ICCA STROKE 2019

WIST

How to treat restenosis after carotid artery stenting

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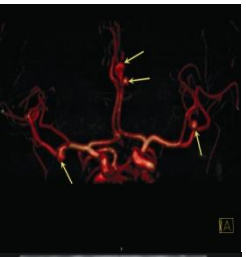
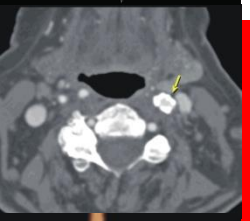
DISCLOSURE STATEMENT OF FINANCIAL INTEREST

AFFILIATION/FINANCIAL RELATIONSHIP	COMPANY
Grant/Research Support	
Consulting Fees/Honoraria	
Major Stock Shareholder/Equity	Company: Balton, Boston, Medtronic, Abbott
Royalty Income	
Ownership/Founder	
Intellectual Property Rights	
Other Financial Benefit	

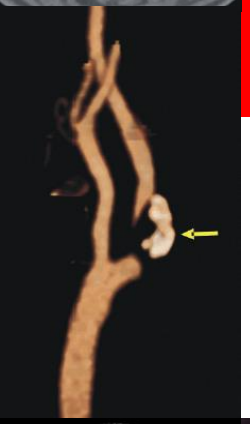
The Krakow Program of Stroke Prevention by Carotid Artery Stenting (from Jan 2001)



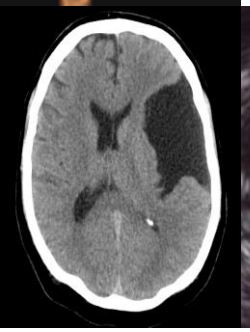
- comprehensive patient evaluation including non-invasive imaging:
  - extra- and intracranial Doppler
  - extra- and intracranial CT angio
  - brain perfusion (MRI)

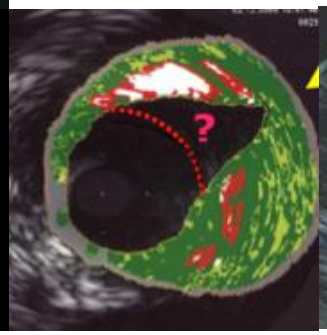


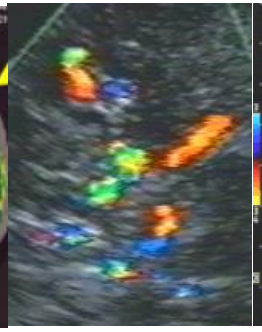
3750 CAS procedures in a single Krakow Center

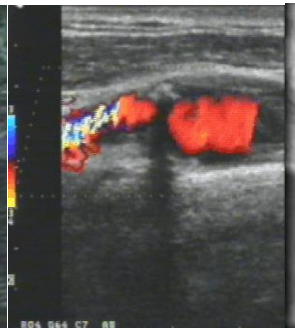


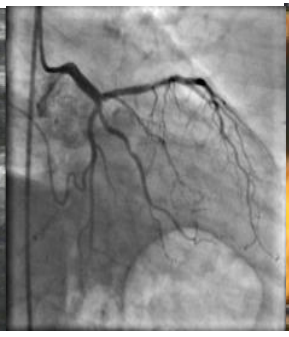
- coronary angiography prior to CAS (except pts. after CABG or recent PCI)
- rigorous follow-up

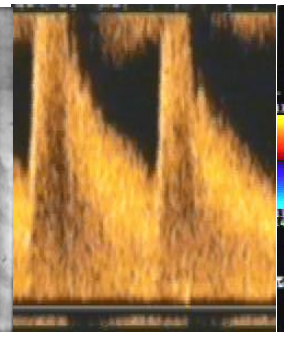


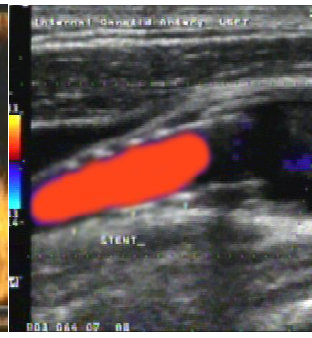






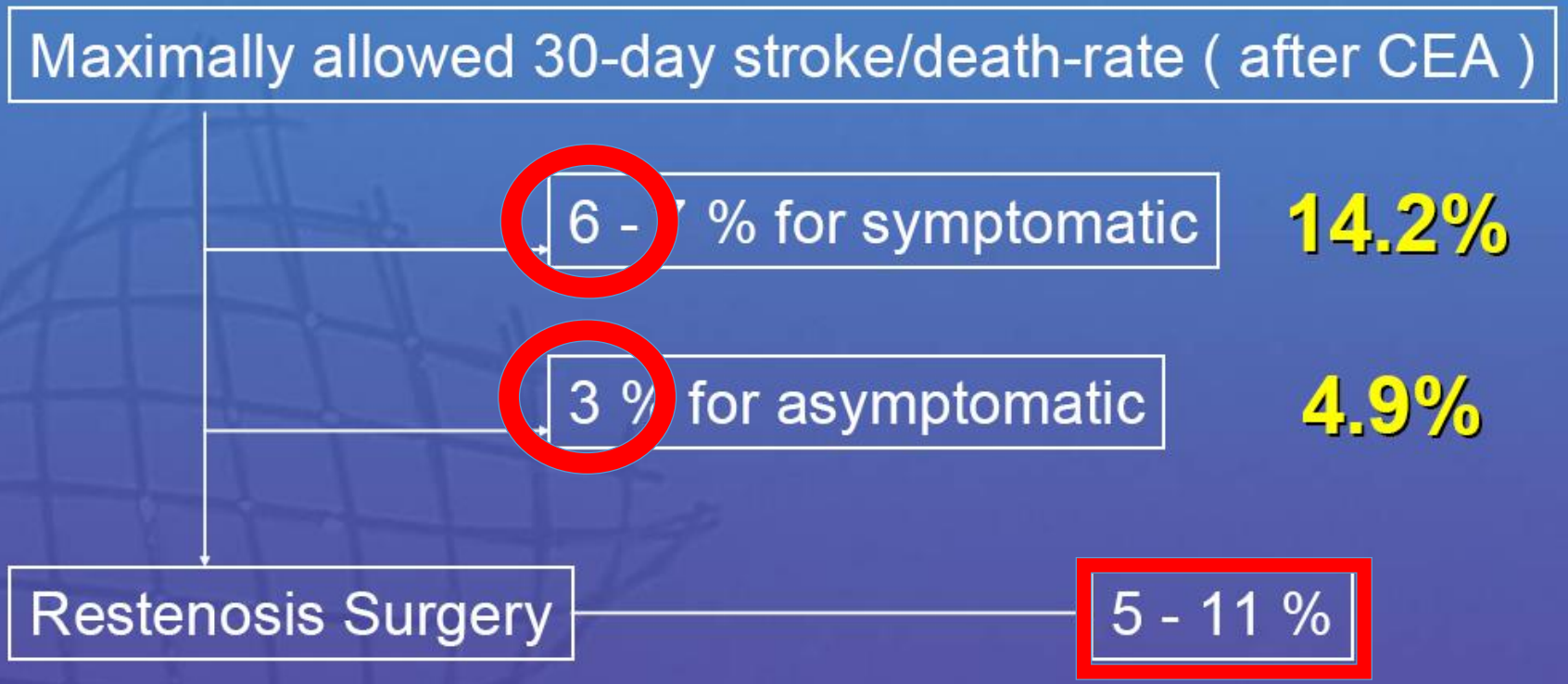






Comparison with CEA recommendation

Ad Hoc Committee, American Heart Association



Moore et al. Stroke 1995;26:188-201.

In-stent restenosis after carotid stenting is not a trivial problem as it still exists.

Occurs much less frequently than in subclavian, vertebral, renal or peripheral arteries.

Is definitely less frequently than restenosis after carotid endarterectomy.

10% restenosis according guidelines is completely not acceptable.

Treatment modality in-stent restenosis is still evolving.

Re- PTA for in-stent restenosis always needs temporary NPD.

In recurrent in-stent restenosis of-label devices needs to be used.

Rigorous US investigation in such patients is mandatory.

J Endovasc Ther. 2009 Aug; 16(4): 397–409.
Published online 2009 Aug 1. doi: 10.1583/08-2685.1
PMCID: PMC5621710
PMID: 19702339

Carotid Revascularization Using Endarterectomy or Stenting Systems (CaRESS): 4-Year Outcomes

Christopher K. Zarins, MD,[1] Rodney A. White, MD,[2] Edward B. Diethrich, MD,[3] Rebecca J. Shackelton, MSc,[4] and Flora S. Siami, MPH[4]

Conclusion:

The risk of death or nonfatal stroke 4 years following CAS with distal protection is equivalent to CEA in a broad category of patients with carotid stenosis. There were no significant differences in stroke or mortality rates between high-risk and non–high-risk patients and no differences in outcomes between symptomatic and asymptomatic patients. After 4 years, CAS had a 2-fold higher restenosis rate compared to CEA. The

Baseline Characteristics of the 184-Patient CMS-Defined High-Risk Subset by Treatment Arm

Caucasian	102 (95.3%)	71 (92.2%)	0.379
Clinical status			
Symptomatic	33 (30.8%)	18 (23.4%)	0.264
Asymptomatic	74 (69.2%)	59 (76.6%)	
Percent stenosis			
50%–75%	11 (10.3%)	1 (1.3%)	0.015
>75%	96 (89.7%)	76 (98.7%)	
Etiology of carotid disease			
Atherosclerosis	93 (86.9%)	58 (75.3%)	0.043
Restenosis	1 (0.9%)	24 (31.2%)	<0.001
Radiation	1 (0.9%)	1 (1.3%)	0.814

J ENDOVASC THER
2010;17:271–272

◆ LETTER TO THE EDITORS

Piotr Musialek, MD, DPhil
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Restenosis After Carotid Artery Stenting Versus Endarterectomy: The Jury is Still Out!

To the Editors:

"...after 4 years, CAS had a 2-fold higher restenosis rate compared to CEA"[1] —if taken in isolation from the baseline characteristics of the CaRESS study groups—might inadvertently fuel the (unproven) notion that "CAS is associated with a restenosis rate higher than CEA."

There were 24 (31.2%) postsurgical restenotic lesions in the CAS arm and only 1 (0.9%) postsurgical restenotic lesion in the CEA arm in the high-risk subset of 184 CaRESS patients ($p<0.001$).[1] There is little

are treated with CAS. Evidence indicates, however, that post-CEA stenosis is an independent risk factor for in-stent restenosis after subsequent CAS[2] (risk increase by 4.28-fold, $p=0.008$).[3] For this reason,[2,3] the high proportion of "baseline" post-CEA restenotic lesions in the CAS arm of CaRESS is likely to have driven (and can explain the finding of) an apparently higher CAS restenosis rate in

never compare incomparable groups.

- it's easy to get compromising conclusions!!!

Treatment modality of in-stent restenosis

Balloon angioplasty only with bigger diameter

Cutting Balloon

Second self expanding stent (stent in stent technique)

Drug eluting balloon (problem with 45 sec inflation)

Self expanding sirolimus coronary stent – STENTYS X position

Surgery should be avoided !!!!

KRAKOW INSTITUTION (3250 index CAS procedures)

Excluded: ostial RCCA & LCCA – (balloon expandable stents)

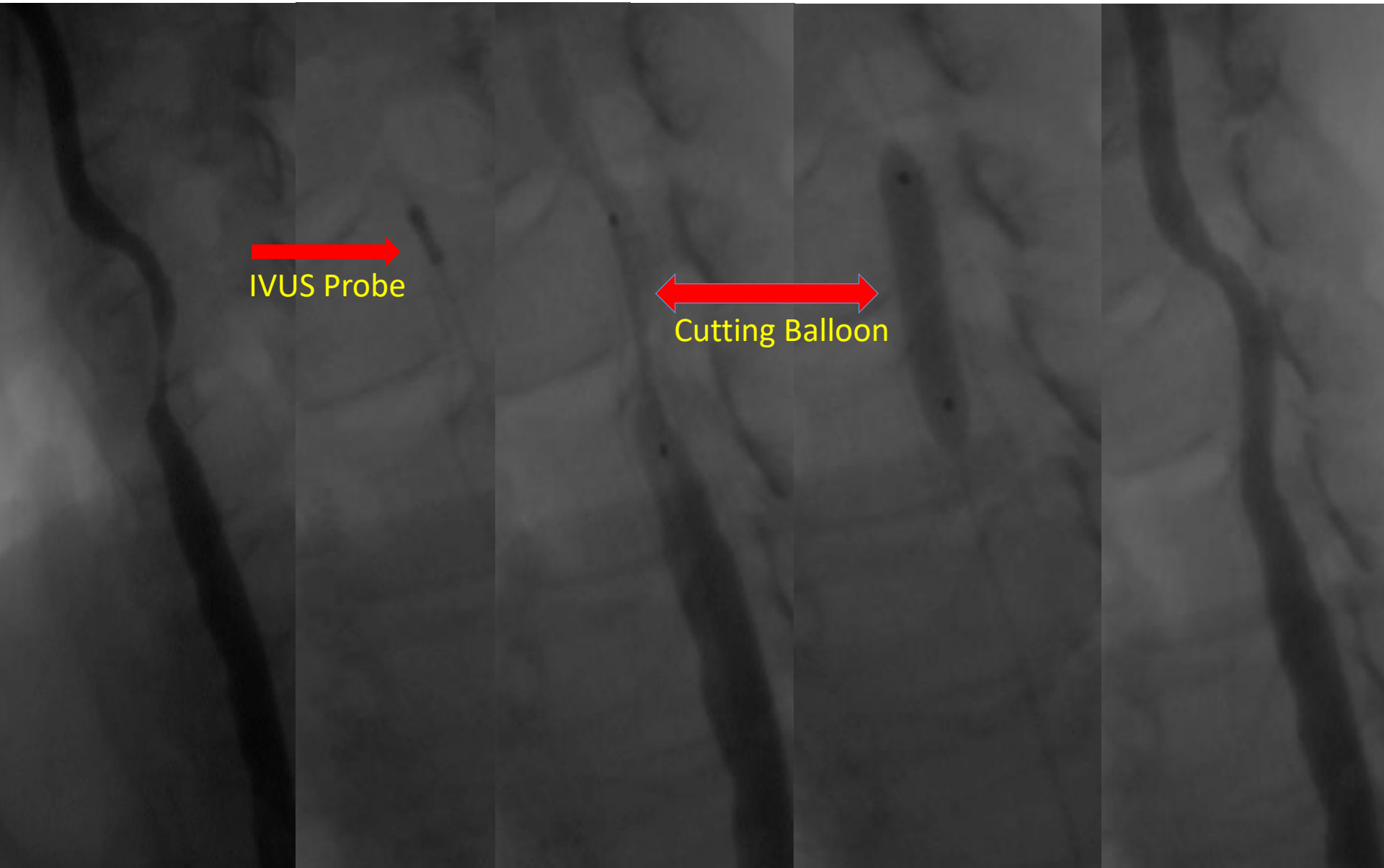
Iatrogenic or spontaneous dissection – no restenosis events

Aneurysm and fibromuscular dysplasia (balloon angioplasty only)

Patients who not survived at least 6 months after index procedure

In stent restenosis requiring re - PTA - 44 pts 1.35%

First in our strategy for Carotid In-Stent Restenosis Standard balloon with bigger diameter or Cutting Balloon were used. In Re-PTA IVUS guided with Cutting Balloon.



J ENDOVASC THER
2012;19:000–000

◆ CLINICAL INVESTIGATION ◆

Zotarolimus-Eluting Stent for the Treatment of Recurrent, Severe Carotid Artery In-Stent Stenosis in the TARGET-CAS Population

Lukasz Tekieli, MD, PhD[1,3]; Piotr Pieniazek, MD, PhD[1,3]; Piotr Musialek, MD, DPhil[1,3]; Anna Kablak-Ziembicka, MD, PhD[1,3]; Tadeusz Przewlocki, MD, PhD[1,3]; Mariusz Trystula, MD, PhD[2,3]; Zbigniew Moczulski, MD[3]; Karolina Dzierwa, MD[1,3]; Piotr Paluszek, MD[3]; and Piotr Podolec, MD, PhD[1,3]

Results: ZES implantation under distal embolic protection was technically successful and uncomplicated. Angiographic stenosis was reduced from 84.6%±7.5% to 10.7%±3.6% ($p<0.01$). In 5 patients with ZES implanted fully within the self-expanding carotid stent, duplex ultrasound follow-up (mean 17 months, range 6–36) revealed no evidence of restenosis or stent fracture/deformation. In the 2 other patients, the ZES had been implanted for distal edge ISS such that the ZES protruded beyond the original carotid stent. This protruding segment of the ZES demonstrated deformation/kinking in both; in one, this led to symptomatic stent occlusion.

Conclusion: The use of coronary ZES in the treatment of recurrent carotid ISS is feasible and appears effective provided the ZES is placed entirely within the original stent. Placement of a coronary ZES outside the carotid stent scaffold should be avoided.

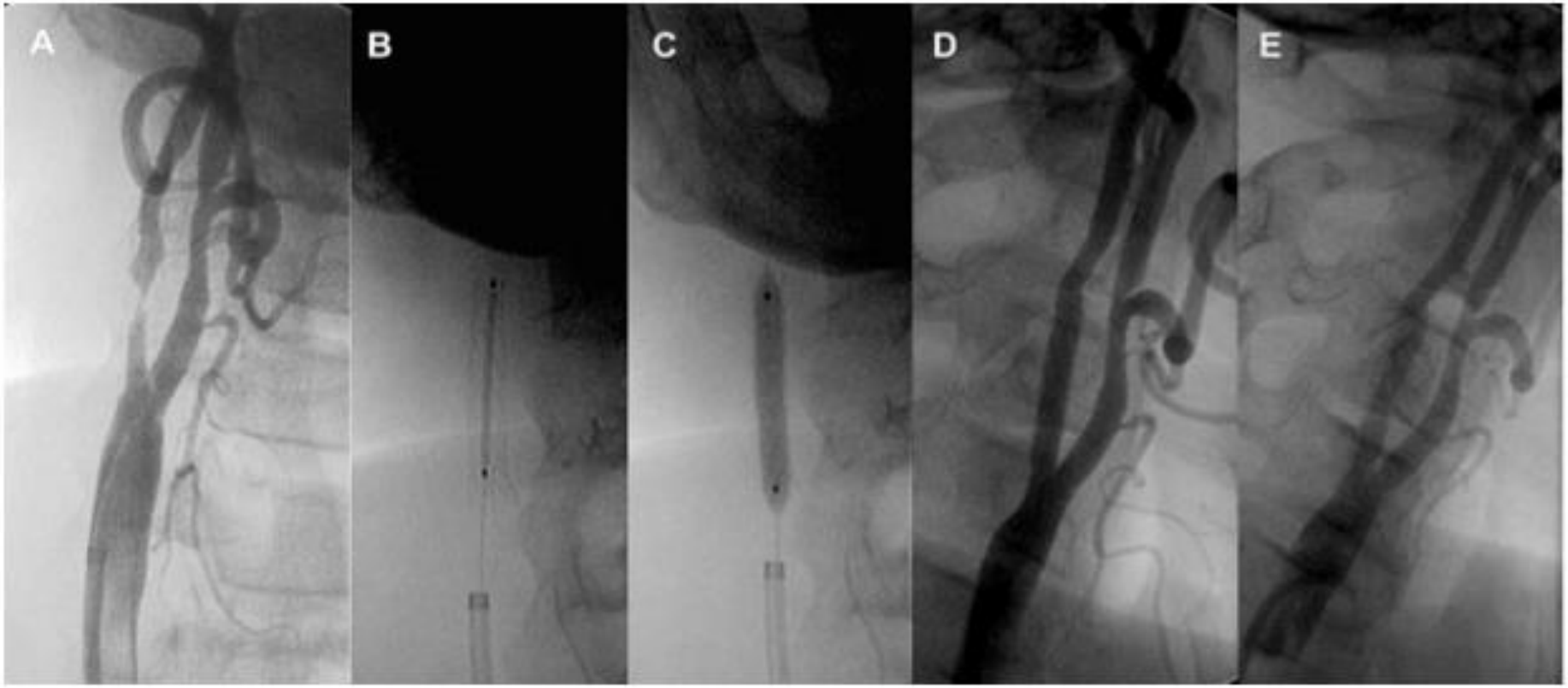


Figure 1 ◆ (**A**) A 50-year-old man treated with CAS 17 months earlier for RICA stenosis presented with asymptomatic recurrent ISS that became critical (92%) 6 months after in-stent balloon angioplasty was performed for the initial ISS. (**B**) A 4.0-×24-mm ZES was positioned within the self-expanding 4–9-×30-mm NexStent. (**C**) The ZES was implanted with up to 16 atmospheres of balloon pressure. Angiographic results immediately after the procedure (**D**) and at 12 months (**E**).

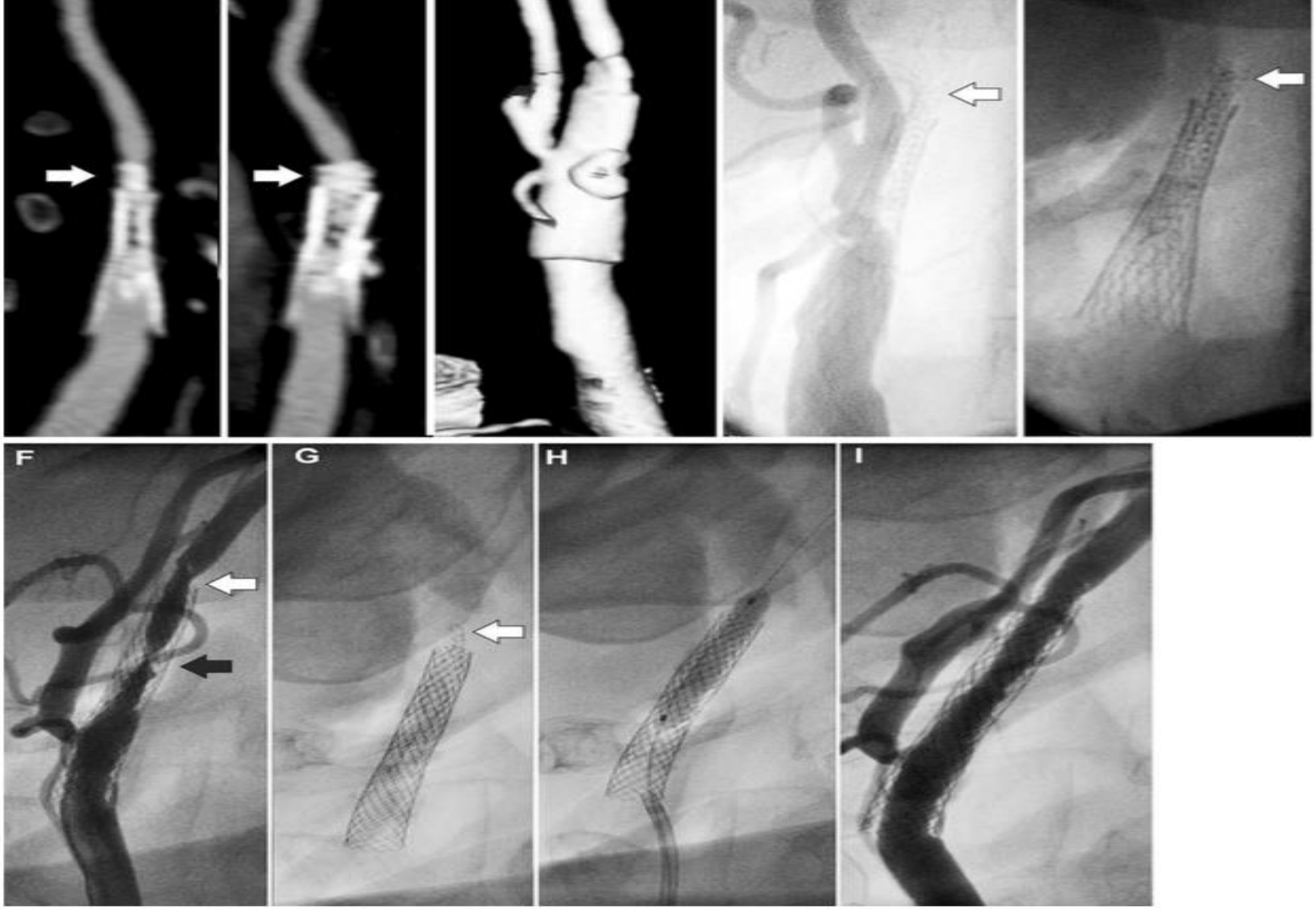
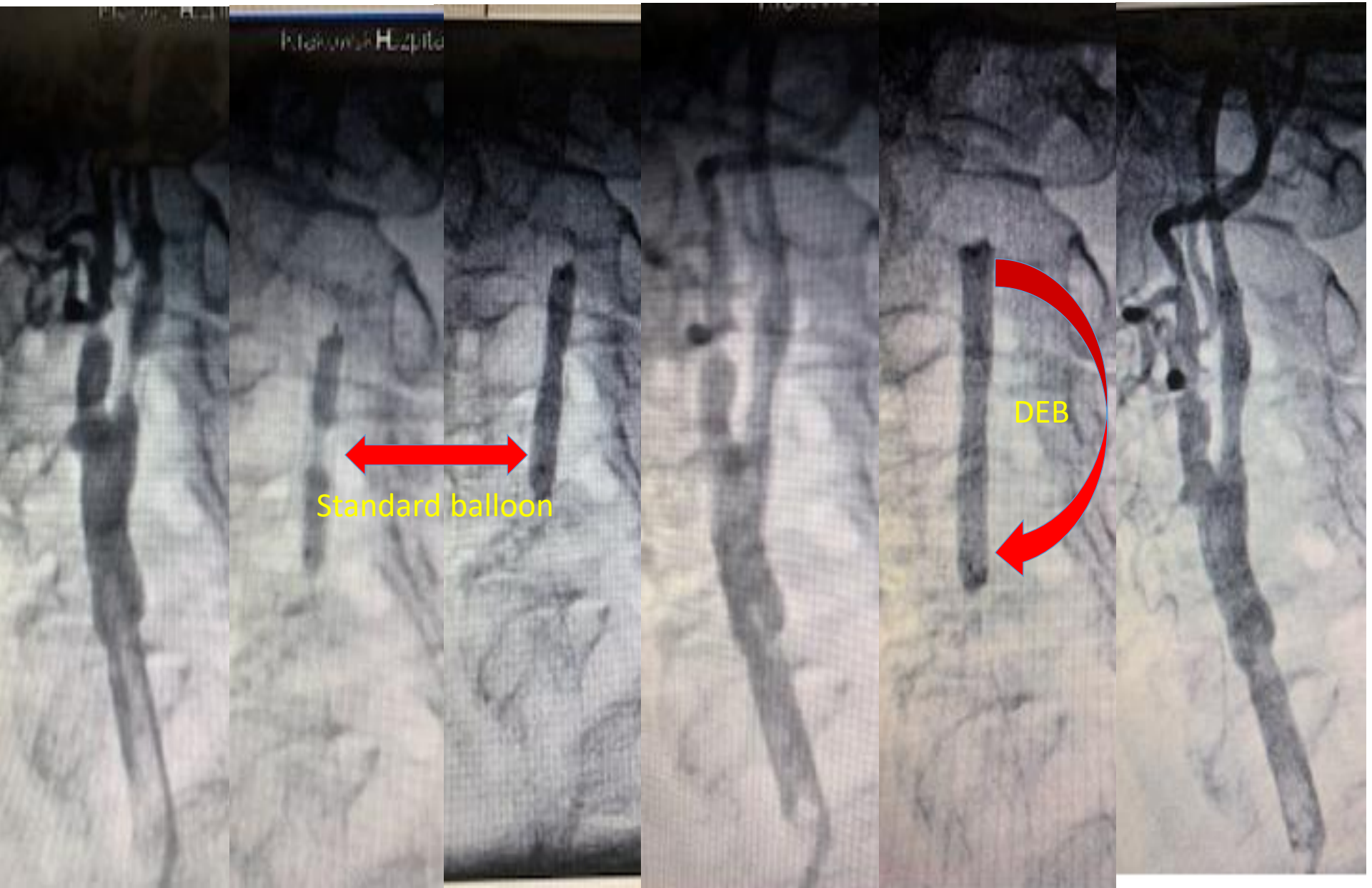
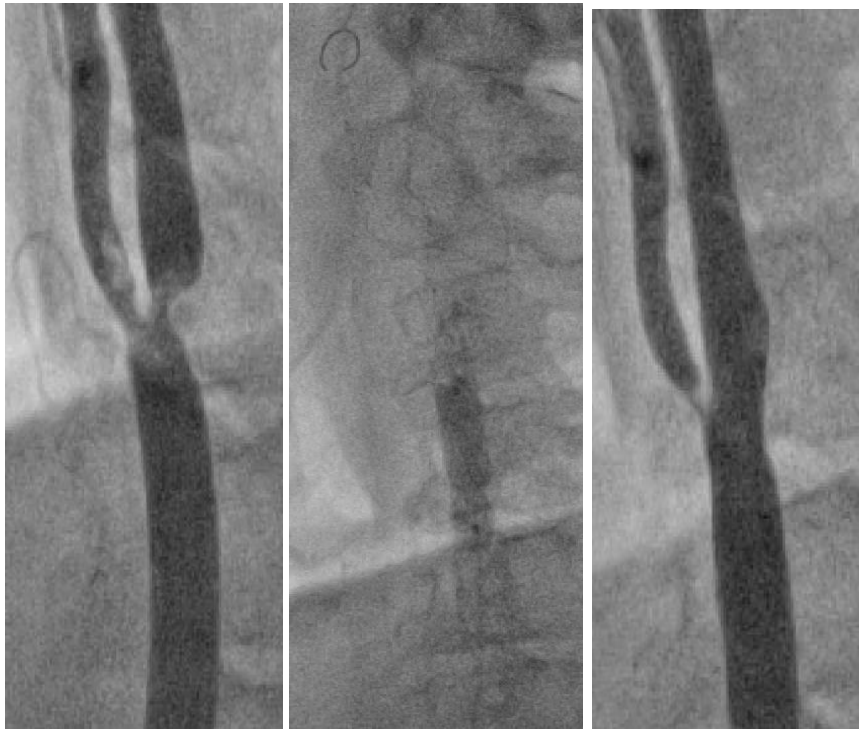


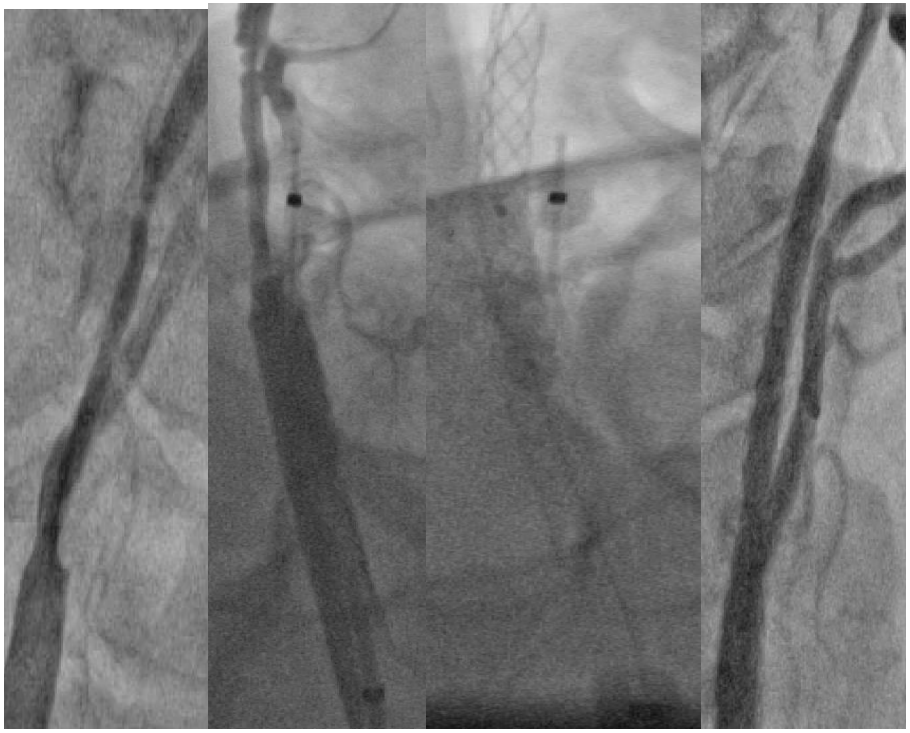
Figure 2 ◆ Two cases of ZES crush. Patient 1: (**A–C**) orthogonal CTA projections of ZES protruding (white arrows) from a self-expanding 7-×30-mm Carotid Wallstent 8 months after ZES implantation. Note the elliptical cross section of distal part of the Wallstent and protruding segment of the ZES. (**D, E**) One month later, angiography showed distal edge ZES deformation (white arrow) resulting in stent occlusion 3 days after an episode of left-hemispheric TIA. Patient 2: (**F,G**) angiography showing in-ZES stenosis (F, black arrow) and distal edge ZES deformation (white arrow) 12 months after ZES implantation. (**H**) In-ZES angioplasty with a 4.0-×20-mm balloon, and (**I**) the final angiographic result.

At present time standard approaches with Carotid In-Stent Restenosis DEB is used after excellent artery preparation with Standard Balloon. Temporary NPD use is mandatory



Treatment modality of ISR



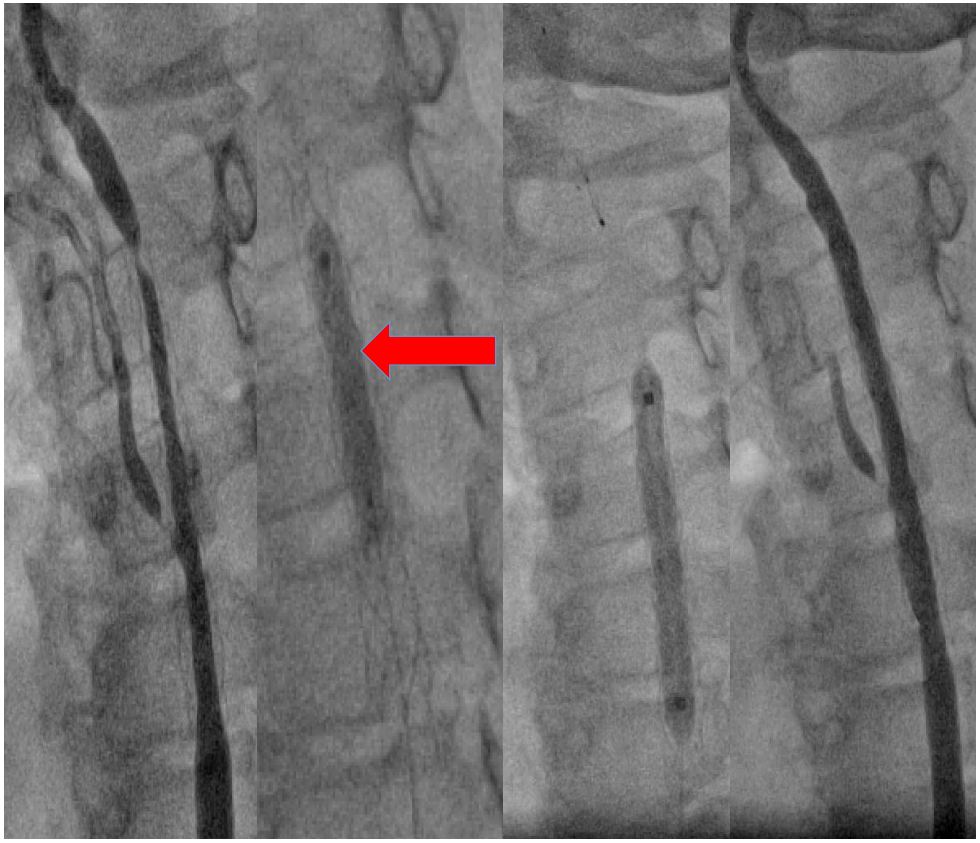


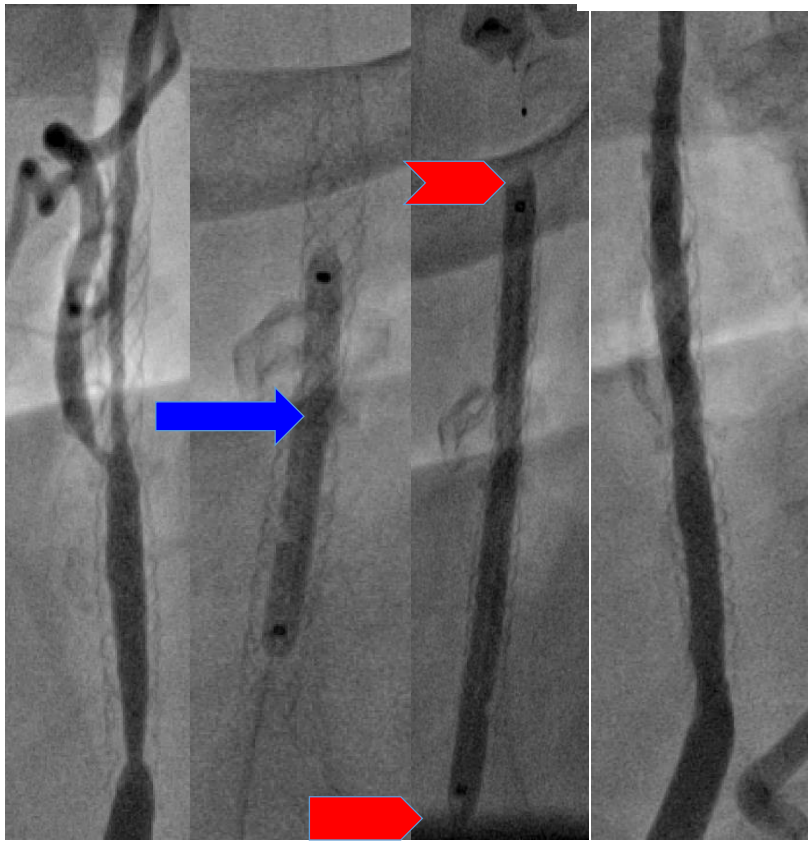
Patient 78 y. with bilateral ICA stenosis after syncope two months ealier

LICA 85% with thrombus containing lesion
CAS - 06 Sep. 2016 Roadsaver 9.0/20mm & Filter Wire EZ

RICA 95% long diffuse lesion
CAS - 04 Nov.2016 Roadsaver 8.0/40mm & Mo.Ma 8 Fr.

Treatmnet modality of ISR



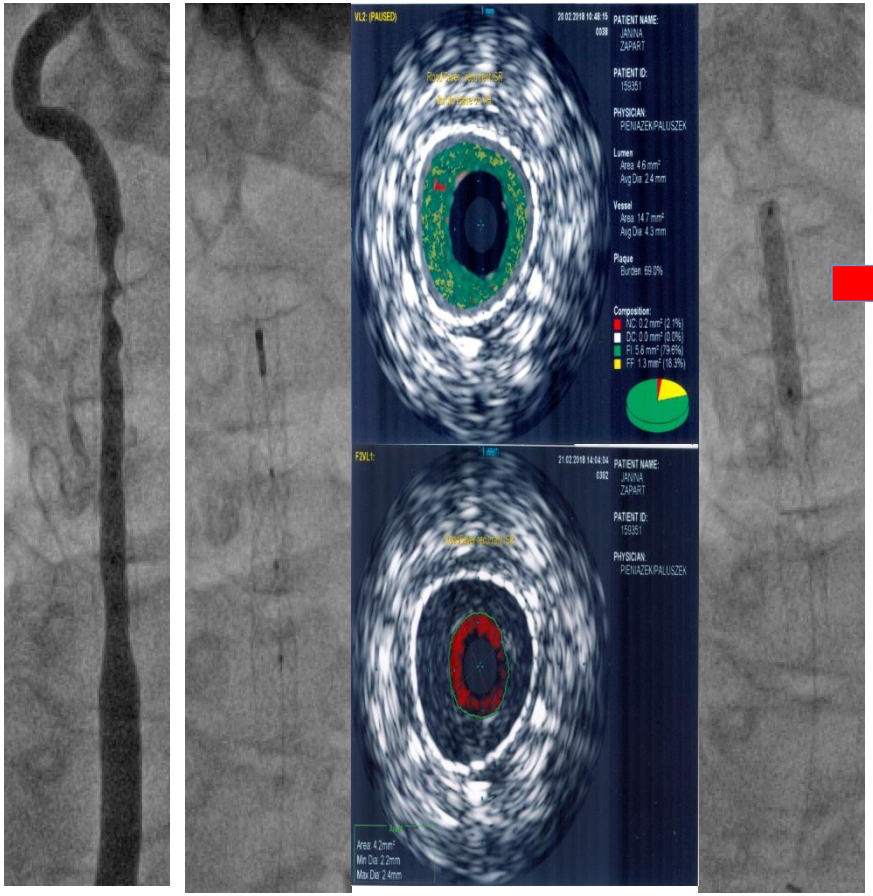


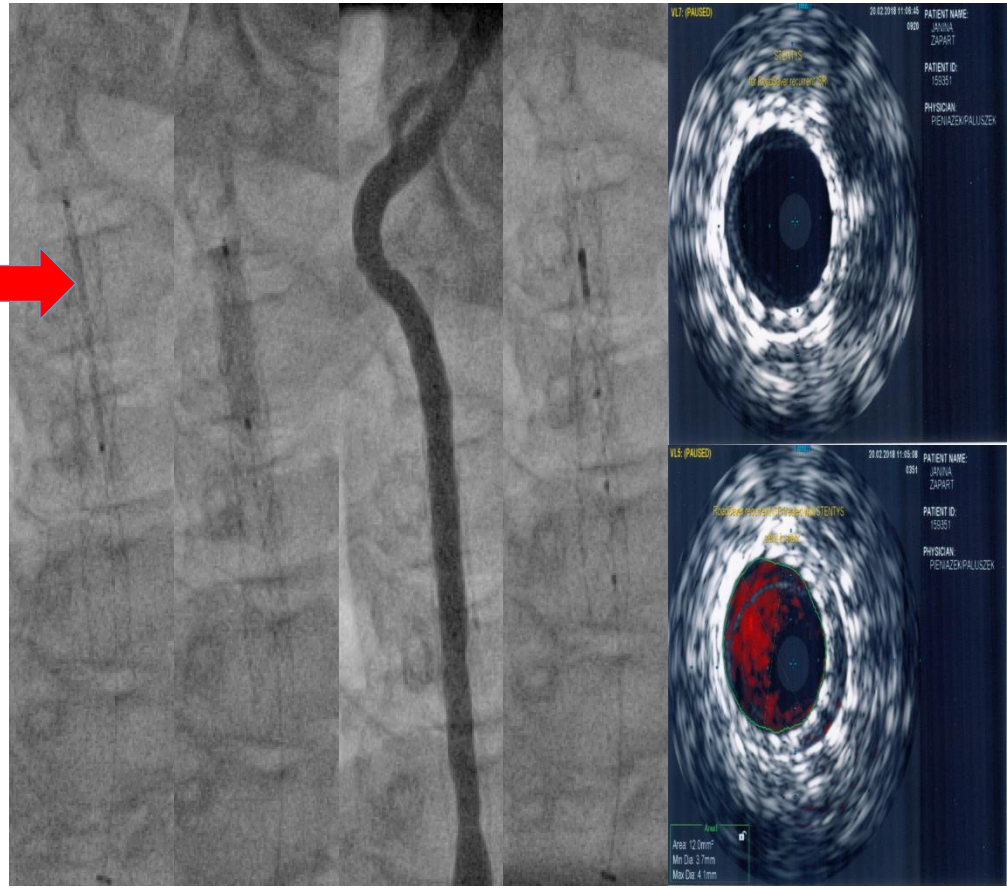
Patient 78 y. with bilateral ICA stenosis after syncope two months earlier - bilateral RESTENOSIS

LICA in-stent restenosis 90% PSV 3.5/0.9m/sec
CAS - 04 Jul.2017 Sterling 4.0/20mm,
DEB Biopath 5.0/30mm & Spider FX

RICA in stent restenosis 80% PSV 3.3/0.8m/s
CAS - 31 Jul.2017 Armada 4.0/40mm, DEB LEGFLOW 5.0/80mm !! & Spider FX

Treatment modality of ISR





Patient 78 y. with bilateral ICA stenosis after syncope two months earlier with recurrent - bilateral RESTENOSIS

LICA ReRe in-stent restenosis 80% IVUS MLA 4.2mm CAS - 20 Feb.2018

Viatrac 4.5/20mm STENTYS X position 3.0-3.5/27mm , MAVERIC 5.0/20mm & FilterWire

Risk of Death Following Application of Paclitaxel-Coated Balloons and Stents in the Femoropopliteal Artery of the Leg: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.

Katsanos K, Spiliopoulos S, Kitrou P, Krokidis M, Karnabatidis D.

J Am Heart Assoc. 2018 Dec 18;7(24):e011245. doi: 10.1161/JAHA.118.011245.

PMID: 30561254 **Free Article**

vascular

Meta-analysis finds a higher risk of death in the long term when paclitaxel-coated devices are used in the leg

New data published in the *Journal of the American Heart Association (JAHA)*, suggest that there is an increased risk of death at two and five years following the use of paclitaxel-coated balloons and stents in the femoropopliteal artery. While the authors, Konstantinos Katsanos (Patras, Greece) and colleagues, write in *JAHA* that this meta-analysis provides good statistical evidence to back these findings, some leading physicians state that it lacks individual patient-level data from the randomised controlled trials.

In the *JAHA* paper, the investigators write that several randomised controlled trials have already shown that paclitaxel-coated balloons and stents significantly reduce the rates of vessel restenosis and target lesion revascularisation after lower extremity interventions.

The investigators conducted a systematic review and meta-analysis of randomised controlled trials investigating paclitaxel-coated balloon angioplasty or paclitaxel-coated metal stents in the femoral and/or popliteal arteries. In all, 28 randomised controlled trials with 4,663 patients (89% intermittent claudication) were analysed. As reported in *JAHA*, they last screened

11:00 - 12:15, Room 1 - Main Arena 1

Long-term safety of drug-eluting technologies in the leg – recent findings, controversies, and future outlook

Moderator: Dierk Scheinert, John Laird
Panel: Konstantinos Katsanos, Peter Schneider, Michael Dake, Thomas Zeller, William Gray, Sean Lyden

11:00 - 11:10

Risk of death following application of Paclitaxel-coated balloons and stents in the femoropopliteal artery – findings from a metaanalysis of RCTs

Konstantinos Katsanos

11:10 - 11:16

A look into the methods: merits and limits of meta-analysis

Timothy Hanson

11:16 - 11:22

Toxicological aspects and safety profile of Paclitaxel

Juan Fernando Granada Solis

11:22 - 11:28

Event adjudication in clinical trials: how does it work?

Marc van Sambeek

PATIENT LEVEL DATA FROM MAJOR CLINICAL TRIAL PROGRAMMES WITH DRUG-ELUTING DEVICES

Subjects and lesion characteristics

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WIST

Variable	SB&CB treatment (n=14)	DEB treatment (n=30)	Total (n=44)	p
Days from CAS/Re-PTA	734.71 (±1181.82	480.93 (±453.99)	561.68 (±758.66)	0.791
Male gender	10 (71.43%)	20 (68.97%)	30 (69.77%)	1.000
Age, years	59.36 (±8.98)	68.17 (±7.08)	65.30 (±8.71)	0.001*
LICA	7 (50.00%)	20 (66.67%)	27 (61.36%)	0.290
RICA	4 (28.57%)	16 (53.33%)	20 (45.45%)	0.124
LCCA	1 (7.14%)	3 (10.00%)	4 (9.09%)	1.000
RCCA	2 (14.29%)	0 (0.00%)	2 (4.55%)	0.096
Symptomatic	0 (0.00%)	5 (16.67%)	5 (11.36%)	0.161
Post CEA restenosis	0 (0.00%)	1 (3.33%)	1 (2.27%)	1.000
Previous contralateral stroke	1 (7.14%)	0 (0.00%)	1 (2.27%)	0.318
Ipsilateral stroke/TIA >6 months	0 (0.00%)	4 (13.33%)	4 (9.09%)	0.290
Contralateral ICA/CCA not patent	1 (7.14%)	4 (13.33%)	5 (11.36%)	1.000
Arteritis	1 (7.14%)	0 (0.00%)	1 (2.27%)	0.318
Death (known)	0 (0.00%)	4 (14.29%)	4 (9.52%)	-
Re-PTA or Death (known)	6 (42.86%)[a]	6 (20.00%)	12 (27.27%)	-
Days to last contact	2137.50 (±1739.68)	1027.17 (±754.56)	1380.45 (±1254.05)	0.044*
Last contact <1 year	3 (21.43%)	6 (20.00%)	9 (20.45%)	0.143
1-3 years	2 (14.29%)	12 (40.00%)	14 (31.82%)	
3-5 years	2 (14.29%)	6 (20.00%)	8 (18.18%)	
≥5 years	7 (50.00%)	6 (20.00%)	13 (29.55%)	

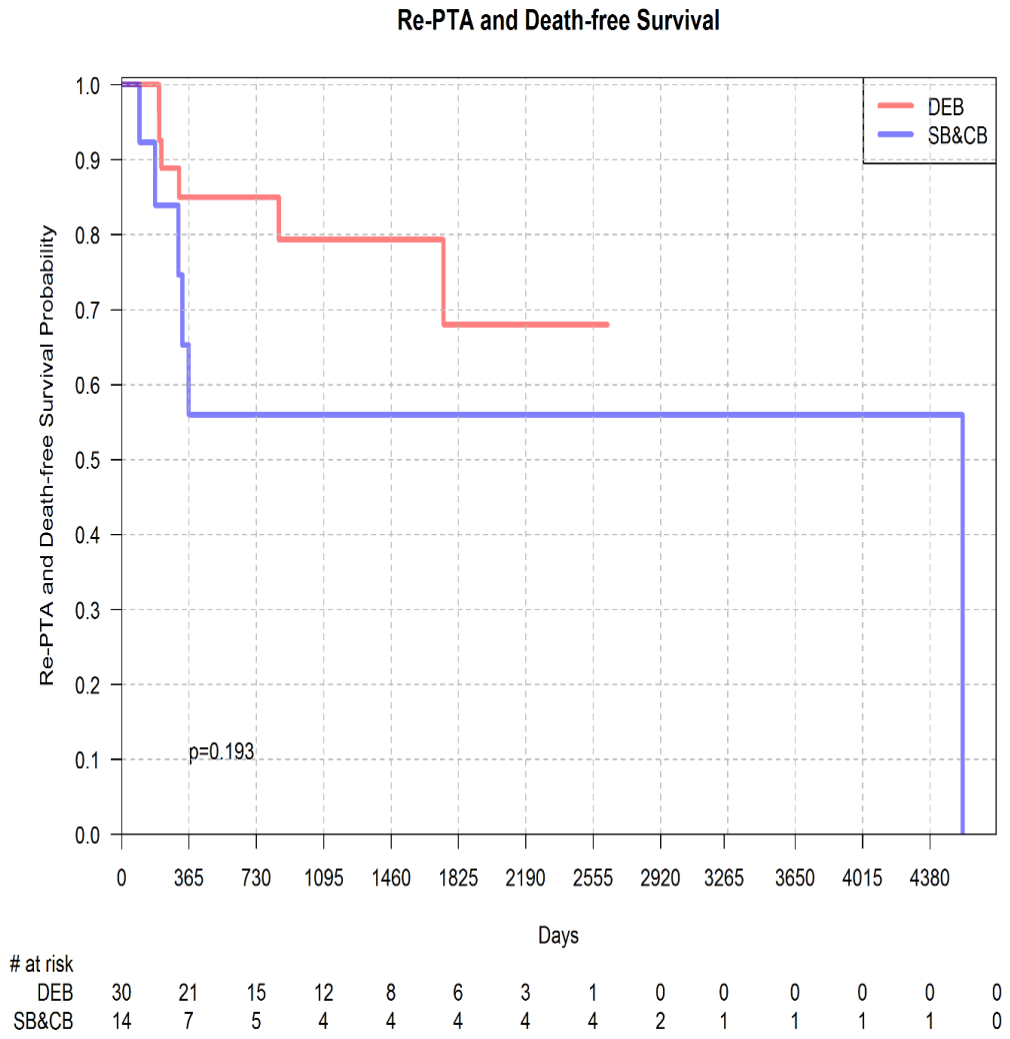
Balloons characteristics – all procedures – including next Re-PTA

Variable	SB&CB (n=15)	DEB (n=37)	Total (n=42)	p
Diameter, mm	5.46 (±0.97)	5.06 (±0.72)	5.17 (±0.80)	0.414
Length, mm	21.15 (±4.16)	30.67 (±14.46)	28.14 (±13.22)	0.013*

- **SB&CB:**
  - CB Avion
  - CB Quantum
  - Sterling
  - Tacker
  - Ultrasoft
  - Viatrac
- **DEB:**
  - Biopath
  - Dior
  - Endeavor
  - Essential
  - Eurocor
  - Freeway
  - InPact Admiral
  - Legflow
  - Lutonix
  - Ranger
  - SeQuent Neo
  - Ultrasoft

Composite endpoint: Re-PTA or Death
SB & CB vs DEB

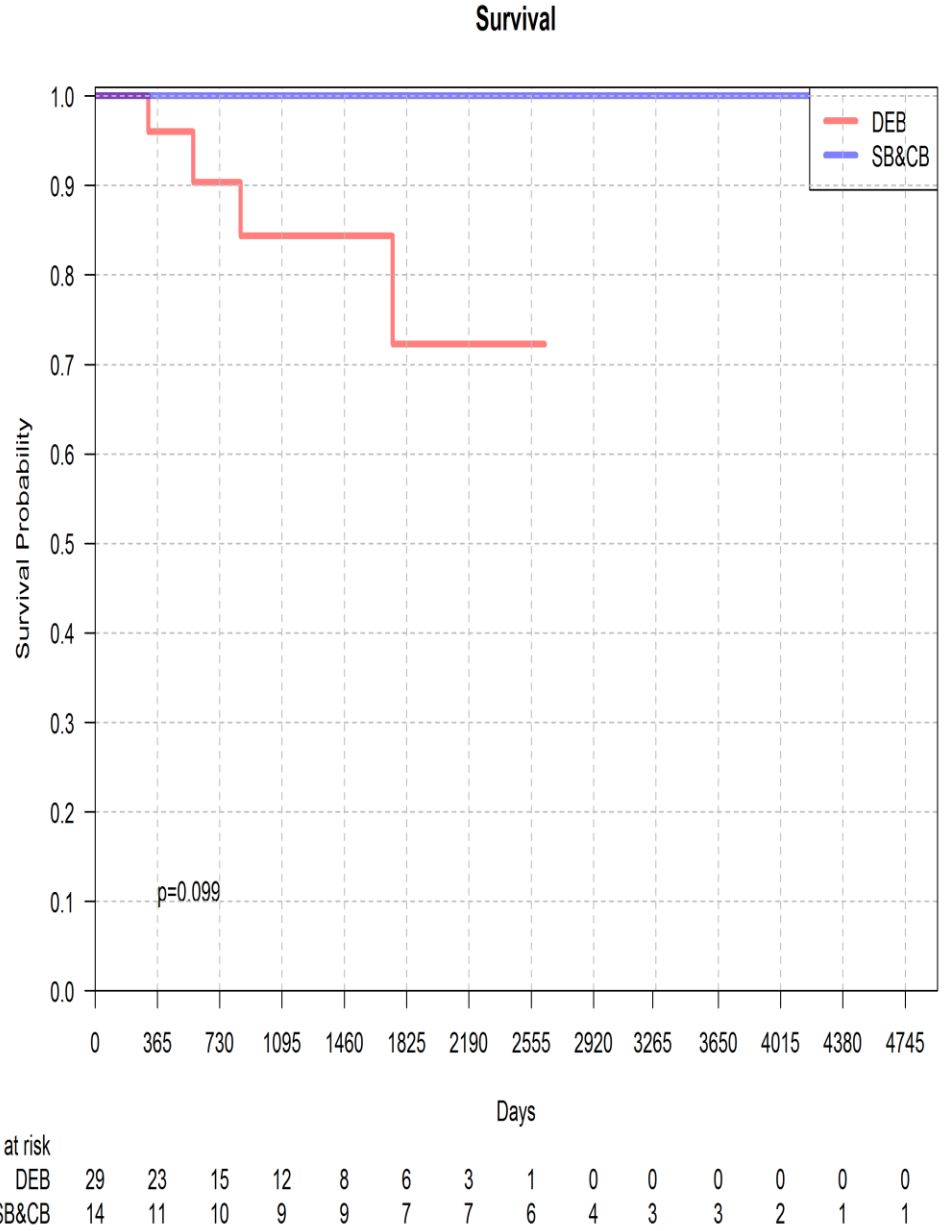
- **Re-PTA or Death free survival** – time to the **first** event
  - 12 events in 44 lesions
  - Log rank test – p=0.193
  - Cox PH model – HR: 2.16 (0.62-7.20), p=0.204



Death
SB & CB vs DEB

Survival

- 4 events in 43 subjects including:
- 1.- SCD
- 2.- CHF
- 3. after abdominal surgery
- 4. Accident
- All deaths occurred in DEB group
- 1 event occurred in DEB after next Re-PTA with DES
- Log rank test – p=0.099



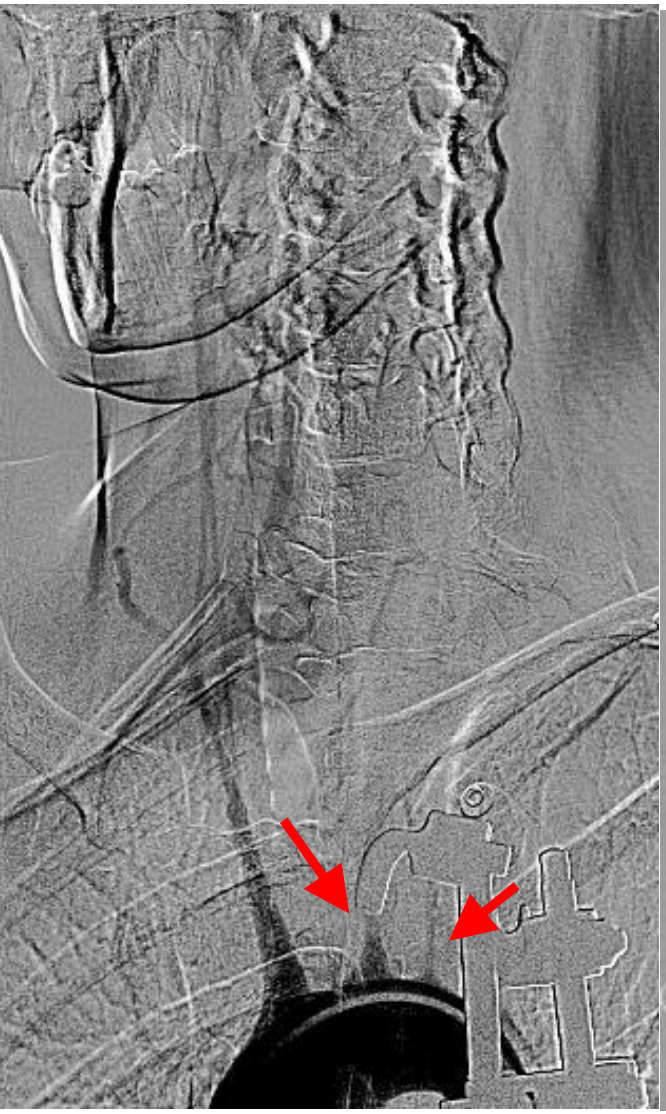
Important knowledge after publication from Dec. 2018 which should be considered:

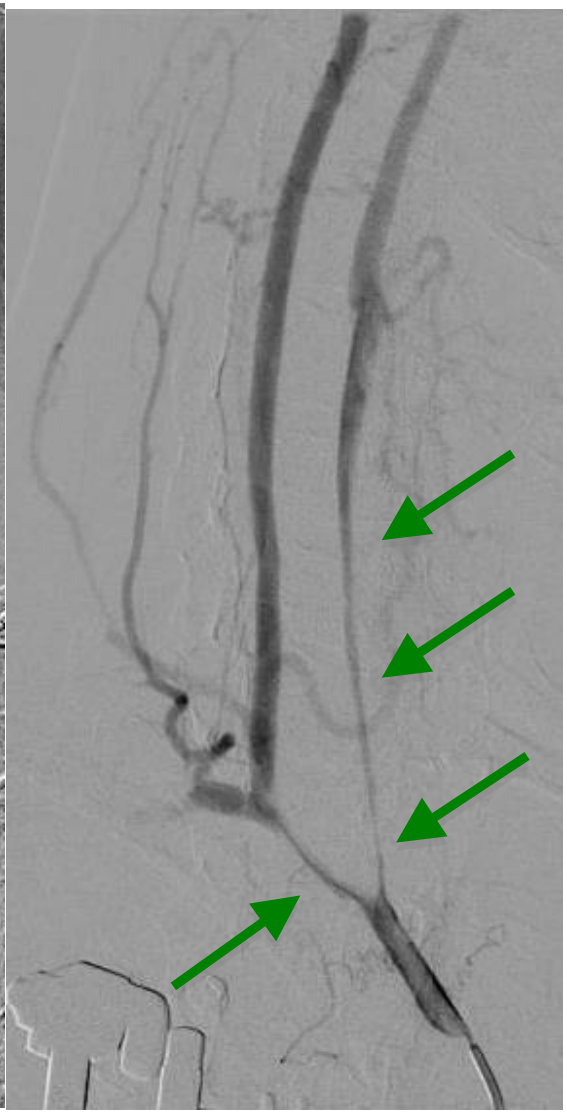
COMPARE : Does Ranger DCB with dose density of 2µg/mm² have similar efficacy compared to and In. Pact DCB with dose density of 3.5µg/mm² ?

Length	Nominal Dose (µg/device) to treat a "typical" COMPARE lesion	
	Ranger 5mm	In.Pact 5mm
120	4809	8448

How to prevent in - stent restenosis in High Risk Lesion/Patient Young female age. 33 with TAKAYASU Syndrome !!!

- (TIA recurrent !!!!!)





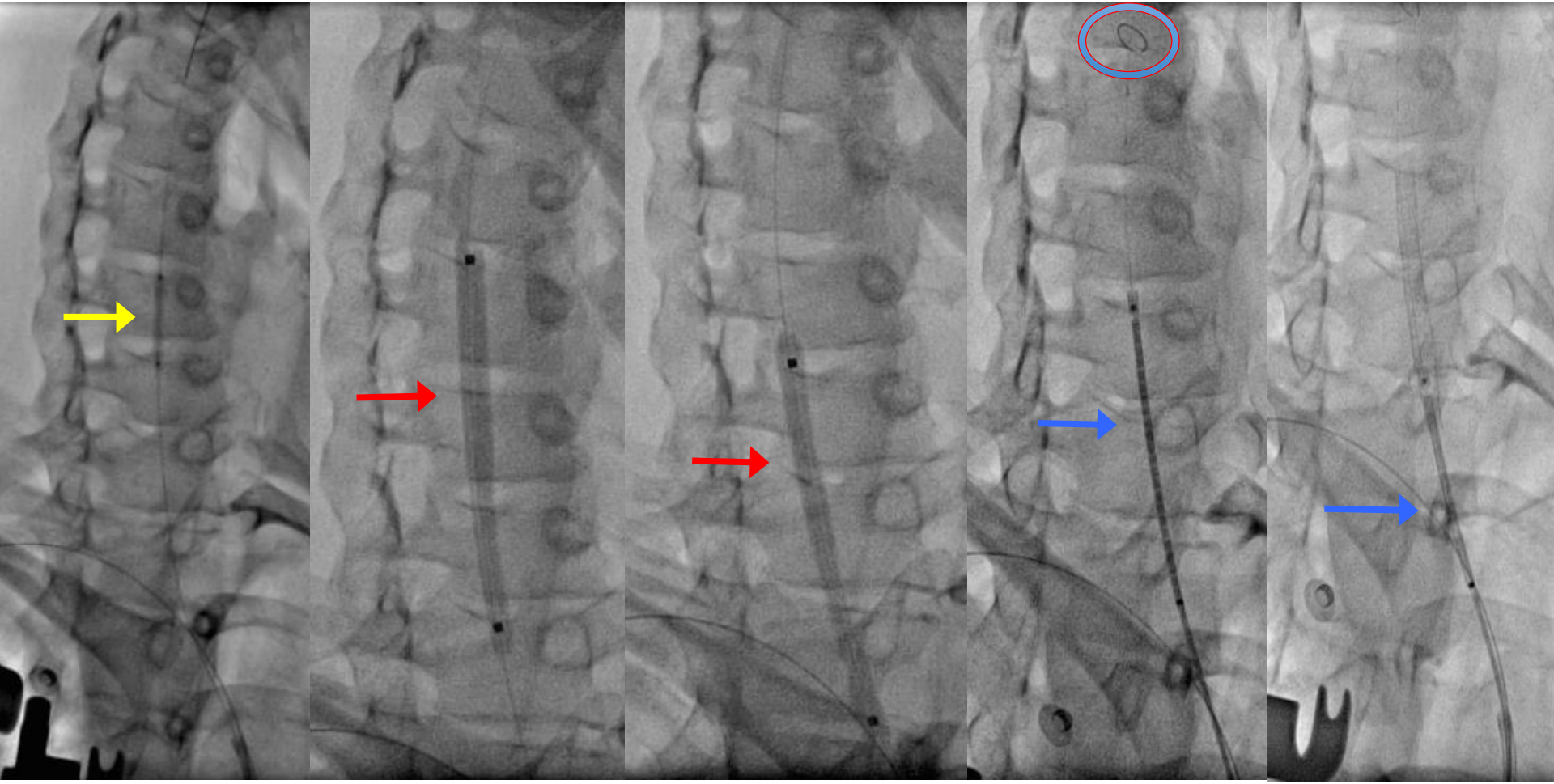
Dramatic image of closing arteries.

RED arrows: LSA&LCCA Occlusions

Green arrows: tight stenosi of RSA & RCCA

Kazibudzki M, Tekieli Ł, Trystuła M, Paluszek P, Moczulski Z, Pieniążek P. Advances in Interventional Cardiology.

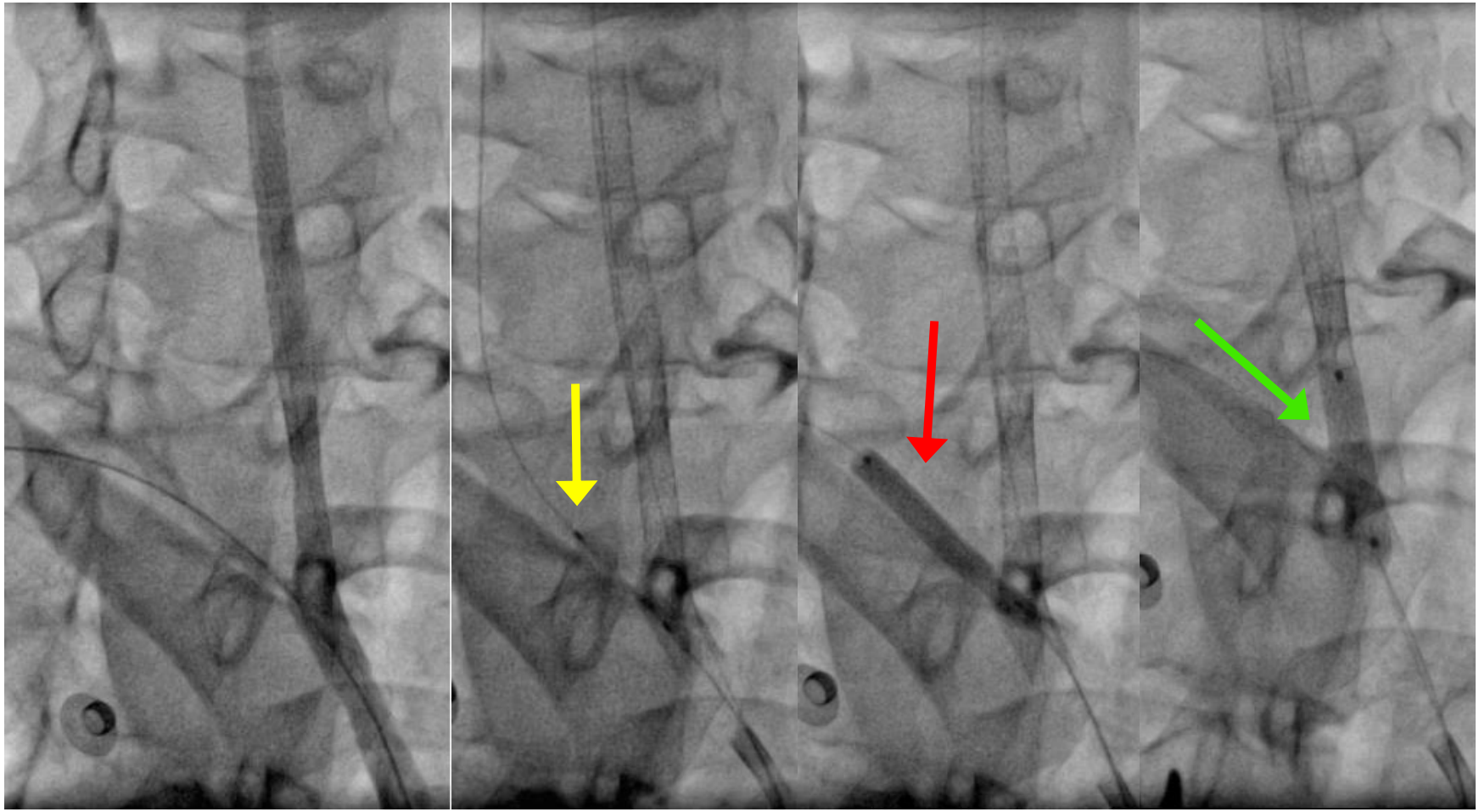
How to prevent in – stent restenosis in High Risk Lesion/Patient
Young female age. 33 with TAKAYASU Syndrome!!!
- (TIA recurrent !!!!!)



2 x DEB, self expandable carotid stents, dystal NPD! EpiFilter Wire

Kazibudzki M, Tekieli Ł, Trystuła M, Paluszek P, Moczulski Z, Pieniążek P. Advances in Interventional Cardiology. 2016;12(2):17

How to prevent in - restenosis in High Risk Lesion/Patient
Young female age. 33 with TAKAYASU Syndrome !!!
- (TIA recurrent !!!!!)



Coronary DES stent with postdilatation implanted to RSA.

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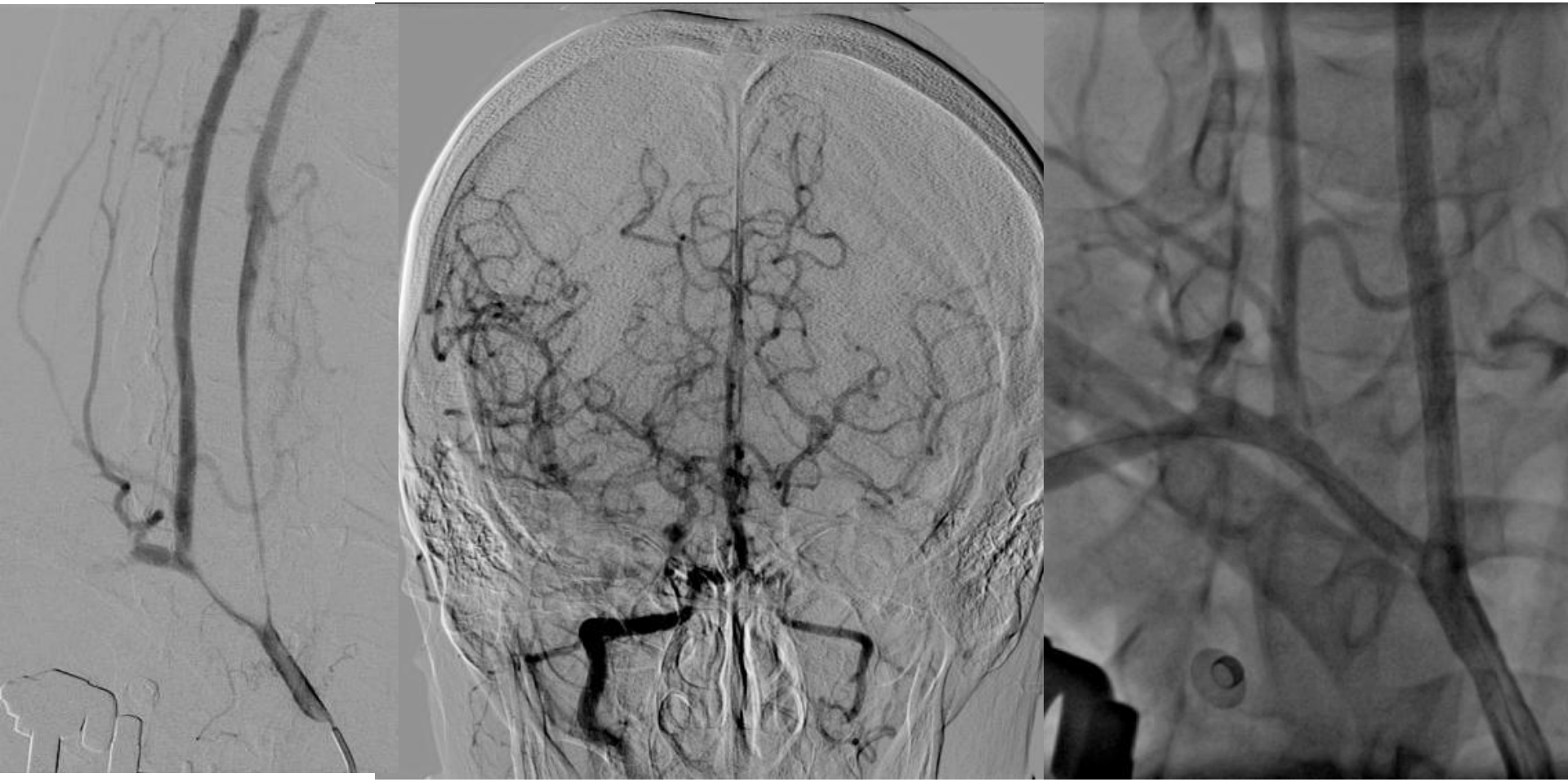

Final angiography . Normal intracranial circulation. Symptoms completely disappeared. !!!!!

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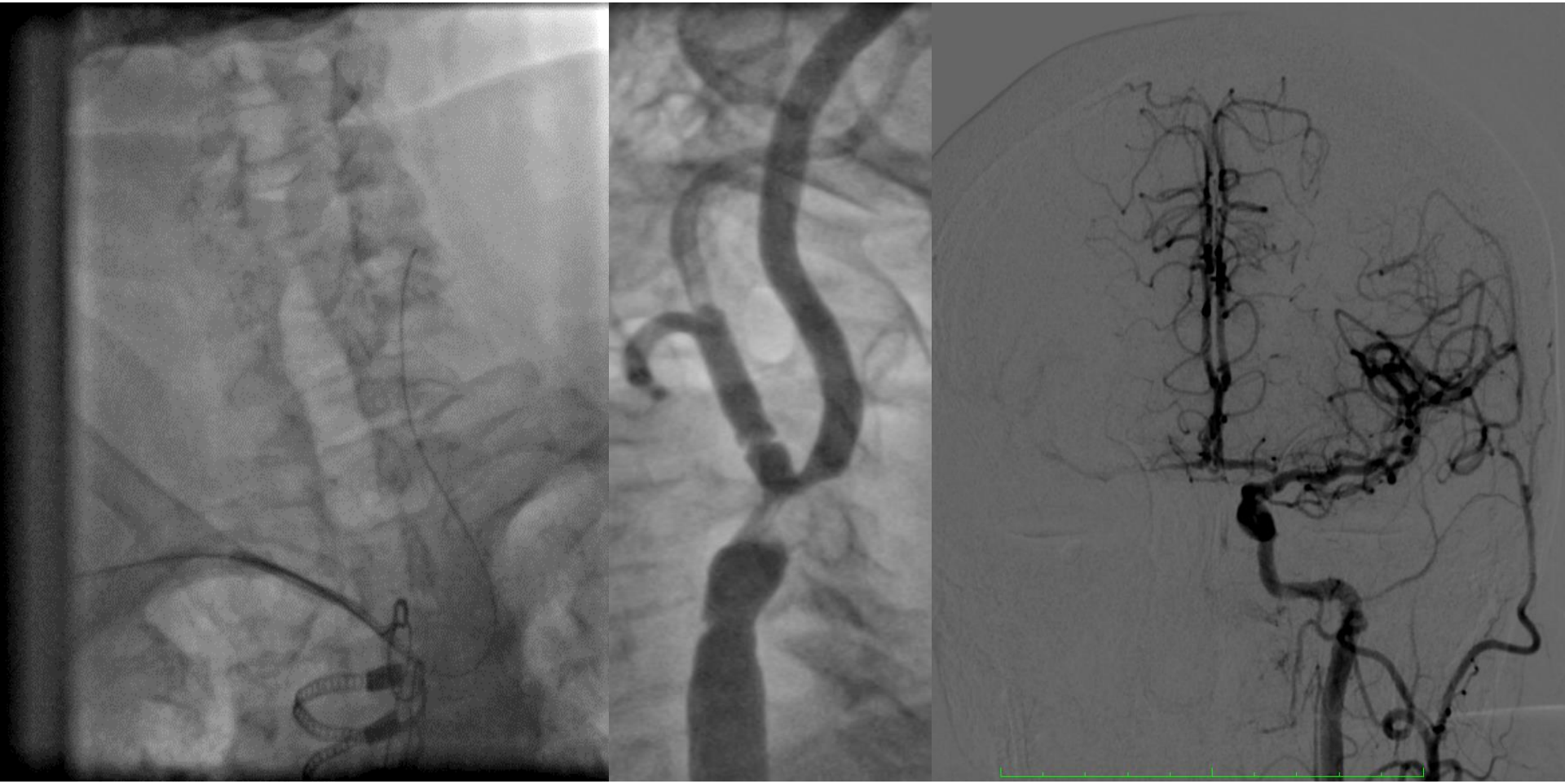
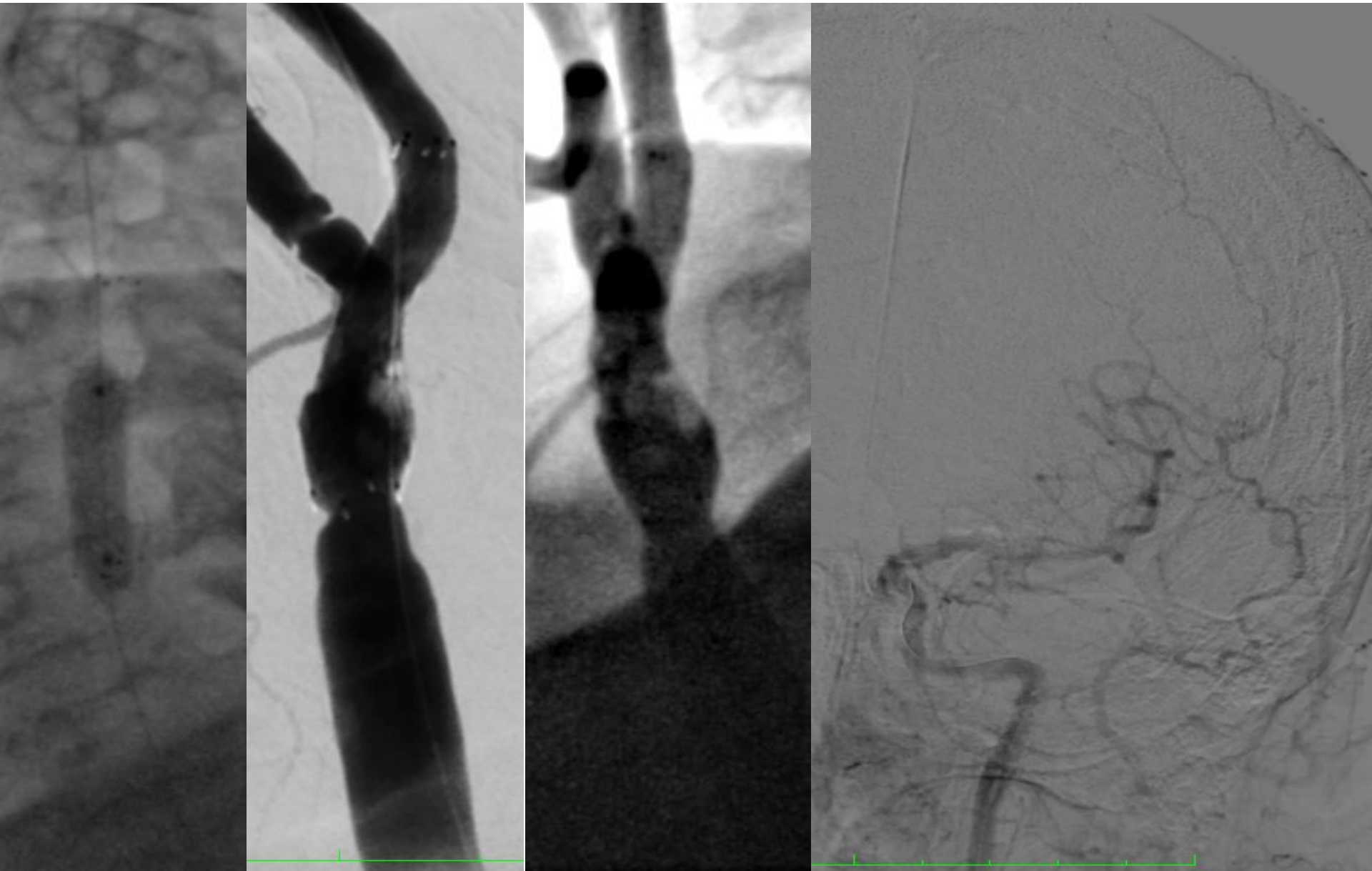
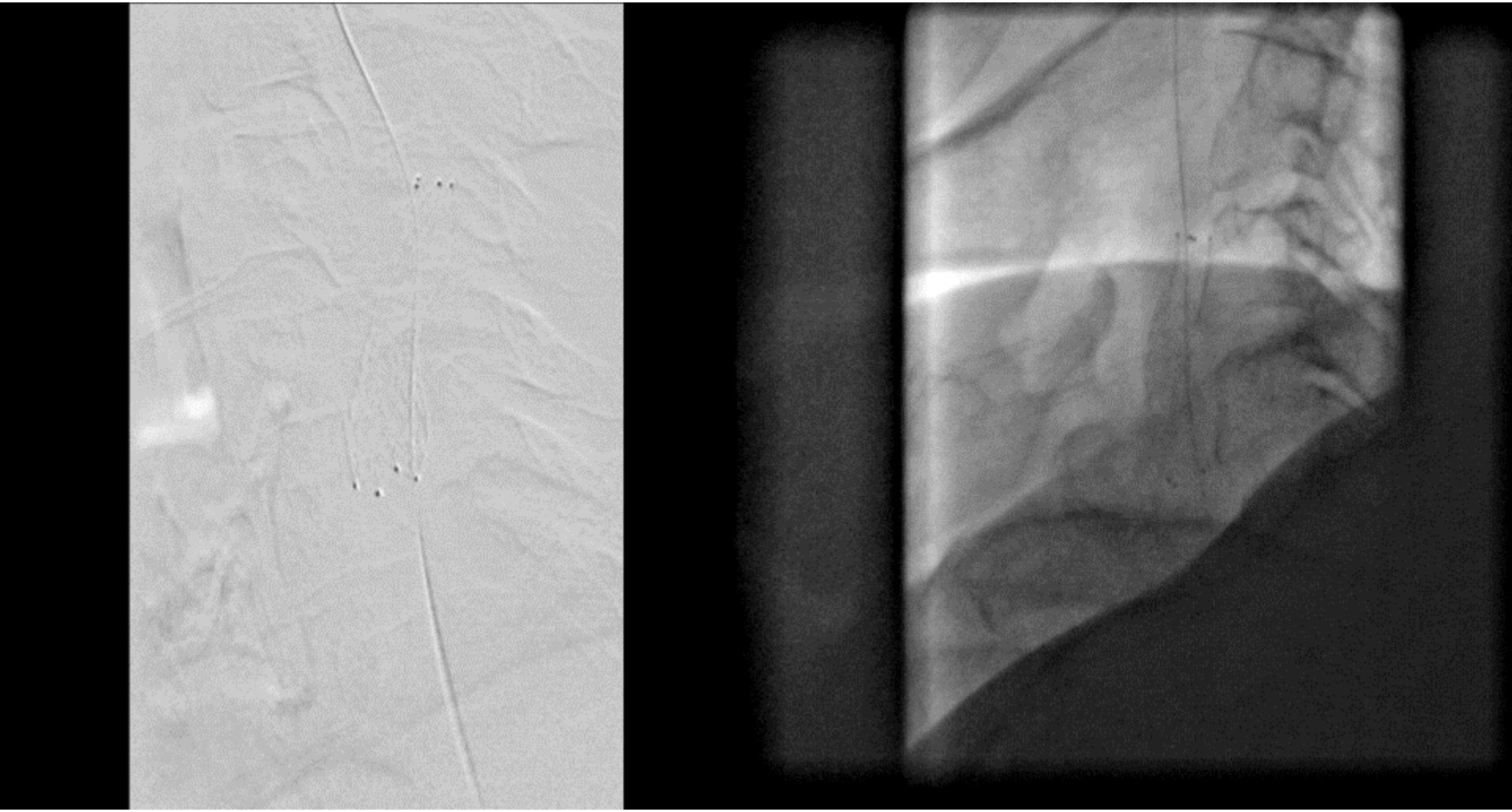
Sometimes, supposedly simple CAS procedure can turn out to be breakneck: Patient after bilateral CEA with RICA occlusion and symptomatic 80% LICA restenosis.
CAS procedure with right radial access with strategy, distal protection and Open Cell stent implantation (Bovine arch our main indication for radial access!!!)



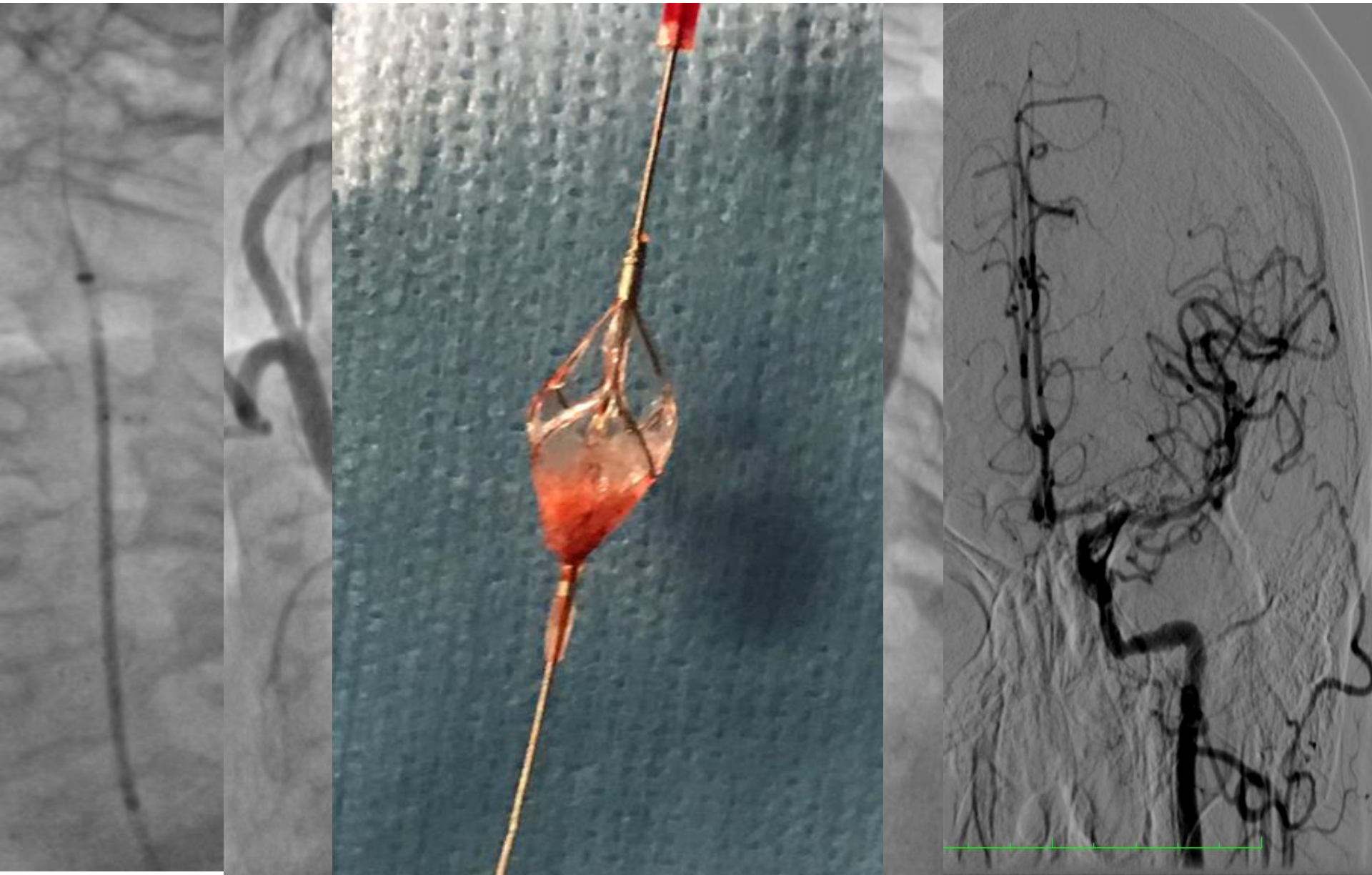
After MER stent implantation and postdilatation – neurological symptoms occurred with slow flow in left hemisphere . MASSIVE PLAQUE BURDEN THRU THE STENT



You never and never can remove the filter and than leave the patient with such angiography without additional treatment. Are there many options???? The best one was to implant asap Roadsaver mesh-stent - 5F easy too cross the first stent and no problem with filter retrieval



Normal angiography after Roadsaver stent in stent implantation.
Example why we need NPD in all CAS procedures!!!
Resolution of neurological symptoms & normal intracranial angiography.



Take home message :

- Restenosis after carotid stenting is not a frequent complication and should not exceed 3% !
- Treatment strategy for in-stent restenosis is changing.
- New technological solutions should be taken into account.
- We need to follow up on further reports about DEB with paclitaxel
- Self expanding coronary DES can be a last option for the patient with malignant restenosis