

Carotid and Intracranial Applications: Defining the Clinical Need and Addressing Technical Challenges

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Disclosure Statement of Financial Interest

I, (insert name) DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

**Drug Coated
Balloon (DCB)
&
Intracranial
Atherosclerosis
(ICAD)**



Treatment of Symptomatic ICAD

Standard of practice: endovascular treatment of intracranial atherosclerosis

M Shazam Hussain,¹ Justin F Fraser,² Todd Abruzzo,³ Kristine A Blackham,⁴ Ketan R Bulsara,⁵ Colin P Derdeyn,⁶ Chirag D Gandhi,⁷ Joshua A Hirsch,⁸ Daniel P Hsu,⁹ Mahesh V Jayaraman,¹⁰ Philip M Meyers,¹¹ Sandra Narayanan,¹² Charles J Prestigiacomo,¹³ Peter A Rasmussen,¹ On behalf of the Society for NeuroInterventional Surgery

J Neurointervent Surg 2012;4:397

I, B

1. Aspirin is preferred over warfarin for the medical management of symptomatic ICAD (AHA level B, class I; CEBM level 1a, grade B).

2. The use of combination aspirin 325 mg daily and clopidogrel 75 mg daily for the first 3 months, followed by aspirin 325 mg daily, along with aggressive risk factor modification of hypertension, hyperlipidemia, diabetes and smoking cessation should be pursued in all patients with symptomatic ICAD (AHA level B, class IIa; CEBM level 1b, grade B).

IIa, B

Medical Treatment of Symptomatic ICAD

The WADIS & SAMMPRIS Trials

Comparison of Warfarin and Aspirin
for Symptomatic Intracranial Arterial Stenosis*

Marc I. Chimowitz, M.B., Ch.B., Michael J. Lynn, M.S.,

WASID trial: ASA vs. Warfarin+ASA

2-year ischemic stroke rate: 19.7% with ASA and 17.2% with Warfarin

Stenting versus Aggressive Medical Therapy
for Intracranial Arterial Stenosis**

Marc I. Chimowitz, M.B., Ch.B., Michael J. Lynn, M.S., Colin P. Derdeyn, M.D.,

**SAMMPRIS trial: Aggressive medical treatment (AMT) vs. AMT
+ stent (self-expanding Wingspan device)**

1-year stroke in the AMT arm: 12.2%

* NEJM 2005; 352:1305
** NEJM 2011;365:993

Treatment of Symptomatic ICAD

Endovascular therapy

Standard of practice: endovascular treatment of intracranial atherosclerosis

M Shazam Hussain,¹ Justin F Fraser,² Todd Abruzzo,³ Kristine A Blackham,⁴ Ketan R Bulsara,⁵ Colin P Derdeyn,⁶ Chirag D Gandhi,⁷ Joshua A Hirsch,⁸ Daniel P Hsu,⁹ Mahesh V Jayaraman,¹⁰ Philip M Meyers,¹¹ Sandra Narayanan,¹² Charles J Prestigiacomo,¹³ Peter A Rasmussen,¹ On behalf of the Society for NeuroInterventional Surgery

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4. In patients with symptomatic 70–99% intracranial stenosis who have failed aggressive maximal medical therapy, angioplasty or stent therapy may be considered (AHA level B, class IIb, CEBM level 2b, grade B).

IIb, B

Endovascular Treatment of Symptomatic ICAD

- **Intracranial circulation is a “peculiar” circuit**
- **Unfavorable anatomy (small diameter, “delicate” arterial wall and tortuous course vessels)**
- **Endovascular treatment extrapolated by other vascular district (i.e. coronary)**
- **Lack of dedicated devices**

Endovascular Treatment of Symptomatic ICAD

Available options and Uncovered issues

	Technical success (TS) or failure (TF)	Procedural complication rate	Restenosis rate	How to improve Role for DCBs?
POBA	Reasonable TS Shorter duration of DAPT Dissection & elastic recoil of target lesion.	4%-40% 5.9% <i>237 pts in 4 studies</i>	24%-40%	"Submaximal" PTA
BMS	Reasonable TS (83%-100%)	6%-68% 7.2% <i>SSYLVIA Trial</i>	13.8%-37% (lower than SES)	Dedicated stent DCB (ISR Rx & prevention)?
SES*	High TS (97%-100%)	6% 14.7%-20% <i>SAMMPRIS Trial</i>	17.6%-31%	DCB (ISR)?
DES**	Sub-optimal deliverability: TF: 4%-14%	5.5% (0%-18%)	10.9% (0%-38%)	Dedicated stent, 3 rd generation DES DCB (ISR)?

* Self-expanding-stent (Wingspan, Enterprise)

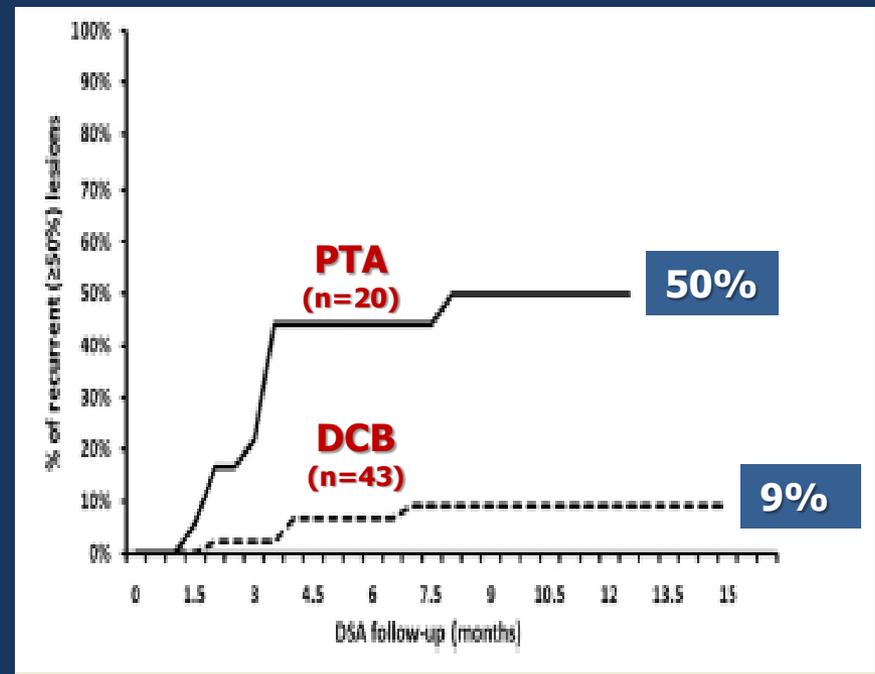
** First (Cypher, Taxus, Coroflex Please) , or 2nd (EES) generations coronary DES.

1. Endovascular Treatment of Intracranial ISR

POBA vs. DCB

- 51 pts with >50% ISR in intracranial circulation underwent re-PTA with POBA (32%) or DCB (SeQuent Please)*
- ASA/Prasugrel LD: 500/600 mg. DAT continued for 1 year. Then, ASA lifelong
- Angio & clinical F/U up to 12 months
- *Technical success (<50% DS): 92% due to DCB failure in 8% (shifted successfully to POBA →100% TS)*
- *End-point (stroke, ICH, SAH): 1.6%*

Angiographic re-ISR rate at F/U (≥50% by DSA)



Vajda Z. *AJNR* 2011;32:1942

* *Coronary DCB (not dedicated for intracranial vessels)*

2. Endovascular Prevention of Intracranial ISR

DCB + Self-expanding stent

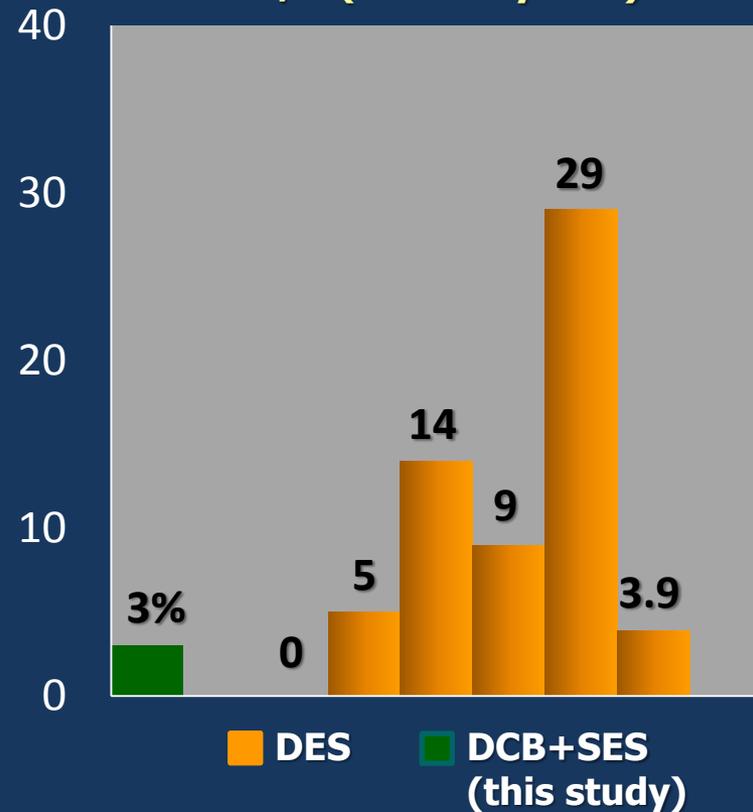
- 52 pts with ICAD underwent DCB (SeQuent Please/Dior) followed by SES (Enterprise)
- ASA/Prasugrel LD: 500/600 mg. DAT continued for 1 year. Then, ASA lifelong
- Angio & clinical F/U up to 12 months
- *Technical success (<50% DS): 81% due to DCB failure in 19% (24% SeQuent, 16% Dior). Pts successfully shifted to POBA → TS 100%*
- *End-point (stroke, ICH, SAH): 5%*

Rigidity of the DCB shaft and stiffness of the balloon tip. Thus,

→ *Dedicated DCB*

→ *Systematic predilation*

Angiographic re-ISR rate at F/U (≥50% by DSA)



Treatment of Symptomatic ICAD

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IIb, B

4. In patients with symptomatic 70–99% intracranial stenosis who have failed aggressive maximal medical therapy, angioplasty or stent therapy may be considered (AHA level B, class IIb, CEBM level 2b, grade B).

5. There is insufficient evidence to recommend between angioplasty and the use of balloon mounted, drug eluting or self expanding stent systems (AHA level C, class III; CEBM level 5, grade D). Further studies comparing these techniques and technologies are required.

III, C

DCB for ICAD

Take Home Message-1

- **ICAD accounts for 8%-10% of all ischemic strokes**
- **Endovascular treatment with POBA/stent may be an option in case of AMT failure (AHA Class IIb, B)**
- **Sub-optimal deliverability and navigability in the intracranial circulation and/or high rate of restenosis are limits to the currently available technology**
- **DCBSs showed promising results in the treatment of intracranial circulation ISR (more studies needed)**

**Drug Coated
Balloon (DCB)
&
Extracranial
Atherosclerosis**



In-stent Restenosis after CAS

A snapshot

- **Rare and usually benign condition
(despite a wide range of occurrence: 1%-50%)**
- **Significant ISR (>80% DS by Doppler/DSA) varies
between 3%-8% and “merits respect” for a small but
definitive risk of progression and/or symptoms
development**
- **Usually occurring during the first year after CAS
(sometime late in the F/u: “neo-atherosclerosis”?)**
- **Previous ipsilateral CEA and diabetes are predisposing
factors**

Treatment Options of Carotid In-stent Restenosis

Endovascular approach

- Plain Old Balloon Angioplasty (POBA)
- Cutting-balloon angioplasty (CB)
- Re-stent* (direct or after POBA/CB)
- Balloon-expandable DES
- ? *Drug Coated Balloon (DCB) ?*

Surgical Approach (*w stent removal*)

- Standard CEA
- Segmental carotid excision w PTFE/reversed safenous vein interposition grafts
- Proximal ICA ligation and CCA-ICA bypass (PTFE/vein)

* self-expandable

Endovascular Treatment of Carotid In-stent Restenosis*

100 interventions in 96 pts in 20 studies (up to January 2009)

Intervention to Treat ISR	No. of Pts.	Restenosis after ISR Intervention
Repeat PTA	→ 54	8 (15)
Balloon angioplasty (PTA)	31	7 (23)
Cutting balloon angioplasty	23	1 (4.3)
Repeat CAS	→ 31	4 (13)
Angioplasty and repeat CAS	24	1 (4.2)
Drug-eluting stent	1	0
CEA with stent removal	9	0
Carotid artery bypass	5	0
Interposition graft with reversed RSV	1	0
Interposition graft: PTFE	3	0
ICA-ECA interposition	1	0
Brachytherapy	1	0

Endovascular treatment (85/100, 85%)

Note.—Values in parentheses are percentages. ECA = external carotid artery; ICA = internal carotid artery; PTFE = polytetrafluoroethylene; RSV = reversed saphenous vein.

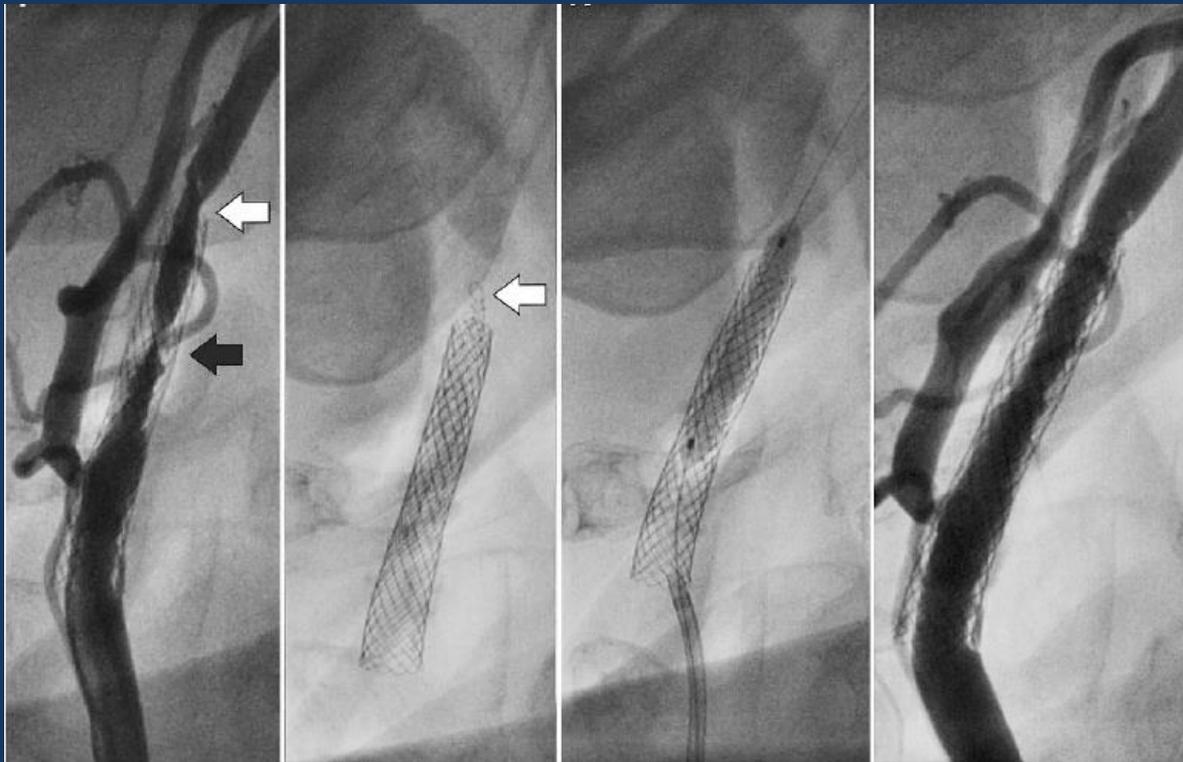
Van Haften AC. *J Vasc Interv Radiol* 2010;21:1471

*≥80% diameter stenosis

DES for carotid in-stent restenosis

A word of caution

7 pts with recurrent ISR >70% treated by ZES (4.0mm)
In 2 pts (28%) with distal edge ISR, the protruding part of the DES distorted and occluded (in 1) the vessel.



Any role for DCBs in Carotid ISR?

◆ CLINICAL INVESTIGATION ◆

Drug-Eluting Balloon for Treatment of In-Stent Restenosis After Carotid Artery Stenting: Preliminary Report

Piero Montorsi, MD; Stefano Galli, MD; Paolo M. Ravagnani, MD; Daniela Trabattoni, MD; Franco Fabbicchi, MD; Alessandro Lualdi, MD; Giovanni Teruzzi, MD; Gianluca Riva; Sarah Troiano, MD; and Antonio L. Bartorelli, MD

Department of Clinical Sciences and Community Health, University of Milan, Centro Cardiologico Monzino, IRCCS, Milan, Italy.

7 pts

◆ CASE REPORT ◆

Drug-Eluting Balloon Angioplasty for Carotid In-Stent Restenosis

Francesco Liistro, MD¹; Italo Porto, MD, PhD¹; Simone Grotti, MD¹; Giorgio Ventoruzzo, MD¹; Rocco Vergallo, MD²; Guido Bellandi, MD¹; and Leonardo Bolognese, MD¹

¹Cardiovascular and Neurological Department, San Donato Hospital, Arezzo, Italy.

²Department of Cardiovascular Medicine, Catholic University of the Sacred Heart, Rome, Italy.

3 pts

**Montorsi P. *J EVT* 2012;19:734
Liistro F. *J EVT* 2012;19:729**

DCB for In-stent restenosis after CAS

Clinical, Ultrasound, and Angiographic Variables

Pts	Age (year) Sex	Sx	Target Vessel	ISR Type*	Time From CAS to ISR (months)	PSV (m/s)	Diameter Stenosis (%)	Stenosis Length (mm)	
1	77/F	-	Left ICA	II	32.7	3.5	80	9.8	
2	74/F	-	Left ICA	III	60.7	4.0	80	15.8	
3	60/M	-	Left ICA	III	12.1	3.2	80	12.3	
4	78/M	-	Left ICA	III	8.3	4.3	90	14.5	
5	80/F	-	Left ICA	III	11.2	4.0	85	15.9	
6	65/F	-	Right CCA	IV	12.3	6.0	90	40.0	
7	64/M	-	Right ICA	III	9.2	4.1	80	17.1	
8	58/F	-	Right ICA	III	8.5	3.5	80	20.2	
					69±8	19±19	4.01	83±4	18±9



* [Lal BK et al. Semin Vasc Surg. 2007;20:259-266](#)

DCB for In-stent restenosis after CAS

Endovascular procedure & pharmacology

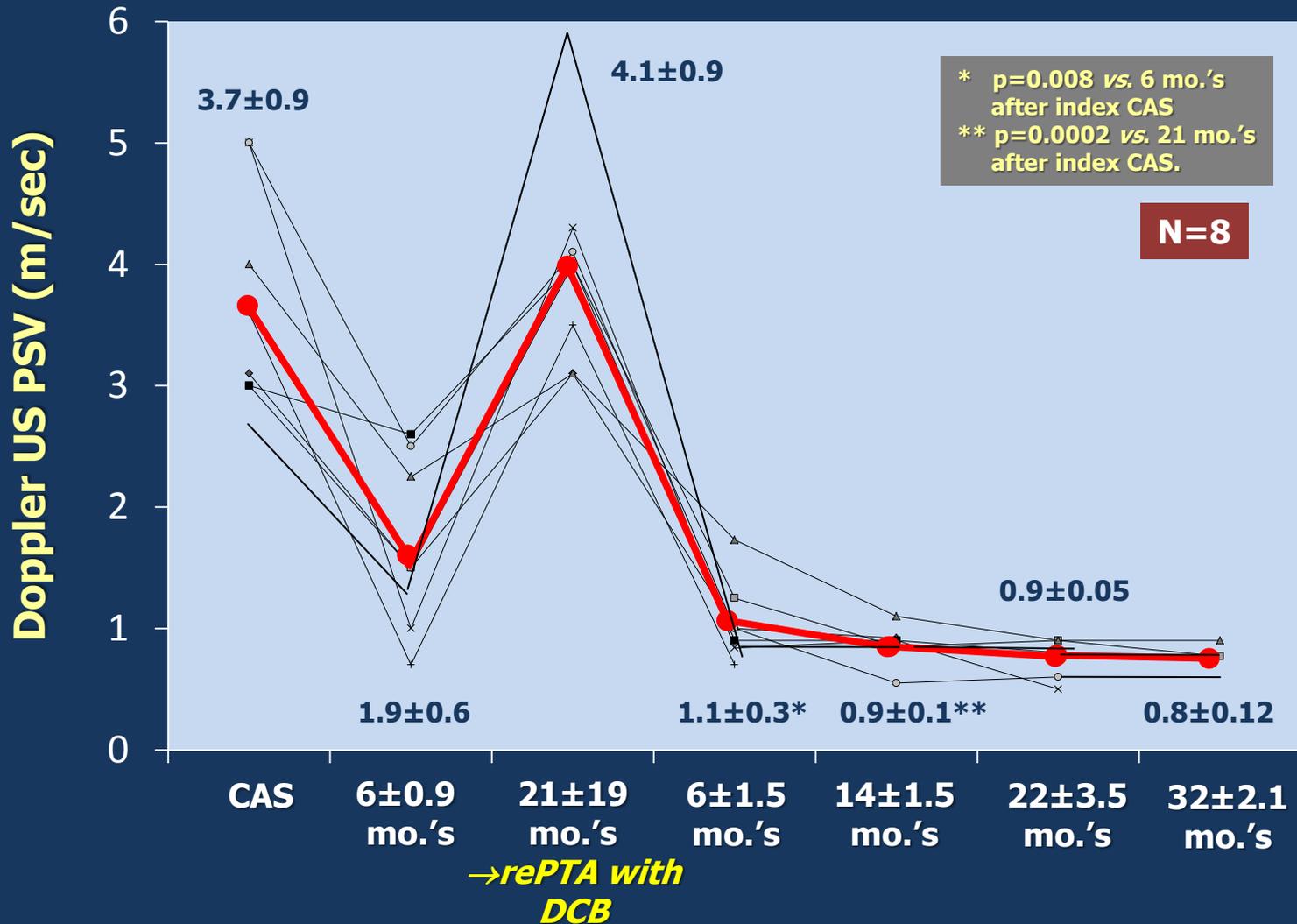
➤ Standard CAS technique

- *Wire "reshaping" technique + 6F sheath*
- *Distal cerebral protection device*
- *IVUS assessment (1:1 stent/DCB ratio)*
- *Predilation mandatory (POBA, CB)*
- *DCBs: **IN.PACT Admiral and Pantera Lux***
(60' inflation; if tolerated, maintained up to 3 min)

➤ Double antiplatelet treatment: 10 days before and up to 3 months thereafter. Then, lifelong ASA.

DCB for In-stent restenosis after CAS

Doppler US results over time



DCB for In-stent restenosis after CAS

Case Example

- 80-yow. Asymptomatic LICA ISR, 11.2 months after initial CAS
- Doppler US: PSV 4.0 m/s (A-B); CTA: LICA ISR in type 2 bovine arch (C-E). Patent intracranial anterior circulation (F-H)



Doppler US

CT-angiography

DCB for In-stent restenosis after CAS

Case Example: Procedural steps



**Baseline
LICA ISR**

**6F sheath in CCA
(right radial
approach)**

**Predilation
Cutting balloon
4x10mm**

Post-CB

**IN.PACT
5x40mm
(3' inflation)**

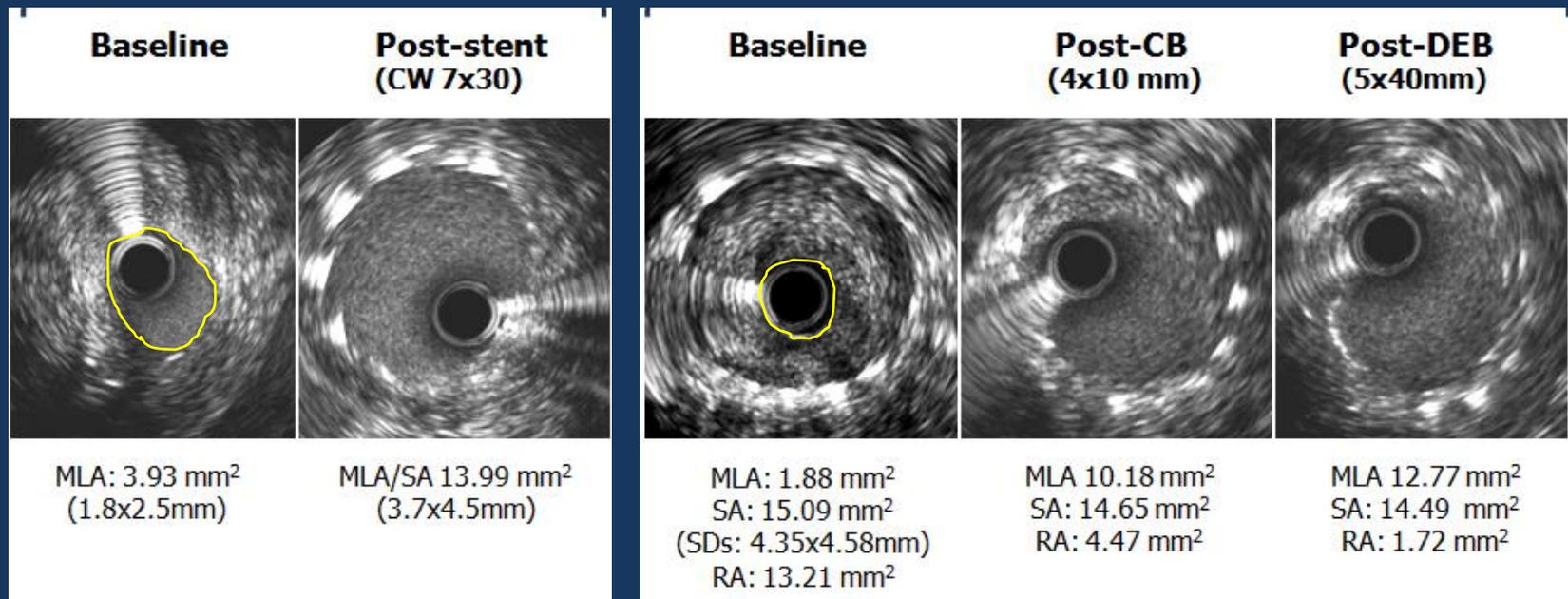
**Final
result**

DCB for In-stent restenosis after CAS

Case Example: IVUS

**Initial CAS
(7/14/2010)**

**ISR; rePTA w DCB
(6/14/2011)**



DCB for In-stent restenosis after CAS

Take Home Messages-2

- **Significant (>80% stenosis by US Doppler/angio) ISR after CAS is a rare complication**
- **Endovascular treatment is recommended**
- **Re-ISR after standard PTA may occur in 0%-50%, in some case symptomatic**
- **DCBs offer promising results over time (up to 3 years)**
- **Large, randomized study comparing DCB vs. standard endovascular treatment is required**
- **DCB with different pharmacology and carrier or/and excipient characteristics may result in different clinical outcome**

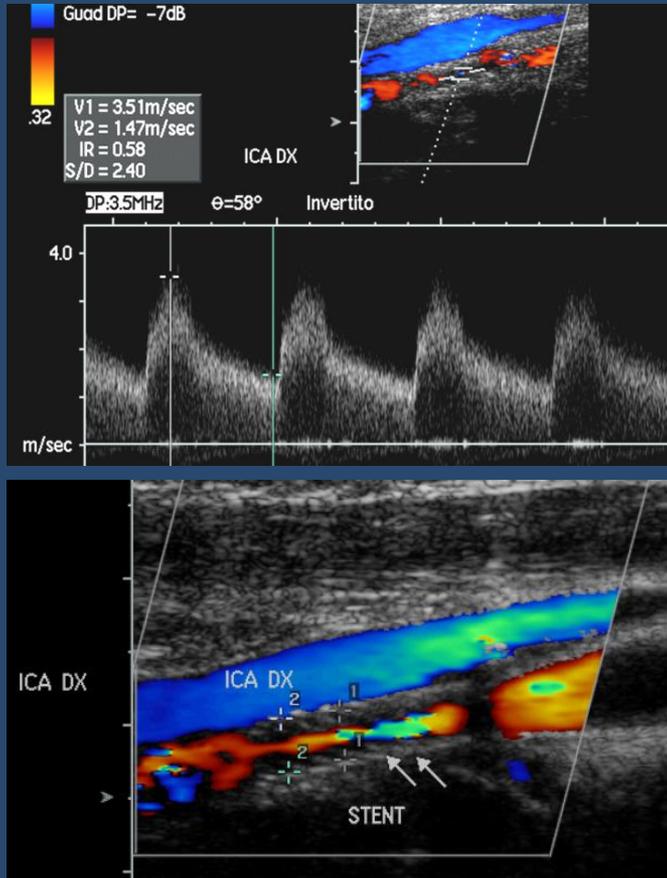
**Carotid and Intracranial Applications:
Defining the Clinical Need and Addressing
Technical Challenges**

BACK-UP SLIDES

DCB for In-stent restenosis after CAS

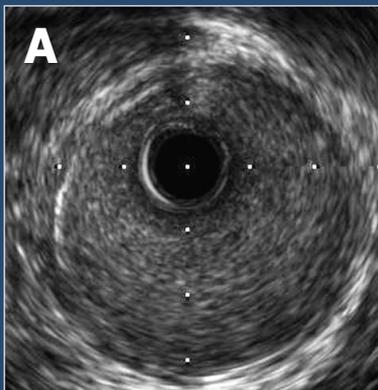
Case Example

- 58 y-o-w
- Systemic atherosclerosis with multiple PTA+stents in the past, included both common femoral arteries.
- 5/2012 Right ICA stenosis. CAS through left radial artery
- 11/2012 Asymptomatic, significant (80%) ISR

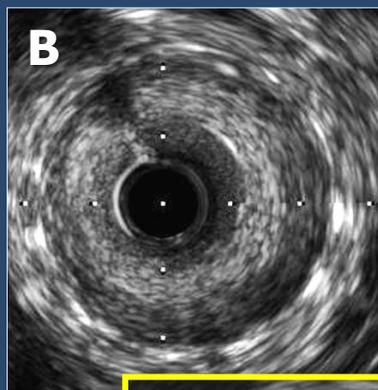


DCB for In-stent restenosis after CAS

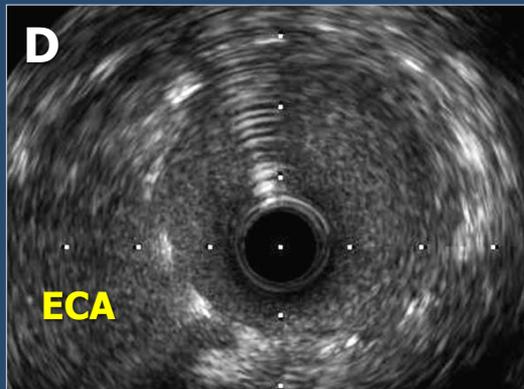
Case Example: IVUS finding



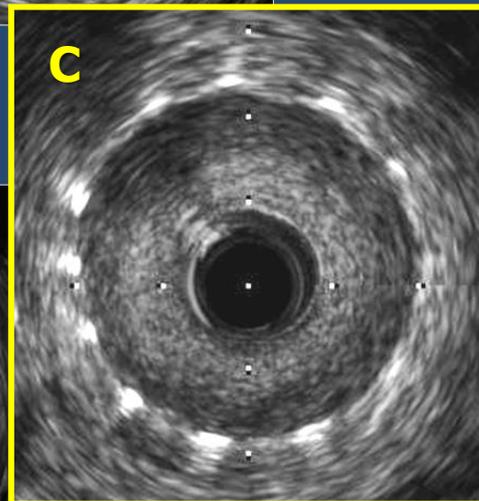
MLA 16.5 mm²
(4.5x4.4 mm)



MLA 3.75mm²
SA: 14.9 mm²
(4.4x4.3 mm)



MLA: 14.8 mm²



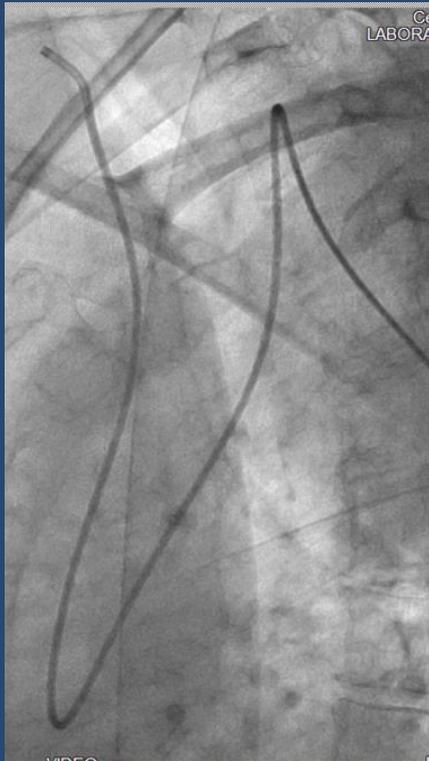
MLA: 1.89 mm²
(1.61x1.51mm)
SA: 13.2 mm²
(3.9x4.2mm)



DCB
Pantera Lux®
4x30mm
(6F guide)

DCB for In-stent restenosis after CAS

Case Example: *Procedural steps*



RCCA engagement
from left brachial
artery (CLARET)



RICA ISR



Engagement of ECA
with 260cm, .035"
Terumo wire



Pantera Lux
4x30mm
(3' inflation)



Final result

DCB for In-stent restenosis after CAS

Case Example: *Procedural steps*



RCCA ISR

6F sheath in RSA over
.035"stiff wire

6F sheath in
RCCA over filter

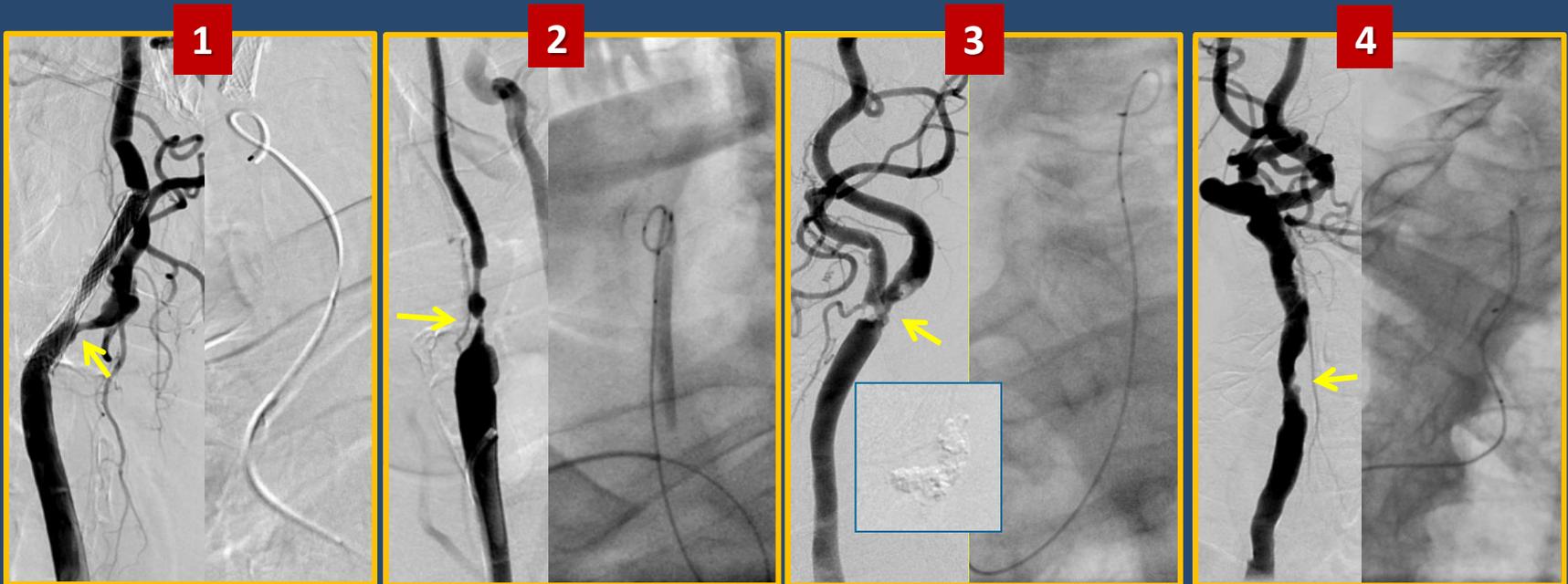
CB
4x10mm

IN.PACT
5x60mm
(3' inflation)

Final result

In-stent restenosis after CAS

The wire "reshaping" technique



In-stent restenosis

ECA occlusion

**Carotid bifurcation
disease (calcification)**

LCCA stenosis