, the hematocrit heterogeneity and the local velocity balancing, prove to be a direct consequence of the bi-phasic nature of blood (plasma and RBCs, Fig.1A). Further analysis on the velocity balancing suggests that well-balanced bifurcations (velocity difference <20%) promote robustness of perfusion and might be key for local regulation mechanisms. Furthermore, we are interested in depth-dependent differences. The trajectories of individual RBCs show that RBCs tend to enter and exit the capillary bed at the same cortical depth (Fig.1B-C). This is surprising because commonly the capillary bed is described as a homogeneous 3D-network where a preferential flow direction would not be expected. Further differences with respect to depth are: a decrease in RBC velocity with depth and a shift of the location of the largest pressure drop from capillaries to descending arterioles. These aspects are relevant for the vascular supply capability and for the up-regulation of flow.

Conclusion: We provide a new mechanistic role of RBCs and propose a strong evolutionary advantage of the existence of the bi-phasic nature of blood. Furthermore, our findings support the hypothesis that for an efficient oxygen up-regulation at least two regulation mechanisms must be playing hand in hand, namely.

FC 2.1

A pericyte-independent role for PDGF-BB in vascular stabilization by stimulating the Semaphorin3A/Neuropilin1+ Monocyte axis

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Objective: Vascular Endothelial Growth Factor (VEGF) is the master regulator of angiogenesis. However its therapeutic potential is challenged by the need to control both the dose and duration of expression: high doses cause aberrant angioma-like tumors, but sustained delivery for 4 weeks is required for new vessel persistence. We previously found that: 1) increasing VEGF doses impair vessel stabilization by inhibiting the endothelial Sema3A/Nrp1+ monocytes (NEM)/TGF-beta1 paracrine axis; and 2) PDGF-BB co-expression restores normal angiogenesis despite high VEGF levels. Here we investigated whether and how PDGF-BB accelerates the stabilization of VEGF dose-dependent angiogenesis.

Methods: Mouse leg muscles were implanted with monoclonal populations of genetically modified myoblasts homogeneously producing specific VEGF levels that cause normal (low and medium) or aberrant angiogenesis (high), alone or with a fixed 1:3 ratio of PDGF-BB (V+P). VEGF signaling was abrogated by systemic treatment with the receptor-body Aflibercept.

Results: PDGF-BB did not change the effects of low and medium VEGF, but it greatly accelerated vascular stabilization with high VEGF (80% at 3 weeks vs 0% with VEGF alone). All normal capillaries induced by different V or V+P doses displayed similar pericyte coverage and functional perfusion, despite different stabilization rates. However, PDGF-BB co-expression restored Sema3A production, NEM recruitment and TGF-beta1 levels in vivo despite high VEGF, leading to endothelial quiescence. PDGF-BB directly increased

Sema3A expression dose-dependently in vivo even without VEGF. Blockade of Sema3A/Nrp1 binding abolished NEM recruitment and greatly reduced vessel stabilization by both V and V+P, but interestingly a Sema3A/NEM-independent fraction of about 30% persisted in all conditions. In vitro VEGF and PDGF-BB had direct and opposing effects on endothelial Sema3A. Co-expression prevented VEGF-induced loss of Sema3A both in vitro and in ex vivo-isolated endothelium, but did not increase it compared to controls. However, in situ hybridization revealed that PDGF-BB specifically and dose-dependently expanded a non-endothelial source of Sema3A expression. **Conclusion:** We identified a novel role for PDGF-BB to promote vascular stabilization independently from pericyte recruitment, by regulating the endothelial Sema3A/NEM/TGF-beta1 axis.

FC 2.2

Immune interactions in afferent lymphatic vessels

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Objective: Afferent lymphatic vessels (LVs) mediate transport of antigen and leukocytes to draining lymph nodes (dLNs), thereby serving as immunologic communication highways between peripheral tissues and LNs. Performing intravital microscopy (IVM) in the murine ear skin we previously found that after entry into lymphatic capillaries, dendritic cells (DCs) and T cells spend several hours patrolling or arresting within lymphatic capillaries before being transported to the dLN in larger collecting vessels. This mode of migration has raised fundamental questions regarding the purpose of intralymphatic leukocyte migration. In order to elucidate upon the purpose of this migration step, we investigated whether DCs and T cells interact inside lymphatic capillaries in the skin.

Methods: In order to image intralymphatic DC-T cell interactions, we performed IVM experiments in contact-hypersensitivity (CHS)-inflamed or ovalbumin (OVA)-specific delayed-type hypersensitivity (DTH)-inflamed ear skin of fluorescent reporter mice. Complementary adoptive transfer experiments were performed to determine the effects of intralymphatic DC-T cell interactions on DC migration from the skin to dLN.

Results: Performing IVM in CHS-inflamed ear skin we found that T cells frequently contacted DCs inside lymphatic capillaries. Majority of these contacts were short-lived (<10 mins) with few long-lasting (>30 min) contacts. Preliminary findings in an OVA-specific DTH model suggest that OVA-pulsed wild type (WT) DCs show a tendency to engage in long-lasting (>30 mins) contacts with T cells compared to OVA-pulsed MHCII-deficient (MHCII-KO) DCs. Previous reports have shown that regulatory T cells (Tregs) constitute a large fraction of T cells that exit from CHS-inflamed ear skin. We show that, in CHS-inflamed ear skin of a three-color fluorescent reporter mouse, Tregs actively patrol lymphatic capillaries and also frequently contact DCs inside lymphatic capillaries. Tregs more frequently contacted DCs inside lymphatic capillaries than in surrounding tissue, and in adoptive transfer experiments, WT DCs that migrated from the skin to dLN had reduced CD80 and CD86 compared to MHCII-KO DCs.

Conclusion: While the functional consequences of these intralymphatic interactions are being further explored, these findings highlight the importance of lymphatic capillaries in the skin as a novel immune compartment in which immune modulation can occur.

FC 2.3

A circadian zip code guides leukocyte homing

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Objective: The process of leukocyte migration to tissues has long been studied. Yet, no broad systematic approach has been undertaken to investigate the effects of multiple molecules, leukocyte subsets and organs with respect to the time-of-day.

Here, we have investigated the hypothesis that leukocyte subsets migrate to organs at specific times of the day by deciphering a leukocyte- and endothelial cell-specific zip code of pro-migratory molecules.

Methods: We employed adoptive transfer and homing assays to functionally screen for factors on both murine leukocytes and their microenvironment involved in trafficking at different times of the day. We tested the previously profiled protein code on leukocytes and endothelial cells in varying mouse models with lineage-specific genetic ablation of the circadian clock. This code was further pharmacologically manipulated and explored in a syngeneic and a xenogeneic model of acute myeloid and B-cell acute lymphoblastic leukemia. Finally, we investigated the rhythmic behavior of human primary leukocytes.

Results: We show this rhythmic molecular signature to govern time-of-day-dependent homing behavior of leukocyte subsets to specific organs. We determined the phase of the day when leukocyte migration to tissues and its respective blockade would show maximal effects to be at the beginning of the behavioral activity phase. Lineage-specific ablation of circadian clock function in endothelial cells and leukocyte subsets demonstrated that rhythmic recruitment is dependent on both microenvironmental and cell-autonomous oscillations. These oscillations extended to mouse and human cancer models, where leukemic tumor burden in blood was dependent on rhythmic homing and engraftment. Rhythms in the expression of pro-migratory factors and migration capacities were preserved in human primary leukocytes, demonstrating the relevance of this phenomenon across species.

Conclusion: Here, we have deciphered an extensive, time-of-day-dependent trafficking zip code on endothelial cells and leukocytes that is specific for each organ and leukocyte subtype. These findings are not only advantageous for scientists to improve the outcome of their experiments based on the time-of-day effects but also open up new avenues to treat patients at different times of the day to reduce costs and maximize efficacy.

FC 2.4

Analysis of differentially expressed lncRNAs between blood vascular and lymphatic endothelial cells identifies LEC-LINC2 as an important factor for endothelial cell survival

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Objective: The blood- and lymphatic-vascular systems are essential in vertebrates to ensure the efficient transport of nutrients, signaling molecules, and circulating immune cells to organs. In the last decade,

several significant advances have been made to gain more understanding how angiogenesis and lymphangiogenesis are regulated especially in cancer progression. Despite intensive works in finding new signaling molecules and transcription factors, little is known about the role of long noncoding RNAs (lncRNAs) in the regulation of angiogenic growth of blood and lymphatic vessels. The recent technological boost in sequencing techniques has revealed lncRNAs as important regulators of gene expression in a cell type-specific manner via multiple mechanisms.

Methods: To identify vascular-associated lncRNAs and characterize their functional role in angiogenesis, we established, for the first time, the landscape of lncRNAs expressed in human primary dermal blood vascular and lymphatic endothelial cells (hBECs and hLECs) using the 5'-accurate RNA-sequencing method called CAGE (capped analysis of gene expression).

Results: Based on conservation, expression level, and specificity, we selected 2 hBEC- and 2 hLEC-associated lncRNAs to be targeted using antisense oligonucleotides (ASO) GapmeRs. Subsequent ASO-mediated knockdown screen followed by transcriptional profiling highlighted a strong impact of LEC-LINC2 on the transcriptome of hLECs, in particular regarding cell growth and migration pathways. Subcellular localization studies showed that LEC-LINC2 localizes predominantly in the nucleus suggesting a chromatin-related function. To identify chromatin-interacting sites of LEC-LINC2, we performed chromatin isolation by RNA precipitation followed by DNA-sequencing. We found that LEC-LINC2 significantly interacts in cis but mainly in trans near genomic loci previously determined as differential expressed genes after ASO-mediated knockdown. Gene set enrichment analysis showed that the majority of these interactions were associated with endothelial cell growth and migration, strongly suggesting that LEC-LINC2 directly regulates the transcription of genes involved in these pathways.

Conclusion: Our results indicate lncRNAs as essential components of vascular development and function that may also provide novel insights into the pathogenesis of diseases associated with increased or impaired (lymph)angiogenesis.

Poster

P1

Supervised exercise training improves physical function in patients with lower extremity artery disease: preliminary results

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Objective: In lower extremity artery disease (LEAD), supervised exercise training (SET) is recommended as one of the primary baseline measure in patients with intermittent claudication to improve walking capacities. The aim of the present study was to investigate the effects of SET on physical function and balance.

Methods: Fontaine stage II LEAD's patients following a 3-month SET were investigated. SET consisted in 3 weekly 50-min sessions. Ankle-brachial Index (ABI), treadmill pain-free walking distance (PFWD) and maximal walking distance (MWD) were measured before and after SET. Monthly time course evolution of physical

function [6-min walking distance (6MWD), Short Physical Performance Battery (SPPB) score, and stair climbing test (SCT)], and balance (posturographic platform) were also assessed (pre-SET, 1 month and 2 months, post-SET).

Results: Fourteen LEAD patients (64.8 ± 2.8 years, 86% men) were analyzed. Following SET, walking performances significantly increased (PFWD: 97.7 ± 14.0 m pre- vs. 208.5 ± 46.6 m post-SET; $P=0.011$; MWD: 370.8 ± 59.0 m pre- vs. 662.3 ± 127.8 m post-SET; $P=0.004$). ABI did not change significantly (0.89 ± 0.07 pre- vs. 0.86 ± 0.04 post-SET; $P=0.86$). 6MWD, SCT, and SPPB score significantly improved during SET ($P \leq 0.001$, $P \leq 0.001$, $P=0.011$; respectively). 6MWD was significantly increased at 1 month (+8%, $P=0.012$), 2 months (+9%, $P=0.004$), and after SET (+10%, $P=0.01$) compared to pre-training. However, increase was not significant at 1 and 2 months compared to end of SET. Similarly, time during SCT significantly decreased at 1 month (-13%, $P=0.003$), 2 months (-17%, $P=0.001$) and after SET (-17%, $P=0.006$) compared to pre-training. Again, no significant difference was found at 1 and 2 months compared to end of SET. SPPB score tended to slightly increase at the end of SET (+8%, $P=0.06$) compared to pre-training. No significant difference was found after 1 or 2 months of SET. Balance did not change significantly during SET.

Conclusion: These results confirm beneficial effects of SET on walking performances. They suggest that SET is also effective in improving physical function in LEAD patients. Monthly time course evolution of physical function revealed that these adaptations mainly occur during the first month of SET, suggesting that training adaptations (volume, intensity) may be considered in the second part of SET to further increase benefit.

P2

Symptomatic internal carotid artery stenosis in the presence of a persistent primary hypoglossal artery: case report and review of the literature

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Objective: Anatomic variations of the extracranial carotid artery are very rare. Among them, a unilateral persistent hypoglossal artery (PHA), arising from the internal carotid artery at the level of C1-C3 and passing through the hypoglossal canal to join the basilar artery in the cranium, appears with a reported incidence between 0.03-0.2%. We report a case of recurrent transient ischemic attacks (TIAs) in a patient with proximal internal carotid artery (ICA) stenosis associated with ipsilateral PHA and propose a classification and a treatment algorithm based on a literature review (Fig. 3-4, Table 1-2).

Methods: Case report of a 78-year-old right-handed man experiencing an acute left hemispheric stroke, 2 hours before being transferred to our emergency department. Two previous TIAs over the past 3 years had been treated conservatively. At presentation, right-sided hemiplegia, right homonymous hemianopsia and anosognosia were documented. After rapid evaluation by the stroke team, intravenous thrombolysis with tissue plasminogen activator (tPA) was administered within 20 minutes, with complete resolution of symptoms over a few hours. Concurrent CT and MR angiography revealed new ischemic lesions in the left territory of the sylvian artery and in the cerebellum; a 50% stenosis of the left ICA; a persistent hypoglossal

Figure 2: Left : Internal carotid stenosis extending from the bifurcation to the origin of the PHA, producing 50% stenosis (top) ; Post-stenting control angiography showing complete reperfusion of the ICA and PHA, with complete stent coverage of the lesion, without residual stenosis (bottom). Notice the balloon exclusion tip of the MoMa device positioned in the ECA (asterisk). Right : 3D reconstruction of carotid CTA at 3 months follow-up verifying excellent stent apposition, without restenosis.

ICA : Internal Carotid Artery ; PHA : Primary Hypoglossal Artery ; ECA : External Carotid artery

P2. Figures.

artery originating 2 cm distal to the bifurcation at the level of the C1–2 vertebra, dominantly perfusing the posterior circulation; and bilateral hypoplastic vertebral arteries (Fig. 1). After multidisciplinary discussion, the patient was transferred to a tertiary university center where protected carotid stenting using a proximal protection device was performed under local anesthesia (Fig. 2).

Results: There were no peri-/postinterventional neurologic events. The patient was discharged after 12 days with dual antiplatelet treatment. At 3-months follow-up, he remains asymptomatic with a patent stent in the ICA on CTA.

Conclusion: Treatment of symptomatic carotid artery stenosis in the presence of PHA is challenging. Preoperative imaging with CTA/MRA along with a multidisciplinary approach is essential to the critical management of this rare and complex extracranial pathology in symptomatic patients. In the case of a high origin of the PHA, protected carotid artery stenting is considered to be the preferred and safest treatment.

Figure 1 a-b : Brain MRI showing old and new ischemic lesions in the cerebellum and in the territory of the left sylvian artery ; c : High-resolution CT angiography of the left carotid showing an ulcerated atheroma in the left internal carotid artery producing 50% luminal stenosis, extending over 2 cm from the carotid bifurcation, up to the origin of the PHA at the level of C2 vertebra (yellow asterisk) ; d : Intracranial and supra-aortic MR angiography revealing bilateral hypoplastic vertebral arteries, with absence of posterior communicating arteries and basilar artery from the PHA dominantly perfusing the posterior circulation ; e : 3D reconstruction on CTA

ICA : Internal Carotid Artery ; PHA : Primary Hypoglossal Artery ; ECA : External Carotid artery

Methods: To report a case of an atypical symptomatic descending aortic dissection.

Results: A 29-year-old woman was admitted to our Department for epigastric and back pain associated with right leg claudication. An angio-CT scan showed a distal aortic dissection with the entry tear located in the descending thoracic aorta at the level of T10. The true lumen was highly compressed, especially at the level of the visceral arteries and the iliac arteries with a stenosis of the right common iliac artery due to a thrombosed false lumen. The patient underwent an infra-renal aorto-bi-iliac bypass with reimplantation of the left inferior polar renal and inferior mesenteric arteries through a median laparotomy. Under supra-renal aortic clamping, a fenestration of the aorta at the level of the renal arteries was performed prior to the confection of the proximal anastomosis. One month later, the patient developed a left leg claudication. A thrombosis of the left limb bypass and a persistent highly stenotic true lumen were seen on the CT-scan. A re-intervention was performed with a left limb bypass thrombectomy. Aortic true lumen remodeling was achieved by implanting 2 large self-expanding uncovered E-XL stents (Jotec GmbH, Hechingen, Germany) from the thoracic aorta till the distal abdominal aorta. The post-operative period was uneventful and the CT of control confirmed the excellent result with complete reopening of the true lumen and normal visceral, renal and limb perfusion.

Conclusion: Atypical dissections arising for the distal part of the descending aorta are rare and their ideal management remains unclear. Indeed, the timing of treatment and the kind of material to implant regarding the risk of spinal cord ischemia are debatable. The E-XL stents (Jotec GmbH) was specifically designed to treat aortic lesions. Its use has been reported to be safe and efficient to improve proximal EVAR fixation or to treat aortic dissection with malperfusion. This specific aortic stent should be part of the armamentarium of the vascular surgeon.

P3

Atypical descending aortic dissection treated by large uncovered self-expanding stents

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Objective: It is now recommended to treat acute complicated type B aortic dissection by covering the proximal tear using a stentgraft. The use of a distal uncovered stent alone or in combination with a stentgraft could be useful in cases of persistent visceral or limb malperfusion and in order to achieve adequate aortic remodeling.

Figure 3: Proposed classification according to lesion localization, based on published cases of ICA stenosis in the presence of PHA. Type I: ICA involvement only; Type II: ICA-PHA bifurcation involvement; Type III distal ICA only (IIIa) or PHA only (IIIb).

ICA: internal carotid artery; ECA: External carotid artery; CCA: Common carotid artery ; PHA : Persistent hypoglossal artery

Figure 4: Treatment algorithm depending on lesion localization for symptomatic ICA stenosis in the presence of PHA

ICA: internal carotid artery; PHA: Persistent hypoglossal artery; CEA: carotid endarterectomy; CAS: Carotid artery stenting; BMT: Best medical treatment

P2. Figures.

Table 1: Literature review of CAS for the ICA stenosis with PHA

Authors	Symptom	Lesion Characteristics	Embolic protection	Stent type	Outcome Follow-up
Huang M et al. 2016	TIA	Rt. 60% stenosis, proximal to the ICA-PHA bifurcation	Spider Fx into the PHA (distal protection)	Protégé stent	Good, 1 year angiography
Kanazawa R et al. 2008	Syncope	Lt. Stenosis ICA, close to ICA-PHA bifurcation	Modified Parodi method with single distal balloon protection at the PHA	Self expanding stent	Good, no follow-up
Nii K et al. 2010	TIA	Lt. 75% stenosis ICA, 18 mm from ICA-PHA bifurcation	Single distal balloon protection (ICA proximal to the origin of PHA)	Wallstent RP	Good, 3 months angiography
Eller JL et al. 2013	Ischemia	Rt 50% stenosis ICA and 80% stenosis HPA	Gore Flow Reversal System in CCA and ICA	Closed cell Wallstent in HPA and CCA	Good, 6 months clinical
Zhang L et al 2016	None	Rt. 80% stenosis ICA to the origin of PHA	Mo.Ma device (ECA and CCA)	Wallstent (closed cell)	Good, no FU
Murai S et al. 2016	Ischemia	50% stenosis proximal to PHA origin	Proximal flow blockade (CCA et ECA) and distal filter	Self expanding stent	Good, no FU
Ryu B et al 2016	None	Lt. 80% stenosis ICA	Single distal balloon at the ICA proximal to the origin of PHA and proximal balloon protection	Wallstent	Good, no FU
Numan et al 2013	Vertigo and syncope	Lt. 80% ICA stenosis	None	Precise self-expanding stent	Good, 1 year angiography
Kaku et al 2017	Left hemiplegia	Rt. 50% ICA stenosis	Proximal flow reversal and distal filter	Self-expanding stent	Good, no FU
Silva CF et al. 2013	TIA	Rt. 75% stenosis ICA to the origin of the PHA	Double distal filter protection in ICA and PHA	Precise stent	Good, 6months angiography
Our Case	Recurrent TIA	Lt. 50% stenosis ICA to the origin of the PHA	Mo.Ma device (ECA and CCA)	Protégé self expanding stent	Good, 3 months CTA

CAS: carotid artery stenting; TIA: transient ischemic attack; ICA: internal carotid artery; CCA: common carotid artery; ECA: external carotid artery; PHA: persistent primitive hypoglossal artery; Lt.: left; Rt.: right; Rt.: right; FU: Follow-Up

P2. Table.

Table 2: Literature review of carotid endarterectomy for the ICA stenosis with PHA

Authors	Symptom	Lesion Characteristics	Surgical Technique	Cerebral Protection	Outcome Follow-up
Katoh M et al 1999	TIA	Lt. severe ICA stenosis close to the origin of PHA	CEA	None	Good, no FU
Megyesi JF et al. 1997	TIA	Rt. ICA stenosis extending to PHA origin	CEA with patch angioplasty	None	Good, no FU
Hatayama T et al. 1999	Vertigo attacks	Lt. 80% ICA stenosis	CEA	T-shaped shunt	Good, no FU
Pinkerton JA et al. 1980	TIA	Lt. severe stenosis ICA proximal to the ICA-PHA bifurcation	CEA	Carotid shunt (proximal to bifurcation)	Good, 6 months clinical
Thayer WP et al. 2005	None	Lt. 75% ICA stenosis	CEA with patch angioplasty	Carotid shunt (CCA-ICA)	Good, distal restenosis at 1 month (CTA)
Cartier R et al. 1996	None	Rt 90% ICA stenosis, PHA arising 4 cm from bifurcation with 60% stenosis (tandem)	Carotid and HPA endarterectomy with vein patch with anterior subluxation of the jaw	CCA-ICA shunt	TIA postop fully recovered, asymptomatic at 1 year FU
Elhammad y MS et al. 2007	TIA	Rt. Severe ICA and PHA stenosis	CEA	None	Good, no FU
Kawabori M et al. 2009	TIA	Rt 70% ICA stenosis	CEA	CCA-HPA shunt	Good, no FU
Stern J et al. 1978	TIA	Rt. ICA and proximal HPA stenosis	Carotid and HPA endarterectomy	CCA-HPA shunt	Good, no FU
Sunada I et al. 1990	Left hemiparesis	Rt. Severe ICA and proximal PHA stenosis	Carotid and HPA endarterectomy with primary closure	CCA-HPA shunt	Right facial paresis, hemiplegia
Osgood CP et al. 1983	TIA	Rt. 50% ICA and PHA stenosis	Carotid and HPA endarterectomy	CCA-HPA shunt	Good, 3 months CTA

CEA: Carotid Endarterectomy; TIA: transient ischemic attack; ICA: internal carotid artery; CCA: common carotid artery; ECA: external carotid artery; PHA: persistent primitive hypoglossal artery; Lt.: left; Rt.: right; Rt.: right; FU: Follow-Up

P2. Table.

P4

Filter-associated inferior vena cava thrombosis with duodenal perforation: case report and literature review

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Objective: The aim of this presentation is to report about the treatment of a case of filter related inferior vena cava thrombosis with perforation of the duodenum and penetration of a vertebral body by the filter struts and to review pertaining literature about the treatment of similar cases.

Methods: A 37 year old woman with a medical history of Behcet's disease treated with corticosteroids, underwent placement of a removable inferior vena cava (IVC) filter because of recurrent iliofemoral venous thrombosis regardless of therapeutic levels of anticoagulation. Despite a correct positioning of the filter, the second follow-up CT-scan, performed at 1 year, showed a complete thrombosis of the infra-renal IVC segment, with perforation of the vessel wall by the filter struts and penetration in the duodenum. The patient remained asymptomatic. Open surgical removal of the filter with resection of the affected vena cava without vascular reconstruction was planned. A review of sporadically reported similar cases has been performed.

Results: The operation was performed under general anesthesia, surgical exposure was performed through a small midline laparotomy, a duodenal Kocher maneuver was then performed to expose the

IVC. The filter struts were found to have completely passed the cava wall in multiple directions. 2 struts penetrated through the duodenal serosa and 1 strut was embedded in the L3 periosteum. The IVC filter was successfully removed in block together with the segment of the thrombosed and retracted IVC. The stumps were closed with 3-0 running polypropylene sutures and the duodenal lesions were closed with vycril seromuscular sutures. No vascular reconstruction was necessary due to the marked development of collateral venous circulation. The patient was discharged home on postoperative day 6 and is doing well 6 months after surgery.

Conclusion: Patients with IVC penetration of filter struts are usually asymptomatic, as was our patient. However, a high level of clinical suspicion for perforation should be maintained when facing non-specific abdominal or back pain, and in episodes of gastrointestinal bleeding in patients with an IVC filter. We recommend that patients with implanted IVC filters, even those who are asymptomatic, should receive regular imaging follow-up, and retrievable filters should be removed as soon as they are no longer needed.

P5

Severe complications after intravascular application of bone cement and hemostatic agent during spinal surgery

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Objective: Posterior surgical approaches to the lumbar spine may cause vascular lesions, due to the proximity of large vessels.. We report two cases with accidental intra-arterial application of bone cement and hemostatic agents during re-do spinal surgery.

Methods: Case I: A 56 year-old women required surgical decompression at the level of L3/4. The patient was placed in prone position. After removal of an old screw massive bleeding occurred from the screw hole. The bleeding stopped after hemostatic agents were applied. The procedure was completed successfully and the patient placed in supine position. A livid, cold and pulseless right leg was noted. Computer tomography angiography (CTA) revealed an occlusion of the right common iliac artery with intra-arterial air. Prompt balloon-embolectomy from the groin restored the circulation to the leg. Foamy looking thrombus was successfully removed. Intraoperative angiography showed extensive embolization of small branches in the buttock, thigh and calf. The postoperative course was uneventful. Without any cardiovascular risk factors the patient suffered severe claudication in the thigh and lower leg at one year.

Results: Case II: A 72 year-old multimorbid women required extended re-decompression at the level of L3-S1 with spondylodesis and an sacral vertebroplasty in a prone position. Massive bleeding occurred after removal of the old screws. The hemodynamic relevant bleeding stopped after application of bone cement and hemostatic agents into the drill hole. Immediately after extubation the patient complained of uncontrollable pain in both legs and showed a complete sensomotoric loss. The CTA showed complete thrombosis of the infrarenal aorta and both iliac axes. Complex time-consuming revascularization of the abdominal, pelvic and lower limb arteries reestablished circulation to both legs. The patient died due to multi organ failure three days later.

Conclusion: Vascular complications after posterior approaches to the lumbar spine are rare and potentially lethal. Early diagnosis and prompt revascularisation is crucial.

P6

Pushing the limits in angioplasty new treatment in pulmonary artery hypertension

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Objective: We will report first experience of 10 patients treated in our institution with pulmonary artery angioplasty for chronic thromboembolic pulmonary hypertension (CTEPH). We will highlight the importance of patient selection in this highly fragile patient cohort.

Methods: Patients underwent selection in a multidisciplinary colloquium with thoracic surgeons, pneumologists and interventional radiologist. All our patients have been treated before with pulmonary endarterectomies and have anticoagulation and are on medication with substance like soluble guanylate cyclase stimulator (sGC) (Riociguat). Some are referred direct to angioplasty because they were poor surgical candidates. According to ESC Guidelines 2015.

Patients suffer from respiratory distress NYHA group III-IV and are oxygen dependent at least for the night and they are handicapped by this condition in their daily life.

Results: In all our patient occurred one minor alveolar bleeding during intervention due to guidewire perforation which had to be coiled during same intervention but remained clinically silent.

Some minor, local pulmonary reperfusion edema occurred which could be proofed by thorax radiography but remained clinically silent and unrecognized by patient.

After two or three treatments they were less oxygen dependent. There was no change in NYHA classification.

Conclusion: Pulmonary artery angioplasty is a safe procedure when patients are carefully selected, intervention should be performed with precaution and postinterventional strict monitoring should be warranted. It can help patients to be less oxygen dependent and they can regain their activity in everyday life.

P7

Correlation between clinical ischemic complications and arterial patencies after Endovascular Abdominal Aneurysm Repair

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Objective: Endovascular aortic aneurysm repair (EVAR) is a safe and effective treatment. Nevertheless, this approach is limited by complication rates from 4-25 % during the follow-up. Early and late ischemic complications are reported in up to 5%. The preoperative arterial, aorto-iliac and visceral anatomy as well as graft characteristics may influence the rate of ischemic complications after EVAR. The purpose of this study was to evaluate the correlation between the global clinical ischemic rate and arterial patencies before and after EVAR.

Methods: We selected 24 patients from a prospectively maintained database (SecuTrial®, interActive Systems GmbH) in a tertiary center. The selection criteria included primary EVAR with Endurant II/IIS aortic graft, from 2014 to 2015. The demographic, intra-

operative and postoperative data were collected from the database and medical records. We analyzed the preop- and postoperative angioCT scan to evaluate patency of peripheral, digestive and renal arteries using Intellispace Portal (Philips®) and Carestream VueMotion (Carestream Health®). Primary outcome was global ischemic event rate defined as peripheral, digestive or renal ischemia. Secondary outcomes were mortality during follow-up and non ischemic-related complication rates

Results: The studied population included a majority of men (78.3%) with a mean age of 75 yo. Most patients had an ASA score of 3 (95.8%). Clinically, no global ischemic event were reported. Only 1 patient (4.16%) had complication which was hematoma. No patient died during a mean follow-up of 181.6 days.

Radiologically, we noticed a significant loss of patency after EVAR in the visceral (superior and inferior mesenteric) arteries (16%, $p < 0.05$, McNemar test). We also noticed a loss of patency in 2% of renal and 1% peripheral arteries.

Conclusion: Even if no ischemic complication occurred, changes in arterial patency were observed after EVAR. This may be explained by progression of pre-existing lesion or graft-related blood flow modifications. It may be important to emphasize that, even if patients were asymptomatic in our study, these changes can lead to symptomatic events at longer term. A bigger cohort study and a longer term follow-up might confirm these preliminary results and might reveal a correlation between clinical events and radiological findings.

P8

An initial experience with the covered endovascular reconstruction of the aortic bifurcation technique (CERAB)

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Objective: The aim of the study was to evaluate the CERAB technique in patients with extensive aortoiliac disease.

Methods: This is a retrospective observational study conducted in two vascular units. From April 2012 to August 2016, we selected all consecutive patients treated with the CERAB technique from two prospective databases. Demographic and perioperative variables were collected and analysed. The follow-up was based on vascular examination by duplex scan.

Primary outcome was primary patency rate at 1 year. Secondary outcome was in hospital complication rates.

Results: We selected 13 patients. The mean age was 68 years [range 53–96] with 70% of male. The indication was intermittent claudication (Fontaine stage IIb) in 80% of the patients. The vascular access was performed with percutaneous approach in 30% of the cases. The mean operation time was 95 ± 22 min. The technical success was 100%. The mean follow-up was 647 days. We observed no occlusion or stenosis of the stentgrafts during the follow-up. We observed no occlusion or stenosis of the stentgrafts during the follow-up. The in hospital complication rate was 38% mainly based on vascular access occlusion (2/13), bleeding (2/13) and distal embolization (1/13).

Conclusion: The CERAB technique has good midterm patency rates. Nevertheless, the initial experience requires caution based on a high in hospital complication rate related mainly to vascular access.

P9

Endovascular procedure as treatment test for unclear median arcuate ligament syndrome

F. Strano, H. Probst (Morges)

Objective: Celiac artery compression syndrome, otherwise known as median arcuate ligament syndrome, is a rare anatomical condition where celiac trunk artery is compressed by a fibrous band of the diaphragm called median arcuate ligament. Most often asymptomatic when isolated, this condition mimics mesenteric angor with chronic postprandial abdominal pain and sequentially weight loss. The treatment is aimed at restoring the normal blood flow in the celiac artery. The first line option is open or laparoscopic decompression of median arcuate ligament followed by eventual revascularisation if symptoms persist.

Methods: A 20 years-old male, had chronic intermittent abdominal pain for 1 year, enhanced by meals and a 20-Kg weight loss. He was submitted to haematological, infectious, metabolic, digestive and oncological investigations, but all of which were normal. An abdominal US-duplex showed a severe stenosis at origin of the celiac trunk with post-stenotic aneurysmal dilation and a significant peak systolic velocity enhance in expiration. Other mesenteric vessels were normal. Injected tomography confirmed US findings. The particular presentation, with both patents mesenteric arteries and a normal network of collaterals, brought us to make a treatment test. After agreement of the multidisciplinary team, in order to lower operation morbidity we decided to perform a percutaneous celiac trunk angioplasty followed by deployment of a bare metal stent with an immediate good revascularisation result at aortogram. The patient was discharged at first post-operative day under double antiplatelet treatment. At the 12 months follow-up, the patient was symptom-free with progressive regain of his lost weight. The US duplex showed a patent celiac artery stent with a normal peak systolic velocity although artery tortuosity.

Conclusion: The celiac trunk lesion in median arcuate ligament syndrome can cause severe symptoms, even in case of both patent mesenteric arteries and a normal network of collaterals. It is usually treated by an hybrid approach comprising ligament decompression and a vascular procedure. An endovascular procedure alone can be considered as a treatment test offering good short-term results and confirming the etiology of the symptoms.

P10

Cold atmospheric plasma therapy with a cold flame by chronic ulcer after balloon dilatation by peripheral arterial disease

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Objective: The aim of this field report is to demonstrate the positive results (reduction of bacterial load, pain and wound size), achieved by using cold atmospheric plasma with a cold flame.

Methods: Five patients with a critical peripheral arterial disease and chronic wounds were first treated by a dilatation of the artery

P10. Figure.

and then the wounds by a cold atmospheric plasma therapy once to twice a week for 2 months. Because of stagnation with the conventional wound treatment by better blood flow, a cold atmospheric plasma treatment was chosen. The plasma device consisted of a pin which generated a cold flame. The gas used was argon. This plasma treatment took place during the usual wound-care in a day-hospital setting. Each session of plasma therapy lasted 30 seconds per square centimetre followed by 10 minutes of wet pack with a wound irrigation solution. In addition, a pain scale was measured during the therapy. A bacteriology culture was taken at the beginning and after each 2 weeks. With a 3D camera the wound size was measured in cm² and cm³.

Results: During the first 2 weeks of treatment all patients showed 75% less pain. The bacteriology culture was 85% negative after 2 weeks and 95% negative after 3 weeks. During the first 12 weeks the reduction of the wound size was 40–50%.

Conclusion: Our results demonstrate that the healing process of chronic wounds can be reactivated by treatment with cold atmospheric plasma in case the critical peripheral arterial disease is result. The implementation is easy, patient-friendly and can be used in a day-hospital setting. A larger number of patients will be included in our next study.

P11

Endoleak evaluation after endovascular repair of abdominal aortic aneurysm

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Objective: One of the main limitations of EVAR during the long-term follow-up is the rate of re-intervention mainly caused by the development of endoleaks (EL). The aim of this study was to analyse the characteristics of patients who developed endoleaks at the CHUV after EVAR.

Methods: Data of all patients who underwent EVAR and who were subject to treatment for endoleaks at the CHUV from 2013 to 2017 were retrospectively collected and analysed. All the parameters at the time of EVAR were analysed

Results: The 25 patients were mainly men (80%) with a mean age of 75 years (62–87) at the time of EVAR. The mean aneurysm

diameter was 64 mm (40–100) with a neck of 22.7 mm in length. The mean oversizing was 12.8%, and 805 of the stent grafts used were Excluder and Endurant. During the mean follow-up of 58 months (4–164), 47 reinterventions were required after a median time of 13 months following EVAR. Most reinterventions were performed during the first two years after EVAR. There was a majority of type 2 ELs (84% of patients) followed by type 1 (48%). Patients with type 1 EL had the shortest neck (17 mm) and mean oversizing inferior to 10%. In the group of patients with type 2 EL, the ratio of circulating blood volume compared to total sac volume was the highest and the thrombus the thinnest and these patients had bigger lumbar arteries.

Conclusion: This single-centre study found type II endoleaks to be the most common type of endoleak and associated with less thrombus and higher ratio of circulating blood. We support the hypothesis that all EVAR should be followed. The preferable way to treat ELs was translumbar embolotherapy for type II endoleaks and prosthetic elongation for type I and III endoleaks. The findings of this study, in parallel to an extensive literature review, enabled a better understanding of local management of endoleaks after EVAR but further studies on bigger population are mandatory.

P12

Massive venous thrombosis in a patient with nephrotic syndrome and a newly diagnosed breast cancer: a case report

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Objective: The association between nephrotic syndrome and thromboembolic events is well established, as it is clear that cancer is one of the most important acquired risk factors for venous thromboembolism (VTE). We report of a patient who presented massive VTE with preexisting hypoplastic inferior vena cava (IVC) related to nephrotic syndrome and who was simultaneously diagnosed breast cancer.

Methods: A 67-year-old man, known for nephrotic syndrome (NS) secondary to nephroangiosclerosis, presented to the emergency department with a 24-hour history of left leg swelling followed by intense pain. The limb was blue, swollen, cold and very painful. No

palpable pulses. Below-knee hypoesthesia and MRC 4/5 were present. Renal function, coagulation profile and inflammatory parameters were normal. D-Dimers 5,6 mg/L. The CT-scan showed iuxta-renal thrombosis of the hypoplastic IVC, involving both renal veins, reaching the left iliac-femoral-popliteal axis, with collateralization to the pelvic and mesenteric veins, associated with bilateral segmental pulmonary embolisms. A suspected left breast nodule was also found. Intravenous heparin was immediately administered and urgent venous angiography and thromboaspiration, liberating the ilio-lumbar collaterals, was performed. A lateral leg fasciotomy was mandatory. The next day, the leg was still swollen but color was normalized and motor and sensory defects were fully recovered. Post-operative Doppler US showed a good venous compressibility of the left leg. Thrombophilia screening was negative. The breast nodule was biopsied and turned out to be an invasive ductal carcinoma. The patient was discharged with oral Rivaroxaban and indication to a left mastectomy and oncological therapy with aromatase inhibitors.

Conclusion: NS facilitates VTE because of glomerular filtration of antithrombin III, plasminogen, protein C and S. The loss of albumin leads to increased hepatic production of fibrinogen. In our case, the presence of neoplasia further boosted the risk for VTE due to the release of tissue factor-rich particles by the cancer cells that are known to promote fibrin formation.

P 13

Foot compartment syndrome – forgotten catastrophe

D. Jaeger, P. Buntschuh, M. Hofmann, Z. Rancic (Zürich)

Objective: Compartment syndrome is a condition in which increased tissue pressure in a closed space results in decreased tissue perfusion. Compartment syndrome after revascularization occurs primarily on the lower leg, but also on the foot, which surgeons often neglect. Diagnosis confirmation is a combination of clinical findings and compartment pressure measurements.

Methods: Case report.

Results: We report on two cases with foot compartment after successful revascularization in acute limb ischemia. First patient (58-year old man) presented with acute swelling of the right lower limb four hours after successful recanalization through thrombectomy of acutely occluded femoro-popliteal PTFE bypass graft, performed for popliteal aneurysm 18 months ago. Immediate fasciotomy decompressed the four compartments of the lower leg. Persistent swelling and tenseness over the distal and median aspect of the foot indicated foot compartment (Fig.1). We performed a decompression with two incisions: on the dorsal (Fig.2) and medial edge of the foot (Fig.3). All fasciotomies were first day closed with negative pressure wound therapy (NWPT). After 6 months follow-up, all ischemic lesions healed (Fig.4). Minor amputation did not impede the mobility of the patient. The second patient (62-year old man) underwent successful catheter-directed thrombolysis of the superficial femoral artery after acute occlusion of unknown cause. After revascularization, the patient presented with compartment syndrome of the lower leg. A fasciotomy of the anterior tibial compartment resulted in positive arterial Doppler immediately. Blisters on the plantar side after eight hours were suspicious of foot compartment. We did a foot

P 13. Figure.

fasciotomy, followed by NWPT treatment and with complete functional recovery after one month.

Conclusion: Foot Compartment often occurs in high-energy fractures and crush injuries but there are rarely cases reported after acute ischemia and revascularization procedures. (1) Foot compartment develops immediately or with delay after revascularization and subsequent lower leg fasciotomy. There is no high-level evidence to guide decision-making for foot fasciotomy. Pressure can be used as objective data but suspicious clinical findings are of utmost importance as indication for necessary fasciotomy. (2) In our patients emergent fasciotomy resulted in limb/foot salvage with no ambulatory disturbances.

P 14

An extremely rare presentation: a cystic hygroma (lymphangioma) of the proximal thigh in an adult

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Objective: We report a case of swelling of the proximal thigh which turned out to be a very rare case of cystic malformation.

P14. Figure.

Methods: Localized merely in the head and neck region of infants cystic lymphangioma (or hygroma) are a rare entity, there are about 100 cases of adult patients reported in the literature, also described mainly in the head and neck region. Only two other adult findings are reported in the thigh and one single case in the distal leg. Trauma has been suggested as etiologic cause in adult patients.

#Under antibiotic treatment, the patient became rapidly asymptomatic and we agreed a wait and watch approach as recurrence after surgical removal is reported to be high. Newer treatment possibilities by means of sclerotherapy (with different agents) seem to have somewhat better results.

Conclusion: We present this extremely rare case to document an unusual but yet important cause of swelling in the lower extremity. We present and discuss the treatment options based on a relevant literature review.

P15

A complex case of celiac-mesenteric revascularization

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Objective: To present a case of mesenteric ischemia highlighting the diagnostic, therapeutic and technical challenges in this pathology.

Methods: Clinical case report.

Results: A 73-years old male patient (hypertension and tobacco use with COPD) with history of aorto-bi-femoral bypass surgery for Leriche-Syndrome underwent right hemicolectomy for ischemic necrosis of the cecum in another institution. After a few weeks the patients came to us for a second opinion with the typical clinical picture of chronic mesenteric ischemia, lasting for more than 1 year. The CT angiography showed a severe stenosis of the celiac trunk due to compression by the arcuate ligament and a long proximal occlusion of

the superior mesenteric artery (SMA) as well as both hypogastric arteries. Because of sudden acute deterioration of the clinical condition with local peritonitis, the patient was urgently operated on. Intraoperatively, no bowel necrosis was found. The operation was completed upon the section of the arcuate ligament followed by stenting of the celiac trunk. Postoperatively the patient suffered a myocardial infarction and underwent urgent aorto-coronary bypass surgery. After a short period of well-being, the abdominal pain reoccurred and the patient presented with an acute abdomen. With clinical and radiological suspicion of small bowel ischemia the patient underwent re-laparotomy and extra-anatomic ilio-mesenteric venous bypass was performed. Early bypass occlusion led to redo laparotomies, featuring reorientation of the graft to an aorto-mesenteric bypass. A hybrid recanalization attempt of the superior mesenteric artery was unsuccessful due to impossible proximal re-entry. Reorientation of the distal anastomosis to the dorsal portion of the SMA was finally successful. In the follow up controls the bypass graft remains patent. Ileo-colonoscopy did not reveal pathologic findings

Conclusion: This case highlights different challenges in the diagnosis and treatment of chronic and acute mesenteric ischemia. In the absence of specific clinical- and radiological signs for acute bowel infarction, the high suspicion leads the therapeutic decision making. Venous bypass orientation is the key and antegrade orientation should be attempted according to current recommendations

P16

Aortic dissections: Proposal for new classification system

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Objective: The objective was to build a new classification based on the Stanford Classification (SC) to integrate patterns that may affect

management including endovascular therapies and evaluate its use in a large population of AD.

Methods: The modified SC proposed includes 3 types (A:dissection involving at least the ascending aorta, B:dissection involving only the descending aorta, C:dissection involving the aortic arch and/or the descending aorta) and 4 subtypes (0:absence of MPS, 1:dynamic MPS, 2:static MPS, 3:static and dynamic MPS)

CT angiography of 228 consecutive patients with proven AD were reviewed. ADs were re-classified according to the new classification.

Results: According the new classification we found: 153 type A, 50 type B (38B0, 5B1, 6B2, 1B3) and 25 type C (18C0, 6C2, 1C3). Thus, type C represented 11 % of all dissections. MPS was present in 28 % of type C ADs. Endovascular treatment was performed in 32 % of type C and 12 % had surgical repair.

Conclusion: The new classification system is easy to use and should be helpful driving the decision making process, especially in integrating the latest development in trans-catheter therapies. Endovascular/surgical management was more frequently done in type C than in type B.

P17

Benefit of arterial preparation by LONGitudinal scoring before paclitaxel eluting balloon angioplasty of the superficial femoral and popliteal artery: concept and inclusion status of the swiss multicentric BELONG Study

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Objective: The immediate benefit of arterial preparation by longitudinal scoring before recanalization of the superficial femoral artery (SFA) and popliteal artery (PA) by angioplasty is already established. Arterial preparation provides a better lumen expansion after balloon angioplasty, reduces the risk of artery dissection and reduces the necessity of stent implantation. Moreover, arterial preparation allows better distribution of paclitaxel to its target tissue: the smooth muscular cells and fibroblasts of the media. We postulate that arte-

Tab. 1:

				A0	A1	A2	A3	B0
799764	1938	70	30.07.2008	1	0	0	0	0
2632669	1947	61	03.08.2008	1	0	0	0	0
799764	1938	70	13.08.2008	1	0	0	0	0
2634284	1947	61	14.08.2008	0	0	0	0	1
381282	1944	64	23.09.2008	0	0	0	0	1
451572	1951	57	14.10.2008	0	0	0	0	1
2642916	1947	61	15.10.2008	1	0	0	0	0
209431	1935	73	24.10.2008	0	0	0	0	1
274695	1925	83	03.11.2008	0	0	0	0	0
223830	1931	77	04.11.2008	0	0	0	0	0
149425	1945	63	09.11.2008	0	0	0	0	0
2645571	1953	55	12.11.2008	0	0	0	0	0
2645571	1953	55	19.11.2008	0	0	0	0	1
2646415	1928	80	20.11.2008	0	0	0	0	0
843995	1935	73	20.11.2008	0	0	0	0	0
2650612	1939	69	28.12.2008	0	0	0	0	1
2457715	1944	65	06.01.2009	0	0	0	0	0
891225	1925	84	06.01.2009	0	0	0	0	0
72994	1943	66	19.01.2009	1	0	0	0	0
2662678	1968	41	27.02.2009	1	0	0	0	0
2663855	1932	77	07.03.2009	0	0	0	0	0
5893356	1927	82	12.04.2009	0	0	0	0	0
2148494	1955	54	01.06.2009	0	0	0	0	0
2686712	1930	79	07.08.2009	1	0	0	0	0
2687861	1950	59	16.08.2009	1	0	0	0	0
2688592	1931	78	21.08.2009	0	0	0	0	1
235749	1947	62	31.10.2009	1	0	0	0	0
2706434	1938	71	16.12.2009	0	0	0	0	1
2712058	1934	76	27.01.2010	1	0	0	0	0
657507	1968	42	27.02.2010	1	0	0	0	0
2718551	1962	48	11.03.2010	1	0	0	0	0
2623229	1946	64	25.03.2010	1	0	0	0	0
2017607	1950	62	02.08.2012	0	0	0	0	0
2532320	1933	79	08.10.2012	1	0	0	0	0
2544001	1929	none		1	0	0	0	0
2549021	1950	none		1	0	0	0	0
833761	1943	64	04.04.2007	0	0	0	0	0
2562973	1924	83	30.04.2007	0	0	0	0	0
910123	1951	49	25.04.2000	0	0	0	0	0
2195034	1946	61	20.08.2007/ 27.08.2007	0	0	0	0	1
773437	1932	75	24.10.2007	0	1	0	0	0
1077682	1960	none		0	0	0	0	0
2659980	1965	44	09.02.2009	1	0	0	0	0
2682479	1936	73	only CR 08.07.2009	0	0	0	0	1
2705769	1941	68	12.12.2009	1	0	0	0	0
2706012	1951	none		0	0	0	0	0
2706035	1939	70	03.12.2009	0	0	0	0	1
2708929	1941	69	06.01.2010	0	0	1	0	0
490933	1934	none		1	0	0	0	0
2682024	8049	88	15.02.2010	0	0	0	0	0

Tab. 1: Continuation

				A0	A1	A2	A3	B0
1045656	1929	0	00.01.1900	0	1	0	0	0
2526992	1928	0	01.01.1900	0	NA	NA	NA	NA
702832	1975	0	00.01.1900	0	1	0	0	0
2630890	1932	0	01.01.1900	0	NA	NA	NA	NA
503090	1932	0	01.01.1900	0	NA	NA	NA	NA
906182	1957	0	00.01.1900	0	1	0	0	0
924839	1926	0	01.01.1900	0	NA	NA	NA	NA
308107	1940	0	00.01.1900	0	1	0	0	0
2441895	1928	0	00.01.1900	0	NA	NA	NA	NA
2499922	1976	0	01.01.1900	0	NA	NA	NA	NA
838728	1922	38387	00.01.1900	0	NA	NA	NA	NA
2436633	1925	38389	01.01.1900	0	0	0	0	1
2437417	1922	38392	00.01.1900	0	1	0	0	0
68830	1959	38400	00.01.1900	1	0	0	1	0
2440469	1928	38409	00.01.1900		0	0	1	0
794129	1961	38418	00.01.1900	0	0	0	0	0
2442435	1951	38420	00.01.1900	0	1	0	0	0
2442624	1949	38421	00.01.1900	0	1	0	0	0
2458269	1931	38517	00.01.1900	0	1	0	0	0
594805	1924	38527	00.01.1900	0	NA	NA	NA	NA
2460104	1926	38530	00.01.1900	0	NA	NA	NA	NA
2224199	1952	38576	00.01.1900	0	0	1	0	0
426651	1969	38577	00.01.1900	0	1	0	0	0
814133	1974	38590	00.01.1900	1	0	0	0	0
2330823	1940	38603	00.01.1900	0	NA	NA	NA	NA
2210866	1927	38604	00.01.1900	0	0	0	1	0
2477783	1935	38653	00.01.1900	0	1	0	0	0
2241774	1940	38660	00.01.1900	0	NA	NA	NA	NA
549322	1942	38681	00.01.1900	0	0	0	0	1
2283680	1949	38697	00.01.1900	0	0	0	0	1
654652	1947	38708	00.01.1900	0	0	1	0	0
760887	1928	38753	00.01.1900	0	0	0	0	1
90009	1925	38758	01.01.1900	0	NA	NA	NA	NA
2283680	1949	38769	00.01.1900	0	0	0	0	1
109638	1941	38778	00.01.1900	0	NA	NA	NA	NA
422106	1932	38779	00.01.1900	0	NA	NA	NA	NA
2500875	1950	38798	00.01.1900	0	0	0	1	0
2468175	1945	38810	00.01.1900	0	1	0	0	0
2458104	1937	38825	00.01.1900	0	0	0	0	0
2288471	1943	38840	00.01.1900	0	NA	NA	NA	NA
2488446	1917	38876	00.01.1900	0	NA	NA	NA	NA
174816	1941	38896	00.01.1900	0	0	0	1	0
178648	1932	38917	00.01.1900	0	1	0	0	0
231635	1941	38936	00.01.1900	0	1	0	0	0
704816	1946	38947	00.01.1900	0	0	0	1	0
				21	14	17	6	16
				A0	A1	A2	A3	B0

P16. Table.

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P 16. Table.

Methods: This prospective, multi-centric, single arm study is aimed to evaluate the benefit of adding artery preparation by longitudinal scoring with the FLEX Scoring Catheter®, before revascularization of the SFA and PA by conventional therapy (paclitaxel-coated balloon angioplasties for all lesions and provisional stenting for residual stenosis). Patients ≥ 18 -year-old, with symptomatic lower extremity occlusive arterial disease, (Rutherford class of symptom 2 to 5) may be included if atheromatous $\geq 70\%$ stenosis or occlusion of SFA and/or PA is present. The main efficacy objective is to evaluate the rate of lumen patency of the target lesion at 12 months. Secondary objectives are 3 and 12 months target lesion patency, absence of major amputation, change in ankle brachial index (ABI) and change in Rutherford class of symptom.

Results: The study is currently running in 5 centers in Switzerland. The planned sample size is 150 patients. Current status of inclusion and early result of index procedures will be presented at the 19th congress of the Union of the Vascular Societies of Switzerland in Lugano in November 2018.

Technical success of the 67 procedures with the FLEX Scoring Catheter®, performed before initiation of the BELONG Study are presented as well (97% technical success, 8.9% provisional stenting, 0% bailout stenting).

Conclusion: Arterial preparation by mean of the FLEX Scoring Catheter® is a promising innovation in the domain of SFA/PA recanalization. If the results we observed in our preliminary experience are confirmed in the BELONG Study and in a larger population, the benefit, in term of efficacy, safety, reduced use of stent, and reduced need for re-intervention, may be considerable.

P 18

Microglia control vessel-associated calcifications in the mouse model of primary familial brain calcification

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Objective: Microglia, the tissue-resident macrophages in the brain, crucially regulate changes in the central nervous system (CNS) during development and in adulthood, such as mediating immune response and clearing cellular debris. However, in neurodegenerative diseases, the role of microglia is highly debated, where they can be either beneficial to the outcome of the disease or can contribute to the progression of the disease, due to their prolonged inflammatory response. Thus, in this study we investigated the role of microglia in a mouse model for primary familial brain calcification (PFBC), a disease characterized by vessel-associated calcifications in the deep brain regions. Previously, we have shown that mouse PDGFB hypomorphs (*Pdgfb* ret/ret) develop brain calcifications similar to PFBC patients. In addition, we have shown that cells around brain calcifications start to express bone cell markers.

Methods: Microglia were characterized using immunohistochemistry, RNAseq and FACS performed on *Pdgfrb* ret/ret mouse brains. Lineage tracing studies, using *Cx3Cr1* CreERT2 and *Sall1* CreERT2 mouse lines crossed with *Pdgfrb* ret/ret animals, were used to examine the expression of osteoclast markers in microglia. We also crossed *Pdgfrb* ret/ret animals with *Trem2* knockout mice to study calcification pathology in the presence of functionally impaired microglia.

Results: Here, we report that microglia express osteoclast markers, indicating their role in the phagocytosis of brain calcifications. We also observed that genetically impairing microglia function by crossing *Pdgfrb* *ret/ret* with *Trem2* *ko* mice, lead to a worsening of calcification pathology. Finally, we have performed RNAseq analysis on tissue around brain calcifications and observed an enrichment of genes, which have been attributed to disease-associated microglia. This finding was validated using immunohistochemistry.

Conclusion: In conclusion, we report that microglia are important in clearing brain calcifications and thus future studies focusing on improving microglia function might lead to an amelioration of calcification load.

P 19

Lineage-specific epigenetic landscapes of lymphatic versus blood vascular endothelium

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Objective: The lymphatic vasculature originates from embryonic cardinal veins. Thus, lymphatic and blood vascular endothelial cells (ECs) share several molecular and development features. However, these two cell types possess distinct genetic signatures, reflecting their different biological functions. Despite significant advances in elucidating how the differentiation of ECs into blood and lymphatic vessels is regulated at the molecular and transcriptional level, the key molecular mechanisms governing the process under physiological and pathological conditions remain poorly understood. We investigated whether EC differentiation might be regulated by epigenetic mechanisms.

Methods: For this purpose, we used matched human primary dermal lymphatic and blood vascular ECs isolated from two different donors, and employed complementary sequencing and array techniques, including RNA-Sequencing, chromatin immunoprecipitation-Sequencing for H3K4me3 and H3K27me3 histone marks, and Infinium MethylationEPIC BeadChip. In addition, we modulated DNA methylation and histone acetylation by using 5-azacytidine and trichostatin A, respectively.

Results: Analysis of global gene expression and histone marks enrichment in the two cell types revealed differences in canonical lymphatic and blood vascular markers, including FLT4, PROX1 and Pdpn, and FLT1, ESAM, and IL-8, respectively, and highlighted developmental and differentiation processes. Surprisingly, we did not observe a significant overlap between DNA methylation of promoters and gene expression indicating that other regulatory mechanisms might play a more prominent role in controlling EC transcription. Notably, when we modulated DNA methylation and histone acetylation, we were able to induce the transcription of classical blood vascular markers in blood vascular ECs and of lymphatic markers in lymphatic EC, but not vice versa.

Conclusion: Overall, these data indicate that, in accordance to their different biological functions, ECs possess a fine regulation of transcription which preserves lineage identity. Understanding how EC gene expression is regulated might serve to identify novel therapeutic targets and/or biomarkers in diseases with hyperactivation or impaired function of the blood and lymphatic vasculature, such as advanced cancer, chronic inflammatory diseases, ischemic heart disease and lymphedema.

P 20

Defining the cellular and molecular mechanisms mediating the migration of human CD4+ effector T-cell subsets across the human BBB in vitro: the role of PECAM-1 and CD99

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Objective: The blood-brain barrier (BBB) strictly controls lymphocyte entry into the central nervous system (CNS). The BBB breakdown, with a subsequent infiltration of inflammatory cells into the CNS, is an early key step in the pathogenesis of multiple sclerosis (MS). Although recent MS drugs targeting immune cell trafficking (e.g. Natalizumab and fingolimod) are highly effective, these treatments are associated with rare but severe side effects like progressive multifocal leukoencephalopathy (PML), suggesting that the current therapies also target immune cells mediating immunosurveillance of the CNS. It is thus essential to differentiate disease relevant pathogenic T cell subsets from non-pathogenic subsets and to explore differences in the molecular mechanisms for entering the CNS. To this end molecular mechanisms has largely been studied in experimental autoimmune encephalomyelitis (EAE), but EAE does not mimic the full picture of MS neuropathology. This underscores the need of meaningful studies with human tissues and cells. We have recently established a novel in vitro human BBB model by co-culturing human CD34+ cord blood cells derived endothelial cells with bovine pericytes. To study if human CD4+ effector T cells cross the BBB through the endothelial junction (paracellular) or through a pore in the endothelial cells (transcellular) we have started to investigate the role of the junctional adhesion molecules PECAM-1 and CD99 in this process. PECAM-1 and CD99 have been shown mediate diapedesis of neutrophils across peripheral vascular beds. Their role in mediating the migration of CD4+ T cell subsets across the BBB remains to be explored.

Methods: We adapted human CD34+ cord blood cells derived BBB in vitro model for use in T-cell migration research. We investigated cellular mechanisms mediating the migration of CD4+ T cell subsets into the CNS. Applying blocking antibodies, we observed the role of CD99 and PECAM-1.

Results: We observed anti-CD99 blocking antibodies reduce CD4+ T cell migration across the BBB in vitro, while anti-PECAM-1 blocking antibodies did not interfere with this process.

Conclusion: These data shows that human effector CD4+ T cell have different molecular mechanisms employed for crossing the BBB compare to innate immune cells.

P 21

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

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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 on a protein level with FACS. In addition, we conducted immunofluorescence (IF) stainings of human skin sections and 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 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 lymph angiogenesis.

P22

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

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Objective: ACKR4 is a member of the atypical chemokine receptor (ACKR) family and binds and scavenges the chemokines CCL19, CCL21 and CCL25. ACKR4 expression by lymphatic endothelial cells (LECs) lining the subcapsular sinus (SCS) ceiling of lymph nodes (LNs) was recently shown to contribute to the formation of a CCL21 gradient across the SCS, which enables 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 and in cellular trafficking.

Methods: We performed experiments using ACKR4-GFP knock-in mice (ACKR4-deficient homozygous ACKR4-GFP/GFP and heterozygous ACKR4-GFP/+) expressing GFP instead of ACKR4, in order to investigate the role of ACKR4 expression on leu-

kocyte trafficking within lymphatic vessels and on lymphatic vessel biology.

Results: Whole-mount-stainings in ACKR4-GFP knock-in mice revealed strong expression of ACKR4 in large lymphatic collectors, while only some of the smaller pre-collectors and no capillaries in the dermis or diaphragm displayed a GFP signal. Co-staining with smooth muscle actin (SMA), a marker of mature collecting lymphatics, revealed that ACKR4 is exclusively expressed in SMA-positive vessels. Interestingly, SMA staining was denser in ACKR4-positive compared to ACKR4-negative lymphatic collectors, suggesting that ACKR4 expression on lymphatics is linked to their collector-maturation state. Upon injection of fluorescently labelled CCL19 into footpad, higher CCL19 signals were detected in lymphatic collectors of ACKR4-GFP/+ as compared to ACKR4-GFP/GFP mice, demonstrating that ACKR4 in collectors is functional. Moreover, upon adoptive transfer of fluorescently labelled T cells into the footpad, fewer T cells were detected in the draining LN of ACKR4-GFP/GFP as compared to wild type mice. We are currently investigating which specific step in T cell trafficking from skin to draining LNs (i.e. entry into capillaries, migration in collectors or entry into the LN parenchyma) could be compromised by ACKR4 deficiency.

Conclusion: Overall, we could show so far that lymphatic collectors express functional ACKR4 and that T cell migration from skin to dLNs is reduced in global ACKR4 knock-outs.

P23

Rapid lymphatic efflux limits cerebrospinal fluid flow to the brain

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Objective: The relationships between cerebrospinal fluid (CSF) and brain interstitial fluid (ISF) are still being elucidated. It has been proposed that CSF will enter paravascular spaces along arteries to flush through the parenchyma of the brain. However, CSF can also directly exit the central nervous system through perineural routes to the lymphatic system. In this study, we aimed to elucidate the functional relationship between CSF efflux and influx into the brain by assessment of the distribution of CSF-infused tracers in awake and anesthetized mice.

Methods: Here we utilized noninvasive imaging techniques that can quantify the transport of tracers to the blood and lymph nodes to quantify the lymphatic outflow of CSF under awake and anesthetized conditions in mice. In vivo imaging by MRI and fluorescence microscopy through the skull were used to monitor the tracer distribution under anesthetized conditions and after death.

Results: We found that during waking conditions lymphatic outflow of CSF was substantially increased compared to anesthetized conditions. Rapid efflux of tracers through lymphatics under awake conditions significantly limited their spread to the paravascular spaces of the brain. Through-skull imaging under anesthetized conditions indicated that tracers remained confined to the surface of the brain, spreading slowly from the PVS of the arteries directly to the PVS of the veins within the pia mater itself. Immediately after the mouse dies, tracers spread along the PVS of

the pia mater and exhibited influx into the brain along the penetrating arteries.

Conclusion: We conclude that under normal conditions a rapid CSF turnover does not enable significant bulk flow into the brain.

P24

Transcriptional profiling of afferent lymphatic capillaries and collectors reveals a new entry site for dendritic cell migration to lymph nodes in inflammation

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Objective: Induction of adaptive immune responses involves the migration of dendritic cells (DCs) through afferent lymphatic vessels (LVs) to draining lymph nodes (dLNs). Recent research has shown that under steady-state conditions DCs enter LVs at the level of afferent capillaries. Subsequently, DCs actively crawl within the capillaries until they reach the contracting collecting vessel segments, where they detach and become rapidly transported to the dLN with lymph flow. In this study we performed a transcriptional analysis of lymphatic capillary- or collector-derived LECs (capLECs and colLECs, respectively) isolated by FACS-sorting from inflamed and uninfamed murine skin, in order to identify new mediators or pathways involved in leukocyte migration

Methods: The methods performed in this study were RNA sequencing, FACS sorting and flow cytometry, whole mount immunostaining and ex vivo assays.

Results: Principal component analysis revealed distinct gene expression signatures for colLECs and capLECs in steady-state and in inflammation. Interestingly, key pathways altered in both capLECs and colLECs during inflammation were “extracellular matrix (ECM) remodelling” and “leukocyte-endothelium interactions”. Specifically, many ECM-degrading enzymes, adhesion molecules and chemokines were strongly upregulated in colLECs during inflammation, suggesting that collectors might also participate in immune cell entry during inflammation. Indeed, whole-mount immunofluorescence confirmed that laminin and collagen in the collector basal membranes were significantly reduced in inflammation. Conversely, VCAM1, CXCL12 and CX3CL1, which have been previously shown to mediate inflammation-induced DC migration, were exclusively detected in inflamed collectors but not in capillaries. Furthermore, performing DC crawl-out studies from murine skin we found that blocking these proteins or blocking ECM degradation significantly reduced DC emigration from inflamed skin. Finally, performing time-lapse imaging we could visualize for the first time DC entry into lymphatic collectors.

Conclusion: Overall, our results shed light on the gene expression differences between capLECs and colLECs and suggest that during inflammatory conditions, collecting vessels in the skin serve as additional entry sites for DCs migrating to dLNs.

P25

Combining live cell imaging and RNAseq analysis to unveil cellular and molecular mechanisms directing T-Cell migration across the blood-brain barrier

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Objective: The endothelial blood-brain barrier (BBB) maintains central nervous system (CNS) homeostasis and strictly controls T-cell trafficking into the CNS. During multiple sclerosis or its animal model, autoaggressive CD4⁺ Th1 or Th17 cells enter the CNS causing neuroinflammation. It has been suggested that Th1 and Th17 cells may use different mechanisms to enter the CNS. Using primary mouse brain microvascular endothelial cells (pMBMECs) as an in vitro BBB model, we previously characterised the multi-step extravasation of Th1 cells across the BBB under physiological flow by means of in vitro live cell imaging. Endothelial ICAM-1 and ICAM-2 are essential for post-arrest Th1 cell polarization and crawling to sites of diapedesis. Interestingly, low levels of ICAM-1 direct Th1 cells to paracellular sites of diapedesis while high levels promote transcellular Th1 cell diapedesis across pMBMEC monolayers. The present study aims to identify the downstream mediators of paracellular and transcellular T cell diapedesis across the BBB integrating potential differences applying for Th1 versus Th17 T cells.

Methods: RNA was isolated 5 times in parallel from pMBMECs expressing high or low levels of ICAM-1. Bioinformatics analysis and sequential selections were made in order to reduce the number of the candidates genes. In vitro live cell imaging was used to investigate the differences between Th1 and Th17 cells. T cells were perfused via a custom-made flow chamber over WT or ICAM-1/2 double knock out pMBMECs. Accumulation of T cells was allowed for 5 minutes at a low flow of 0.1 dyn/cm² followed by physiological flow of 1.5 dyn/cm².

Results: RNAseq analysis identified ACKR1 as potential candidate gene able to direct T-cell diapedesis to para or transcellular pathway. In vitro live cell imaging shows reduced number of arrested Th17 cells – compared to Th1 – on WT pMBMECs monolayer. Absence of endothelial ICAM-1 and ICAM-2 completely abrogates T-cell crawling, by the same extent between Th1 and Th17.

Conclusion: Biological validation of the role of ACKR1 will be done by taking advantage of in vitro live cell imaging using ACKR1 knock out pMBMECs. ICAM-1 and ICAM-2 are necessary for Th1 and Th17 crawling over the pMBMECs. Reduced arrest of Th17 cells compared to Th1 on WT pMBMECs might correlate with reduced expression of alpha4 integrin by Th17 cells. Further experiments are planned to confirm this hypothesis.

P26

Defining the cellular and molecular mechanisms mediating the migration of human CD4⁺ effector T-cell subsets across the human BBB in vitro under physiological flow

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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. Thus, we have recently transferred an existing in vitro human BBB model using brain like endothelial cells (BLECs) into a flow chamber that we recently developed called μ SiM-CVB with “ μ ” highlighting the small volumes utilized and SiM denoting the use of a silicon-based membrane. Thanks to the high-quality imaging of this platform we can visualize live cell interactions between immune cells and the endothelium under a physiological flow. Thereby, we will use different effector CD4⁺ T cells subsets such as Th1, Th17 and Th2 sorted from the blood of healthy donors or the CSF of MS patients, and infuse them on our BLECs monolayer stimulated with pro-inflammatory cytokines. Finally, we have also started to investigate the role of the junctional adhesion molecules PECAM-1 and CD99 in the process of transmigration in static condition and plan to confirm our data under shear flow.

Methods: The CD34⁺ ECs are co-cultured in the μ SiM-CVB system with a pericyte conditioned medium until they acquire a BLECs phenotype. Placing the flow chamber under an inverted microscope allows for real time imaging of the behaviors (crawling, probing, diapedesis) of the effector CD4⁺ T cell subsets with BLECs. We can also block different adhesion molecules such as PECAM-1 and CD99 on the BLECs with blocking antibodies and look at the effect on the interactions with the CD4⁺ T cell subsets.

Results: We have already shown that our μ SiM-CVB system can be used to visualize the different behaviors of Th1 cells on the BLECs. We now aim to compare other subsets of healthy donors and MS patients. Preliminary results showed us that in our model we could reduce the number of Th1 cells interacting with the BLECs when blocking ICAM-1 and we will look at the results when blocking CD99 and PECAM-1.

Conclusion: We will look at the differences of interaction between BLECs and different CD4⁺ T cell subsets, and also try to block the adhesion molecules PECAM-1 and CD99 under physiological flow.

P27

Characterization of human blood vascular and lymphatic endothelial cells by single cell sequencing

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Objective: Lymphatic endothelial cells (LECs) differentiate from the cardinal vein during embryonic development. The blood vascular and lymphatic endothelium, hence, share a close developmental relationship and yet display a large extent of phenotypical and molecular differences. Despite the well-characterised lineage commitment at early stages, the molecular network governing their lineage specificity during vascular remodelling in, for instance, diseases like cancer or inflammatory conditions, is less defined. Intriguingly, it has been shown that lymphatic endothelial markers could also be expressed by blood endothelial cells (BECs) and vice versa under pathological conditions.

Methods: While realistically individual cells do not display synchronised states and such intercellular heterogeneity may be masked in bulk RNA-Seq, we aim to identify the intermediate subpopulation of endothelial cells using single cell RNA-sequencing (scRNA-Seq) that could help to better depict the underlying gene regulatory network.

Results: In our study, by using the scRNA-Seq technology from the 10X Genomics, we investigated the transcriptomic profiles of in vitro cultured endothelial cells derived from neonatal human skin. By performing unsupervised cluster analysis we were able to identify two main clusters namely LECs and BECs defined by the expression patterns of certain well-known lineage-specific markers, such as ESAM, VEGFR1, Podoplanin and PROX-1. Notably, within the two main clusters, we identified endothelial cell subpopulations exhibiting distinctive gene-expression signature. Furthermore, we harnessed ‘pseudo-time’ reconstruction with the key markers to examine the dynamics in the transcriptome of these endothelial cells along a continuum.

Conclusion: Our study has unveiled, other than the requisites for maintaining the lineage specificity of endothelial cells, the heterogeneity within subpopulations represented by differential molecular interactions in the transcriptomic network. This may increase our understanding of how aberrant transcriptomic landscape of the vasculatures relates to vascular remodelling in diseases.

P28

A specific NOX1 inhibitor decreases tumor growth, angiogenesis, lymphangiogenesis and enhances PD-1 based immune therapy

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Objective: NADPH oxidases (NOXs) are enzymes involved in the production of reactive oxygen species (ROS). ROS participate in different cellular functions depending on their concentration and cellular localizations. The NOXs enzymes play a major role in numerous cellular processes such as apoptosis, host defense against pathogens, intracellular signal transduction and angiogenesis. NOX1 is highly

expressed in colon cancer where it appears to promote tumor growth. By using the novel and highly selective NOX1 inhibitor GKT771 and NOX1-deficient mice, we investigated how NOX1 inhibition could become a new anticancer strategy.

Methods: To this end, we treated MC38 colorectal carcinoma and B16-F10 melanoma in immunocompetent mice and analyzed tumor growth and stromal cells composition by Flow Cytometry analysis. Experiments were also realized in immunocompromized mice in order to determine the involvement of immune cells in the NOX1 inhibition effects on tumor development.

Results: We treated MC38 colorectal carcinoma and B16-F10 melanoma in immunocompetent mice and found tumor growth reduced. This treatment also reduced tumor angiogenesis and lymphangiogenesis in the tumors. These results were confirmed in NOX1 deficient mice in which tumor development was reduced compared to WT mice. The use of tumors in immunodeficient mice revealed that the GKT771 effect is dependent on the presence of immune cells. In immunocompetent mice, we found that GKT771 increases the recruitment of anti-tumor immune cells such as pro-inflammatory macrophages and Natural Killer like T lymphocytes, both could stimulate T lymphocytes. When we combined the NOX1 blocker GKT771 with the anti-tumor properties of the checkpoint inhibitor anti-PD1 antibody, we found increased inhibition of colon carcinoma tumors.

Conclusion: In conclusion, inhibition of NOX1 constitutes a novel therapeutic strategy for the targeting of colorectal tumors.

P29

Consequences of Foxc2 depletion in adult lymphatic vasculature

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Objective: Lymphatic vessels regulate body fluid homeostasis, immune cell transport and lipid uptake. Foxc2 is a mechanoresponsive transcription factor crucial for the development of collecting lymphatic vessels and mutated in human hereditary disease lymphedema-distichiasis. Early postnatal Foxc2 inactivation causes degeneration of valves, loss of collecting vessel phenotype and disruption of endothelial cell-cell junctions, leading to lymph leakage and chylothorax. However, the long-term systemic consequences of Foxc2 inactivation in adulthood are still unknown.

Methods: Analysis of lymphatic endothelial specific Foxc2 loss-of-function mouse model (Foxc2lecKO)

Results: We report that Foxc2 maintains adult collecting vessel structure and function. Intriguingly, we also observed that Foxc2lecKO mice develop enlarged lymph nodes, increased number of tertiary fat-associated lymphoid clusters in the peritoneum and thoracic cavity, dilated intestinal lymphatic capillaries and bacterial translocation into mesenteric lymph nodes. The ongoing studies investigate the impact of Foxc2 deficiency on immune responses and gut microbiota and correlation of the phenotype with the symptoms observed in lymphedema-distichiasis patients.

Conclusion: Our data indicate that chronic dysfunction of collecting lymphatic vessels leads to important systemic effects, which go beyond local immunodeficiency generally described in lymphedema. Such effects potentially could contribute to the pathogenesis of many common human diseases.

P30

Normal and transformed intestinal stem cells maintain normoxia through suppression of VEGF signaling and vessel normalization

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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 (Wnt high), which make up 70% of CRC cases.

Methods: Blood vessels in Wnt high colon cancer 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: Here we show that Wnt high normal and transformed intestinal stem cells actively suppress VEGF signaling and slowly expand VEGF-independent vessels, through SEMA3F and apelin, resulting in a sustained normoxic microenvironment. This unusual vessel growth pattern is necessary as Wnt high intestinal stem cells preferentially utilize oxygen-consuming metabolism. Our results provide a mechanism and rationale for resistance to anti-VEGF therapies in Wnt high CRC.

Conclusion: Intestinal stem cells paradoxically repress VEGF-mediated angiogenesis to promote efficient oxygen delivery for metabolic function. Our results provide a mechanism and rationale for resistance to anti-VEGF therapies in Wnt high CRC.

P32

Tissue-specific activation of endothelium drive organ-specific metastasis

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Objective: Metastasis is primarily responsible for the morbidity and mortality of cancer. Improved therapeutic outcomes and prognosis depend on improved understanding of mechanisms regulating metastasis progression. The cross-talk between tumor cells and the local microenvironment is crucial for the outcome of the metastatic process. Thus, we test the hypothesis that 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 is to study the role of the microvascular endothelium in metastasis.

Methods: We plan to compare RNA transcriptomes of activated endothelial cells from two different metastatic sites/foci (lung and liver) using three different spontaneous metastatic mouse models. Identified changes in RNA transcripts will be analyzed by bioinformatic tools to determine common pathways involved in lung and liver endothelial cells activation and their role will be verified in vitro and in vivo. In parallel, we will analyze RNA transcriptomes from tumor cells and myeloid cells located at metastatic sites.

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: We showed that endothelial cells from metastatic lung foci express activation markers such as E-selectin, VCAM1 and ICAM1 in breast and lungs of spontaneously metastatic tumor models when compared to the naïve mice. In contrast, less activation of liver endothelial cells was observed in tumor-bearing mice. In parallel, we observed a significant increase of myeloid cells in metastatic lungs and livers of tumor-bearing mice.

Conclusion: Our data indicate that tumor cells induce a different endothelial activation depending on a metastatic site. The analysis of gene expressions and miRNAs specific for the lung or the liver metastasis in two different cancer types is ongoing.

P33

Role of ICAM-1 and ICAM-2 in Th1 versus Th17 cell mediated CNS autoimmunity

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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 demonstrated an essential role of endothelial intercellular adhesion molecule-1 (ICAM-1) and ICAM-2 in CD4⁺ T-cell crawling on the BBB under physiological flow. Here we have compared the cellular and molecular mechanisms mediating Th1 versus Th17 cell migration across the BBB into the central nervous system (CNS) of mice during EAE.

Methods: We have 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 intravital microscopy. We have compared the ability of in vitro polarized Th1 and Th17 cells to infiltrate the spinal cord versus the brain by immunohistology and to induce EAE in C57BL/6 mice.

Results: We observed the same number of Th1 and Th17 cells adhesion to 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 microvascular endothelium, absence of endothelial ICAM-1 and ICAM-2 abrogated post arrest crawling of both, Th1 and Th17 cells on the inflamed BBB. We saw ameliorated EAE upon adoptive transfer of in vitro polarized Th1 or Th17 cells into ICAM-1/ICAM-2^{-/-} when compared to wild-type C57BL/6 mice.

Conclusion: Endothelial ICAM-1 and ICAM-2 are essential for post-arrest crawling of both, Th1 and Th17 cells on spinal cord microvascular endothelium during EAE. Absence of ICAM-1 and ICAM-2 ameliorates EAE induced by the adoptive transfer of both Th1 and Th17 cells underscoring that ICAM-1 and ICAM-2 are equally important for Th1 versus Th17 cell mediated CNS autoimmunity.

P34

Role of Myct1 in retinal and tumor angiogenesis

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Objective: The development of a functional vascular network is a complex process requiring a coordinated response of endothelial and perivascular cells, adjusted to the organ needs. Aberrant formation of blood vessels is associated with several diseases such as chronic inflammation and cancer. Despite great advances in the field of vascular biology, there is still a need to improve our knowledge of the molecular mechanisms.

Methods: In this project we investigate the role of a novel endothelial gene Myc target 1 (Myct1). To study Myct1 function in the vasculature, we generated a conditional knockout mouse model for its endothelial-specific ablation (Myct1/Pdgfb-iCreERT2).

Results: We found that Myct1 controls pericyte recruitment, vascular network expansion and tip cell selection both in postnatal retinal angiogenesis and in subcutaneously implanted tumor models.

Conclusion: Ongoing experiments investigate the role of Myct1 in adult mice.

P35

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

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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. 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 immunostainings using ACKR3GFP/+ reporter mice and RNA sequencing on FACS-sorted lymphatic and blood endothelial cells of 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 and performed chemokine uptake assays using human LECs and primary dermal LECs isolated from ACKR3-deficient and wild type mice.

Results: Results obtained by whole mount immunostainings and RNA sequencing showed expression of ACKR3 in adult murine lymphatic capillary and collector type vessels. Notably, its ligands CXCL12 and adrenomedullin were also abundantly expressed in these vessels.

In an in vitro uptake assay using a fluorescently labeled, ACKR3-specific chimeric chemokine CXCL11/12, we showed ACKR3 mediated chemokine scavenging activity in human LECs. To further study ACKR3 function in adult LVs in vivo, we have generated a conditional tamoxifen-inducible ACKR3 knockout model (Prox-1CreERT2ACKR3fl/flRedstopfl/fl). In primary dermal LECs isolated from this model, CXCL11/12 uptake is abrogated compared to wild type controls.

Conclusion: In summary, we showed ACKR3 expression in murine adult LVs and confirmed its scavenging function in vitro. In future experiments, we plan to further investigate its contribution to LV biology and function in vivo.

P36

Absence of PECAM-1 promotes transcellular over paracellular T-cell diapedesis across the BBB under flow in vitro

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Objective: Activated T cells enter the central nervous system (CNS) during immunosurveillance and neuroinflammatory disorders such as multiple sclerosis (MS). To gain access to the CNS, T cells migrate across the blood-brain barrier (BBB), which shields the neural tissue from an uncontrolled influx of molecules and cells. T-cell migration across the BBB is a multistep process, in which as a last step T cells cross the BBB either via a paracellular route through the highly specialized endothelial cell-cell junctions or via a transcellular route via a pore through the endothelial cell bodies. Platelet endothelial cell adhesion molecule-1 (PECAM-1) is a transmembrane protein highly enriched in interendothelial junctions. Absence of endothelial PECAM-1 has previously been shown to impair the vascular barrier and increase inflammatory cell trafficking across the BBB during experimental autoimmune encephalomyelitis (EAE), the animal model for human MS. Here we show that PECAM-1 is profoundly upregulated in initial (pre-phagocytic) white matter as well as active cortical grey matter lesions in brain sections of MS patients. Making use of primary mouse brain microvascular endothelial cells (pMBMECs) as in vitro model for the BBB we therefore investigated the role of endothelial PECAM-1 in BBB integrity and the multi-step migration of encephalitogenic T cells across the BBB under physiological flow in vitro.

Methods: Using pMBMECs utilized as in vitro BBB model, we investigated BBB property by transendothelial electrical resistance (TEER) and tracer permeability and imaged dynamic interactions of antigen-activated encephalitogenic CD4⁺ effector T cells with pMBMECs under physiological flow.

Results: Absence of endothelial PECAM-1 affected BBB barrier properties as shown by reduced TEER and increased tracer diffusion. Under physiological flow conditions neither shear resistant arrest of T cells or crawling of T cells on pMBMECs nor T cell diapedesis frequencies across the monolayers were affected by endothelial PECAM-1 deficiency under flow in vitro, but absence of PECAM-1 leads to a shift of the preferential T cell diapedesis pathway from the paracellular to a transcellular route.

Conclusion: Endothelial PECAM-1 expression was not essential for transmigration of T cells, its absence, however, changes the preferential T cell diapedesis route from paracellular towards transcellular diapedesis.

P37

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

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Objective: Under homeostasis lymphocyte trafficking into the central nervous system (CNS) is tightly controlled by the blood-brain barrier (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. It has been demonstrated that pericytes play an important role in the development of the BBB but further studies are needed to better define the role of pericytes in regulating immune cell trafficking in the CNS.

Methods: We use adult pericyte-deficient (Pdgfrb 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. The following techniques are used: immunohistochemistry, histochemistry, confocal microscopy, electron microscopy and flow cytometry.

Results: The analysis of brains of adult Pdgfrb ret/ret mice has shown increased extravasation of leukocytes into the CNS. Immunization of Pdgfrb ret/ret mice with MOG peptide leads to an early, atypical EAE phenotype. An increased number of CD45hi leukocytes can be detected in the brain parenchyma in pericyte-deficient mice compared to controls, with a significant increase in the CD11b⁺ and Ly6Chi populations. In the spinal cord of Pdgfrb ret/ret mice show a decreased number of CD45hi leukocytes compared to the control. Pdgfrb ret/ret; 2D2 mice present an early onset of atypical EAE symptoms compared to control mice and show an infiltration of T-cells into the brain parenchyma.

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 and accelerates spontaneous activation of self-reactive T-cells.

P38

Identification of transcription factors and key molecular pathways determining the fate and function of the afferent lymphatic endothelium

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Objective: The main aim of my project will be to investigate and dissect the following unresolved fundamental questions: How do capillary LECs (Lymphatic endothelial cells) differentiate and which TFs (Transcription factors)/molecular pathways might be involved. What is the influence of these TFs on the molecules expressed by the

Figure 1: Phenotypic and functional characteristics of lymphatic capillary and collector vessels. A) Lymphatic capillaries allow uptake of tissue fluid, macromolecules, and leukocytes. B) Lymphatic collectors are specialized for transport of lymph constituents. Valves prevent backward lymph flow, and contractility from smooth muscle cells propagates lymph. Picture modified from Vranova et al. 2014 3. ECM: extracellular matrix; LEC: lymphatic endothelial cell.

Figure 2: Principal component analysis (PCA) plot of the RNA-sequenced samples (n = 5-6 per conditions), in all present genes. The samples of the different endothelial subsets cluster differentially both under steady state (CTR) and under inflammatory conditions (CHS). CTR: Control, steady-state. CHS: Contact hypersensitivity, inflamed

Figure 3: Volcano plot showing the distribution of the up- and down-regulated genes, between the capLECs and colLECs in steady state. TFs that are significantly differentially expressed were identified using the reactome tool from Metacore, clustering at intermediate fold change levels. Lyve1 and Itih4 (VEGFR3) are known signature genes up-regulated in the capillary LECs.

Figure 4: Immunofluorescent whole mount images of the lymphatics in mouse ear skin. LYVE1 staining is specific for capillary LECs, CD31 is a pan-vascular marker, while podoplanin is a marker for both capillary and collector LVs.

P38. Figures.

capillary and collector LECs, and what does this infer about their differential functions. These questions will be experimentally assessed, first by bioinformatic analysis of RNAseq data from these two cell subsets available in our lab, followed by in vitro and in vivo validation of candidate TFs/molecules.

Methods: Chosen candidate genes from our bioinformatic analysis will be validated based on their expression patterns in vivo in mouse tissues. Genes with a favorable expression patterns will be tested in vitro in LECs, by modulating their expression (over-expression or knocking-out/silencing). The effects of this modulation on the gene expression phenotype (qPCR, FACS, immunohistology) and cellular function (e.g. LEC migration, tube formation, permeability of monolayers) will be evaluated. Finally, TFs that we hypothesize to be important for the differential development of capillary LECs or collector LECs, will be assessed in vivo in developmental mouse studies or by addressing lymphatic function (e.g. lymphatic drainage and network analysis, leukocyte migration) in adults.

Results: Current bioinformatic analysis has been conducted with the interactome tool from the curated database Metacore, which estimates the interconnectedness between the input genes and upstream TFs. A preliminary analysis comparing capLECs and colLECs, utilising the above-mentioned tool, reveals several TFs differentially expressed in both endothelial subsets. An interesting example of our TF list is FoxC1. It is a less studied TF in the lymphatics, and closely related to the known FoxC2.

Conclusion: Identifying TFs and molecular pathways involved in the differential development of lymphatic capillary and collectors will be important for a better understanding of the lymphatic vasculature. Given that lymphatic capillaries and collectors have distinct functions, of which both are desirable in a functional lymphatic network, insight into these processes could be valuable for modulating lymphatic generation and function in the future.

P39

Protection of myocardial vasculature by over-expression of membrane cofactor protein in the context of myocardial ischemia reperfusion injury

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Objective: Human membrane cofactor protein (hCD46), a membrane-bound complement regulator gene, was introduced into porcine cells to overcome hyperacute rejection in pig-to-primate xenotransplantation. We hypothesized that hCD46 transgenic animals can be used to validate the results obtained from small animals in the context of the interaction of vascular endothelial cells (EC) with the plasma cascades in a large animal model. Formerly, such studies with transgenic animals were only possible in mice.

Methods: A closed chest porcine model of acute myocardial ischemia reperfusion (I/R) injury (60 min ischemia, 120 min reperfusion) by balloon catheter occlusion of the left anterior descending coronary artery was used. Human CD46 transgenic pigs (n=6) were used, with wild type (wt) pigs (n=8) as controls. Triphenyl tetrazolium chloride was applied to slices of the area at risk (AAR) to determine the percentage of necrotic ischemic tissue (NIT) within the AAR. Immunofluorescence staining of myocardial sections was done to analyze the vascular endothelial integrity and plasma cascade activation within the NIT.

Results: There was a statistically significant reduction in the percentage of NIT within the AAR (p=0.04) for hCD46 trans-

genic versus wt. Healthy EC markers, heparan sulfate proteoglycan and CD31 were preserved in NIT of hCD46 pigs ($p=0.03$ & 0.08 respectively) as compared to wt. Control animals showed a trend to express more E-selectin compared to the hCD46 group ($p=0.07$). Plasma cascade activation markers; mannose binding lectin, factor B, fibrinogen like protein-2 and fibrin deposition were all reduced either significantly or showing a trend in the hCD46 compared to wt animals ($p=0.06$, 0.0007 , 0.003 and 0.04 respectively).

Conclusion: In conclusion, the transgenic overexpression of the complement-regulatory protein hCD46 indeed led to vascular EC protection and reduced activation of complement and coagulation in the context of myocardial (I/R) injury. The present study succeeded in validating the results that have previously been shown in a small animal model in a clinical related large animal model.

P40

Endothelial calcineurin signaling restrains metastatic outgrowth by regulating Bmp2

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Objective: Here, we investigated the role of endothelial calcineurin signaling in physiological and pathological angiogenesis and tumor metastasis.

Methods: We analyzed tumor progression in genetic mouse models, in which we inactivate calcineurin specifically in endothelial cells, in combination with different in vitro set ups.

Results: We show that it is dispensable for retinal and tumor angiogenesis, but is implicated in vessel stabilization. Importantly, while ablation of endothelial calcineurin does not affect the progression of primary tumors nor tumor cell extravasation, it potentiates outgrowth of lung micrometastases. We identify Bmp2 as a downstream target of calcineurin/NFAT pathway in lung endothelium, potentially inhibiting 3D cancer cell growth. We reveal a dual role of calcineurin/NFAT signaling, in vascular regression/stabilization and in the tissue specific production of an angiocrine factor restraining cancer cell outgrowth.

Conclusion: Our results suggest that in addition to targeting the immune system, post-transplantation immunosuppressive therapy also directly targets the endothelium contributing to aggressive cancer progression.

P41

Imaging of porcine endothelial glycocalyx by confocal microscopy and assessment of its shedding by human serum in an in vitro microfluidic model of pig-to-human xenotransplantation

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Objective: The endothelial glycocalyx (EG) is a brush-like surface layer consisting of heparan sulfate (HS) proteoglycans, sialic acid-containing glycoproteins and glycolipids. It plays important

roles such as mechanotransduction, regulation of the vascular permeability and prevention of blood cell adhesion to the endothelium. EG perturbation has been linked to several pathophysiological conditions such as ischemia/reperfusion injury, atherosclerosis and sepsis. In xenotransplantation, donor graft endothelium interfaces with the recipient's blood, resulting in a switch of the graft endothelium to a pro-coagulant and pro-inflammatory phenotype. This study focused on the reliable visualization of the EG by confocal microscopy as well as on the assessment of its shedding after perfusion of porcine aortic endothelial cells (PAEC) with normal human serum (NHS) using a microfluidic system.

Methods: Wild type PAEC were cultured in microchannels of 550 μm diameter with round cross-sections until confluence. A flow of 600 $\mu\text{l}/\text{min}$, corresponding to a shear stress of 10 dyn/cm^2 , was applied using a peristaltic pump. Flow-adapted PAEC as well as PAEC grown under static conditions were stained using fluorescent wheat germ agglutinin (WGA), which binds to N-acetyl-D-glucosamine (GlcNAc) and N-acetyl neuraminic acid (NeuAc) components of the EG. HS was also stained using a specific antibody. Subsequently, PAEC microchannels were perfused for 2 hours with 10% NHS or cell culture medium.

Results: PAEC exposed to physiological flow for 48 hours considerably upregulated the expression of HS as compared to static culture conditions ($43\% \pm 3\%$ increase of HS-staining). After 5 days of physiological flow we observed an increased WGA staining compared to day 1. Perfusion of PAEC-coated microchannels with 1:10 diluted NHS at 10 dyn/cm^2 led to a significant, time-dependent reduction of both HS ($38\% \pm 6\%$ reduction after 10 minutes) and WGA staining ($43\% \pm 9\%$ reduction). Longer perfusion times led to increasing detachment of PAEC, which could be visualized by confocal microscopy.

Conclusion: Flow and shear stress are important factors affecting the composition of the EG. The reduced staining of these sugar molecules during NHS perfusion supports the idea that in a pig-to-human xenotransplantation setting the porcine EG is shed after contact with human serum.

P42

Pulmonary microvasculature-on-a chip for drug testing

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Objective: The principal pathobiology in idiopathic pulmonary fibrosis (IPF) is very intricate. More light is starting to be shed on IPF pathogenesis with the introduction of tyrosine kinase inhibitors such as nintedanib used to treat IPF. Differences in the cellular responses observed in standard in vitro studies, animal models, and human clinical studies may be confounding the efficient development of new therapeutic strategies. This is particularly true for disease such as IPF with complex correlation of fibrosis and angiogenesis. In vitro microvasculature models that mimic in vivo conditions are one strategy to investigate the efficacy of therapeutic compounds. The aim of this study was to explore how nintedanib acts on vascular remodeling on an isolated 3D network of pulmonary microvasculature.

P41. Figure.

Methods: Firstly, we established a 3D and perfusable microvasculature network by co-culturing primary human lung fibroblasts and human umbilical vascular endothelial cells within 3D fibrin gel network. Then, we explored the impact of nintedanib on this in vitro model by investigating changes in vascular permeability, vessel density, fibroblast invasion, and endothelial-fibroblast interactions.

Results: Although nintedanib did not adversely affect cell viability, but it affected the in vitro microvasculature architecture. Using our in vitro microvasculature model, we showed that treatment with nintedanib significantly increased vascular permeability, decreased vessel density by both reducing number of vessels and shrinking the vessels themselves, inhibited fibroblast recruitment

to endothelial vasculatures, constrained fibroblast invasion toward the vasculature region, and weakened vessel-vessel connections of existing microvessels.

Conclusion: Our results revealed that nintedanib treatment at clinically relevant concentrations considerably affect neovasclogenesis. The effect of nintedanib on microvasculature architecture has formerly been studied in vivo, and our in vitro 3D model of pulmonary microvasculature represents an exciting approach because it allows to study of the effect of nintedanib on isolated human microvessels and resolve cell-cell interactions in greater detail than in vivo studies. Such advanced in vitro platforms can address fundamental questions of drug effects on neovasclogenesis and be used for developing and optimizing drug treatments in personalized vasculature models.

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Role of CD112 in T cell migration

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Objective: Endothelial junctional proteins play an important role in regulating vascular permeability and leukocyte trafficking across the vasculature. We found CD112 (Nectin-2), an adherence junction molecule, to be highly expressed in both lymphatic and blood vascular endothelial cells (ECs). CD112 belongs to the immunoglobulin superfamily and was shown to engage in homophilic interactions as well as heterophilic interactions with a variety of binding partners expressed on ECs and on leukocytes. In this project, we aimed at exploring the role of CD112 in T cell trafficking, since T cells reportedly express the CD112-ligands DNAM-1, TIGIT and CD112R.

Methods: CD112 expression levels in lymphatic endothelial cells (LECs) and blood endothelial cells (BECs) were analysed in cultured cells and in tissues by FACS and immunofluorescence. To investigate a functional role of CD112 on T cell migration, in vitro transmigration assays, involving murine T cells and endothelial cells, were performed. CD112 was blocked with a commercial blocking antibody or an in-house generated fusion protein, consisting of the high-affinity CD112-ligand CD112R and an antibody Fc moiety (mCD112R-Fc). T cell migration was further investigated in CD112-deficient (CD112^{-/-}) mice in adoptive transfer (AT) studies by FACS and immunofluorescent staining on frozen tissue sections. Lymphatic and/or blood vessel coverage was assessed in several organs.

Results: We found that CD112 protein is expressed in cultured murine LECs and BECs in vitro and by the lymphatic and blood vasculature in murine tissues. In functional in vitro assays, treatment with anti-CD112 antibody or with mCD112R-Fc significantly reduced naïve CD4⁺ T cell migration across BEC monolayers. Interestingly, TH1 transmigration was not affected by CD112 blockade. In vivo, naïve T cell homing to the spleen, but not to other SLOs, was significantly reduced in CD112^{-/-} as compared to WT mice. At the same time, we found the blood vessel coverage of the spleen of CD112^{-/-} mice to be significantly increased compared to control mice, indicative of CD112's role in angiogenesis. We are currently performing AT experiments in WT mice in presence of mCD112R-Fc to further investigate the impact of CD112 blockade on T cell homing.

Conclusion: Collectively, our data reveal a novel role for CD112 in modulating naïve T cell migration into spleen.

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

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Objective: Glioblastoma multiforme (GBM) is the most common primary brain tumor with high severity and low therapeutic success. One important aspect in treating GBM is to achieve an effective drug concentration in tumor. It is well known that GBM vasculature is leaky to plasma proteins; however, the drug delivery into the GBM is not successful. Most of prescribed drugs are small lipid soluble molecules, which are effectively removed from the brain endothelial cells via ABC transporters. Until now, the development and homeostatic regulation of human blood-brain barrier (BBB) is poorly understood. The BBB is a multicomponent system and 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: We aim to characterize the transcriptome and proteome of the human BBB in health and GBM. Endothelial cells (EC) are isolated from GBM and normal brain tissue using anti-human CD31 antibody coupled to magnetic beads, followed by lysis and isolation of RNA and protein, which is subjected to RNA seq and protein profiling.

Results: Our preliminary analysis of RNA seq data shows deregulated expression of SLC transporters in GBM endothelial cells compared to controls, whereas the expression of several ABC transporters remained unaltered. Preliminary analysis suggests that deregulation of several transporters in GBM ECs maybe occurring due to loss of BBB-specific phenotype of GBM EC. Our future analysis will be extended to characterize EC changes on a single cell level isolated from distinct GBM regions showing differences in vessel permeability. Furthermore, we want to understand which BBB characteristics (i.e. closed cell-cell junctions, expression of SLC and ABC transporters, low rate of transcytosis) are specifically altered in GBM ECs and whether we will find GBM specific changes that can be exploited for drug delivery (e.g. upregulation of a specific SLC transporter).

Conclusion: Preliminary analysis suggests a deregulation of several transporters (e.g. SLC2A1) in GBM ECs, which may occur due to a loss of some BBB-specific EC genes in GBM samples. For future, we aim to extend our analysis by RNA sequencing of single endothelial cells isolated from GBM regions showing differences in vessel permeability.

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