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First Report of the DEFLECT I Trial
A Prospective, Single Arm Feasibility Study to Evaluate the Safety and Performance of the KeyStone Heart TriGuard™ Embolic Deflection Device in Patients Undergoing Transcatheter Aortic Valve Replacement (TAVR)

Michael Mullen, Andreas Baumbach, Stephanie Meller, Adam Brickman, Pauliina Margolis, Jan Kovac, David Hildick Smith, Cody Pietras, Peter Den Heier, Szilard Voros, Alexandra Lansky

PCR EAPCI EUROPEAN SOCIETY OF CARDIOLOGY EACTS

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I have financial relationships to disclose

Consultant for: Edwards Lifesciences, Nobles Medical Technology

Research support from: Keystone Medical, Edwards Lifesciences, Medtronic, Abbott Vascular, Direct Flow Medical

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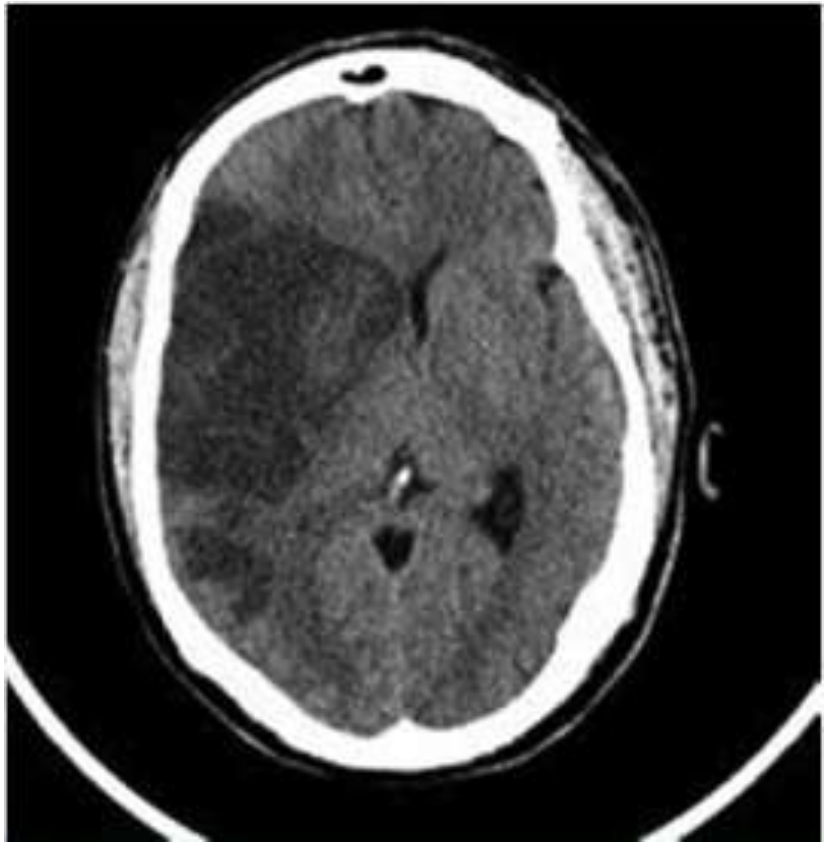
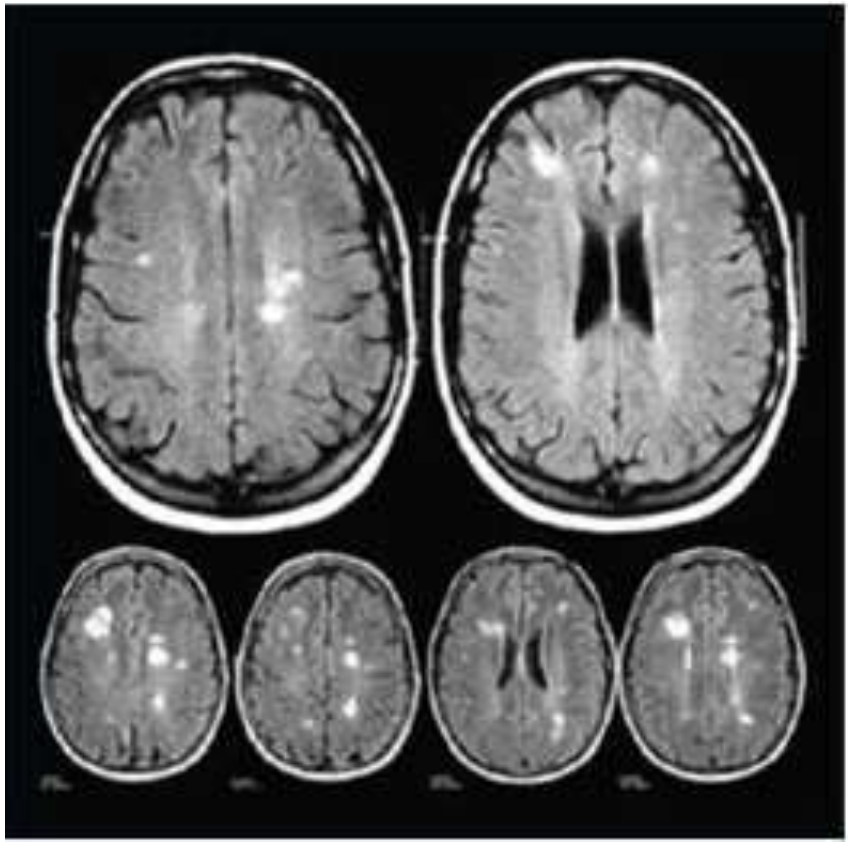
Cerebral injury post TAVR





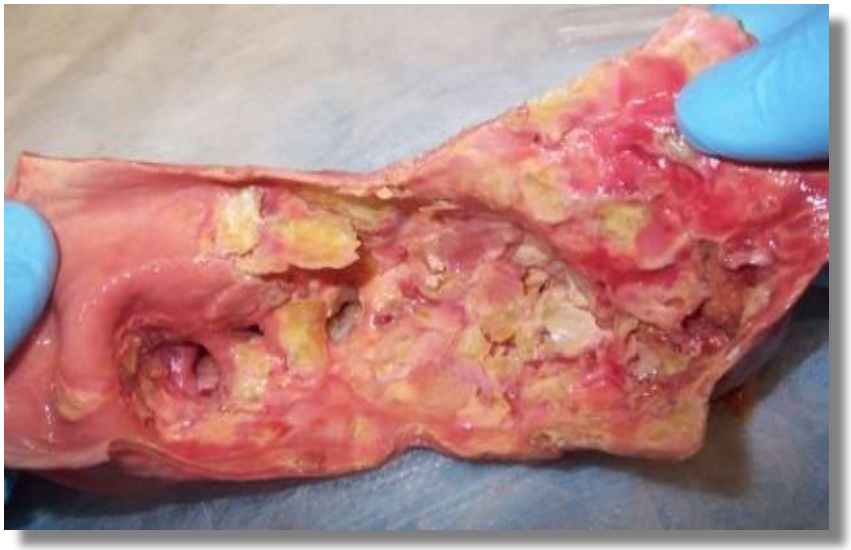
Stroke 3.8 – 6.7% (Partner trials)
Majority are major with significant disability

New DW MRI lesions 58 – 91%

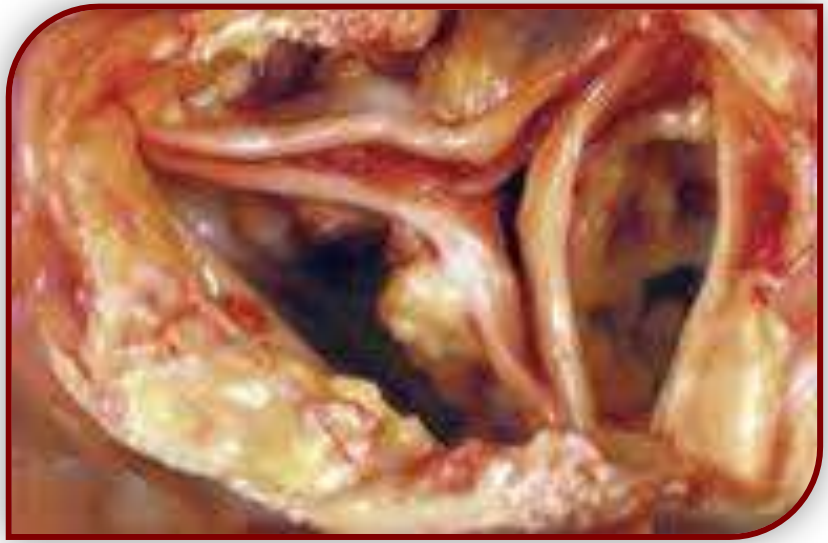
Kahlert 2010, Knipp 2010, Ghanem 2011, Astarci 2011, Stolz 2004, Arnold 2010, Rodes 2011

Athero-Calcific Embolism

Primary source of embolic material following TAVR



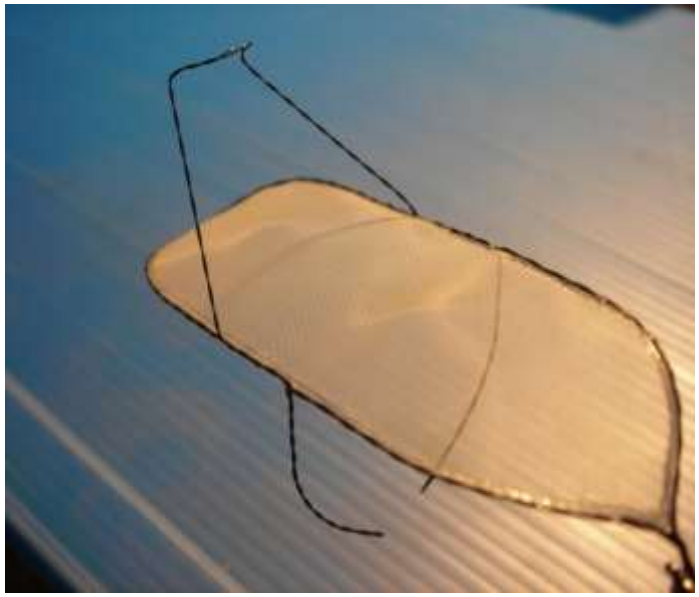
Aorta

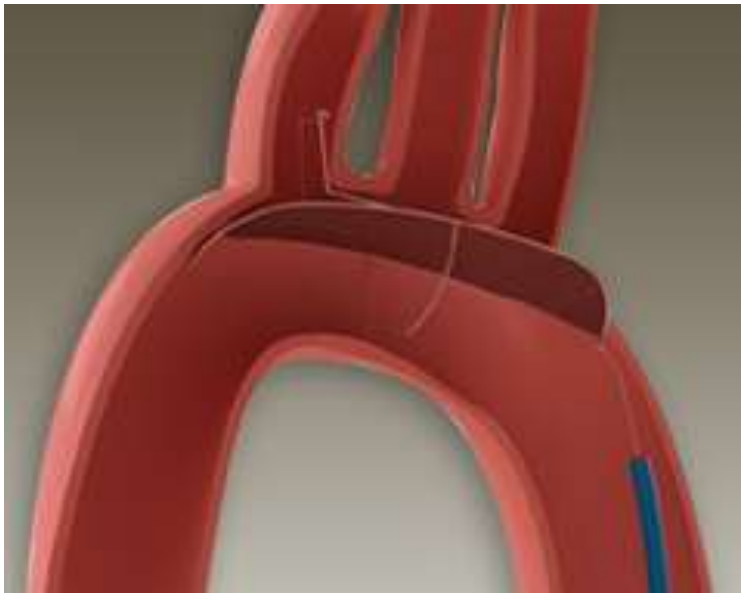


Valve

TriGuard™ Embolic Deflection Device

- The TriGuard™ EDD is a nitinol mesh filter with a pore size of 250µm designed deflect cerebral emboli while allowing maximal blood flow.
- The filter's positioning across all 3 cerebral vessels is maintained by stabilizers.
- Delivered via 9 Fr sheath from femoral artery





EDD in position

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DEFLECT I Trial Design

- Purpose
  - To evaluate the safety and performance of the TriGuard™ EDD in patients undergoing TAVR procedures
  - CE Mark Submission on first 20 consecutive patients
- Study Design
  - Prospective, multi-center, single arm registry design
  - A minimum of 36 subjects up to a maximum of 60 to be enrolled at up to 10 centers in the European Union and Canada

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Inclusion and Exclusion Criteria

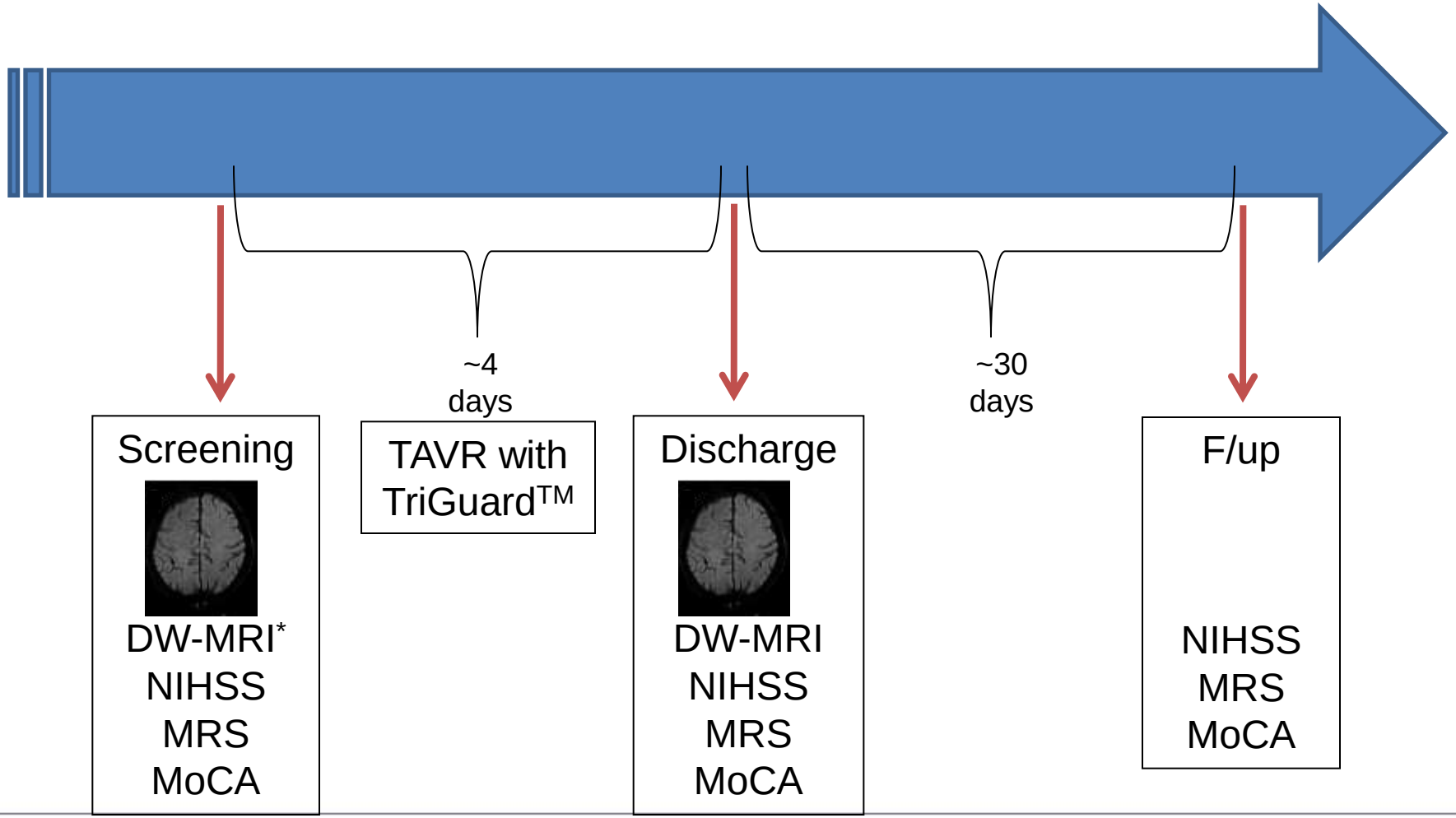
Inclusion Criteria

- ≥ 18 years of age
- Meets indications for TAVR procedure
- Willing to comply with protocol specified follow-up procedures
- Written informed consent

Exclusion Criteria

- TAVR to be performed via trans-axillary, or direct aortic approach
- Acute myocardial infarction within 72 hrs of procedure
- Impaired renal function (GFR < 30 ml, Cockcroft-Gault formula)
- History of stroke or transient ischemic attack within 6 mo
- Severe peripheral arterial disease that precludes 9 Fr sheath
- Documented friable or mobile atherosclerotic plaque in the aortic arch

Key Study Procedures and Time points



Screening DW-MRI*: Performed up to 21 days prior to TAVR

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DEFLECT I Trial Design

Primary endpoints

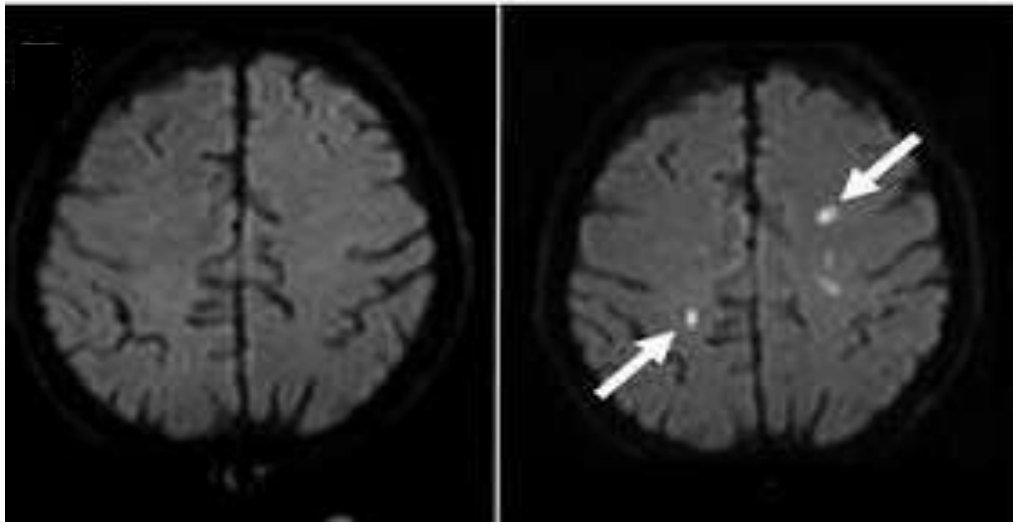
- ***Device performance***
  - EDD access to the aortic arch
  - Able to deploy the EDD
  - Position the EDD across all 3 cerebral vessels during TAVR procedure
  - Retrieve the EDD delivery system
- ***In-hospital device-related safety (hierarchial Composite)****
  - Cardiovascular Death
  - Major Stroke disability
  - Life threatening bleed
  - Acute CV surgery

**All events adjudicated by independent CEC (VARC2)*

DEFLECT I Trial Design

Secondary endpoints

- ***Powered efficacy endpoint:***
- Number of patients with new DW MRI lesions
  - Average and total volume of new lesions in each patient



- Procedure related MACE (non EDD)*

**All events adjudicated by independent CEC (VARC2)*

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DEFLECT I Trial Organization

Principle Investigator	Michael Mullen, MD
Heart Hospital, University College London	Michael Mullen, MD
Bristol Heart Institute	Andreas Baumbach, MD
University Hospitals of Leicester	Jan Kovac, MD
Brighton and Sussex University Hospital	David Hildick-Smith, MD
Amphia Ziehenhuis Molengracht Breda	Peter den Heijer, MD, PhD
Data Analysis, Clinical Events Committee, Angiographic Core Laboratory	Yale Cardiovascular Research Alexandra Lansky, MD
DW MRI Core Laboratory	Global Institute for Research Szilard Voros, MD, PhD
Trial Management, Monitoring	MedPass International Sarah Sorrel
Sponsor	Keystone Heart Pauliina Margolis, MD, PhD

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Baseline Demographics

Data on the first 28 consecutive patients with 20 paired DW MRI

Characteristic	N=28
Age	82.9±6.2
Female	21 (75%)
DM	3 (11%)
COPD	5 (17.9%)
Prior CABG/PCI	5 (18%)/ 3 (11%)
NYHA Class I, II, III, IV	4(15%)/5 (19%)/ 17(63%)/ 1(4%)
Prior CVA	2 (7%)
Atrial fibrillation	9 (32%)
Renal insufficiency	4 (14%)
Corevalve/Edwards Sapien	64%/36%

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TriGuard™ Performance

Characteristic	Before TAVR	Post TAVR	After TAVR Removal
TriGuard™ access to Aortic Arch	28 (100%)		
TriGuard™ positioned in arch	28 (100%)	27 (96%)	22 (79%)
TriGuard™ Covers all 3 vessels	26 (93%)	23 (82%)	19 (68%)
TriGuard™ stabilized anchored in innominate	24 (86%)	23 (82%)	18 (64%)
TriGuard™ retrieved intact			28 (100%)

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Primary TriGuard™ Related Safety

	TriGuard™ Device Related		Procedure (NOT TriGuard™) Related	
Characteristic	In-hospital	30 Days	In-hospital	30 Days
Composite Safety/MACCE	0%	0%	7.1%	10.7%
All cause Death	0%	0%	0%	3.6%
Major Stroke Disability	0%	0%	7.1%*	7.1%*
Life threatening Bleed	0%	0%	0%	0%
Distal Embolization	0%	0%	0%	0%
Major Access complication	0%	0%	3.6%	3.6%
Urgent CV surgery	0%	0%	3.6%	3.6%
Acute Kidney Injury-Stage 3	0%	0%	3.6%	3.6%

2 disabling strokes not TriGuard™ related occurred 1 day after TAVR.
(1) in association with urgent surgical conversion of failed TAVR and
(2) following cardiac resuscitation.

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DW-MRI Results

Lesion Volume Reduction vs. Historic Controls

(Kahlert 2010, Ghanem 2011, Astarci 2011, Stolz 2004, Rodes Cabau 2011)

Parameter	DEFLECT-I N=20	Historical Data N=150
Proportion of Patients with New Lesions	**70%**	**76%**
Number of New Lesions	**5.1 (0 - 28)**	**4.4 (0 -39)**
Average New Lesion Volume	**0.12 (0 - 0.39) cm^3**	**0.34 cm^3**
Max Single New Lesion Volume	**0.39 cm^3**	**6.45 cm^3**
Total New Lesion Volume	**0.70 (0 – 3.94) cm^3**	**1.64 (0 – 70.3) cm^3**

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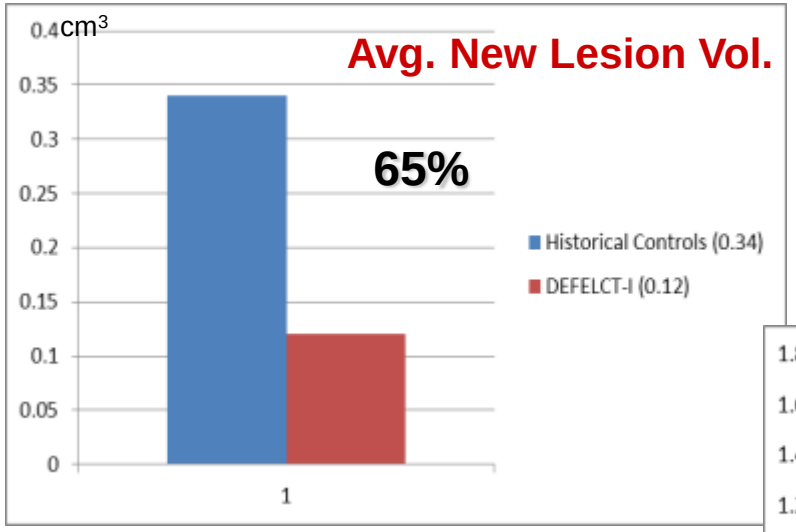

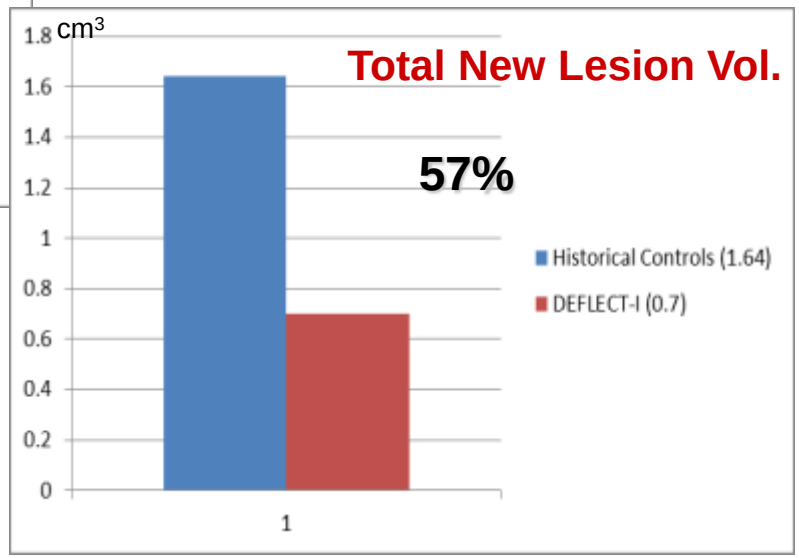

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Conclusions

- Use of the TriGuard™ Embolic Deflection Device is feasible and safe in patients undergoing TAVR
- The TriGuard™ performed as intended in 82% of cases with full coverage of all 3 cerebral vessels until completion of TAVR deployment
- There were no TriGuard™ device related adverse events
- Use of TriGuard™ resulted in similar number of new lesions as historical controls
- However, Average New Lesion Volume was smaller by 65% and the Total New Lesion Volume was 57% lower than historical controls
- Further studies will further determine the role of TriGuard™ EDD in preventing ischaemic brain injury during TAVR and other cardiac interventions