BUILDING ENDOVASCULAR SYNERGIES

MEET 2015
MULTIDISCIPLINARY EUROPEAN ENDOVASCULAR THERAPY

Recurring in-stent restenosis: what is the best management ?

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Disclosure

Speaker name:

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

Consulting

Abbott, Alvimedica, Bard, Biotronik, Boston-scientific, Cook, Cordis, Gore, Lutonix, Medtronic, Spectranetric

Vessel preparation native vessel

- Necessary for maximum efficiency
- Pre-dilatation and adequate (size and time) inflation
- We have learnt a lot with DEB use
  - Global IM.PACT on SFA
  - Deep IM.PACT on BTK

Vessel preparation native vessel

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DEB IV

In.Pact Deep – What went wrong and why?

Effectivity – angiographic control

12-month Outcomes [1]	DEB	PTA	p
Mean Lesion Length (mm±SD)	59.1 ± 41.7	79.7 ± 74.6	*0.060*
Binary (50%) Rest. Rate (%)	41.0% (25/61)	35.5% (11/31)	*0.609*
Occlusion Rate (%)	11.5% (7/61)	16.1% (5/31)	*0.531*
Longitudinal Restenosis (%) [2]	62.7 ± 56.2	93.2 ± 60.8	*0.167*

Revalidated Lumen Loss [3]	DEB	PTA	p
12-month LLL (mm, mean ± SD)	0.51 ± 0.66	0.60 ± 0.97	*0.654*

- Problem of the control group: Only 35% restenosis after 12 months = best data ever reported
- Qualtity of angiograms good enough to detect a difference of 0.2 mm?
  - bad flow in BTK arteries
  - CLI patients with slow run-off + no artefact free image
- Selection of the angiographic cohort

Vessel preparation native vessel

Use the correct technique!

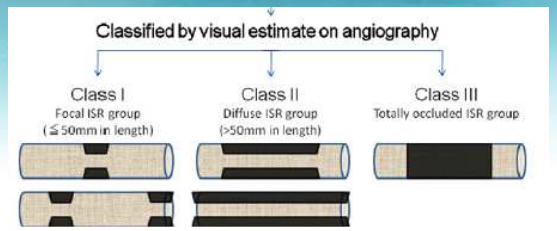
	Inflation Time (sec)		
	30	180	*P* Value
Major dissection (grades 3 and 4)	16	5	.010
Minor or no dissection (grades 1 and 2)	21	32	.010
Further interventions	20	9	.017
Stent	4	1	
Further dilation (prolonged dilation, dilation with larger diameter)	16	8	
Residual stenosis (>30%)	12	5	.097
Complication (embolization, thrombosis)	1	1	
Mean ankle-brachial index (before, after intervention)	0.66, 0.87	0.65, 0.84	

Prolonged inflation (180 sec) improves the immediate result of BTK angioplasty compared to short dilatation times (30 sec)

Significantly fewer major dissections and a modest reduction of residual stenoses are observed

Zorger et al. 2002. *J Vasc Interv Radiol*

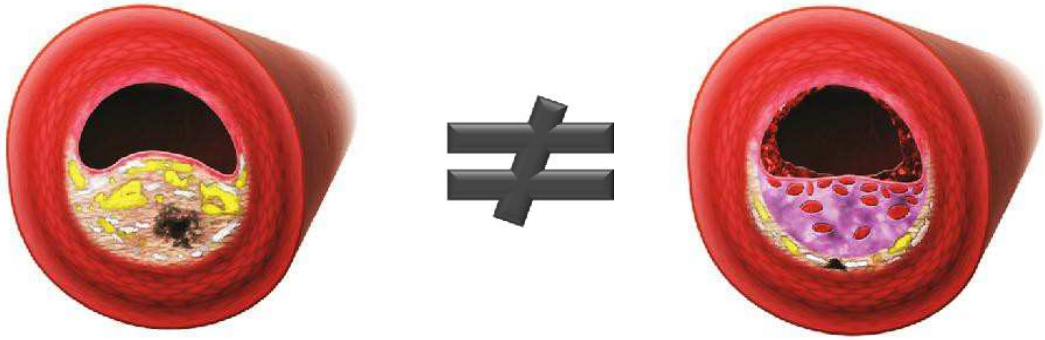
Vessel preparation for ISR



- Does it really exist ?
- PTA: very bad results (TOSAKA III ++++)
- Cutting Balloon : poorly reported
- New stent ? DES ?
- Debulking : not adapted or any recommendation for use
- Laser excimer : FDA approval after EXCITE study

de novo Atherosclerosis v. Restenosis

Morphologically, *de novo* atherosclerosis is distinct from restenosis of peripheral arteries.



ATHEROSCLEROSIS —

Complex, heterogeneous morphology with areas of compact calcium.[1]

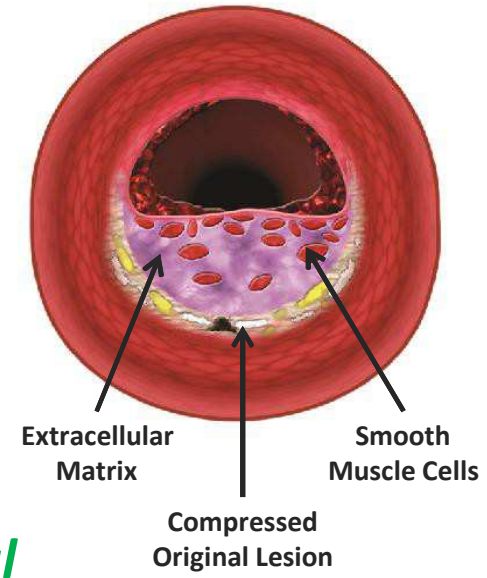
RESTENOSIS —

Soft, aqueous neointimal hyperplasia tissue, with areas of thrombus. [2,3]

1. Thompson and Towler (2012). Nature Reviews. 8: 529-543
2. Soor et al. (2008). Pathology. 40(4): 385-391
3. Amann, Kerstin (2008). Clin J Am Soc Nephrol. 3:1599-1605.

UNIQUE COMPOSITION OF RESTENOTIC LESIONS

- **Extracellular matrix dominant player in NIH**
  - Contributes to 60-80% of restenotic volume
  - Determines the mechanical characteristics of the lesion
  - **Highly-compliant**, soft and aqueous structure
    - Smooth muscle cells initially migrate and propagate into intima
    - Produce and recruit proteoglycans and collagen
      - Increased concentration of hydrophilic elements
      - Contribute considerably to water content and volume of lesion



Removal of ECM and its components is critical in the regression of the lesion

- Brodmann M et al. (2013). Cardiovasc Intervent Radiol. 36: 69-74
- Dieter RS and Larid JR. (2004). Endovasc Today. Oct: 36-38
- Iijima R et al. (2004). Heart. 90: 1071-1072
- Kenagy RD et al. (2005). J Histochem Cytochem. 53(1): 131-140
- Simon, Daniel

TREATMENT IMPLICATIONS: *ANGIOPLASTY*

- Angioplasty is largely ineffective in restenotic NIH tissue.

– Balloon inflation squeezes water content out of aqueous ECM.

  – Upon deflation and removal, the lesion rehydrates within 100 mins
    - ***'Acts like a sponge'***

– Acute, immediate restenosis development

- Future role of Drug-Eluting Balloons + Debulking?

- Iijima R et al. (2004). Heart. 90: 1071-1072
- Singh S et al. (2013). Endovasc Today. Aug: 36-39
- Laird JR et al. (2010) Circ Cardiovasc Interv. 3: 267-276
- Mauradin GSR et al. (2001). Radiology. 10: 288-297
- Micardi A et al. (2013). Endovasc today. Aug: 50-53

TREATMENT IMPLICATIONS:

MECHANICAL ATHERECTOMY

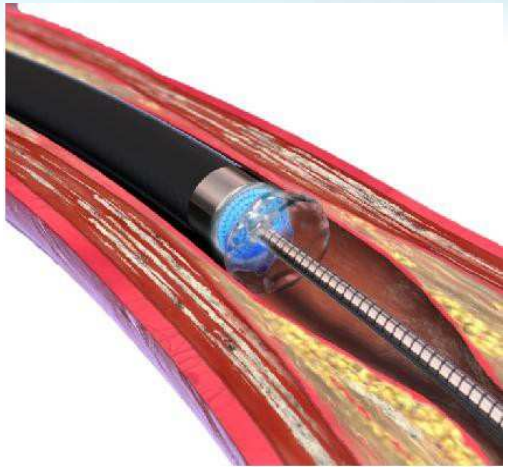
- Mechanical Atherectomy relies upon differential hardness of lesion
  - *Neointimal tissue is soft & aqueous*
  - ***Cannot effectively cut/sand***[1-4]
  - ***'Spinning in mud'***

- Clinically demonstrated to be less effective in restenotic lesions[1]
  - 12mo TLR 44% vs. 16% in de novo
  - Predictor of TLR at 1 year
- Risk embolization from displacement of soft NIH material[4]
  - Restenotic lesions have significantly higher risk (15x) of embolization
  - SilverHawk was associated with a significant increase in clinically significant distal embolization
    - 31-fold higher chance of distal embolization compared to PTA

1. Brodmann M et al. (2013). Cardiovasc Intervent Radiol. 36: 69-74
2. Shammas NW et al. (2013). 2013 TCT Abstracts: TCT-539.
3. Shammas NW et al. (2012) Cardiovasc Revasc Med. 13:224-227
4. Shammas NW et al. (2008) J Endovasc Ther. 15: 270-276

TREATMENT OF RESTENOSIS WITH LASER

- Laser highly absorptive in the unique aqueous morphology of NIH
  - Extracellular matrix, smooth muscle cells, collagen and thrombus



- Photoablation **vaporizes** NIH material, debulking the restenosis
  - Without mechanical components that could tear or shear the easily fragmented structure
  - Reducing embolic potential

ATHERECTOMY DEVICE CHOICES

Mechanical Atherectomy

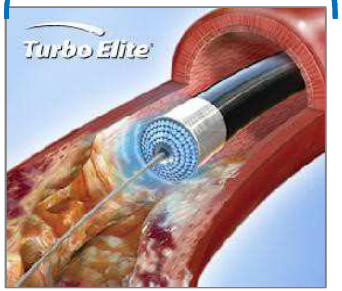
Directional

Orbital

Rotational

Reliant upon **DIFFERENTIAL HARDNESS** of lesion to ***cut, scrape or sand*** hardened, calcific atherosclerotic lesions

Laser Atherectomy



Laser

VAPORIZES the full-spectrum of PAD lesion morphologies

IMAGES: http://www.ev3.net/peripheral/us/plaque-excision/turbohawk.htm, http://www.medgadget.com/2009/12/pathway_medicals_peripheral_plaque_drill_gets_510k_classification.html

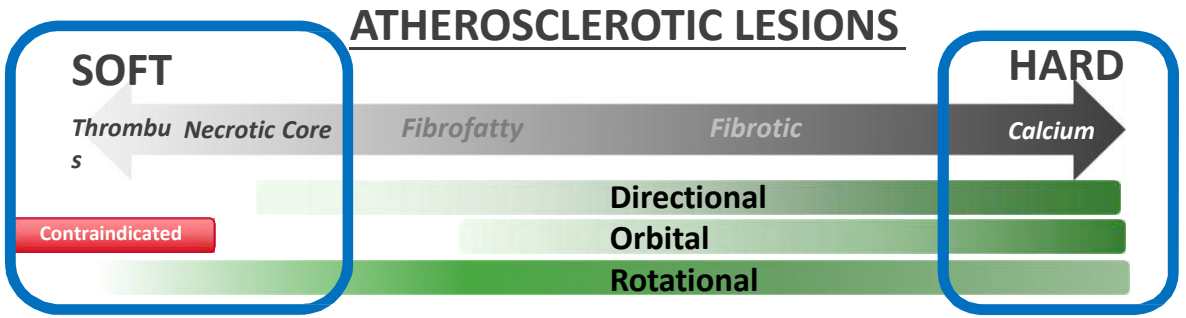
MECHANICAL ATHERECTOMY DEVICES

Directional

Orbital

Rotational

Less effective or contraindicated in softer morphologies[1-3]



Because mechanical devices rely upon cutting, scraping or sanding, ideal for hard, calcific lesions

Mechanical devices relying upon the differential hardness of plaques may not effectively remove soft, aqueous restenotic tissue[1-3]

1. Brodmann M et al. (2013). Cardiovasc Intervent Radiol. 36: 69-74.
2. Shammas NW et al. (2013). 2013 TCT Abstracts: TCT-539. Shammas
3. NW et al. (2012). Cardivasc Revasc Med. 13: 224-27.

IMAGES: http://www.ev3.net/peripheral/us/plaque-excision/turbohawk.htm, http://www.medgadget.com/2009/12/pathway...html

MECHANICAL VS. LASER ATHERECTOMY

Effectiveness of Different Types of Atherectomy Devices for Treating Forms of Plaque Composition and Thrombus

Atherectomy Device	Thrombus	Soft Plaque	Mild Calcification	Moderate Calcification	Severe Calcification
Excimer Laser	+ +	+ +	+ +	+ +	+ +
Diamondback	– –	+	+ +	+ +	+ +
TurboHawk	– –	+ +	+ +	+ +	+
Jetstream	+ +	+ +	+ +	+	+
Phoenix	– –	+ +	+ +	+	+

+ + Very Effective, + Effective, – Less Effective, – – Ineffecti

This table modified from Mustapha EVT 2011, and represents the opinions of the author based on personal experience and does not necessarily reflect data from clinical

http://evtoday.com/pdfs/EVT1011_feature_mustapha.pdf

LASER EXCIMER

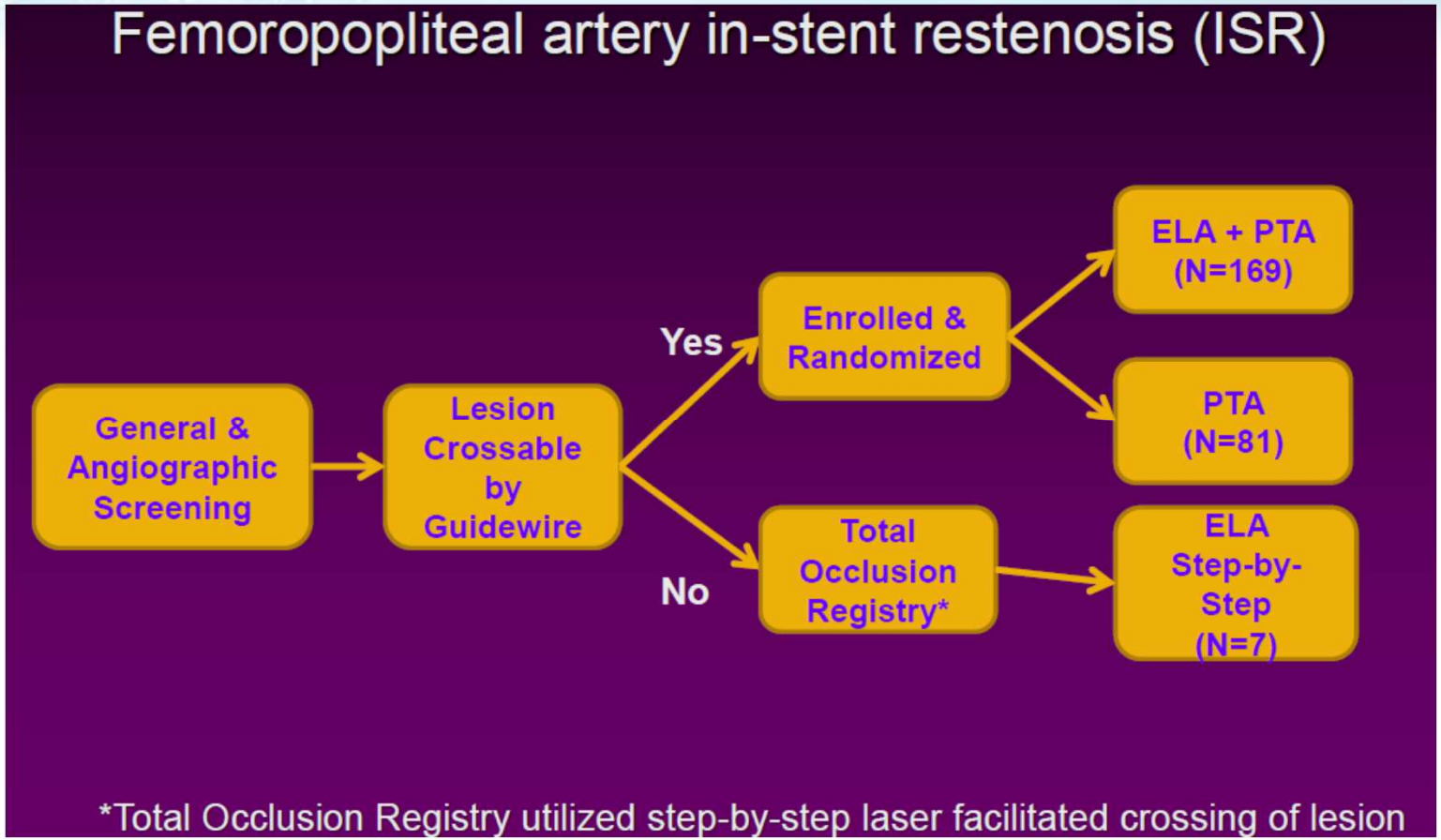
- Debulking with fibrotic pulverisation
  - Reduce the residual ISR
  - May progress into long occlusion
  - Avoid immediat recoil we observe in TOSAKA III
  - Fibrotic residual lesion after LASER ablation is smoother and adequate for final remodelling

LASER EXCIMER

EXCITE ISR

- RCT with 35 sites
- Randomization 2:1
- ISR- PTA Vs Laser + PTA
- 250 Pt included

LASER EXCIMER
EXCITE ISR
study design



LASER EXCIMER
EXCITE ISR
primary endpoints

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- Primary Safety Endpoint
  - Major Adverse Events through 30 days:
    - Death
    - Unplanned Major Amputation
    - Target Vessel Revascularization (TLR)
- Primary Efficacy Endpoint
  - Freedom from clinically driven TLR at 6 months

LASER EXCIMER
EXCITE ISR
demographic data

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	ELA + PTA (N=169)	PTA Alone (N=81)	P-value
Age (mean)	68.5	67.8	0.60
Male	62.7 %	61.7 %	0.89
Hypertension	95.8 %	93.8 %	0.53
Hyperlipidemia	96.4 %	95.0 %	0.73
Diabetes Mellitus	47.0 %	47.5 %	1.00
CAD	64.3 %	68.8 %	0.57
Previous ISR	32.5 %	29.6 %	0.77
Smoking	75%	91.3%	0.05
Rutherford Class			0.54
1	3.0%	3.7%	
2	18.9%	14.8%	
3	62.1%	69.1%	
4	15.4%	11.1%	
5	0.6%	0.0%	
6	0.0%	0.6%	

LASER EXCIMER
EXCITE ISR
angiographic core lab assessment

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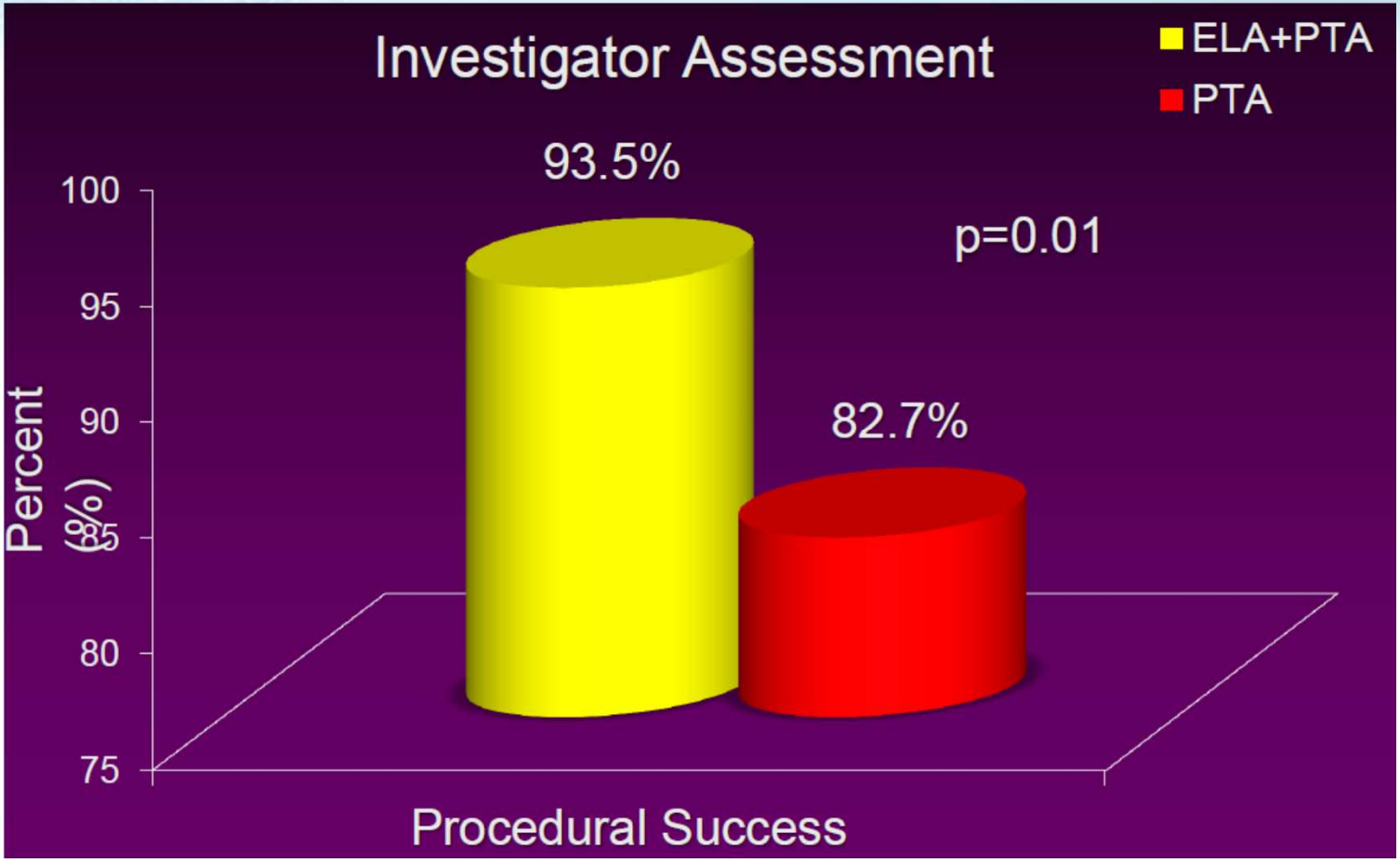
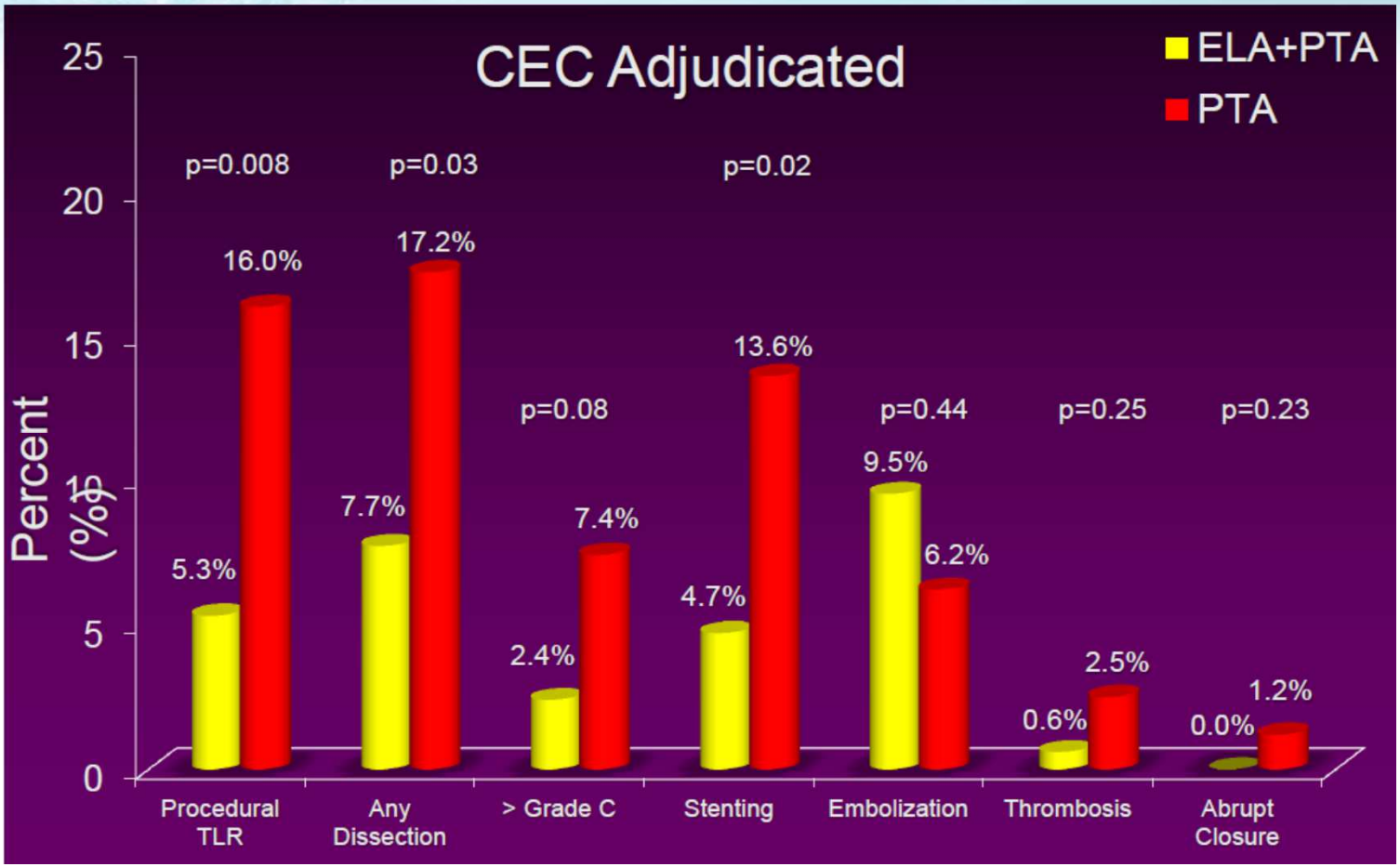
	ELA + PTA (N=169)	PTA Alone (N=81)	P-value
Mean Lesion Length (cm)	19.6	19.3	0.85
Diameter Stenosis (%)	81.7%	83.5%	0.42
Popliteal Lesion	21.3%	23.4%	0.93
Total Occlusion	30.5%	36.8%	0.37
Calcium (Mod/Sev)	27.1%	9.1%	0.005
Stent Fracture			0.16
0	85.8%	95.8%	
1	5.0%	0.0%	
2	6.4%	4.2%	
3	2.1%	0.0%	
4	0.0%	0.0%	
5	0.7%	0.0%	

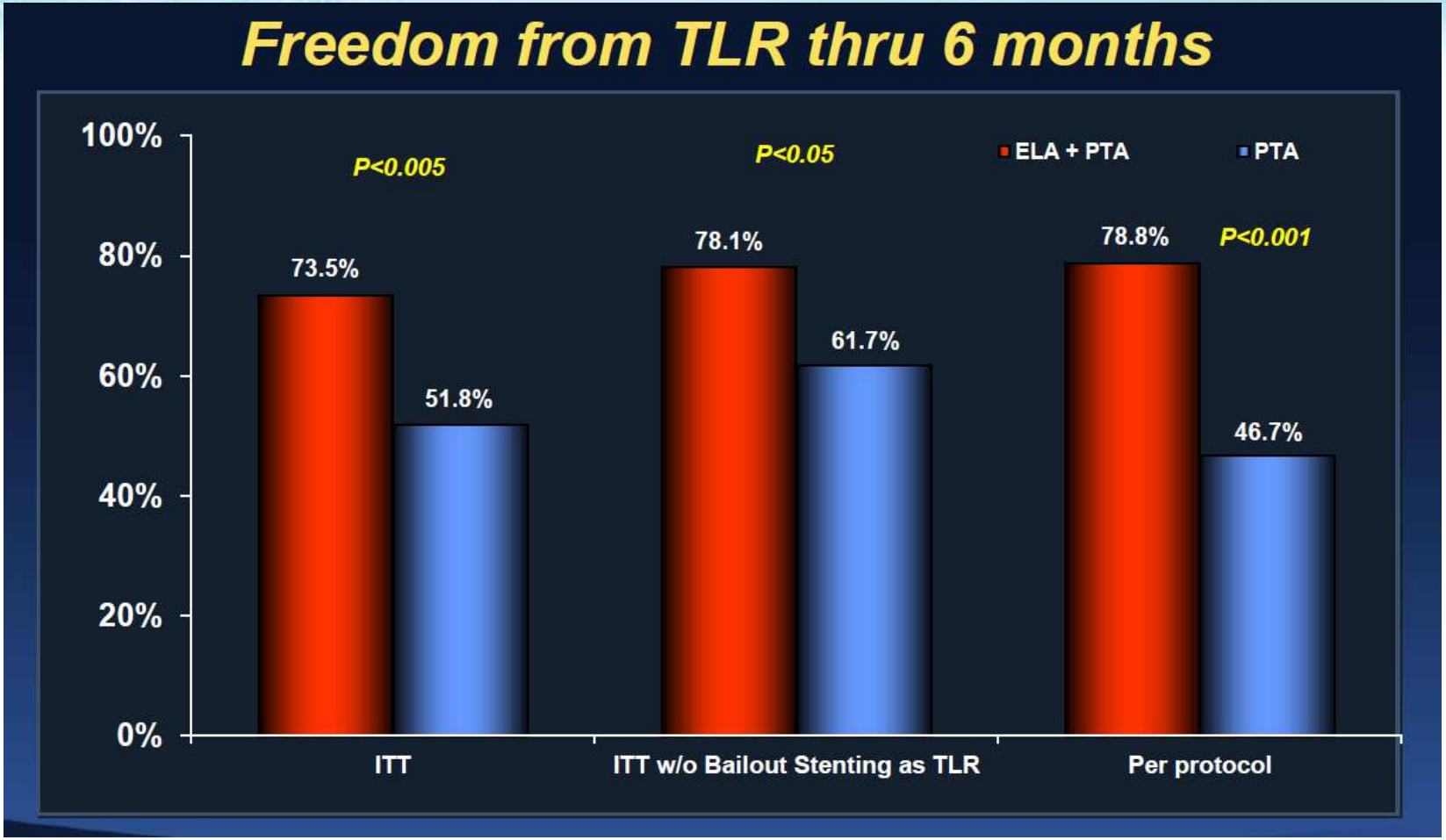
LASER EXCIMER
EXCITE ISR
technical success



LASER EXCIMER
EXCITE ISR
procedural complications



LASER EXCIMER
EXCITE ISR
freedom from TLR



LASER EXCIMER
EXCITE ISR
lesion length and TLR

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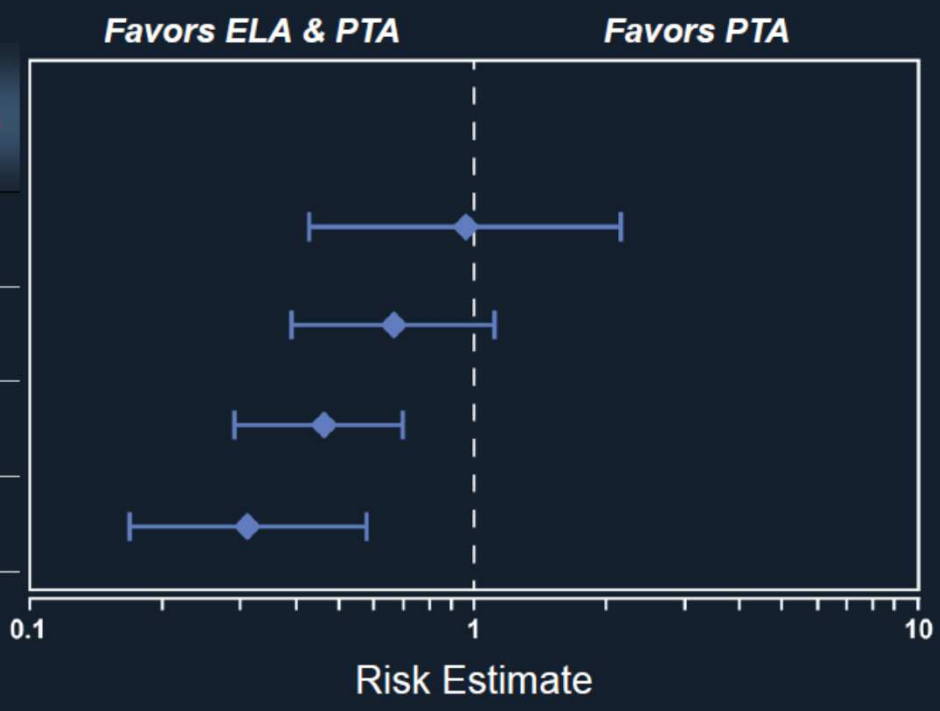
Variable (Lesion Length)	Estimate	Lower CL	Upper CL
5 cm	0.96	0.43	2.14
15 cm	0.66	0.39	1.12
25 cm	0.46	0.29	0.70
35 cm	0.31	0.17	0.58

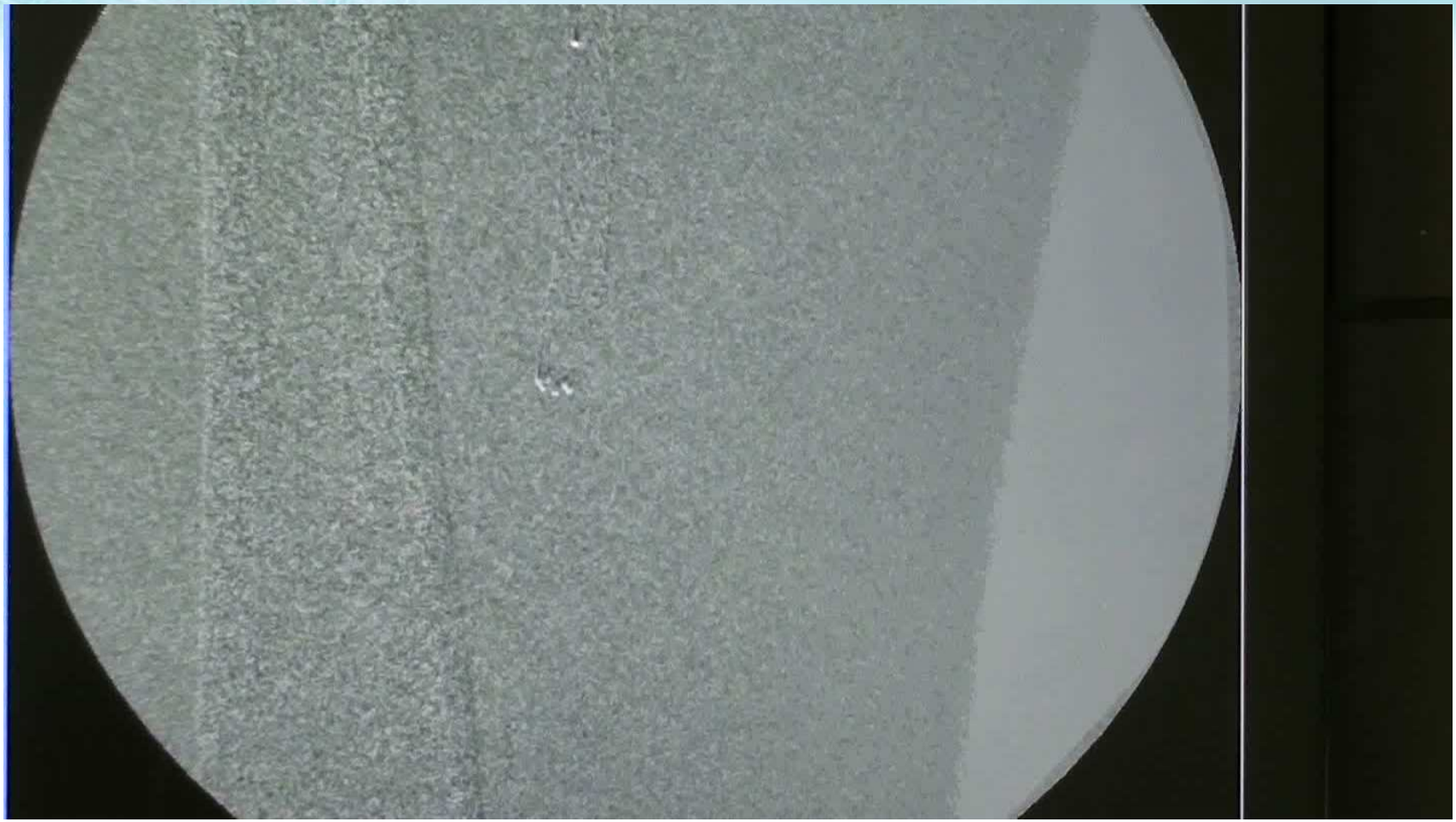


LASER EXCIMER

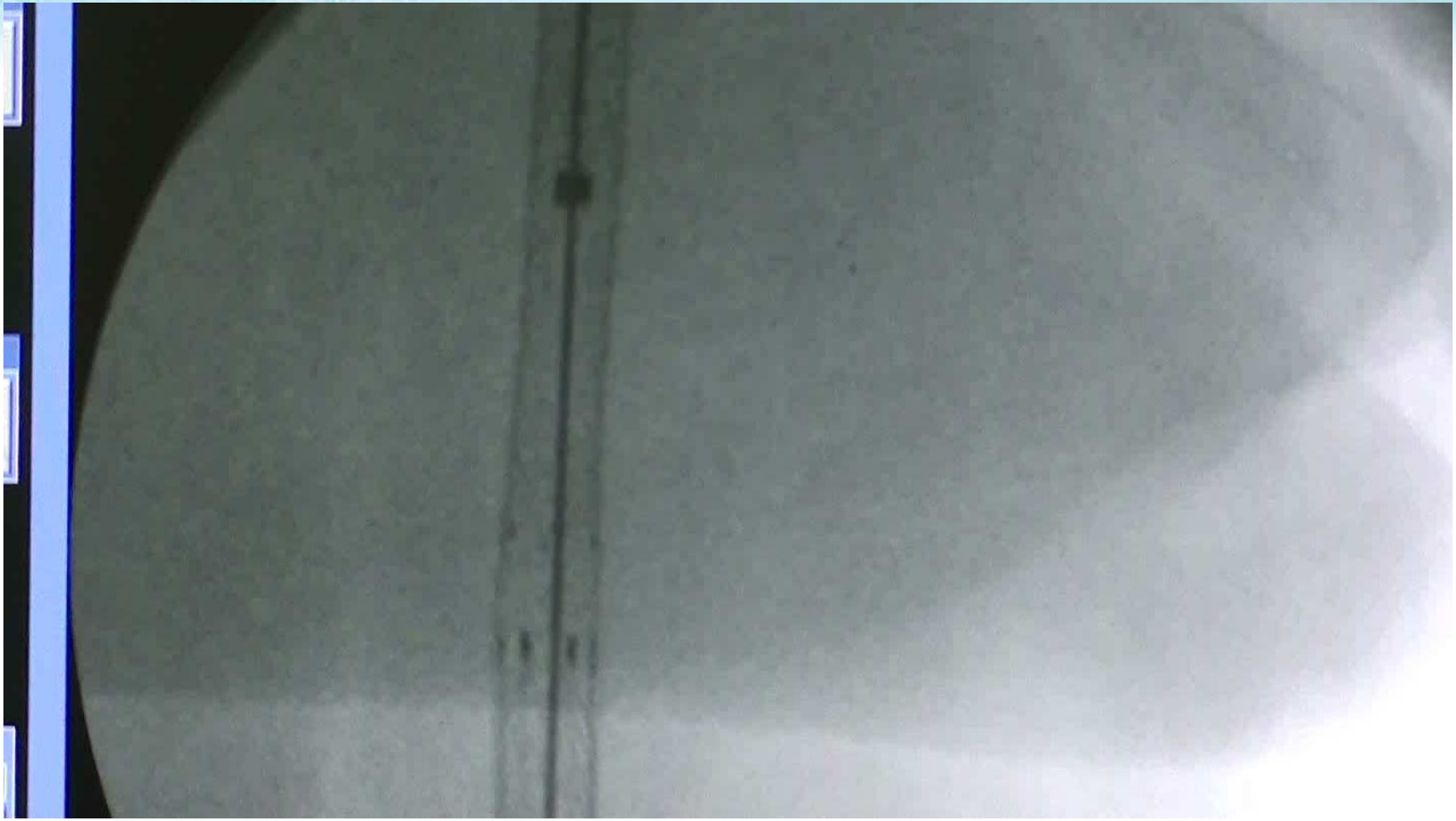
- Case: lady 62 years
- SFA recanalisation 16 months ago
- ISR after 10 months
- ISR inflation using PTA 12 months
- New symptomatic ISR (90-95%) on duplex investigation

Clinical case

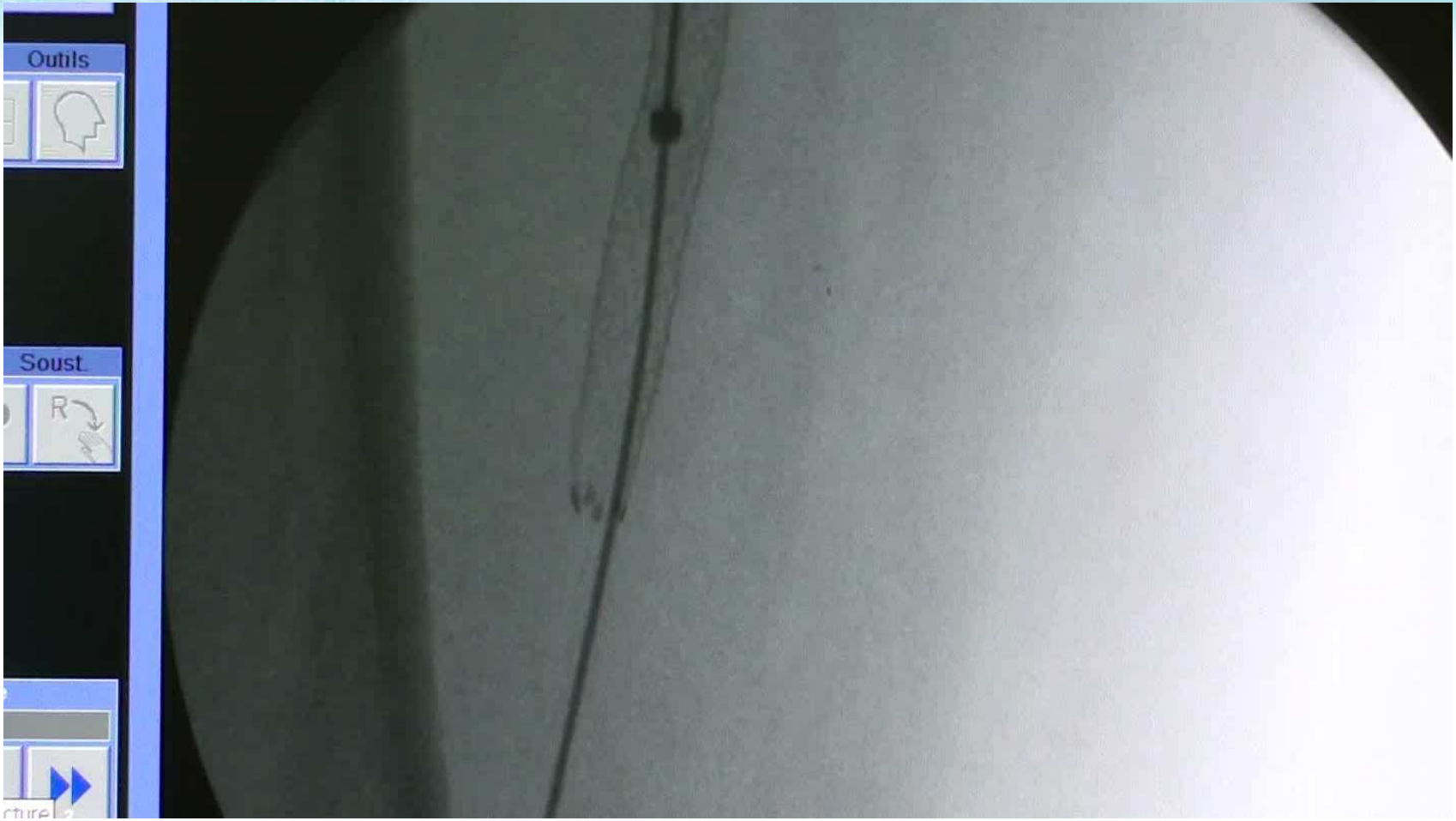
Clinical case



Clinical case



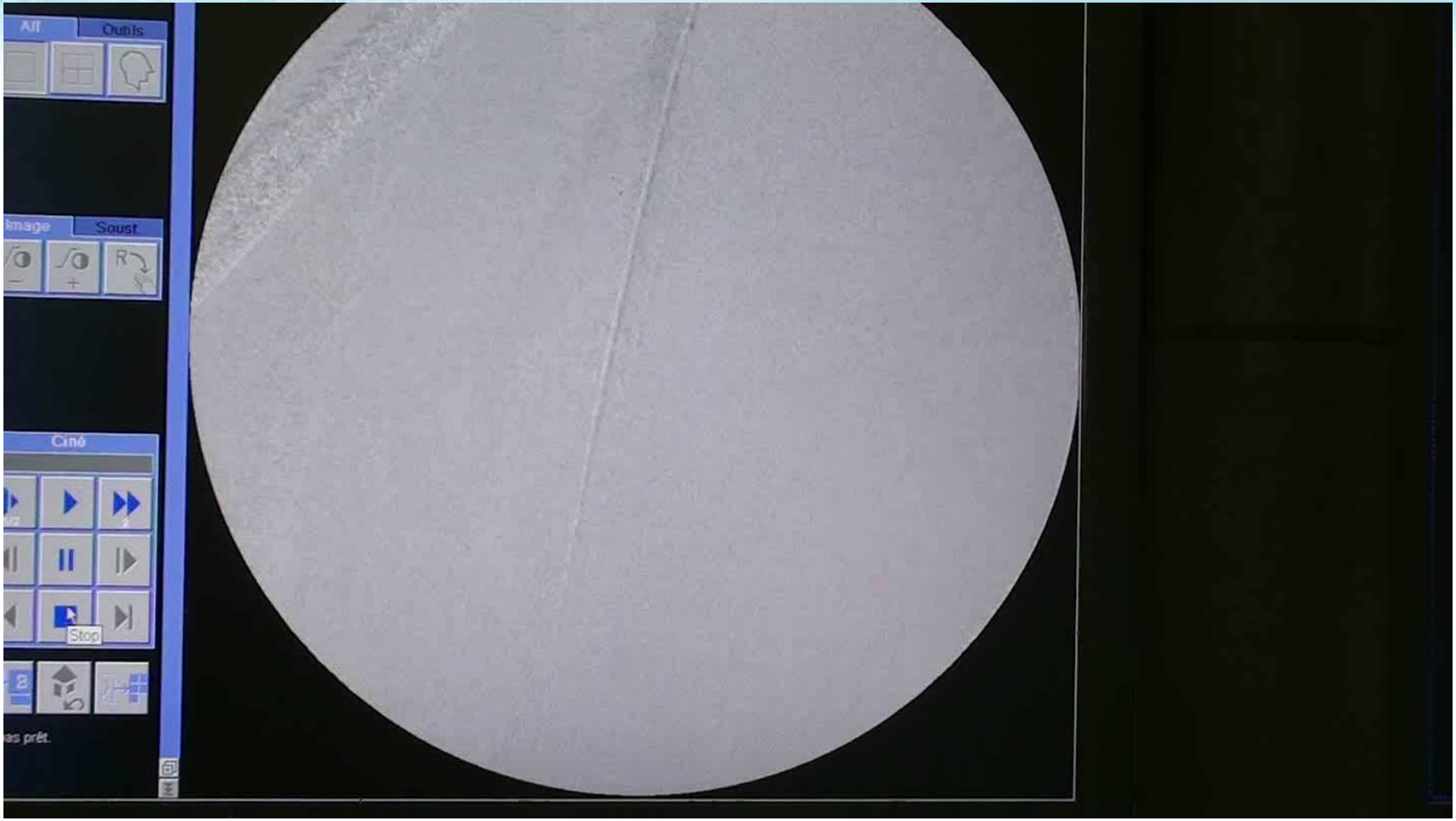
Clinical case



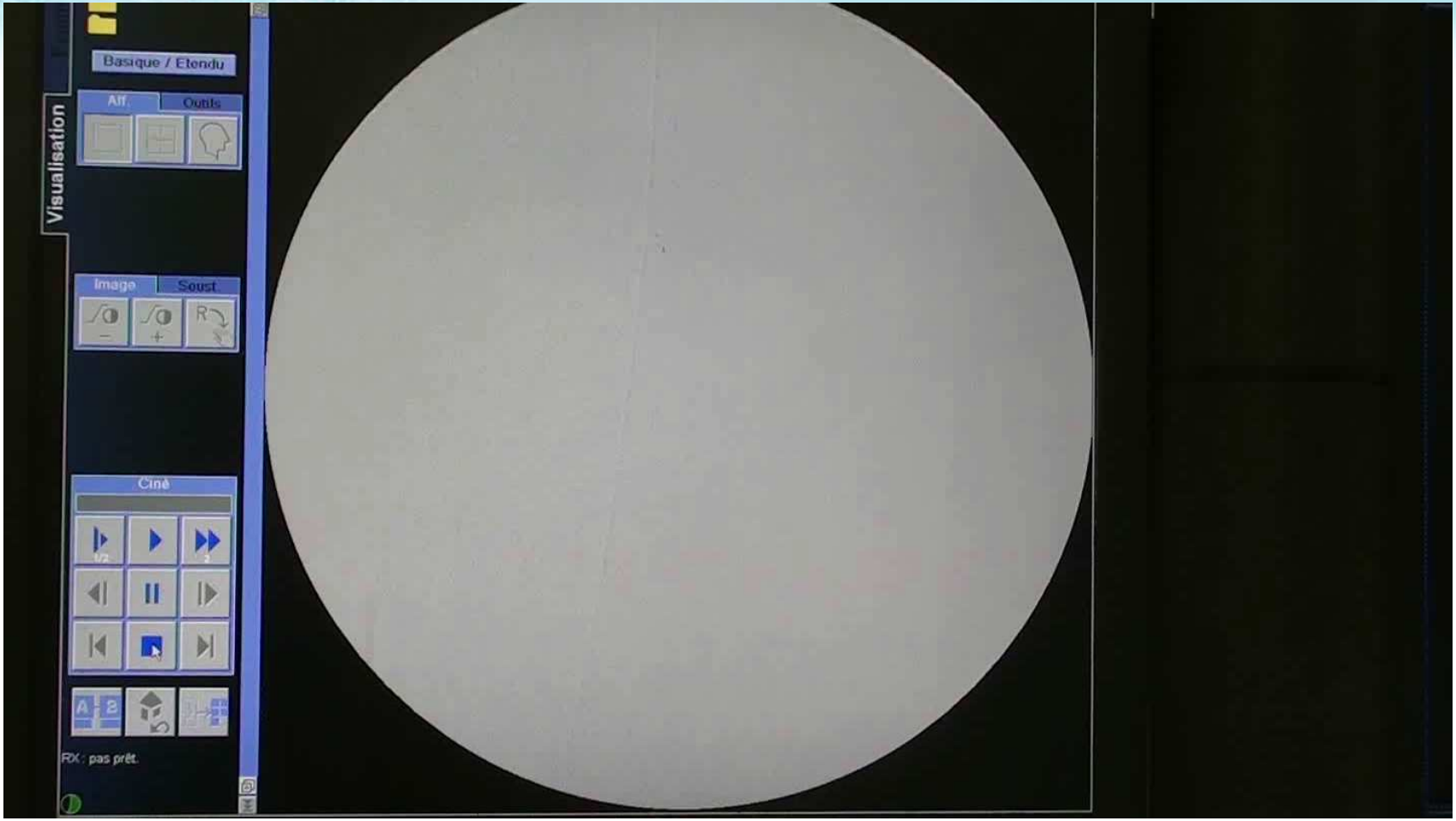
Clinical case

Clinical case

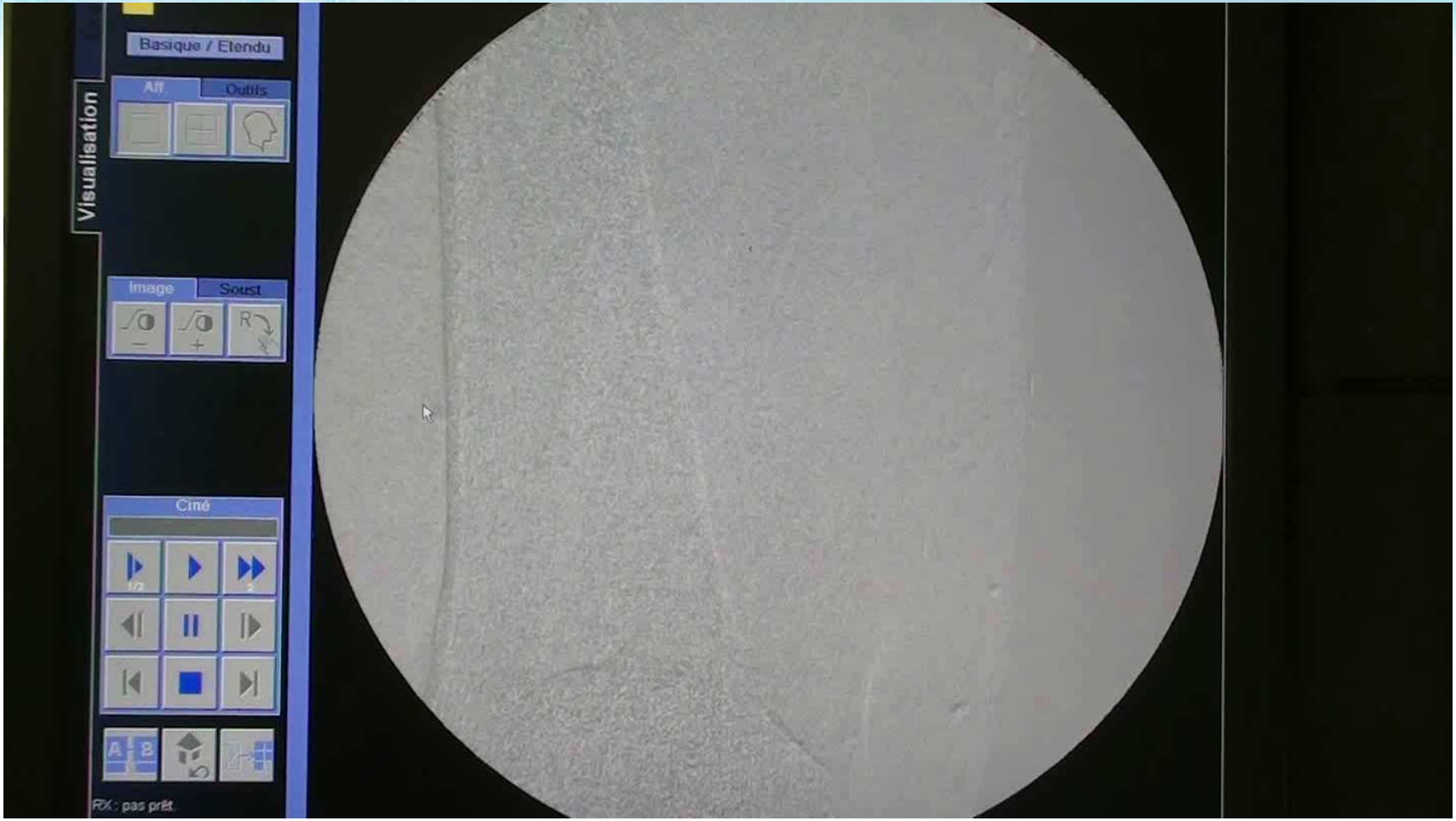
Clinical case



Clinical case



Clinical case



CONCLUSION

- Vessel preparation is the key for native vessels and moreover for ISR
- We have now dedicated tools
- Perfect protocol need to be clarified
  - **INTACT** RCT: PTA/DCB/Laser + DCB
  - 246 Pt – 18 Months FU- clinical + economical evaluation
- Endovascular treatment is progressing also in terms of FU and durability