DIDACTICS
DEVELOPMENT
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LOLINAD treated with third generation DCB

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Disclosure slide

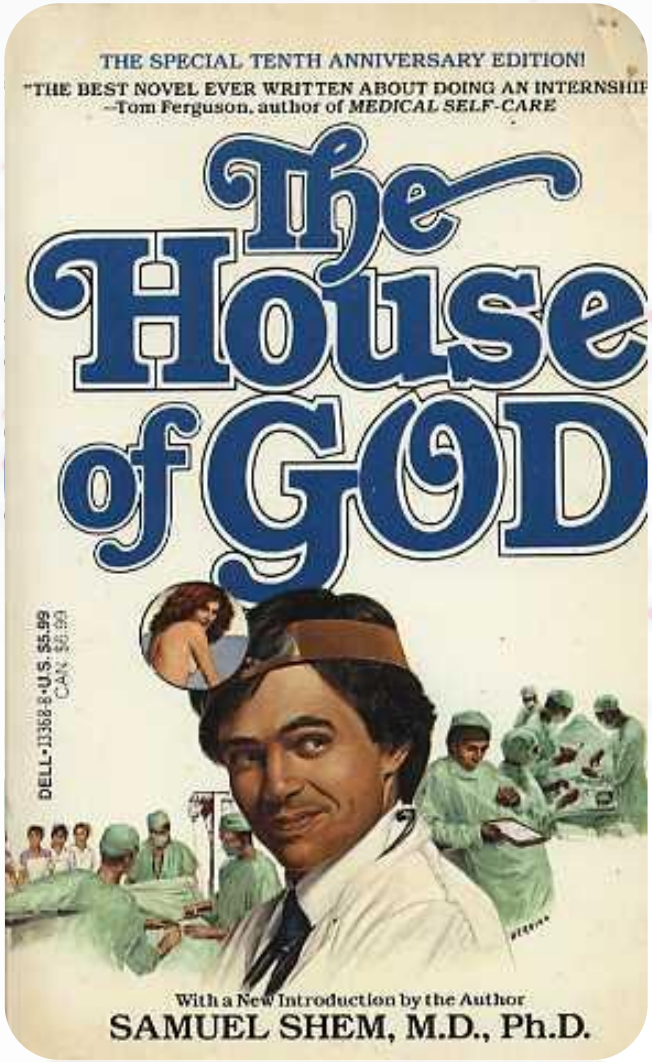
Speaker name: Koen Deloose, MD

❑ I have the following potential conflicts of interest to report:

- ☒ Consulting: Medtronic, Spectranetics, Biotronik, Abbott, Bard iVascular, Bentley, Cook, GE Healthcare, Terumo, Boston Scientific, Contego Medical, Cardionovum
- ❑ Employment in industry
- ❑ Stockholder of a healthcare company
- ❑ Owner of a healthcare company
- ❑ Other(s)

❑ I do not have any potential conflict of interest

LOLINAD : female patient 74yr



LOLINAD

means

Little Old Lady in No Apparent Distress

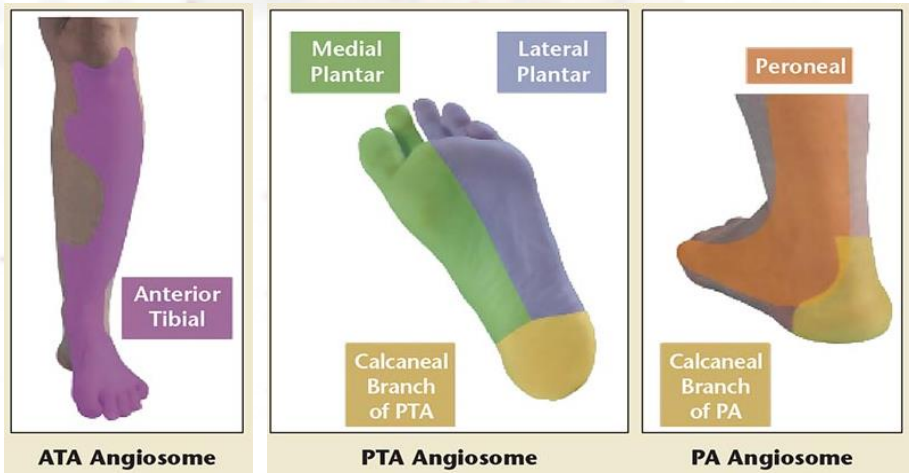
CLI case : female patient 74yr

- Risk factors
  - ✓ *IDDM type 2*
  - ✓ *AHT*
  - ✓ *Hypercholesterolemia*

- Comorbidities
  - ✓ *CABG*
  - ✓ *PTAS right + left SFA*

- Present state
  - ✓ *Non healing ulcer right foot (dorsum)*
  - ✓ *DUS : triphasic signal CFA, more distal weak monophasic signal*

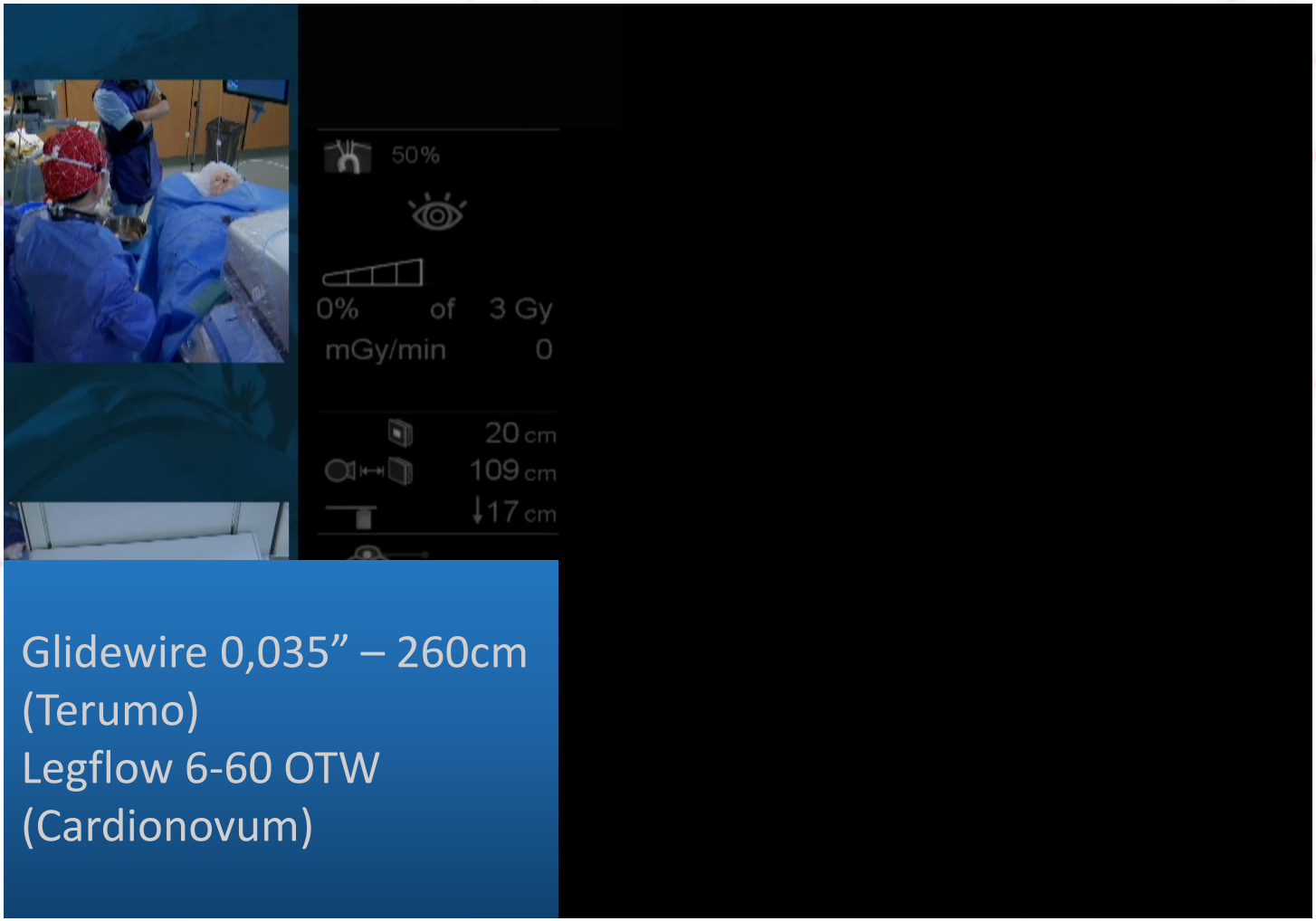
Diagnostic angiography



Strategy

- Ipsilateral antegrade approach
- 6F, 12-45 cm sheath (Terumo)
- Passage : intraluminal – subintimal
- Popliteal artery treatment ?
- Below the knee strategy ?

Popliteal artery treatment

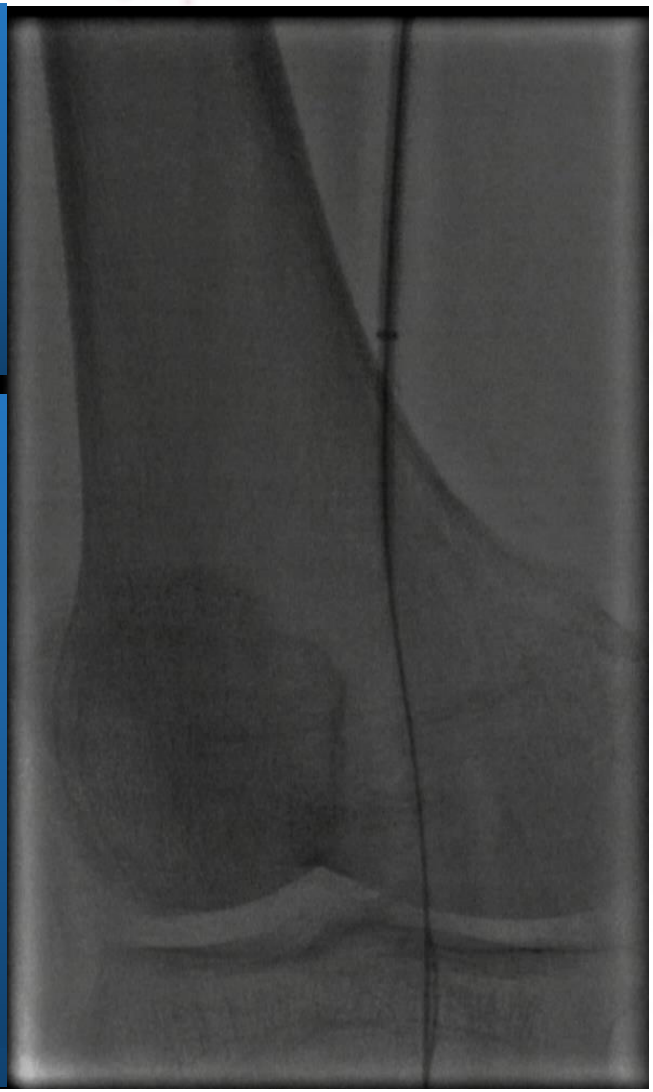


Glidewire 0,035” – 260cm (Terumo)
Legflow 6-60 OTW (Cardionovum)

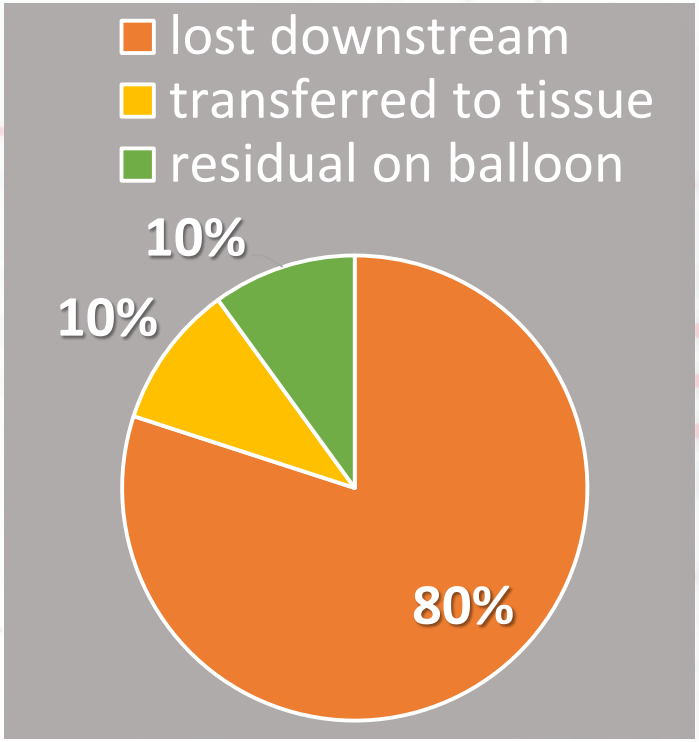
BTK treatment

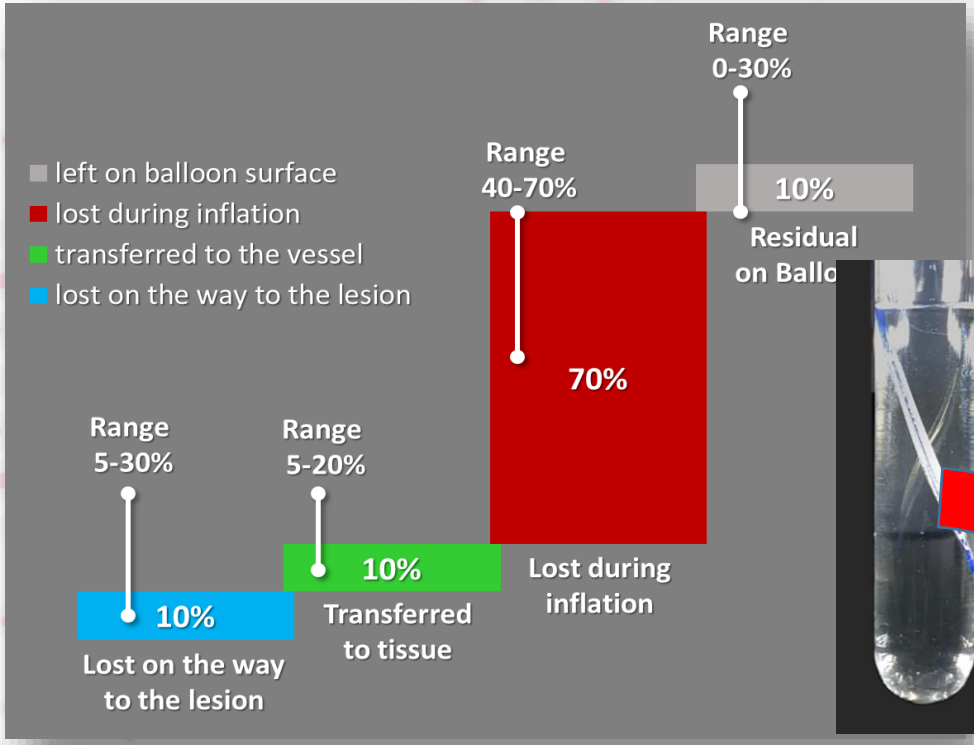
Advantage 0,014”– 300 cm (Terumo)
CXI cath 2,3F – 90 cm (Cook)

DCB as definitive treatment?



First & second generation DCB's : Most PTX is lost downstream



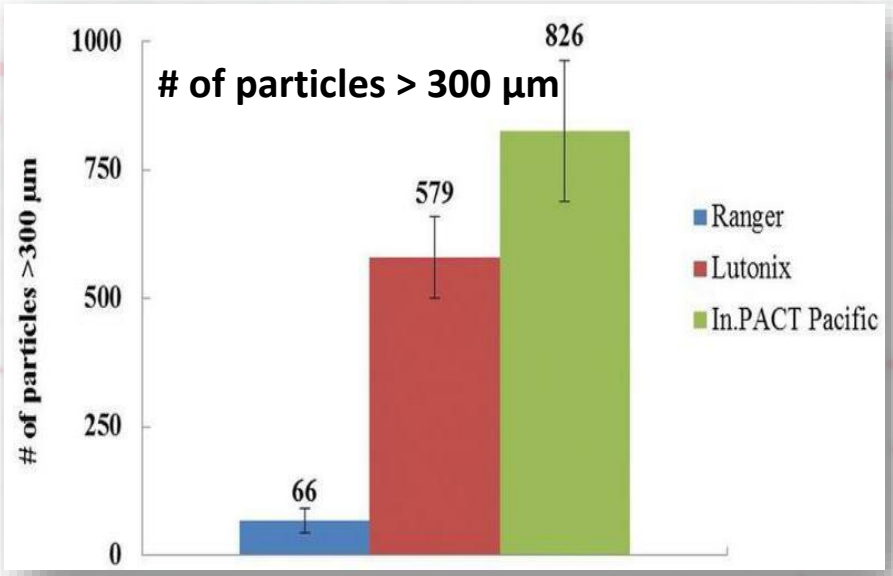


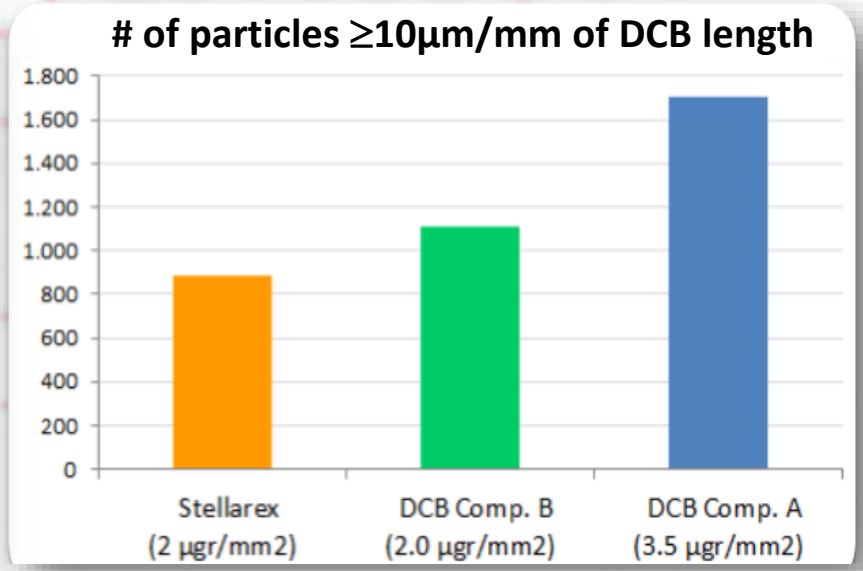
Mass effect : obliteration of microcirculation distally (cfr atherosclerotic debris)

Drug effect : potential local tissue toxicity

Mass effect : obliteration microcirculation

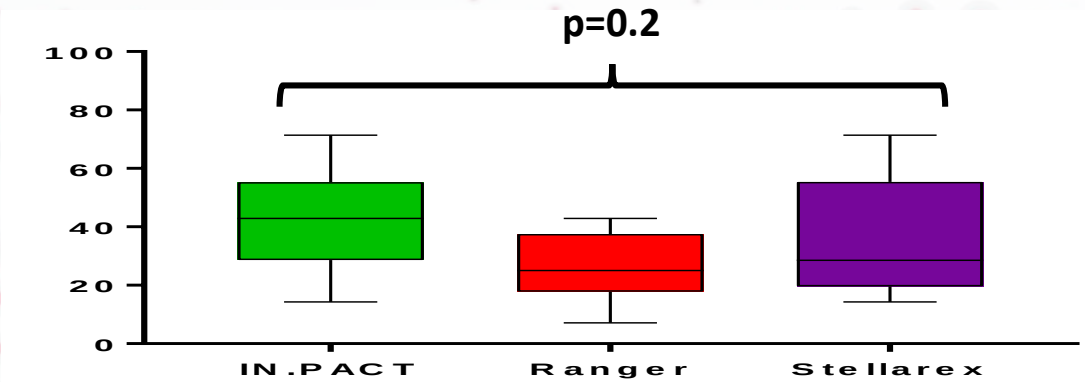
- Particle sizes > capillaries (5~10 µm) should matter





1. Gongora CA, Shibuya M, Wessler JD, McGregor J, Tellez A, Cheng Y, Conditt GB, Kaluza GL, Granada JF. Impact of Paclitaxel Dose on Tissue Pharmacokinetics and Vascular Healing: A Comparative Drug-Coated Balloon Study in the Familial Hypercholesterolemic Swine Model of Superficial Femoral In-Stent Restenosis. JACC Cardiovasc Interv. 2015 Jul;8(8):1115-1123

Drug effect : distal PTX effects ?

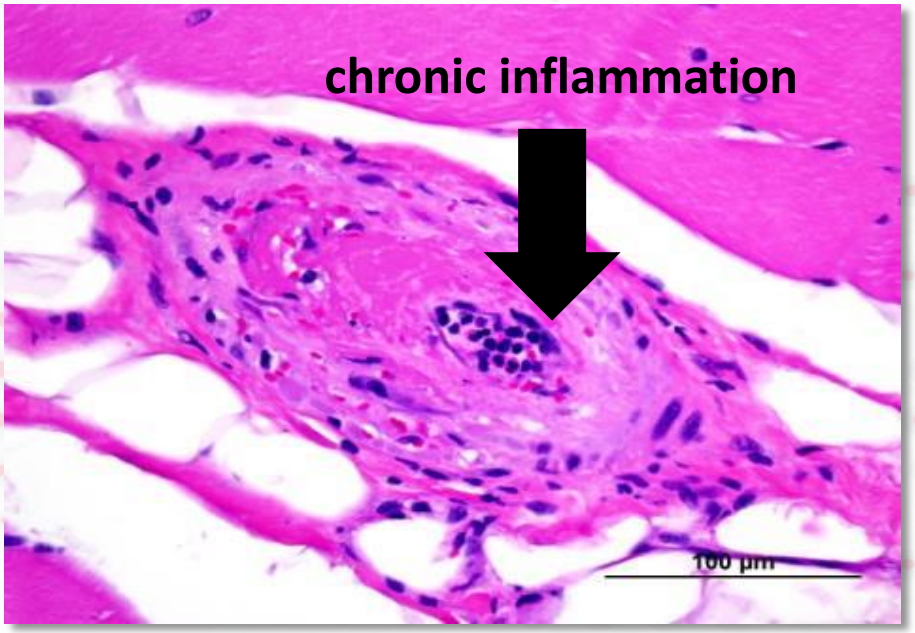


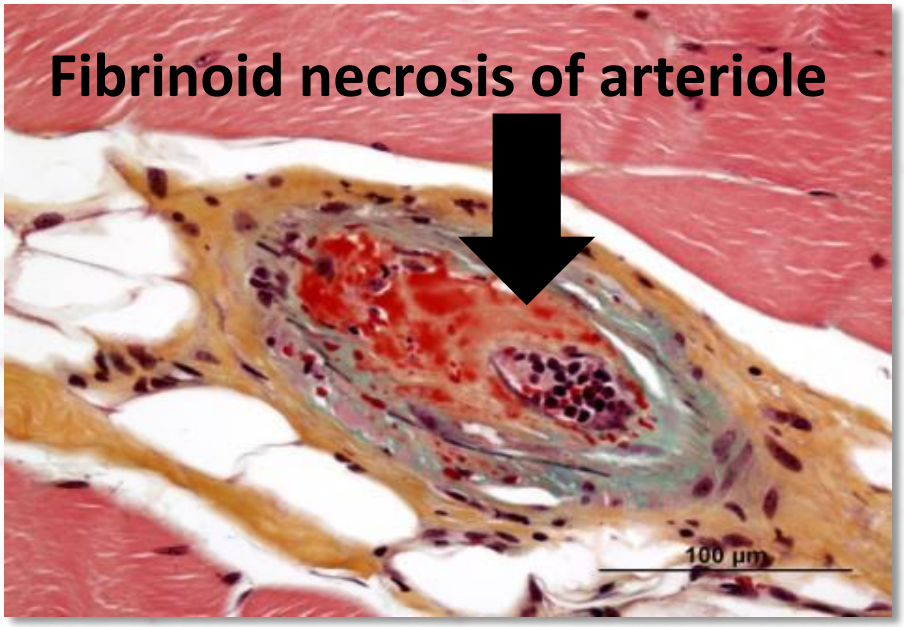
	Survival Treatment	Second Comparative Study		
		IN.PACT (n=12)	Ranger (n=6)	Stellarex (n=6)
Sections with vascular changes in downstream nontarget tissues (%)	28-day (3x)	42.9	25	30

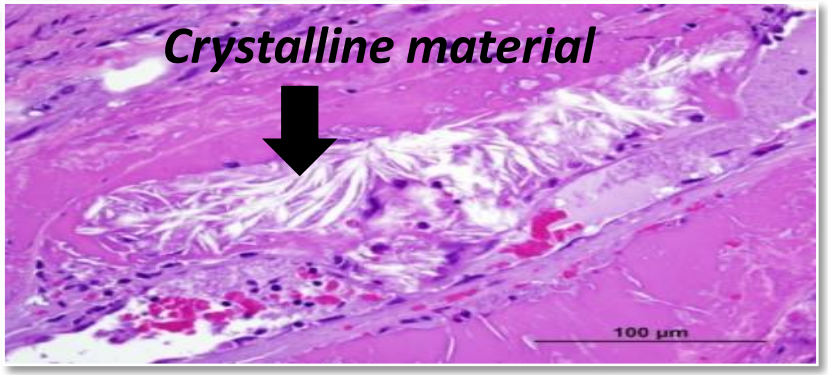
	Survival Treatment	Second Comparative Study					
		IN.PACT		Ranger		Stellarex	
		Skeletal muscle	Coronary band	Skeletal muscle	Coronary band	Skeletal muscle	Coronary band
Paclitaxel concentration in downstream tissues (ng/g)	28-day (3x)	216.5 (326.1-146.2)	911.3 (691.3-1773.8)	91.5 (44.8-116.9)	822.5 (347.9-1450.6)	101.9 (44.6-163.8)	962.3 (149.9-1160)

With the courtesy of Aloke Finn, CVPath institute Gaithersburg, USA

Drug effect : distal PTX effects ?







Kolodgie FD et al. J Vasc Interv Radiol 2016 Sep,27(11), 1676-1685 ; with the courtesy of Aloke Finn, CVPath institute Gaithersburg, USA

What is the clinical relevance of these theoretical findings?

12-Month Key Safety Outcomes

	LEVANT II[1]		Global[2]	IN.PACT SFA[3]	IN.PACT Global				ILLUMINATE			
					Long[4]	CTO[5]	ISR[6]	Clinical[7]	FIH	EU RCT	US Pivotal	Global
	PTA	Lutonix 035		PTA	IN.PACT Admiral							
Subjects	160	316	691	111	220	157	126	131	1406	80	328	300	371
All Thrombosis				3.7% (4/107)	1.4% (3/207)	3.7% (5/134)	4.3% (5/115)	0.8% (1/124)	2.9% (38/1311)				
Revasc. due to Thrombosis	0.7% (1/140)	0.4% (1/285)	1.3% (8/634)										
Major Amputation	0.0% (0/140)	0.3% (1/286)	0.5% (3/635)	0.0% (0/107)	0.0% (0/207)	0.0% (0/134)	0.0% (0/115)	0.0% (0/124)	0.2% (3/1311)	0.0%	0.0%	0.0%	0.3%

1. Rosenfield K, et al. NEJM:373:145-53 (2015).
2. Presented by Laurich C, SVS Chicago 2015.
3. Tepe G, et al. Circ 131:495-502 (2015).
4. Presented by Scheinert D, PCR Paris
5. Presented by Tepe G, Charing Cross London 2016.
6. Presented by Brodmann M, VIVA Las Vegas 2015.
7. Presented by Jaff M, VIVA Las Vegas 2016; includes subjects of imaging cohorts

IN CLAUDICANTS, THERE DOESN'T SEEM TO BE ANY IMPACT ON SAFETY

What is the clinical relevance of these theoretical findings?

Primary IN.PACT DEEP Outcomes

Primary Efficacy	DEB	PTA	p
12-month LLL (mm) [1]	0.61 ± 0.78	0.62 ± 0.78	*0.950*
12-month CD-TLR [2]	9.2% (18/196)	13.1% (14/107)	*0.291*

Primary Safety	DEB	PTA	p
6-month Death, Major Amputation or CD TLR	17.7% (41/232)	15.8% (18/114)	*0.021* (non-inferiority) *0.662 (superiority)*

1. Angio Cohort, Corelab adjudicated. Angiogaphic Imaging 12-month FU compliance = 70.9% (DEB) vs. 71.4% (PTA)
2. Clinically driven TLR of the target lesion in the (major) amputation free surviving subjects at 12 months. "Clinically driven TLR" defined as any TLR of the target lesion associated with: a) deterioration of RC and / or b) Increase in size of pre-existing wounds and / or c) occurrence of a new wound(s), with b) and c) adjudicated by the Wound Healing Core lab

Secondary Safety Outcomes

12-month Safety	DEB	PTA	p
Major Amputation	8.8% (20/227)	3.6% (4/111)	*0.080*
All-Cause Mortality	10.1% (23/227)	8.1% (9/111)	*0.551*
Death and Amputations [1]	35.2% (80/227)	25.2% (28/111)	*0.064*
Death, Major Amp, CD TLR [2]	26.9% (61/227)	23.4% (26/111)	*0.496*
Amputation Free Survival	81.1% (184/227)	89.2% (99/111)	*0.057*
Wound Healing (site reported)	73.8% (121/164)	76.9% (70/91)	*0.579*

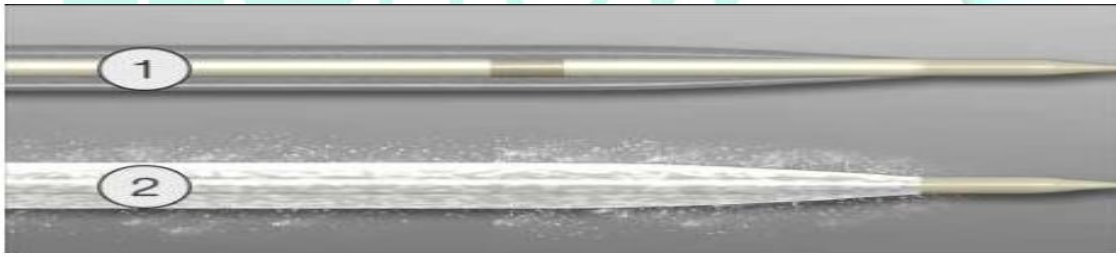
1. Death of any Cause, Major or Minor Amputation of target limb (MAE per protocol)
2. Death of any Cause, target limb Major Amputation and clinically driven TLR

DOES DISTAL DOWNSTREAM PARTICLE EMBOLIZATION IMPACT WOUND HEALING AND COULD IT AFFECT CLINICAL OUTCOMES FOR CLI PATIENTS?

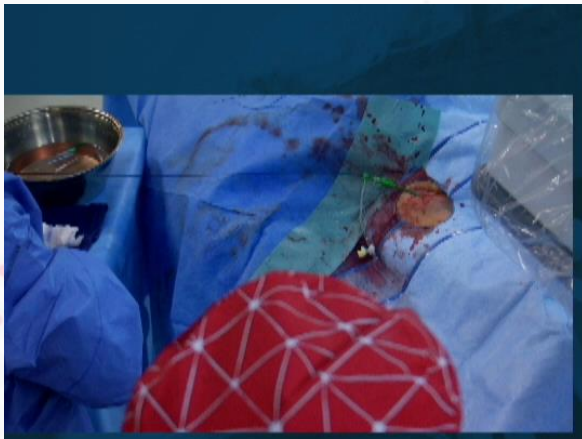
Definitive treatment Legflow (Cardionovum)

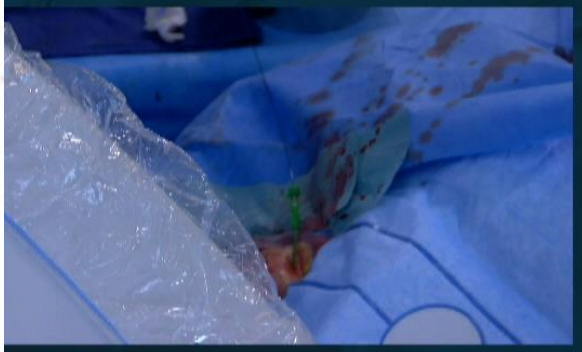
~~MASS EFFECT~~ : nanostructural organization of 0.1µm PTX particles

~~TOXIC EFFECT~~ : SAFEPAX coating technology : hydrophobic during tracking, lipophilic during inflation -> homogenous drug release and wall absorption



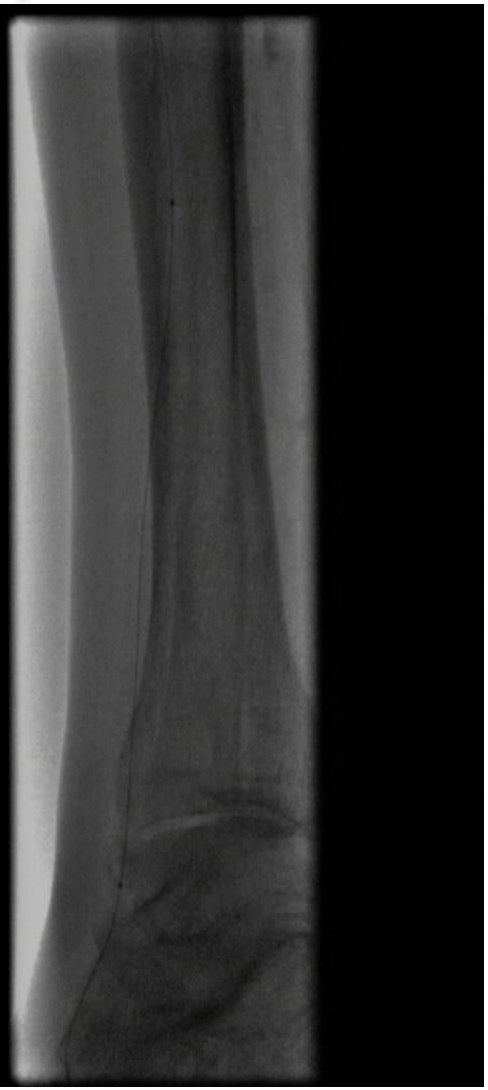
BTK treatment





DEFINITIVE TREATMENT

Legflow 0,014” balloon 3mm-150mm (Cardionovum)



BTK treatment : RESULT

Remaining questions

- More extensive foot arch recanalization?
- Antegrade/retrograde posterior tibial recanalization?
- Routine use of anti spasm medication?
- Role for IVUS
- DCB or just POBA BTK?

Little old lady in no distress anymore!!!

Conclusions

- Downstream PTX particulates is a real phenomenon, present post dilatation with all DCB's, but with clear differences between different brands

- Impact (mass- & toxic effect) of large PTX particles downstream on woundhealing in CLI patients with poor distal vessel run-off is still unknown

- With a third generation of DCB, like the Legflow DCB (Cardionovum), with homogenous PTX release (0.1µm) and efficient SAFEPAX mediated vessel uptake, physicians are feeling more comfortable in treating CLI patients