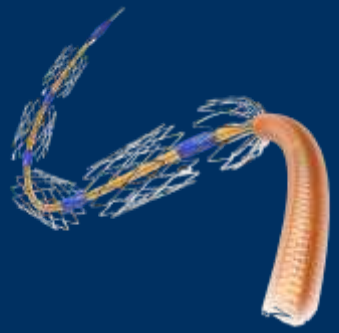
Scrub-in with the experts: Interventional techniques for complex femoropopliteal obstructions

Final results and insights of the ***LOCOMOTIVE Registry*** (full cohort)



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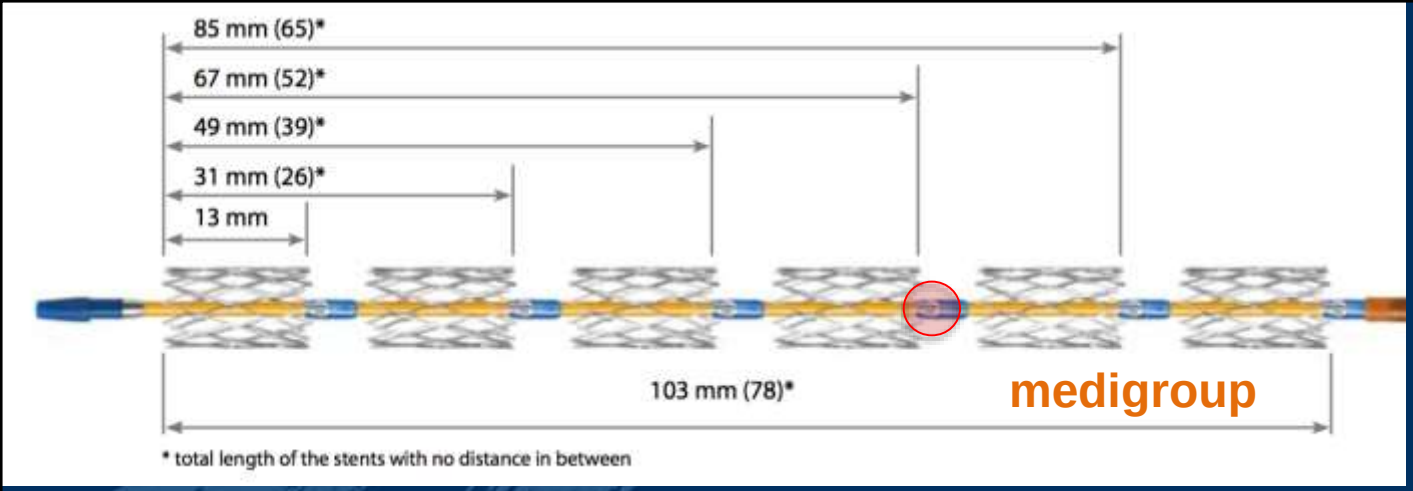
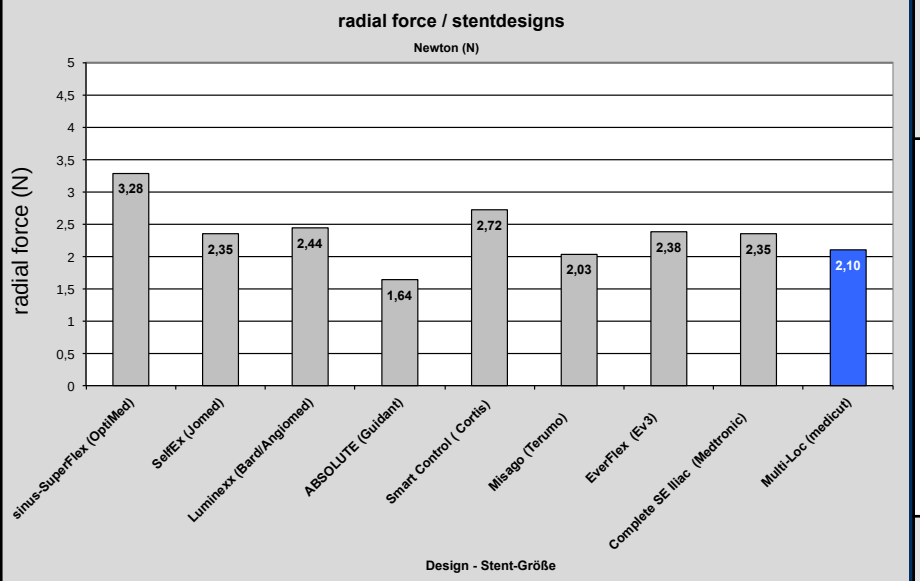
Disclosure

Speaker name: Dr. Klaus Amendt

I have the following potential conflicts of interest to report:

- [X] Consulting: B.Braun, Bayer AG
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [X] Owner of European and US-patent on Multiple Stent Delivery System





Components

MSDS	
Sheath	6F
Stents	6 ML-Stents
Working length	80 cm, 130 cm
Guide-wire	0,035``
Individual Stent	
Length	13 mm
Diameter	5, 6, 7, 8 mm
Radiopaque marker	1/stent
Design	closed cell designe
Radial force	comparable to standard nitinol stents
Treated vessel diameter	4 – 8 mm

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DEKRA: CE – marking: ***27.05.2015; FIM 17.06.2015***

ClinicalTrials.gov Identifier: NCT02531230)
24.08.2015 - 31.12.2016
ClinicalTrials.gov Identifier: NCT02900274)
End: 31.12.2018

LOCOMOTIVE: Closed registry

Objective: to assess ***safety and efficacy*** of the ***multi-LOC*** peripheral stents system to treat de novo and restenotic lesions

Design: non randomized prospective, multi-center registry
common femoral to distal popliteal artery, all comers registry: RCC 2-5, Fontaine II- IV

Intended Use: flow limiting dissections and recoil after POBA and DCB-dilatation.
„whenever stenting is indicated“

Primary endpoint: ***6 month TLR- rate (LINC 2017, CX 2017)***
Additional variables: ***12 month TLR rate (LINC 2018, CX 2018)***
@ 6 and ***12 months:*** walking distance (S1, S2)
ABI , CCD: patency- rate
RCC, amputation rate

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Conclusions: results of the closed LOCOMOTIVE-Registry (n: 75) in 2018

ClinicalTrials.gov Identifier: NCT02531230)
24.08.2015 - 31.12.2016

These data @ 6 and 12 months show that the MSDS strategy is safe and effective in patients with PAOD (RCC 2-5) with complex femoro-popliteal lesions:

- ***High procedural success rate (100%)*** to release the individual stent segments also in morphologically challenging lesions.
- ***No stent-loss***, ***no conversion*** to standard stenting
- ***half of the lesion length could be saved from stenting*** as compared to the "long stent" strategy.

- ***Ff TLR rates: @ 6 months: 94,7% (CLI: 95.0%, IC: 94.5%)***
  @ 12 months: 90.7% (CLI: 95.0%, IC: 89.9%)
- ***primary patency rate: @ 6 months: 90,7% (CLI: 95.0%, IC: 89.1%)***
  @ 12 months: 85.7% (CLI: 93.3%, IC: 83.3%)
- ***No stent fractures***
- ***Sustained clinical benefit in CLI and IC (RFCCL, ABI)***

LOCOMOTIVE Registry

Extended registry

ClinicalTrials.gov Identifier: NCT02900274

End: 31.12.2018

N: 357

Site	City	PI
DE - Diakonissenkrankenhaus Mannheim	Mannheim	Dr. med. Klaus Amendt
DE - Universitätsklinikum Heidelberg	Heidelberg	Prof. Dr. med. Christian Erbel
DE - Universitäts-Herzzentrum Freiburg - Bad Krozingen	Bad Krozingen	Prof. Dr. Thomas Zeller
DE - Klinikum Lippe-Detmold	Detmold	Dr. med. Dirk Härtel
DE - Klinikum Magdeburg	Magdeburg	PD Dr. med. habil. Jörg Tautenhahn
DE - Sankt Gertrauden-Krankenhaus	Berlin	Dr. Ralf Langhoff
DE - Heinrich-Braun-Klinikum Zwickau	Zwickau	Prof. Dr. med. Andreas Hansch
DE - Asklepios Klinikum Harburg	Hamburg	PD Dr. Hans Krankenberg
DE - Agaplesion Bethesda Krankenhaus Wuppertal	Wuppertal	Dr. Jawed Arjumand
DE - Städtisches Klinikum Dessau	Dessau-Roßlau	Dr. med. Karsten Stock
DE - Ev. KH Königin Elisabeth Herzberge gGmbH	Berlin	Dr. Jens Stegemann
DE - Klinik Kösching	Kösching	Prof. Dr. med. Alexander Hansen
DE - SRH Klinikum Karlsbad-Langensteinbach	Karlsbad	Prof. Dr. med. Erwin Blessing
DE - Ev. Krankenhaus Mülheim	Mülheim an der Ruhr	Prof. Dr. Claus Nolte-Ernsting
DE - SLK-Kliniken Heilbronn (Bad Friedrichshall)	Bad Friedrichshall	Prof. Dr. med. Thomas Dengler
DE - St. Marien-Krankenhaus Siegen	Siegen	PD Dr. med. Christian Hohl
DE - Universitätsklinikum Jena	Jena	Prof. Dr. med. Ulf Teichgräber
DE - Universitätsklinikum Leipzig	Leipzig	Prof. Dr. Dierk Scheinert
FR - CHU Lille	Lille	Dr. Jonathan Sobocinski
FR - CHU Cote de Nacre	Caen	Dr. Etienne Joguet
FR - CHU Bordeaux - Hôpital Pellegrin	Bordeaux	Prof. Eric Ducasse
FR - CHU de la Timone à Marseille	Marseille	Prof. Philippe Piquet
HR - Clinical Hospital Merkur	Zagreb	Prof. Vinko Vidjak
HR - UHC Sisters of Mercy	Zagreb	PhD Tomislav Krčmar
IT - Nuovo Ospedale San Giovanni di Dio	Firenze	Dr. Nicola Troisi
PL - Centrum Kardiologii Józefów	Józefów/Warsaw	Dr. Robert Proczka

Lesion morphology

	All patients n=357	CLI n=60	Non CLI n=297	p-value
Target lesions	448	81	367	
Distal run off				
No vessel	12 (3.5%)	5 (8.5%)	7 (2.5%)	0.001
1	92 (26.7%)	24 (40.7%)	68 (23.8%)	
2	117 (34.0%)	19 (32.2%)	98 (34.4%)	
3	123 (35.8%)	11 (18.6%)	112 (39.3%)	
SFA I	176 (39.2%)	31 (37.8%)	145 (39.5%)	0.775
SFA II	235 (52.3%)	37 (45.1%)	198 (54.0%)	0.148
SFA III	263 (58.6%)	47 (57.3%)	216 (58.9%)	0.798
P1	140 (31.2%)	30 (36.6%)	110 (30.0%)	0.243
P2	74 (16.5%)	18 (22.0%)	56 (15.3%)	0.140
P3	14 (3.1%)	3 (3.7%)	11 (3.0%)	0.755
TASC C/D lesions	200 (44.5%)	45 (54.9%)	155 (42.2%)	0.037
Diffuse vessel disease	383 (85.3%)	71 (86.6%)	312 (85.0%)	0.716
Calcification	385 (85.7%)	67 (81.7%)	318 (86.6%)	0.247
Total occlusion	141 (31.4%)	22 (26.8%)	119 (32.4%)	0.324
Total lesion length, cm (range)	16.0±9.7	16.2±9.1	16.0±9.8	0.926

LOCOMOTIVE Registry

Extended registry

ClinicalTrials.gov Identifier: NCT02900274

End: 31.12.2018

N: 357

Procedural details and device characteristics

	All patients	Critical limb ischemia	No critical limb ischemia	p-value
Patients	357	60	297	-
Total number of released stent segments	1741	308	1433	-
Total length of stent segments per lesion L	0.56±0.59	0.53±0.37	0.57±0.62	0.691
Lesion length saved from stenting	**0.44±0.59**	**0.47±0.37**	**0.43±0.59**	**0.691**
Predilatation target lesion ***DCB (with or w/o POBA)*** **POBA only** **No predilatation**	 202 (45.0%) 243 (54.1%) 4 (0.9%)	 25 (30.5%) 56 (68.3%) 1 (1.2%)	 **177 (48.2%)** 187 (51.0%) 3 (0.8%)	 **0.014**
Procedural success per patient	351 (98.3%)	59 (98.3%)	292 (98.3%)	0.993

LOCOMOTIVE EXTENDED Registry

NCT number: ***NCT02900274***

End: 31.12.2018

Clinical outcomes at 6 months

	All patients	Critical limb ischemia	No critical limb ischemia	p-value
Patients	**357**	**60**	**297**	-
Pre-procedure				
Target leg ABI before procedure	**0.58±0.31**	**0.46±0.28**	**0.59±0.30**	**0.026**
Target leg ABI after procedure	**0.90±0.24**	**0.81±0.27**	**0.91±0.24**	**0.105**
6 months				
Number of follow-ups sonographic, clinical and by telephone relative to *TLR, TVR*	337 (94.4%)	56 (93.3%)	281 (94.6%)	0.694
Follow-up duration, months (including time to event)	6.1±0.9	5.8±1.5	6.2±0.8	0.006
Primary *unassisted patency of* target *vessel*, diameter stenosis<70% and/or TLR	**299 (88.7%)**	**50 (89.3%)**	**249 (88.6%)**	**0.884**
All Target lesion revascularizations (Re-PTA, lysis, surgical)	**15 (4.5%)**	**4 (7.1%)**	**11 (3.9%)**	**0.285**
Target vessel revascularization (Re-PTA, lysis)	24 (7.1%) 15 **+9**	6 (10.7%) 4 **+ 2**	18 (6.4%) 11 **+ 7**	0.252
Non-target *vessel* revascularization	**14 (4.2%)**	**6 (10.7%)**	**8 (2.9%)**	**0.007**
All *non Target lesion* revascularisation (n)	**23 (6.8%)**	**8 (14.2%)**	**15 (5.3%)**	
Target leg ABI	0.89±0.26	0.77±0.31	0.90±0.24	0.006
Rutherford shift pre vs. 6 months	1.8±1.3	**2.6±1.7**	1.6±1.2	**<0.001**
Major amputations, target and non-target leg	6 (1.8%)	**5 (8.9%)**	1 (0.4%)	**<0.001**
Death	15 (4.5%)	8 (14.1%)	7 (2.5%)	**<0.001**

LOCOMOTIVE EXTENDED Registry

NCT number: ***NCT02900274***

End: 31.12.2018

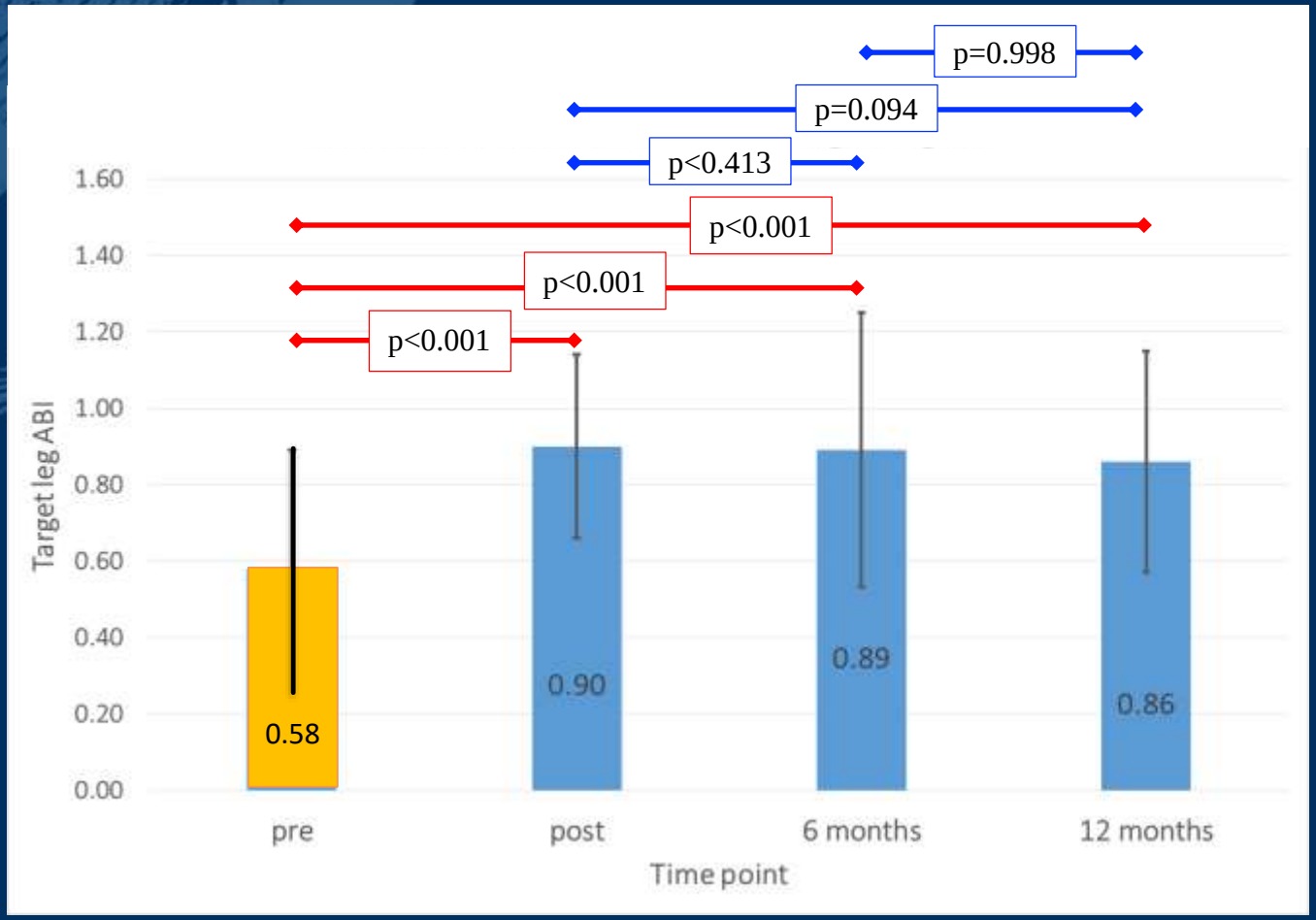
Clinical outcomes at 12 months

	All patients	Critical limb ischemia	No critical limb ischemia	p-value
Patients	**357**	**60**	**297**	**-**
12 months				
Number of follow-ups sonographic, clinical and by telephone relative to *TLR, TVR*	303 (84.9%)	47 (78.3%)	256 (86.2%)	0.121
Follow-up duration, months (including time to event)	11.8±3.2	**10.8±4.0**	12.0±3.0	**0.012**
Primary unassisted patency of *target vessel*, diameter stenosis<70% and/or TLR	248 (81.8%) N=303	38 (80.9%) N=47	210 (82.0%) N=256	0.847
All Target *lesion* revascularizations (Re-PTA, lysis, surgical)	**35 (11.6%)**	**7 (14.9%)**	**28 (10.9%)**	**0.435**
+ TLR vs 6 months (n)	+20 (+6.6%)	+3 (+6.3%)	+17 (+6.6%)	
Target *vessel* revascularization (Re-PTA, lysis)	43 (14.2%) 35 +8	9 (19.1%) 7 +2	34 (13.3%) 28 +6	0.289
Non-target vessel revascularization	23 (7.5%)	7 (14.3%)	16 (6.3%)	**0.051**
All *non Target lesion* revascularisation (n)	31 (10.2%)	9 (19.1%)	22 (8.6%)	
Target leg ABI	0.86±0.29	0.86±0.374	0.90±0.22	0.909
Rutherford shift pre vs. 12 months	**1.8±1.3**	**2.6±2.0**	**1.7±1.2**	**<0.001**
Difference in Rutherford shift 6 - 12 months[2]	**-0.09±1.17**	**0.03±1.66**	**-0.11±1.07**	**0.502**
Major amputations, target and non-target leg	8 (2.6%) N=304	**5 (10.6%) N=47**	3 (1.2%) N=257	<0.001
Death	22 (7.3%)	10 (26.3%)	12 (4.7%)	**<0.001**

LOCOMOTIVE EXTENDED Registry

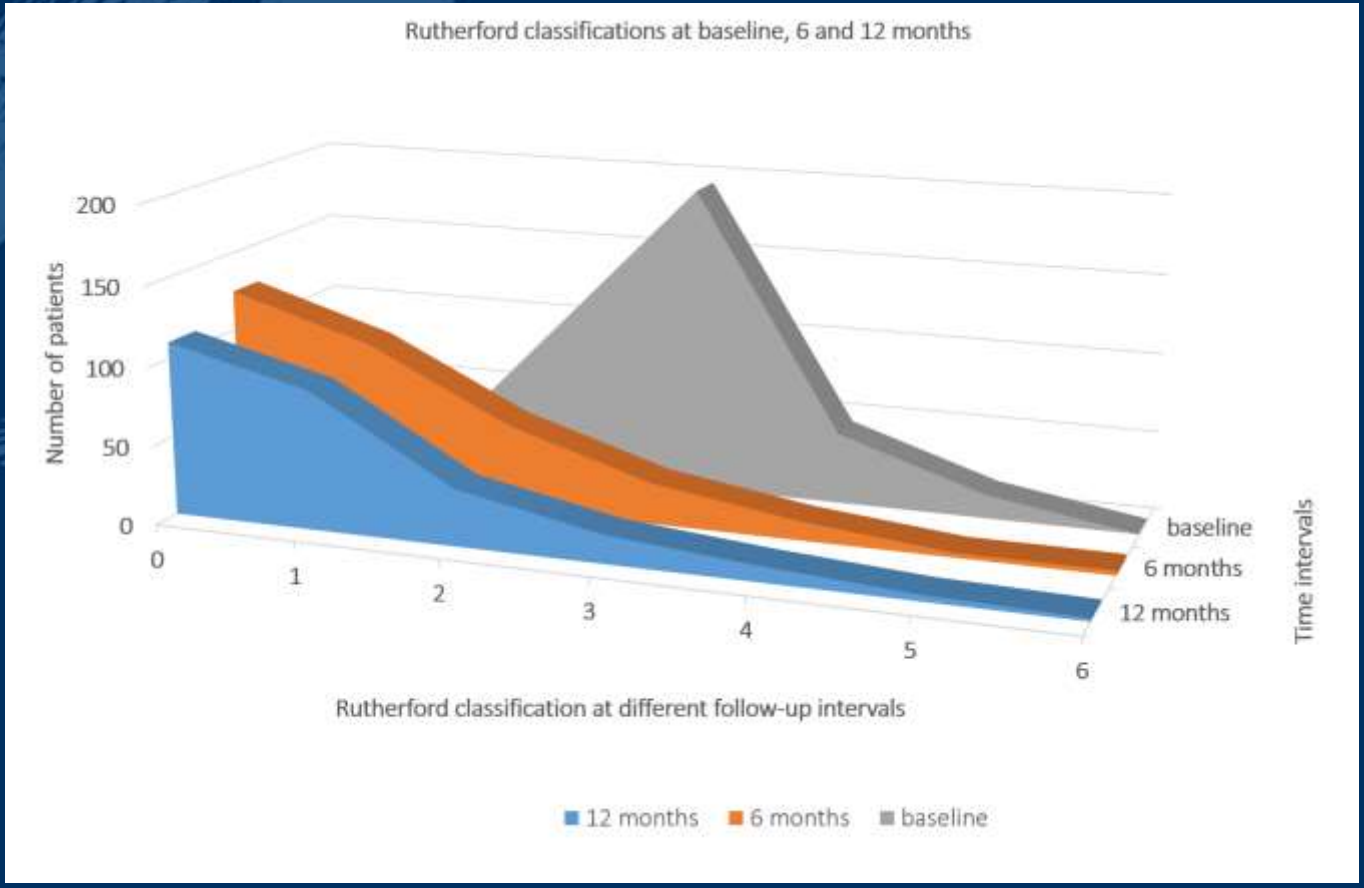
NCT number: ***NCT02900274***

End: 31.12.2018



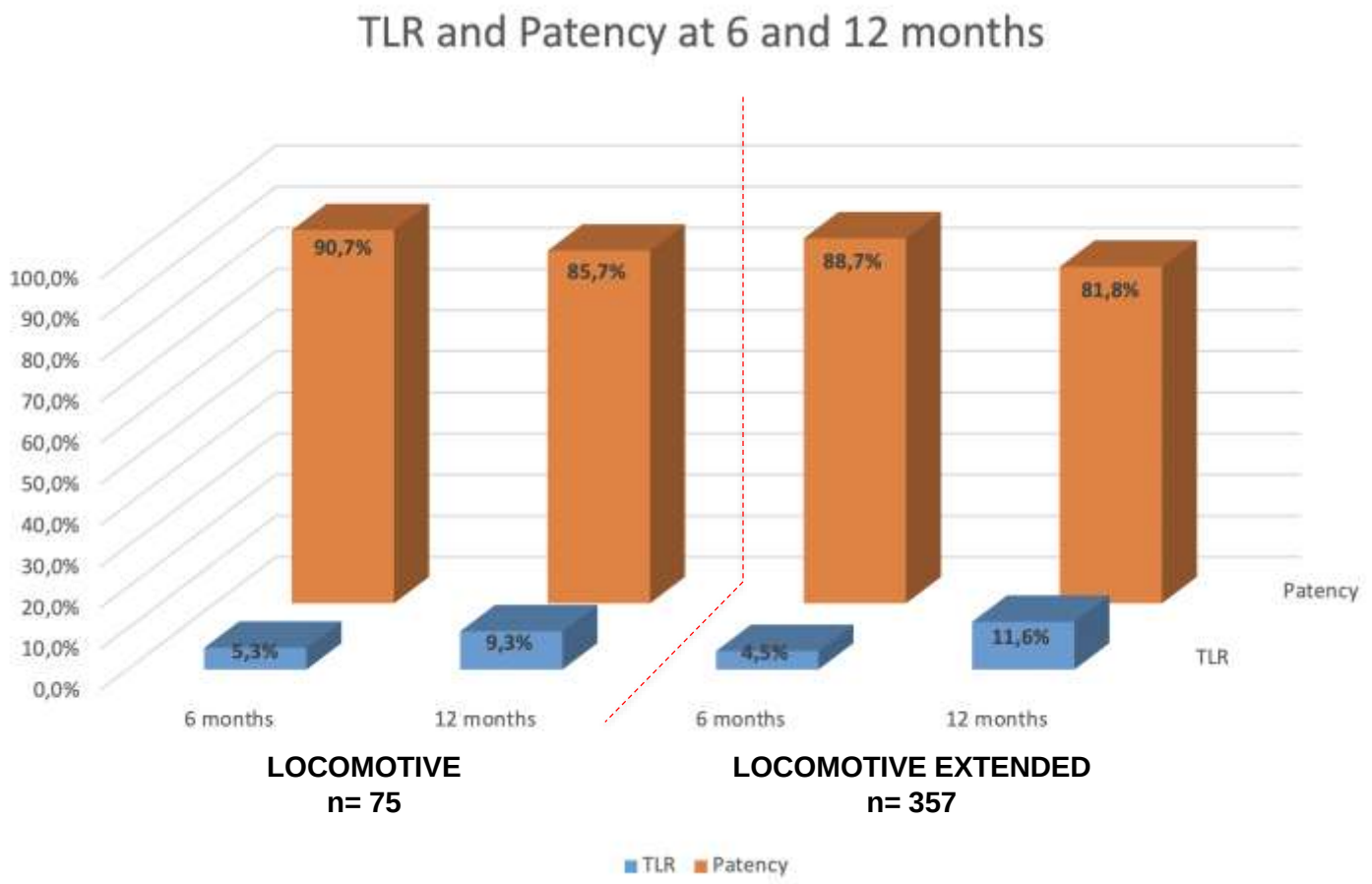
LOCOMOTIVE EXTENDED Registry

NCT number: ***NCT02531230***



ClinicalTrials.gov Identifier: NCT02900274)
End: 31.12.2018

LOCOMOTIVE Registry



Conclusions: results of the extended LOCOMOTIVE-Registry (n: 357)

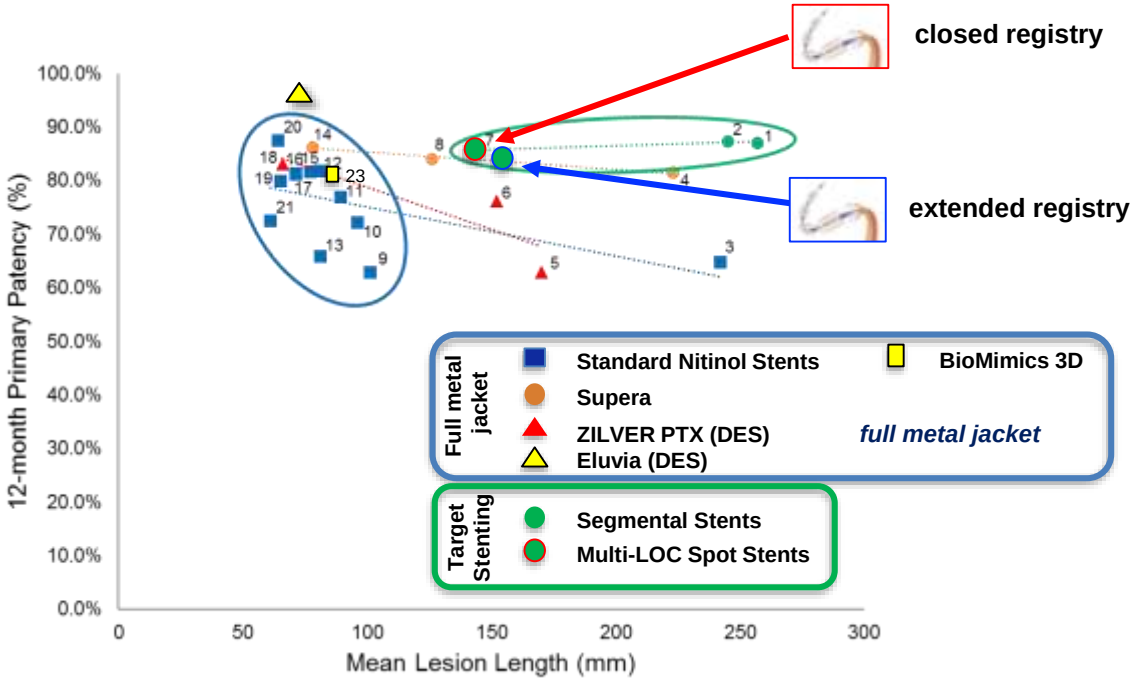
These data @ 6 and @ 12 months show that the MSDS strategy is safe and effective in patients with PAOD (RCC 2-5) with complex femoro-popliteal lesions:

- ***High procedural success rate (98%)*** to release the individual stent segments also in morphologically challenging lesions.
- ***No stent-loss***, ***no conversion*** to standard stenting
- ***half of the lesion length could be saved from stenting*** as compared to the "long stent" strategy.

- ***Ff TLR rates: @ 6 months 95,5% (CLI: 92.9%, IC: 96.1%)***
  @ 12 months 88.4% (CLI: 85.1%, IC: 89.1%)
- ***primary patency rate: @ 6 months 88,7% (CLI: 89.3%, IC: 88.6%)***
  of target vessel @ 12 months 81.8% (CLI: 80.9%, IC: 82.0%)
- ***No stent fractures***
- ***Sustained clinical benefit in CLI and IC (RFCCL, ABI)***
- ***Progession of disease within lesion and outside is comparable***

SFA stent performance related to lesion length

RTCs and Registries



Note: Results from clinical trials are not directly comparable. This chart is for educational purposes only.

1 HONG SPOT: Hong S-J et al. J Am Coll Cardiol Intv 2015;8:472–80. 2 PARADE: Young-Guk K. 12-month results of PARADE trial. LINC 2018. 3 DURABILITY 200: Bosiers M et al. J Vasc Surg. 2011;54:1042-1050. 4 SUPERA 500 LL: Scheinert D. Results from the SUPERA-500 Registry. LINC 2013. 5 ZEPHYR: Iida O et al. JACC Cardiovasc Interv. 2015;8:1105-12. 6 REAL: Scheinert D 2-year results of the REAL PTX trial. Presented at LINC 2017. 7 LOCOMOTIVE: Amendt K. LOCOMOTIVE All comers study 12-month results. LINC 2018. 8 SUPERA 500: Scheinert D. Results from the SUPERA-500 Registry. LINC 2013. 9 ABSOLUTE: Schillinger M et al. N Engl J Med. 2006;354:1879–1888. 10 DURABILITY: Bosiers M et al. J Endovasc Ther. 2009;16:261-269. 11 DURABILITY II: Matsumura JS, Yamanouchi D, et al. J Vasc Surg. 2013 Jul;58(1):73-83. 12 MIMICS-2: Zeller T. MIMICS-2 Study: 1-Year Results. LINC 2018. 13 ASTRON: Dick P et al. Catheter Cardiovasc Interv. 2009;74:1090–1095. 14 SUPERB: Garcia L et al. Circ Cardiovasc Interv. 2015 May;8(5). 15 STROLL: William A et al. J Vasc Interv Radiol 2015;26:21–28. 16 RESILIENT: Laird JR et al. Circ Cardiovasc Interv. 2010;3:267-276. 17 4EVER: Bosiers M et al. J Endovasc Ther. 2013;20:746–756. 18 ZILVER PTX: Dake M et al. Circ Cardiovasc Interv. 2011;4:495–504. 19 MIMICS: Zeller T et al. Circ Cardiovasc Interv. 2016;9:e002930. 20 MISAGO 2: Schulte K et al. J Endovasc Ther. 2012;19:774-784. 21 COMPLETE SE: Laird JR et al. J Endovasc Ther. 2014;21:202-212. 22. Majestic Trial: Müller-Hülsbeck S et al. 2016; JEVT 23(5):701-707. 23. MIMICS-2 Study Th. Zeller @LINC 2018.

Restenoses after Fem-Pop ***Spot-Stenting***

–monocenter analysis –
Diakonissenkrankenhaus Mannheim
N: 129 patients, 646 ML-stents ***out of these***

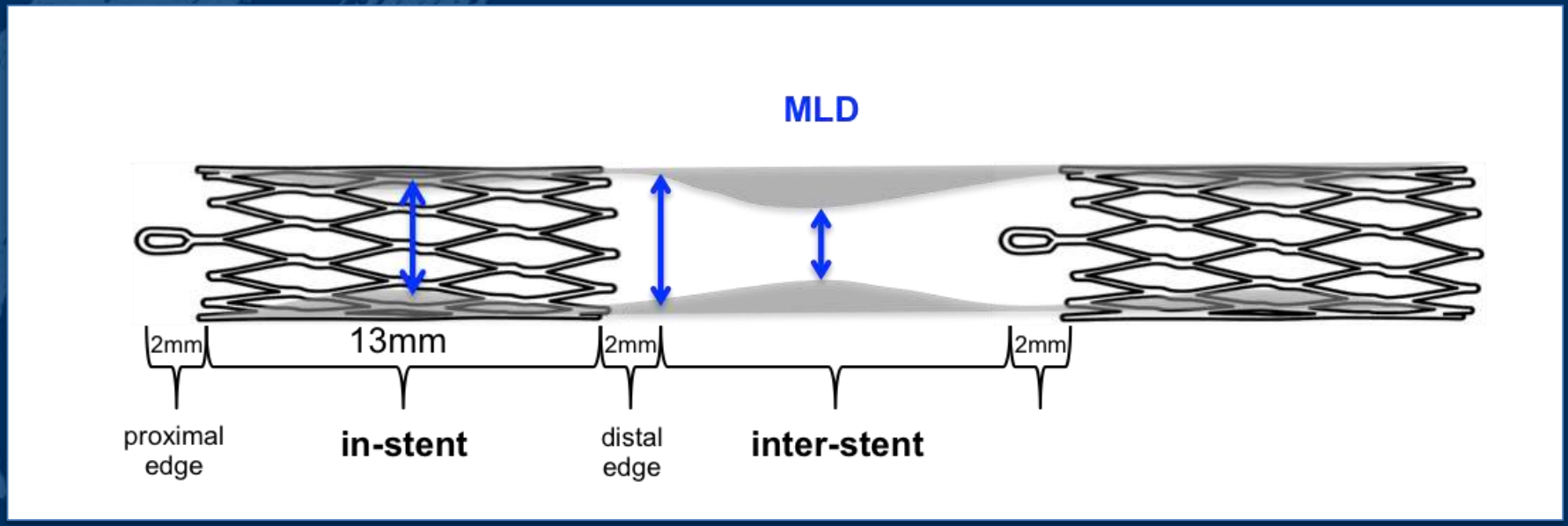
10 konsecutive pat. / 10 „clinically-driven TLR“
Including 51 Multi-LOC Stents

patients characteristics

	Index-Intervention	Re- Intervention
Patients (n)	**10**	
Age (y)	74.1 ± 8.5	75,1 +- 8.7
Time to TLR		**11.5 months** (1-16)
RF CCL (n) 4-6 2 3	 0 3 7	 0 3 7
ABI pre intervention	0.62 ± 0.22	0.70 ± 0.28
max. walking capacity treadmill (m)	108 ± 71	94 ± 41
Active smoking RR, D.m., HLP	10 =	10 =
Statins (n) ASS, Clopi,	10 =	**8** **=**
Balloon-treatment POBA **DEB**	 **10** 0	 0 **10**

Restenoses after Fem-Pop ***Spot-Stenting***

Restenosis: model for analysis



Schematic diagram of quantitative vascular measurements. To determine the pattern of restenosis, the minimal lumen diameter (MLD) was measured along the target lesion at predefined sites. According to the manufacturer's instructions for use, a minimum distance of 5 mm between

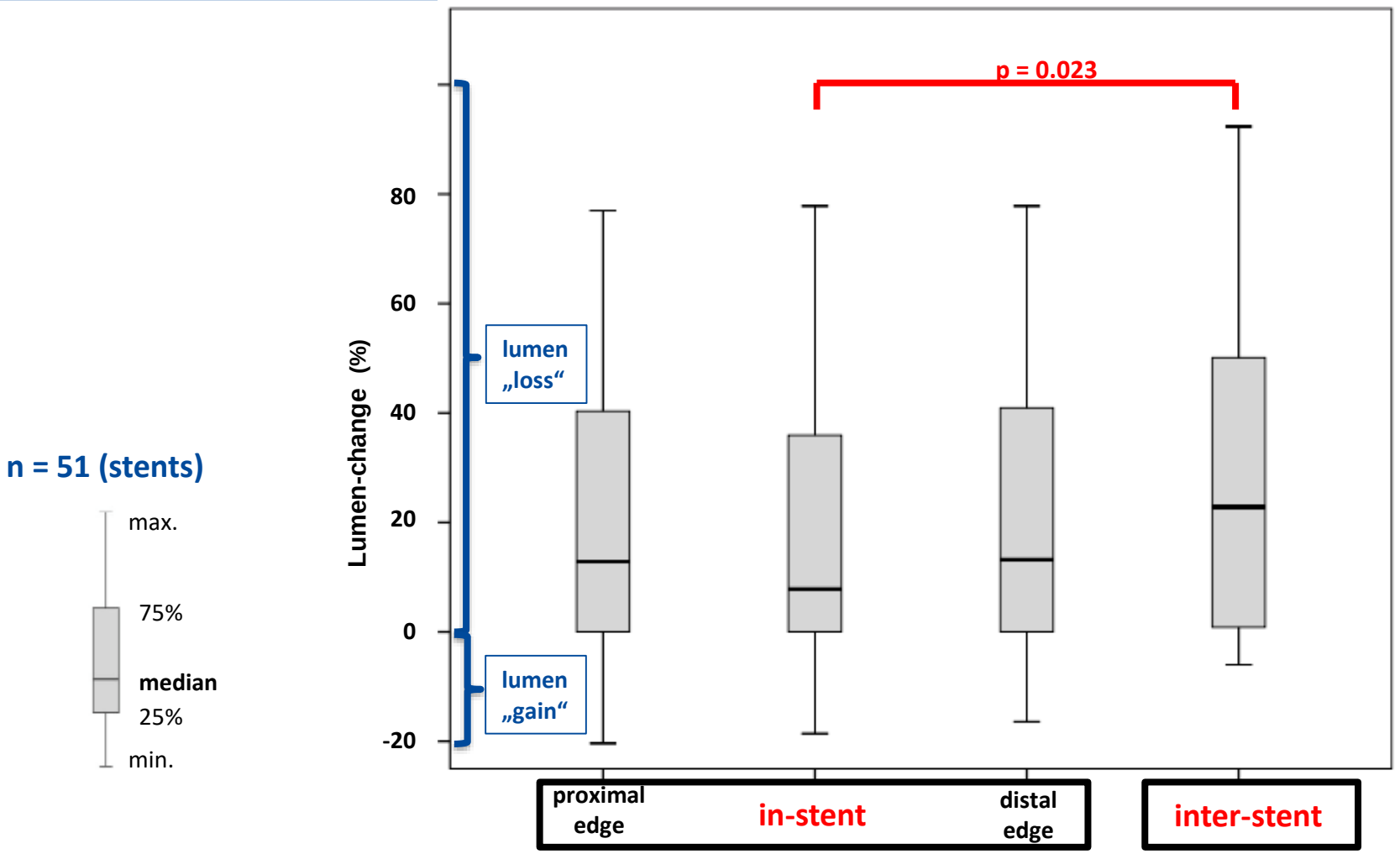
2 of 10 lesions were analysed after catheter thrombolysis

Sigl M, Amendt K et al. In vivo 2020;34:433-439

Restenoses after Fem-Pop ***Spot-Stenting***

Restenosis: model for analysis

Localisation of restenosis



Sigl M, Amendt K et al. In vivo 2020;34:433-439

Morphology of restenoses

Out of *129 patients*, ***10 patients*** with ***10 fem-pop.-lesions***,***11.5 months*** after ML-Stent implantation, showed ***restenoses*** (CCD > 50%),
out of these

- 6 with exclusive „inter-stent“ localisation
- 4 with „inter-stent“ and „in-stent“ localisation
- ***no „isolated in-stent“ stenoses and***
- ***no stent fractures in 51 short stents***

Preliminary conclusions:

1. **Spot-, target-, fokal stenting shows better TLR and patency rates compared full metal-jacket-stenting**
2. **Multi-LOC- stents do not fracture, = $f_{(Stent\text{-}Länge)}$**
3. **Multi-LOC-stents show *less stent associated intimal hyperplasia* (stent lumen and stent-edges)**

but

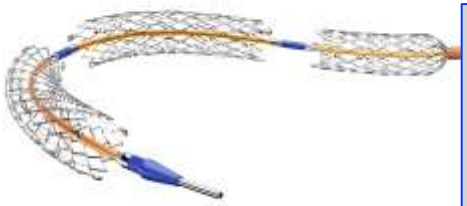
4. **In rare cases with long and calcified dissected membranes after balloon angioplasty 13 mm long spot-stents *might be to short***
5. **Multi-LOC- stenting also does not prevent further progression of atherosclerois**

Solutions as a complement to spot stenting with multi-LOC (13mm) x 6 ?

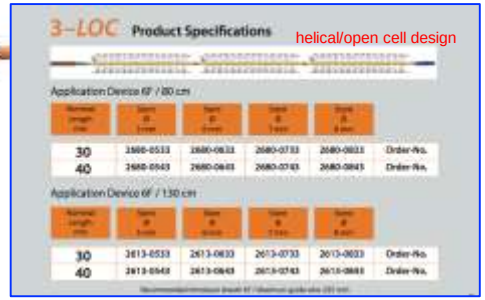
medigroup

ad 4: ***longer*** **spot-Stents:** ***3-LOC **** **und** ***2-LOC ****

30 or 40 mm length (helical). **(3 stents/device)** **(2 stents/device)**



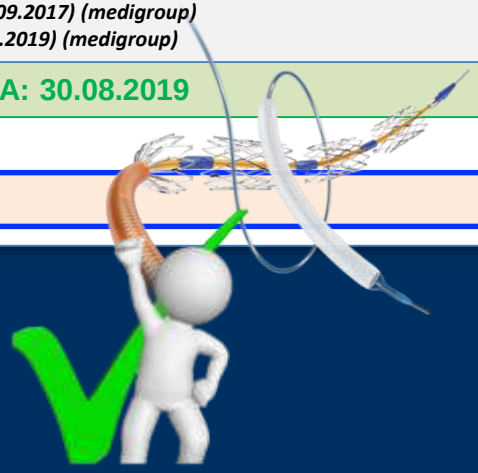
Ø: 5, 6, 7, 8 mm



European Patent ***2775968 (06.09.2017) (medigroup)***
US-Patent ***10,245,168 B2 (2.4.2019) (medigroup)***

*** CE-Marking DEKRA: 30.08.2019**

ad 5: Debulking, ***drug-eluting balloon-angioplasty + focal stenting***



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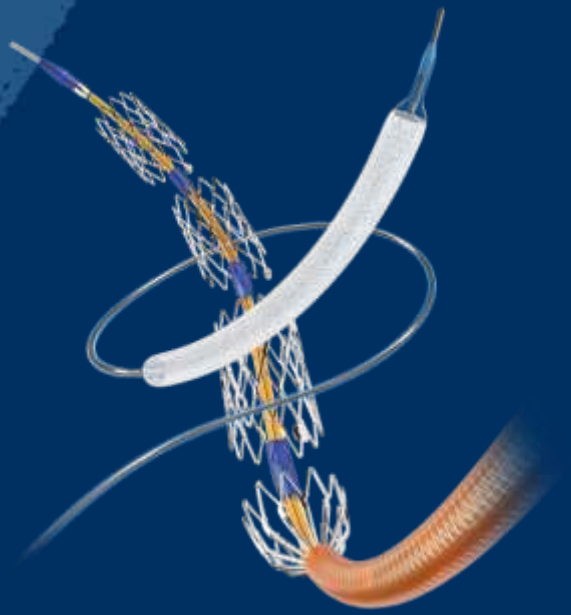
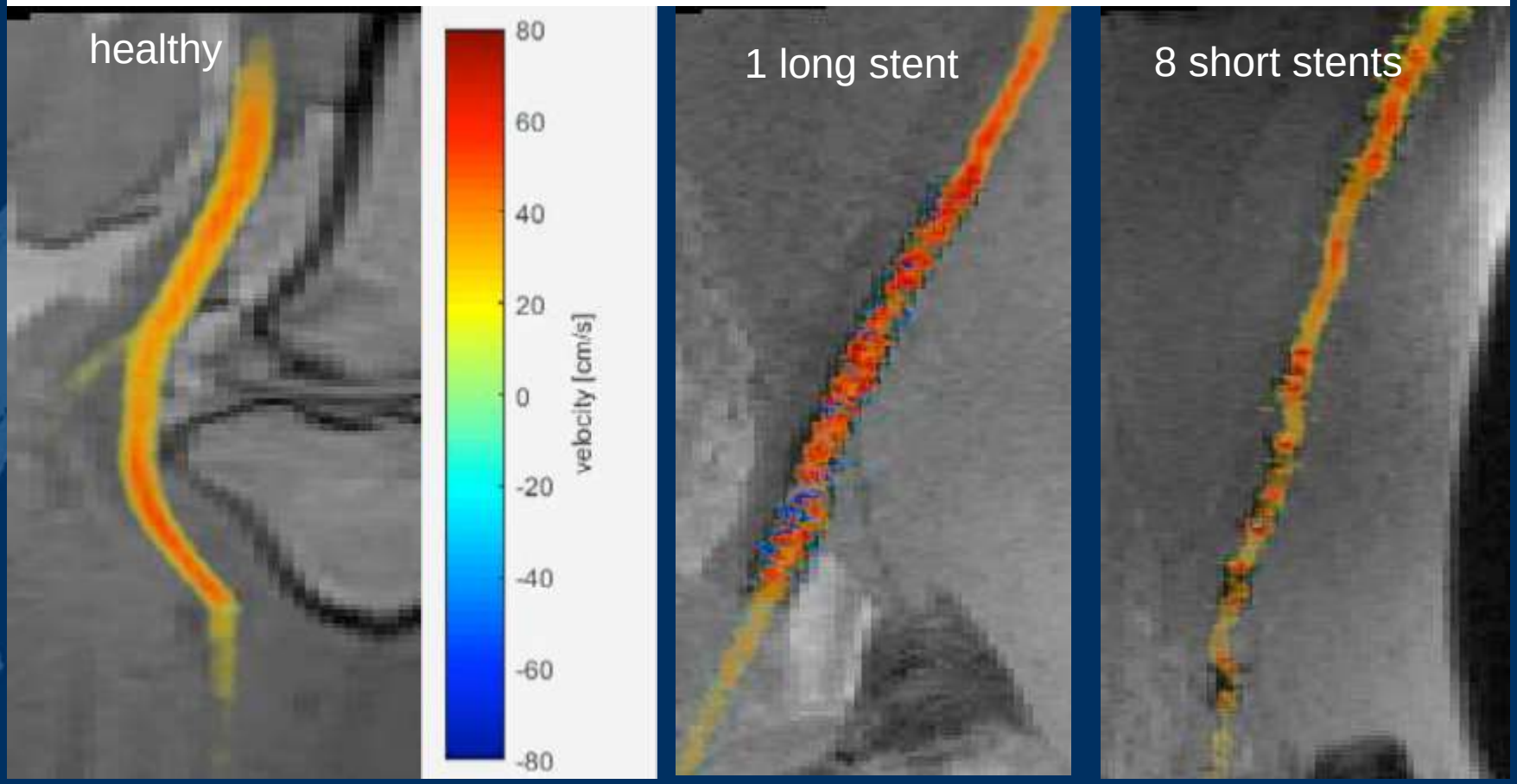
Multi-LOC: future studies planned:



Controlled studies with combination of DEB and spot-stenting with the Multi-LOC

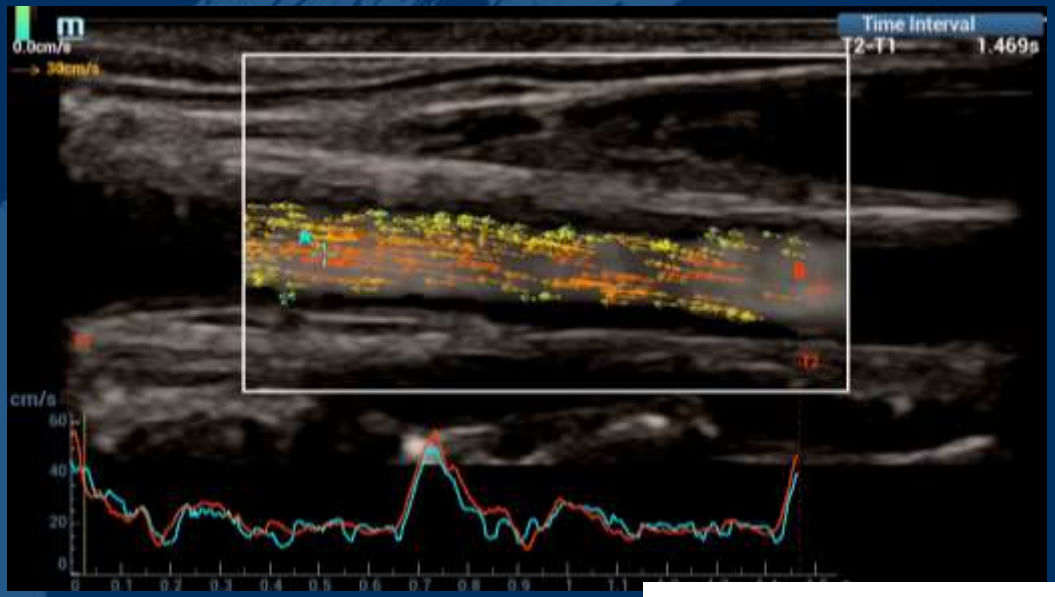
4D – flow MRI

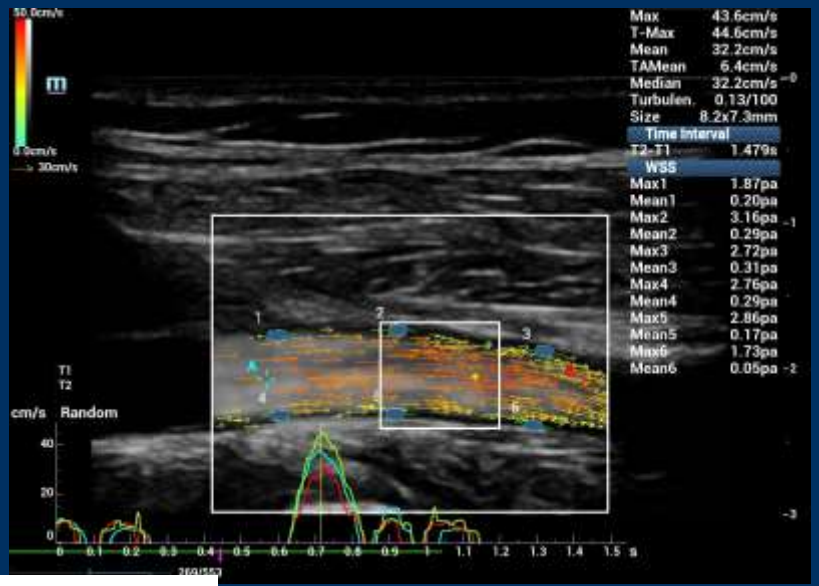


Dr. Martin Sigl, Universitätsklinikum Mannheim, Dr. K. Amendt, Diakonissenkrankenhaus Mannheim

High frame rate ultrasound: Vector Flow Imaging

Estimating local PWV



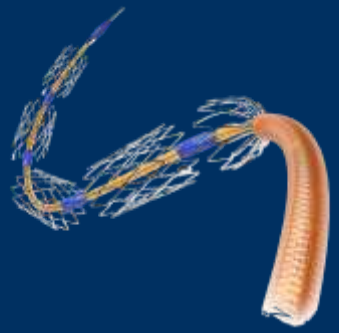


Popliteal hemodynamics
in normal an diseased PA
in different Stent-typs
= PV
= wall shear stress (WSS)

Dr. Martin Sigl, Universitätsklinikum Mannheim, Dr. K. Amendt, Diakonissenkrankenhaus Mannheim

Scrub-in with the experts: Interventional techniques for complex femoropopliteal obstructions

Final results and insights of the ***LOCOMOTIVE Registry*** (full cohort)



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