The C-GUARDIANS IDE Trial for the C-Guard MicroNet Stent, and Context from Longer term European Data

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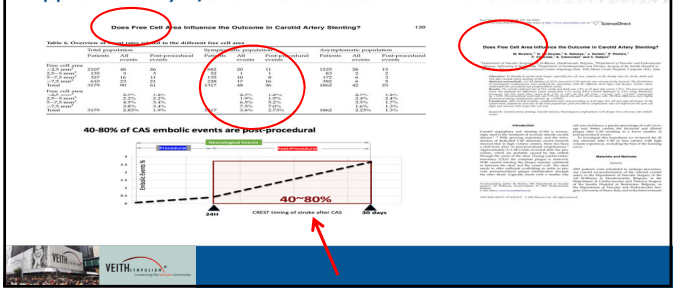
Disclosures

- ***Symposia Honoraria & Proctor Fees***:
  - Abbott, Endologix
- ***Symposia Honoraria***:
  - Boston Scientific, Shockwave, Gore, Penumbra
- ***National PI/Co-PI***: C-GUARDIANS, Confidence, SAPPHIRE WW, CANOPY
- ***VIVA Board Member***
- ***Research Grants, Stocks, Equity***
  - None

Important Note: The C-GUARD stent is an *investigational device ONLY* in the US

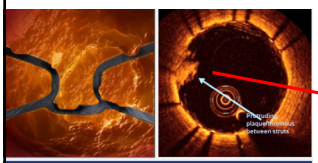
Why a Micro-mesh Carotid Stent?

Approximately 2/3 of Events Occur AFTER the CAS Procedure

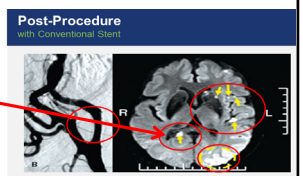


- So, with standard conventional carotid stents, there is some early post-procedure risk of stroke regardless of the access routes or embolic protection type chosen (***TCAR, proximal protection***, etc.)

Post CAS Strokes: Plaque Protrusion Through Stent Cells



Conventional Open Cell Stent (1ST GEN):
Bare or dual layer approach, with plaque protrusion risk



Successful opening of the carotid artery

MRI reveals new multiple micro-infarcts (obstructions) due to liberation of embolic particles

Ideal Characteristics of a Carotid Stent

- Conformable, works in majority of carotid anatomies, AND
- Maximizes plaque coverage to reduce protrusion/ embolization

Available Conventional Carotid Stents

Open Cell Stents: Conformable, but least plaque coverage

Closed Cell stents: Better plaque coverage, but rigid and less conformable

C GUARD Micro-Mesh Carotid Stent:
"The Ideal Carotid Stent Design"?

Important Note: The C-GUARD stent is an *investigational device ONLY* in the US

C GUARD Micro-Mesh Stent

- Theoretically combines the "best of two worlds":
- Extremely conformable through proprietary "Smart Fit" technology, AND
- Has by far the best plaque coverage through the micro-mesh layer with the smallest stent cell size to date

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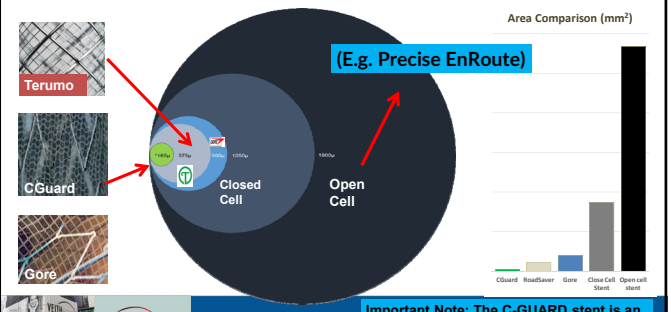
MicroNet™ Technology Around The CGuard™ Stent



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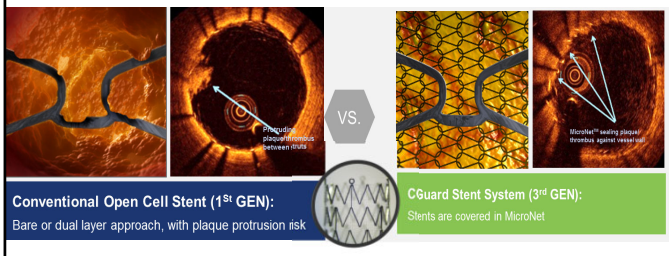
Stroke Prevention Strategy: MicroNet Technology



Conventional Open Cell Stent (1St GEN):
Bare or dual layer approach, with plaque protrusion risk

CGuard Stent System (3rd GEN):
Stents are covered in MicroNet

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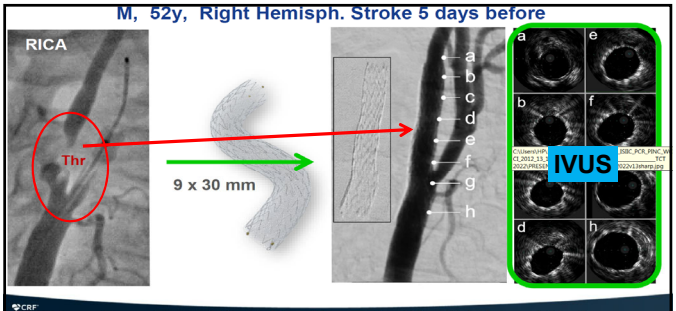
M, 52y, Right Hemisph. Stroke 5 days before



TCT Trans-Femoral MoMa Flow Reversal + MicroNet-Covered Stent

P. Musialek @ TCT 2022

OPTIMA Clinical Trial

Randomized Controlled Trial: CGuard™ MicroNet™ vs Acculink

Superior Protection from New DW-MRI Lesions

YEAR:	STUDY:	HIGHLIGHT:
2020	SIBERIA	Randomized trial; CGuard demonstrates neuroprotection vs conventional stents

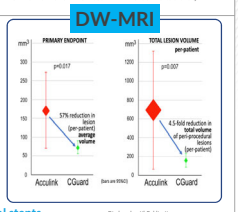
✔ CGuard demonstrates SUPERIORITY to other stents

Андрей Анатольевич Карпенко
FGBU "SFBMITS them. AK. E.N. Meshalkin "of the Ministry of Health of Russia Center of Vascular and Hybrid Surgery,,SCIENTIFIC RESEARCH INSTITUTE OF CARDIOVASCULAR PATHOLOGY Novosibirsk city

CLINICAL RESULTS:
- The study data provide, for the first time, Level-1 evidence for a novel role of MicroNET-covered carotid stent (stent as a peri- and post-procedural cerebral protector)

Study Overview (N)	#/N (%) DSMI 30d CGuard	#/N (%) DSMI 30d Acculink
SIBERIA Randomized Trial	0/50 (0%)	3/50 (6.00%)
MINOR STROKE/TIA	0/50 (0%)	2/50 (4%)
MAJOR STROKE	0/50 (0%)	0/50 (0%)
MYOCARDIAL INFACTION	0/50 (0%)	1/50 (2%)
RELATED DEATH	0/50 (0%)	0/50 (0%)
NON-RELATED DEATH	0/50 (0%)	0/50 (0%)
1y IN-STENT RESTENOSIS/OCCLUSION	0/50 (0%)	3/50 (6%)

DW-MRI



Randomized Trial; CGuard™ demonstrates Neuroprotection vs Conventional stents

2020 PCR e-Course by Pavel Ignatenko
2021 LINC Sarv Bugurov

C GUARD : Potential Advantages over Other Micro-Mesh Carotid Stents

- ↑ Conformability with "auto-tapering"
- *Exact length* compared to elongating stents
- Smaller mesh pores, sewn on *outside* of stent, no coating
- C GUARD has significantly less restenosis and occlusion issues, with good long term durability data
- Easier to size and deliver the stent
- Larger matrix stent sizing options; no supply issues

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MESH STENTS, SPECIFIC PLATFORMS AND FEATURES

Second Generation Stents

Mesh Design

* Mesh for permanent plaque coverage

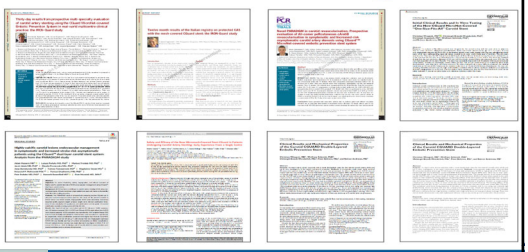
* Open Cell Stent for conformability

Name	RoadSaver / Casper	Gore® Carotid Stent	CGuard ™
Manufacturer	Terumo / Microvention	Gore®	InspireMD
Clinical data	2014 CE Approved	2018 FDA Approved	2015 CE Approved/IDE
Stent frame	Nitinol closed-cell	Nitinol open-cell	Nitinol open-cell
Mesh position in relation to frame	inside	outside	outside
Mesh material	Nitinol	PTFE Polytetrafluoroethylene	PET Polyethylene terephthalate
Mesh structure	braided	inter-woven	20 µ single - fibre knitted
Pore size	375 - 500 µm	500 µm	150 - 180 µm

C GUARD: Excellent Data, Results

Carotid Solution: Our Well Studied Mesh-Covered Technology

More than **1,600** patients in Clinical Publications & Studies



European Data for C-Guard

YEAR	STUDY	PUBLICATION HIGHLIGHTS
2015	CARENET	Safety, Efficacy & Neuroprotection over other stents data
2016	PARADIGM	All comers population; Excellent clinical results
2017	CASANA	Large surgical center; Clinical results over conventional stents historical data
2017	WISSGOTT	Clinical & mechanical assessment; Mechanical advantages vs competitive stents
2017	IRON-GUARD 1	Real world multicentric 30d results; Excellent clinical results in multicentric
2018	WISGOTT 10MM	"One-Size-Fit-All"; 10 mm CGuard OSFO demonstrates safety and efficacy
2019	IRON-GUARD 1	Real world multicentric 1y results; Excellent long-term results in multicentric
2020	IRON-GUARD 2	Large real world multicentric; Large Multicentric validate Best-In-Class clinical results
2020	SIBERIA	Randomized Trial; CGuard demonstrates Neuroprotection vs Conventional stents
2021	POLISH VASCULAR REGISTRY	Large Real-World multicentric; Expected excellent clinical results
2022	OCTOPVS	OCT comparison CGuard vs CEA; Anticipated CGuard superior procedural results than CEA
2022	PARADIGM EXTEND	Large long-term study for all commers; CGuard to prove excellent long-term results
2022	OPTIMA	IVUS assessment after CGuard; Anticipated Plaque exclusion demonstrated
2023	FLOW-GUARD	Use of CGuard as flow diverter in very high-risk patients beyond carotids; Potential new CGuard indications

CGuard™ Real Life Registry (733 Patients, 20 Centers)

YEAR: 2020 | STUDY: IRONGUARD 2 | HIGHLIGHT: Large real world multicentric: Excellent clinical results to date | ✔ CGuard™ demonstrates safety and feasibility in real-world

Prof. Speziale, Umberto I Hospital, Rome — Dr. Sirignano, Umberto I Hospital, Rome

CLINICAL RESULTS:
- Procedure success 100%
- No major stroke @30 days, @1y
- DSMI at 30d 8/733 (1.09%)

CONCLUSIONS:
"Our analysis suggests that use of the CGuard-EPS in routine clinical practice was associated with an extremely low occurrence of adverse neurologic events."

Study Overview (N)	#/N (%) DSMI 30d	#/N (%) 1y IpsS	#/N (%) 1y ISR	#/N (%) DSMI 30d + 1y IpsS + 1y ISR
IRONGUARD 2 (733)	8/733 (1.09%)	1/726 (0.14%)	6/726 (0.83%)	15/726 (2.07%)
MINOR STROKE	4(*)/733 (0.41%)			
MAJOR STROKE	0/733(0.14%)			
MYOCARDIAL INFACTION	4/733 (0.55%)			
RELATED DEATH	0/733 (0%)			
NON-RELATED DEATH	1(* Hem. Transf.)/733 (0.14%)			

JACC ; LINC 2021

Additional Information:
- Prospective multicenter (20) independent Investigator Initiated Study.
- 17.% Symptomatic. 80.9% EPS and proximal occlusion 18.82%). Pre-dilatation 23.05%, and Post-dilatation in 82.81%.
- Procedural success 100%. Technical success 99.86%.

Ongoing Trial: CGuard™ All Comers

CGuard™ Provides Sustained Benefit in Unselected Patients

YEAR: 2022 | STUDY: PARADIGM EXTEND | HIGHLIGHT: Long-term study for all comers; CGuard to evaluate long-term results | ✔ CGuard™ demonstrates long term safety and feasibility

Piotr Musialek, MD, DPhil — Jagiellonian University Professor of Cardiovascular Medicine and Dept. of Cardiac & Vascular Diseases; Consultant in Vascular Medicine and Cardiology, John Paul II Hospital, Krakow, Poland

CLINICAL RESULTS:
- 480 (from 550 expected) all comers, high risk patients
- With on going 5 years FU will demonstrate CGuard™ EPS long term safety

Study Overview (N)	#/N (%) DSMI 30d	#/N (%) 1y IpsS	#/N (%) 1y ISR	#/N (%) DSMI 30d + 1y IpsS + 1y ISR
PARADIGM EXTEND (480)	5/480 (1%)	1/354 (0.28%)	1/354 (0.28%)	7/354 (1.98%)
MINOR STROKE	2/480 (0.42%)			
MAJOR STROKE	0/480 (0%)			
MYOCARDIAL INFACTION	1/480 (0.21%)			
RELATED DEATH	0/480 (0%)			
NON-RELATED DEATH	2/480 (0.42%)			

MicroNET-covered stent: clinical and duplex 5-year outcomes

PARADIGM-Extend Study n = 480

	12 mo	24 mo	36 mo	48 mo	60 mo
Ipsilateral stroke	1*	0	0	0	1
Any stroke	1	2	1	1	1
Stroke related death	0	0	0	0	1
MI or other non - cerebral	1	1	1	1	0
Restenosis	1	0	0	0	0
Any death	2	2	2	2	2

0.83%

ESC Congress 2020 — The Digital Experience

Carotid Disease: Essential Update 2020

C-GUARDIANS TRIAL

- FDA US Pivotal IDE Trial
- US and Europe Trial 315 High risk CEA patients, up to 50 sites; FU 3-5 years
- Primary Endpoint: D/S/MI at 30 days and ipsilateral stroke 1 year
- All trial patients approved by screening committee
- Core lab, CEC, DSMB adjudicated
- Sponsor: INSPIRE MD
- PI: Chris Metzger (US); Piotr Musialek (Europe)

C-GUARDIANS US IDE Pivotal Trial

Careful Design and Oversight

- Requires NAV6 distal embolic protection or MoMa Proximal embolic protection systems (best in class protection)
- Clinical sites and (limited) operators carefully selected
- All cases must be approved by a screening committee
- Protocol carefully prepared and revised
- All cases reviewed early after completion
- Trial combines an excellent stent with experienced operators, mandated procedural techniques, and carefully selected cases

C-GUARDIANS IDE Trial Progress…

- First patients enrolled July 21, 2022
- 235 patients enrolled to date (74.5% enrolled)
- DSMB, CEC reviews: No concerns
- Promising results to date
- ***C-Guard stent now included in CREST 2 Trial***

Conclusions

- The C-Guard MicroNet stent is a unique technology with potential additional "neuroprotection" in a conformable stent with provides maximizes lesion coverage and scaffolding
- Long term comparative data from Europe demonstrates excellent results which are durable in high risk lesions, with intra-lesion imaging confirming excellent plaque exclusion, and lowered DW-MRI emboli
- The C-GUARDIANS IDE pivotal trial is ongoing and should provide additional rigorous data

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Thank You for Your Attention!