

Flash presentation:
Clinical trials in carotid disease: What is
the state-of-the-art post-CREST?

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Disclosure

Speaker name: Ravish Sachar

I have the following potential conflicts of interest to report:

- Consulting: Boston Scientific, Medtronic
 - Employment in industry
 - Stockholder of a healthcare company: Contego Medical
 - Owner of a healthcare company
 - Other(s)
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- I do not have any potential conflict of interest

CREST Trial: 30 Day Outcomes

Per protocol	CAS N = 1,131	CEA N = 1,176	Difference	Unadjusted p-value*
All Death, Stroke, or MI	5.8% (65)	5.1% (60)	0.7%	0.5200
Death	0.53% (6)	0.26% (3)	0.27%	0.3335
Any Stroke	4.1% (46)	1.9% (22)	2.2%	0.0019
Major Stroke	0.9% (10)	0.4% (5)	0.5%	0.2005
Minor Stroke	3.2% (36)	1.5% (18)	1.7%	0.0088
MI	2.0% (22)	3.4% (40)	-1.5%	0.0387

CREST Trial

CREST Era

- Enrollment 2001-2009
- First generation technology
- Early in operator experience
- Majority of events in the first half of the study

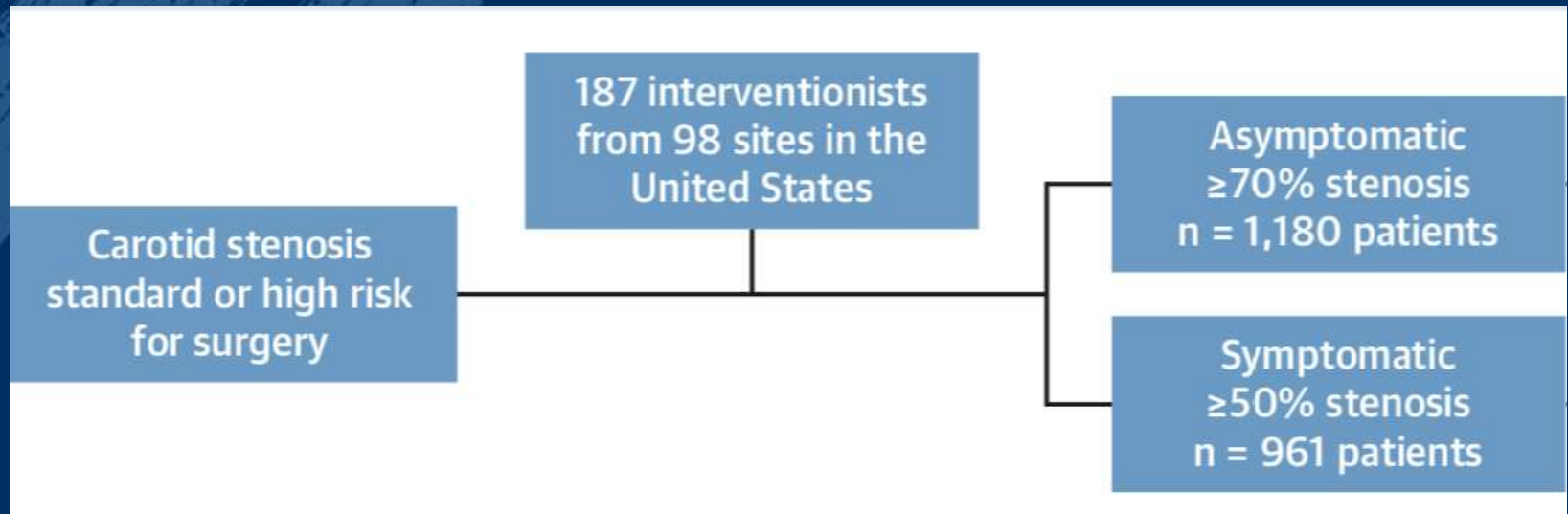
Post CREST Era

- Newer Devices
- Improvement in technique
- Better patient selection
- More through use of adjunctive therapy
- Significant increase of endovascular treatment of acute ischemic and dedicated stroke centers

ACT I: 30 Day Outcomes (Enrollment 2005-2013)

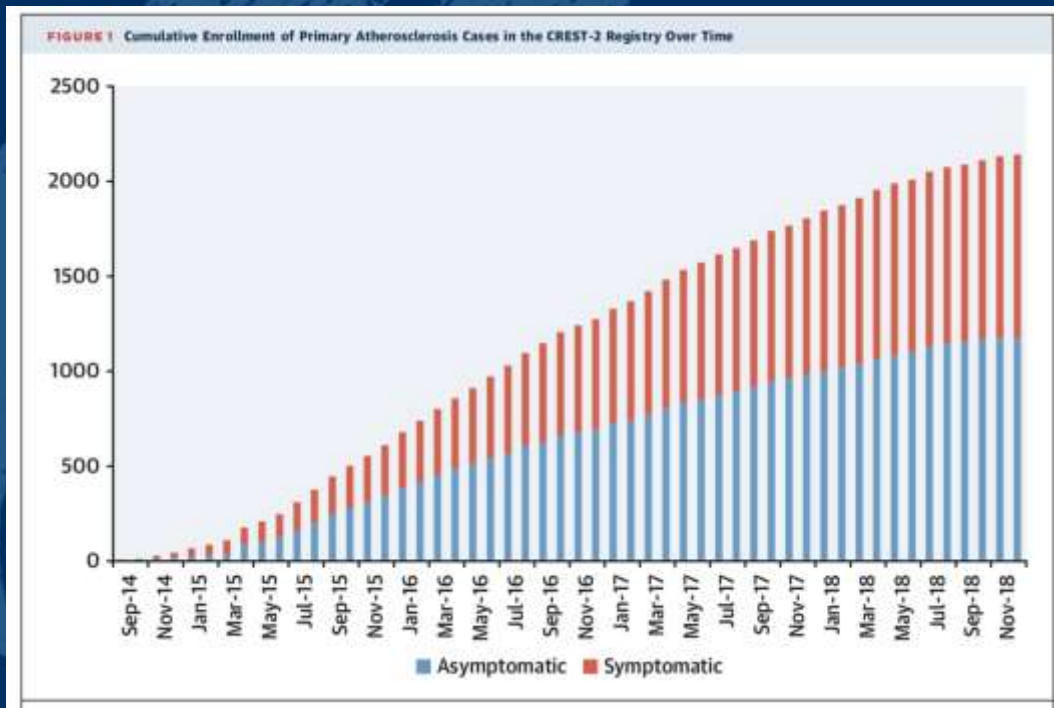
Outcome	Stenting (N=1089) <i>no. of patients/total no. (%)</i>	Endarterectomy (N=364) <i>no. of patients/total no. (%)</i>	P Value†
Death, stroke, or myocardial infarction	35/1072 (3.3)	9/348 (2.6)	0.60
Death or stroke	31/1072 (2.9)	6/348 (1.7)	0.33
Death or major stroke	6/1072 (0.6)	2/348 (0.6)	1.00
Death	1/1072 (0.1)	1/348 (0.3)	0.43
All stroke	30/1072 (2.8)	5/348 (1.4)	0.23
Major stroke	5/1072 (0.5)	1/348 (0.3)	1.00
Ipsilateral	4/1072 (0.4)	1/348 (0.3)	1.00
Nonipsilateral	1/1072 (0.1)	0/348	1.00
Minor stroke	26/1072 (2.4)	4/348 (1.1)	0.20
Ipsilateral	22/1072 (2.1)	4/348 (1.1)	0.36
Nonipsilateral	4/1072 (0.4)	0/348	0.58
Myocardial infarction	5/1072 (0.5)	3/348 (0.9)	0.41

Crest 2 Registry (Enrollment 2014-2018)



2141 Patients
45% Symptomatic

Broad Group Of Enrolling Physicians



85 Interventional Cardiologists (45.5%)

44 Vascular Surgeons (23.5%)

25 Interventional Radiologists/Neuro-Radiologists (13.4%)

23 Neurosurgeons (12.3%)

10 Interventional Neurologists (5.3%)

The median # of patients enrolled per interventionalist: 8

The median rate of enrollment: 40.5 patients/month

C2R – Procedural DATA

TABLE 2 Details of Carotid Stenting Procedures Performed in C2R for Primary Atherosclerosis

	All Patients (N = 2,141*; 100%)	Asymptomatic (n = 1,180; 55.1%)	Symptomatic (n = 961; 44.9%)
Medications			
Pre-procedure† DAPT‡	1,733 (80.9)	964 (81.7)	769 (80.0)
Pre-procedure statin therapy	1,641 (76.7)	910 (77.2)	731 (76.1)
Post-procedure§ DAPT	1,999 (93.5)	1,096 (93.1)	903 (94.1)
Stents			
Closed cell stents	1,500 (70.1)	805 (68.3)	695 (72.5)
Open-cell stents	639 (29.9)	373 (31.6)	266 (27.7)
No stent used (balloon angioplasty)	1 (0.05)	1 (0.08)	0 (0.0)
Embolic protection			
Distal filter protection	1,960 (91.5)	1,074 (91.0)	886 (92.2)
Proximal flow-reversal	153 (7.1)	94 (8.0)	59 (6.1)
No embolic protection	28 (1.3)	12 (1.0)	16 (1.7)
Anesthesia 			
Local	1,919 (94.1)	1,066 (95.3)	853 (92.7)
General	120 (5.9)	53 (4.7)	67 (7.3)

- 80.9% Pre-Proc DAPT
- 93.5% Post-Proc DAPT
- 70% Closed Cell Stents
- 99% EPD use
- 94% Local Anesthesia

Values are n (%). *The first C2R-eligible revascularization for 2,141 patients. †Pre-procedure includes medication taken within 36 h of the CAS procedure. ‡DAPT (dual antiplatelet therapy) is defined as aspirin + any other antiplatelet. §Post-procedure includes medications prescribed to the patient at the time of discharge. ||"Local" includes minimal sedation (anxiolysis), moderate sedation/analgesia (conscious sedation), local, and regional anesthesia. "General" includes deep sedation/analgesia, local converted to general, and general anesthesia.

DAPT = dual antiplatelet therapy; other abbreviations as in [Table 1](#).

Crest 2 Registry – 30 Day Outcomes

TABLE 3 Periprocedural Adverse Events Among Patients Undergoing Carotid Stenting in C2R for Primary Atherosclerosis

	All Patients (N = 2,141*; 100%)	Asymptomatic (n = 1,180; 55.1%)	Symptomatic (n = 961; 44.9%)
Stroke or death	43 (2.0)	16 (1.4)	27 (2.8)
Any stroke, regardless of laterality	35 (1.6)	12 (1.0)	23 (2.4)
Stroke ipsilateral to the index artery	31 (1.5)	9 (0.8)	22 (2.3)
Stroke contralateral to the index artery	10 (0.5)	5 (0.4)	5 (0.5)
Death	8 (0.4)	4 (0.3)	4 (0.4)
Stroke, death, or MI	47 (2.2)	18 (1.5)	29 (3.0)
MI	4 (0.2)	2 (0.2)	2 (0.2)
Stroke, death, MI, or major† access site complications	59 (2.8)	27 (2.3)	32 (3.3)
Major access site complications	13 (0.6)	9 (0.8)	4 (0.4)

Values are n (%). *The first C2R-eligible revascularization for 2,141 patients. †Access site complications are considered major if there is a need for blood transfusion or surgical evacuation/repair.

C2R = CREST-2 Registry; MI = myocardial infarction.

What do these data tell us about CREST 2 Randomized?

TABLE 4 Perioperative Adverse Events Among Asymptomatic Patients Undergoing Carotid Stenting in C2R for Primary Atherosclerosis, Stratified by Potential CREST-2 Trial Eligibility

	All Asymptomatic Patients (N = 1,180*; 100%)	CREST-2 Trial Ineligible (n = 916; 77.6%)	CREST-2 Trial Eligible (n = 264; 22.4%)
Stroke or death	16 (1.4)	14 (1.5)	2 (0.8)
Any stroke, regardless of laterality	12 (1.0)	11 (1.2)	1 (0.4)
Stroke ipsilateral to the index artery	9 (0.8)	8 (0.9)	1 (0.4)
Stroke contralateral to the index artery	5 (0.4)	5 (0.6)	0 (0.0)
Death	4 (0.3)	3 (0.3)	1 (0.4)
Stroke, death, or myocardial infarction	18 (1.5)	16 (1.8)	2 (0.8)
MI	2 (0.2)	2 (0.2)	0 (0.0)
Stroke, death, MI, or major† access site complications	27 (2.3)	23 (2.5)	4 (1.5)
Major access site complications	9 (0.8)	7 (0.8)	2 (0.8)

Values are n (%). *1,180 asymptomatic patients out of the total 2,141 C2R patients with primary atherosclerosis. †Access site complications are considered major if there is a need for blood transfusion or surgical evacuation/repair.

CREST-2 = Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Study; other abbreviations as in Table 2.

Perspectives on C2R 30-day Data

- As compared to earlier studies:
 - Interventionists in C2R were more experienced
 - Each interventionist was reviewed for prior training, total CAS experience, and current CAS volume
 - Specific recommendations were made for CAS technique
 - Arch and great vessel atherosclerosis, type 3 arches, circumferential lesion calcification, and lesion tortuosity excluded
 - Adjunctive therapy with DAPT, statins, and HTN medications better specified

Nationwide Trends in Carotid Endarterectomy and Carotid Artery Stenting in the Post-CREST Era

Tyler S. Cole, MD; Andrew W. Mezher, BS; Joshua S. Catapano, MD; Jakub Godzik, MD; Jacob F. Baranoski, MD; Peter Nakaji, MD; Felipe C. Albuquerque, MD; Michael T. Lawton, MD; Andrew S. Little, MD; Andrew F. Ducruet, MD

- The Nationwide Readmissions Database from 2010 to 2015 was obtained from the Healthcare Cost and Utilization Project
- Nationwide trends in CAS and CEA and associated periprocedural stroke, MI, death, cost, and readmission rates since CREST was published
- 378 354 CEA and 57 273 CAS patients were treated between 2010 and 2015
- Patients were matched based on demographics, comorbidities, and severity of illness.

30 Day Outcomes

	CAS	CEA	OR	P-value
30-Day Stroke - All Pts	1.9%	2.6%	1.47 [CI, 1.29–1.68]	<i>P</i> <0.001
30-Day Stroke - ASX	0.2%	0.3%		<i>P</i> =0.113
30-Day Stroke - SX	5.6%	8.1%	1.47 [CI, 1.29–1.68]	<i>P</i> <0.001
Inpatient Mortality	1.4%	0.8%	0.57 [CI, 0.48–0.68]	<i>P</i> <0.001
30-day Readmission	8%	7.2%	0.90 [CI, 0.84–0.96]	<i>P</i> =0.018
Cost	\$19,172	\$14,433		<i>P</i> <0.001

Lower stroke rate was in CAS was driven by higher stroke risk among symptomatic CEA patients, with no significant difference among asymptomatic patients.

Scaffold Trial – Per Protocol Population

	Analysis Population (n = 265)
Patients evaluable for 30-day MAE*	99.6 (264)
Death/stroke/MI†	3.0 (8) (1.3–5.9)
Stroke/death	1.5 (4)
Death	0.4 (1) (0.0–2.1)
MI (all non-Q-wave)	1.5 (4) (0.4–3.8)
Stroke	1.1 (3) (0.2–3.3)
Major stroke	1.1 (3)
Ischemic stroke (all ipsilateral)	0.8 (2)
Hemorrhagic stroke (ipsilateral)	0.4 (1)

12.8% Symptomatic

Armour Trial

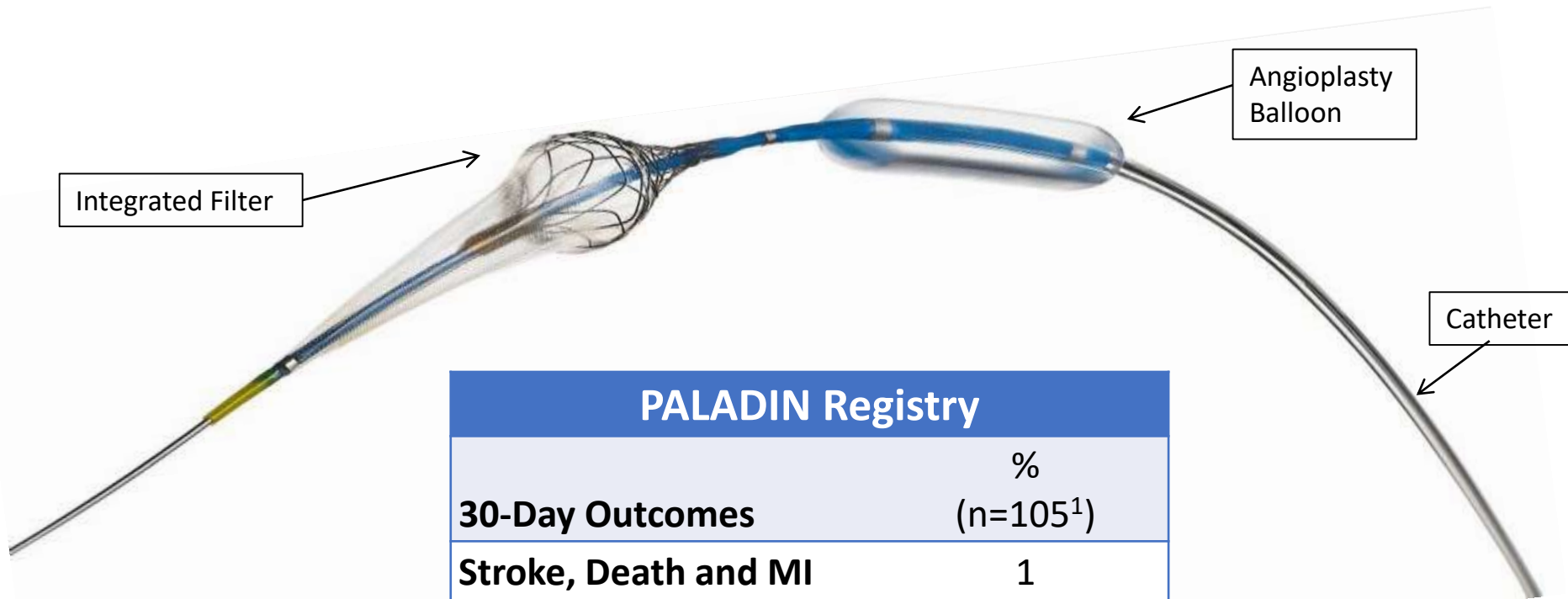
TABLE V. Primary and Secondary Endpoints

Endpoints	ITT population (N = 220)	Roll-in (N = 37)	Full analysis population (N = 257)
Primary endpoint			
Composite rate of MACCE to 30 days post-procedure	2.7% (6/220)	0.0% (0/37)	2.3% (6/257)
Any myocardial infarction	0.0% (0/220)	0.0% (0/37)	0.0% (0/257)
Stroke	2.3% (5/220)	0.0% (0/37)	1.9% (5/257)
Minor ipsilateral stroke	1.4% (3/220)	0.0% (0/37)	1.2% (3/257)
Minor contralateral stroke	0.0% (0/220)	0.0% (0/37)	0.0% (0/257)
Major ipsilateral stroke	0.9% (2/220)	0.0% (0/37)	0.8% (2/257)
Major contralateral stroke	0.0% (0/220)	0.0% (0/37)	0.0% (0/257)

No Strokes in Symptomatic Patients

Paladin Registry – 106 Patients

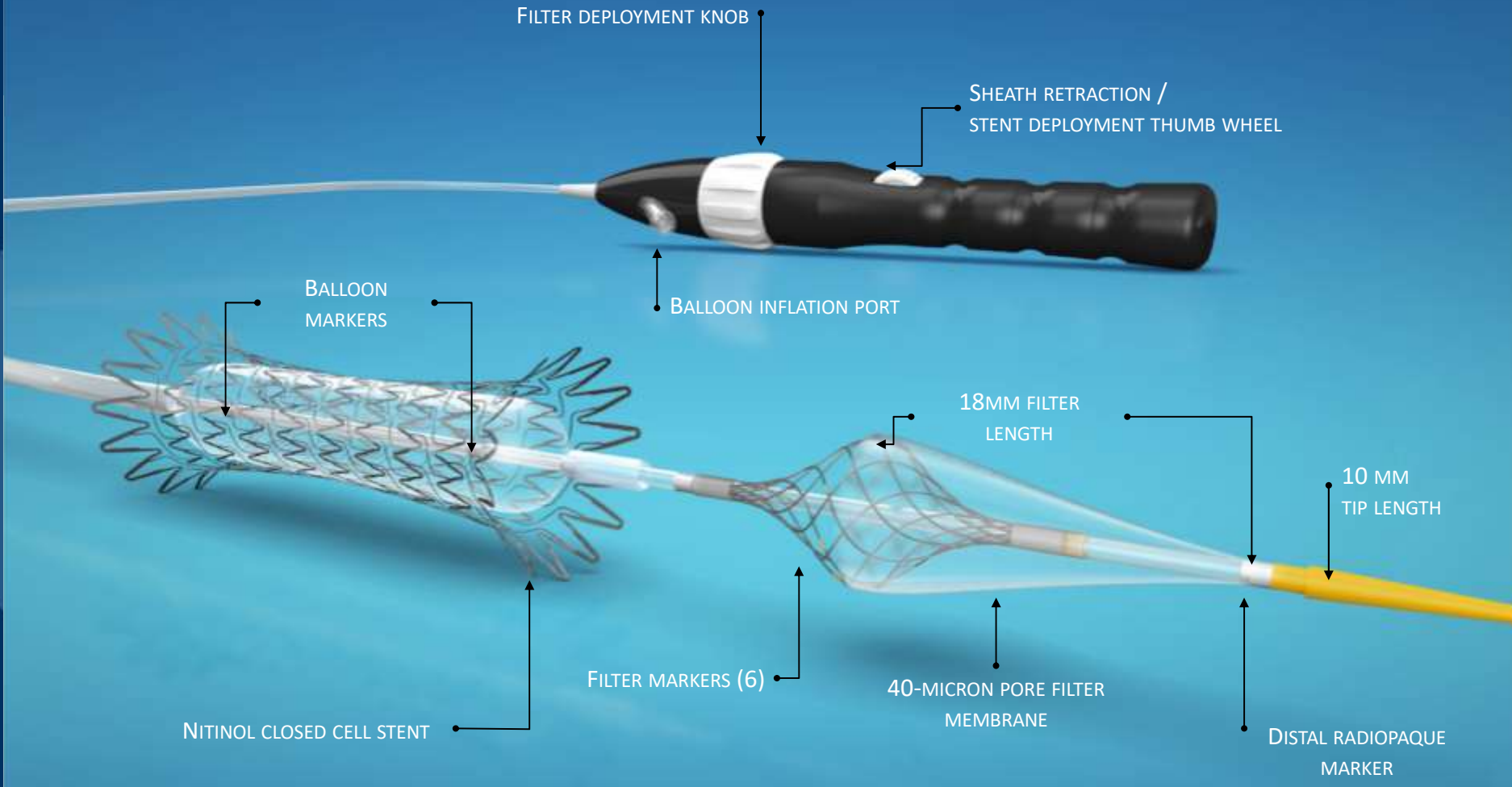
Carotid Balloon with Integrated Embolic Protection



PALADIN Registry	
	%
30-Day Outcomes	(n=105¹)
Stroke, Death and MI	1
Death	0
Stroke	1
Myocardial Infarction	0
Stroke and Death	1

¹Of the 106 subjects enrolled, one (1) subject withdrew consent following discharge, and 105 were eligible for follow up at 30 days. This patient had no neurological events

Neuroguard IEP®



PERFORMANCE I Study:

30 day, 6- and 12-month Outcomes

Long Term Outcomes	30 days (n=67)	6 months (n=67)	12 months (n=62)
Neurological Death	0	0	0
Stroke	0	0	0
Major	0	0	0
Minor	0	0	0
Stroke and Neurological Death	0	0	0
Myocardial Infarction	1	1	1
Total	1	1	1

Summary

- Carotid stenting technology and experience have both steadily evolved in the post-CREST era
- We should expect 30-day stroke rates in ASX patients in the 1-2 % range
- Newer therapies hold promise for even better outcomes, especially for symptomatic patients
- Narrowing or elimination of the delta between ASX and SX patient



Conclusion:

State of the Art in the Post-Crest Era?

- Patients have more choices than ever before with multiple approaches for CAS, many of which offer excellent outcomes at a significantly improved risk profile
- However, currently in the US, re-imburement remains a barrier for equal access to these technologies



Thank you!

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