Flow diversion and Neck bridging devices

S Lamin
Queen Elizabeth Hospital
Birmingham

ECMINT
Oxford
June 2019

University Hospital Birmingham NHS
NHS Foundation Trust

How does FD work

- FD provides endoluminal reconstruction as opposed to endosaccular reconstruction with coils
- Immediate effect: mechanical flow disruption.
- “Days to weeks” Thrombus formation, the rate of thrombus formation varies according to size and configuration of the aneurysm.
- Biological: “weeks to months” after the flow to the aneurysm is reduced, thrombus stabilizes and endothelial growth starts.

What is porosity and pore density?

- POROSITY: Ratio of metal free surface area in a stented vessel
- PORE DENSITY: Number of pores per unit surface area i.e., holes/mm^2 (may be important in the efficacy of flow diverters*)

DIAGRAM A

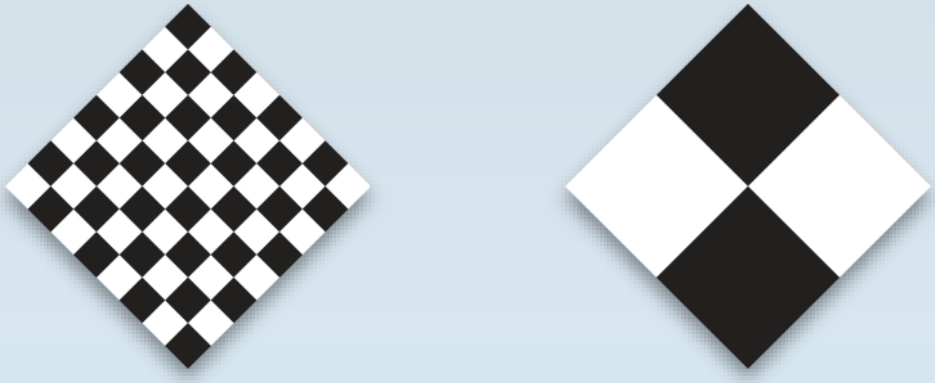


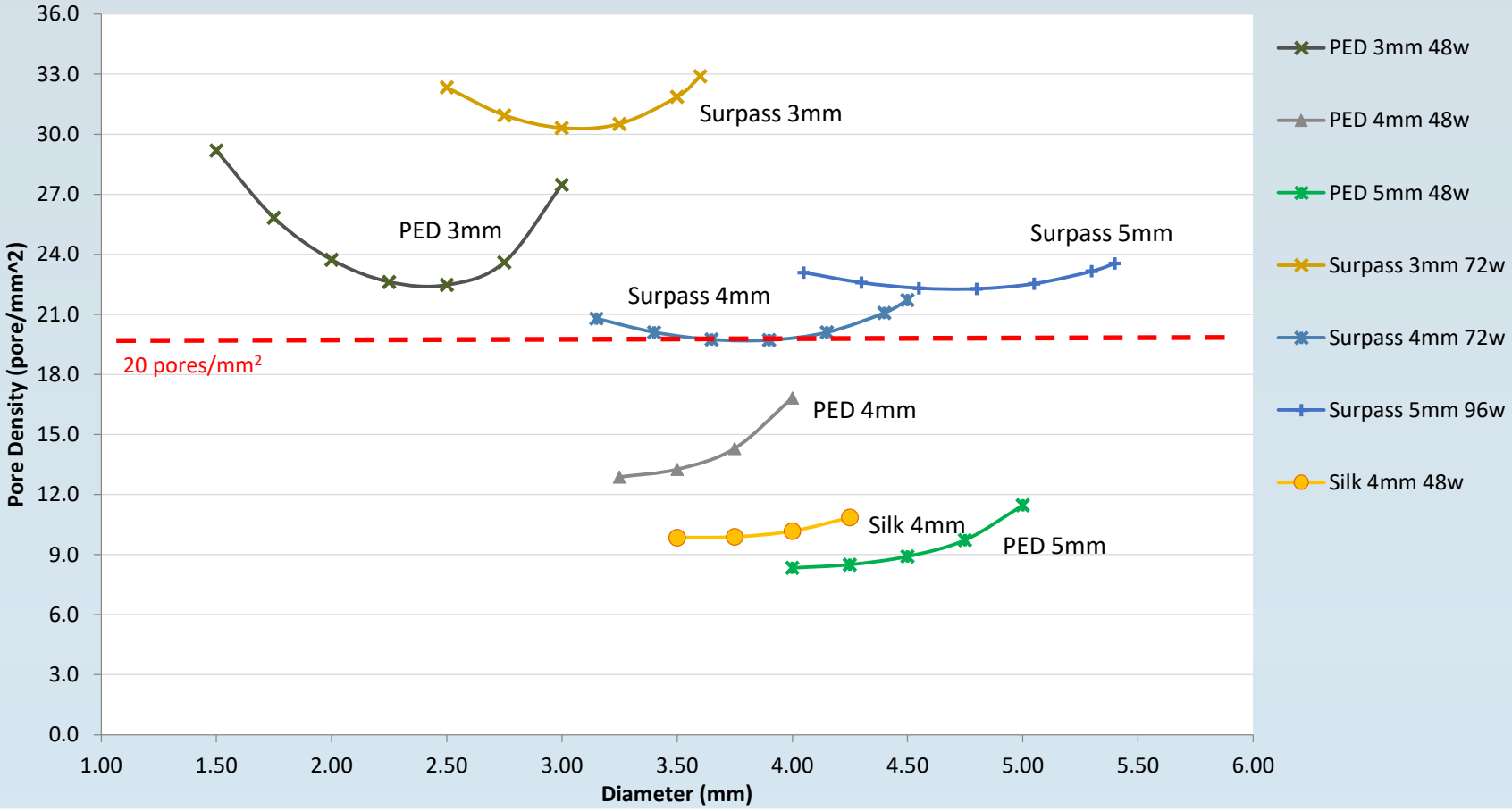
DIAGRAM B

Schematic showing equal porosity (50%) but different pore densities. Diagram A has 16 times higher pore density than diagram B.

* Stroke. 2009;40:952-958

Pore density

No Surpass™ Device has a pore density of < 20 pores/mm² even in the larger vessel diameters



Available devices

- Pipeline shield
- Surpass
- FRED
- P64/48 +pHPC
- SILK
- Derivo
- BRAVO

Indications

- Fusiform Aneurysms
- Dissecting aneurysms
- Large wide neck aneurysms

Less strong indications

- Recurrent aneurysms
- Small aneurysms with wide neck
- Multiple adjacent small aneurysm
- Small ruptured aneurysms that can not be coiled or clipped.
- Aneurysms with potentially high recurrence rate.

Study Comparison

	IntrePED[1]	PUFs[2]	Surpass multicenter study Wakhloo et	Stent-Assisted Coiling Meta Analysis[3]	Neuroform Stent™* Registry[4]	Enterprise™ * Stent Registry[5]
Type	Retrospective registry	Prospectiv e trial	Prospectiv registry	Meta-Analysis	Prospective registry	Retrospective registry
# Patients	793	107	165	1517	284	213
# Institutions	17	10	24	39 articles	2	10
Follow-up Time	19.3 mo avg	1 yr	6 mo	13 mo avg	12.9 mo avg	6 mo avg
Follow-up Rate	100%	95%	86.8	60%	58%	51%
Aneurysm Types	All	Large, giant ICA	All	All	All	All

1. IntrePED Presentation by Dr. David Kallmes, SNIS Conference, July 28, 2013.
2. Becske T, Kallmes DF, Saatci I, et al. Pipeline for Uncoilable or Failed Aneurysms: Results from a Multicenter Clinical Trial. Radiology. Published online before print February 15, 2013, doi: 10.1148/radiol.13120099
3. Shapiro, Becske, Sahlein, Babb, Nelson. Stent-supported aneurysm coiling: A literature survey of treatment and follow-up. AJNR Am J Neuroradiol 33:159-63, Jan 2012.
4. Fiorella, Albuquerque, Woo, Rasmussen, Masaryk, McDougall. Neuroform stent assisted aneurysm treatment: evolving treatment strategies, complications and results of long term follow-up. J NeuroIntervent Surg (2009), doi:10.1136/jnis.2009.000521.
5. Mocco et al. Delayed thrombosis or stenosis following Enterprise-assisted stent-coiling: Is it safe? Midterm results of the interstate collaboration of Enterprise stent coiling. Neurosurgery, Vol 69, No 4, Oct 2011

Results Summary

	IntrePED[1]	PUFs[2]	Surpass[5] multicenter study Wakhloo etal	Stent-Assisted Coiling Meta Analysis[3]	Neuroform™ * Stent Registry[4]	Enterprise™ * Stent Registry
Complete occlusion rate	71% (12-24 mo f/up)	86% (12 mo f/up)	75%	61%	48.2% (progressive thrombosis at 12.9 mo avg f/up)	40%[5]
Recurrence rate	0%	0%	0%	14%	27.7%	Not reported
M&M	8.3%	5.6%	8.7%	5.3%	8.1%	4.8%[6] (periprocedural)
Neurologic death	3.8%	2.8%	2.7%	2.1% (periprocedural)	3.2%	2%[6] (periprocedural)

1. IntrePED Presentation by Dr. David Kallmes, SNIS Conference, July 28, 2013.
2. Becske T, Kallmes DF, Saatci I, et al. Pipeline for Uncoilable or Failed Aneurysms: Results from a Multicenter Clinical Trial. Radiology. Published online before print February 15, 2013, doi: 10.1148/radiol.13120099
3. Shapiro, Becske, Sahlein, Babb, Nelson. Stent-supported aneurysm coiling: A literature survey of treatment and follow-up. AJNR Am J Neuroradiol 33:159-63, Jan 2012.
4. Fiorella, Albuquerque, Woo, Rasmussen, Masaryk, McDougall. Neuroform stent assisted aneurysm treatment: evolving treatment strategies, complications and results of long term follow-up. J NeuroIntervent Surg (2009), doi:10.1136/jnis.2009.000521.
5. Mocco et al. Delayed thrombosis or stenosis following Enterprise-assisted stent-coiling: Is it safe? Midterm results of the interstate collaboration of Enterprise stent coiling. Neurosurgery, Vol 69, No 4, Oct 2011.
6. Mocco et al. Treatment of intracranial aneurysms with the Enterprise stent: a multicenter registry. J. Neurosurg. Vol 110, January, 2009.

Recurrence Rate

	IntrePED[1]	PUFs[2]	Surpass$_5$ multicenter study Wakhloo etal	Neuroform™ * Stent Registry[3]	Enterprise™ * Stent Registry[4]
Recurrence	0%	0%	0%	27.7%	Not Reported
Follow-up Time	19.3 mo avg	1 year	≥6 MO	12.9 mo avg	6 mo avg
Follow-up %	100%	95%	86.8%	58%	51%

1. IntrePED Presentation by Dr. David Kallmes, SNIS Conference, July 28, 2013.
2. Becske T, Kallmes DF, Saatci I, et al. Pipeline for Uncoilable or Failed Aneurysms: Results from a Multicenter Clinical Trial. Radiology. Published online before print February 15, 2013, doi: 10.1148/radiol.13120099
3. Fiorella, Albuquerque, Woo, Rasmussen, Masaryk, McDougall. Neuroform stent assisted aneurysm treatment: evolving treatment strategies, complications and results of long term follow-up. J NeuroIntervent Surg (2009), doi:10.1136/jnis.2009.000521.
4. Mocco et al. Delayed thrombosis or stenosis following Enterprise-assisted stent-coiling: Is it safe? Midterm results of the interstate collaboration of Enterprise stent coiling. Neurosurgery, Vol 69, No 4, Oct 2011.

Neurologic Death

	IntrePED[1]	PUFs[2]	Surpass$_5$ multicenter study Wakhloo etal	Neuroform™ * Stent Registry[3]	Enterprise ™* Stent Registry[4]
Neurologic Death	3.8% 30/793	2.8% 3/107	1.6% ant 7.5 post	3.2% 9/284	2.1% 3/141 (periprocedural)

IntrePED Notes:

- **Posterior – 5 (0.6%)**
- **Ruptured – 6 (0.7%)**

1. IntrePED Presentation by Dr. David Kallmes, SNIS Conference, July 28, 2013.
2. Becske T, Kallmes DF, Saatci I, et al. Pipeline for Uncoilable or Failed Aneurysms: Results from a Multicenter Clinical Trial. Radiology. Published online before print February 15, 2013, doi: 10.1148/radiol.13120099
3. Fiorella, Albuquerque, Woo, Rasmussen, Masaryk, McDougall. Neuroform stent assisted aneurysm treatment: evolving treatment strategies, complications and results of long term follow-up. J NeuroIntervent Surg (2009), doi:10.1136/jnis.2009.000521.
4. Mocco et al. Treatment of intracranial aneurysms with the Enterprise stent: a multicenter registry. J. Neurosurg. Vol 110, January, 2009.
5. Wakhloo et al AJNR AUGUST 14, 2014

Aneurysm Rupture Post-Treatment

	IntrePED[1]	PUFs[2]
Late Aneurysm Rupture	0.6% 5/793	0.9% 1/107

1. IntrePED Presentation by Dr. David Kallmes, SNIS Conference, July 28, 2013
2. Becske T, Kallmes DF, Saatci I, et al. Pipeline for Uncoilable or Failed Aneurysms: Results from a Multicenter Clinical Trial. Radiology. Published online before print February 15, 2013, doi: 10.1148/radiol.13120099.

Late Aneurysm Rupture

Meta- analysis of 30 published studies

- 1,379 patients
- 703 available to determine the bleeding rate: 0.9% per year
- Only incompletely coiled aneurysms larger than 10 mm
- Laterna et al: Neurosurgery 55:767-778 (2004)

Intracranial Hemorrhage (ICH)

	IntrePED[1]	PUFs[2]	Surpass[5] multicenter study Wakhloo et	Neuroform™* Stent Registry[3]	Enterprise™* Stent Registry[4]
Total ICH	3.0% 24/793	4.7% 5/107	5% 2.5 SAH	3.2% 9/284	1.4% (periprocedural) 2/141
Major ICH	2.4% 19/793	1.9% 2/107		1.4% 4/284	Not reported
Minor ICH	0.6% 5/793	2.8%* 3/107		1.8% 5/284	

* Includes one patient with major stroke caused by thrombosis and minor ICH caused by head trauma

1. IntrePED Presentation by Dr. David Kallmes, SNIS Conference, July 28, 2013
2. Becske T, Kallmes DF, Saatci I, et al. Pipeline for Uncoilable or Failed Aneurysms: Results from a Multicenter Clinical Trial. Radiology. Published online before print February 15, 2013, doi: 10.1148/radiol.13120099
3. Fiorella, Albuquerque, Woo, Rasmussen, Masaryk, McDougall. Neuroform stent assisted aneurysm treatment: evolving treatment strategies, complications and results of long term follow-up. J NeuroIntervent Surg (2009), doi:10.1136/jnis.2009.000521.
4. Mocco et al. Treatment of intracranial aneurysms with the Enterprise stent: a multicenter registry. J. Neurosurg. Vol 110, January, 2009.

Ischemic Stroke

	IntrePED[1]	PUFs[2]	Surpass[5] multicenter study	Neuroform™* Stent Registry[3]	Enterprise™* Stent Registry[4]
Total Ischemic Stroke	6.6% 52/793	4.7% 5/107	6.4%	9.5% 27/284	7.3% 8/110 (stenosis events)
Major Ischemic Stroke	4.7% 37/793	2.8% 3/107	3.7%	5.3% 15/284	Not reported
Minor Ischemic Stroke	1.9% 15/793	1.9% 2/107	2.7%	3.5% 10/284	

IntrePED Notes:

- **Major Strokes – 4 in posterior locations, 33 in anterior locations**
- **85.9% received dual anti-platelet medication prior to procedure**
- **71.7% had platelet aggregation testing prior to procedure**

1. IntrePED Presentation by Dr. David Kallmes, SNIS Conference, July 28, 2013
2. Becske T, Kallmes DF, Saatci I, et al. Pipeline for Uncoilable or Failed Aneurysms: Results from a Multicenter Clinical Trial. Radiology. Published online before print February 15, 2013, doi: 10.1148/radiol.13120099
3. Fiorella, Albuquerque, Woo, Rasmussen, Masaryk, McDougall. Neuroform stent assisted aneurysm treatment: evolving treatment strategies, complications and results of long term follow-up. J NeuroIntervent Surg (2009), doi:10.1136/jnis.2009.000521.
4. Mocco et al. Delayed thrombosis or stenosis following Enterprise-assisted stent-coiling: Is it safe? Midterm results of the interstate collaboration of Enterprise stent coiling. Neurosurgery, Vol 69, No 4, Oct 2011.

SAFE study (Safety and efficacy Analysis of FRED Embolic device in aneurysm treatment): 1-year clinical and anatomical results

Laurent Pierot,[1] Laurent Spelle,[2] Jérôme Berge,[3] Anne-Christine Januel,[4] Denis Herbreteau,[5] Mohamed Aggour,[6] Michel Piotin,[7] Alessandra Biondi,[8] Xavier Barreau,[3] Charbel Mounayer,[9] Chrisanthi Papagiannaki,[10] Jean-Paul Lejeune,[11] Jean-Yves Gauvrit,[12] Anne-Laure Derelle,[13] Emmanuel Chabert,[14] Vincent Costalat[15]

ABSTRACT

Background and purpose Flow diversion is an innovative and increasingly used endovascular treatment for intracranial aneurysms. Its initial evaluation with the first devices available showed good efficacy of this

Conclusions SAFE study analysis at 1 year confirms the excellent safety profile of the FRED device for aneurysm treatment, with low morbidity and mortality rates (2.9% and 1.9%, respectively) and demonstrates its efficacy (adequate occlusion in 73/90 (81.1%)).

Results Thirteen interventional neuroradiology centers included 103 patients/aneurysms. Aneurysm locations were supraclinoid internal carotid artery (ICA) in 71 (68.9%), cavernous ICA in 15 (14.6%), anterior cerebral or anterior communicating artery in 9 (8.7%), and middle cerebral artery in 8 (7.8%). Most aneurysms were small (<10 mm) in 71 patients (68.9%). Cumulative 1-year mortality and morbidity rates were 2/103 (1.9%) and 3/103 (2.9%), respectively, one death being related to cancer. At 1 year, anatomical results were: complete occlusion in 66/90 patients (73.3%), neck remnant in 7/90 patients (7.8%), and aneurysm remnant in 17/90 patients (18.9%).

Conclusions SAFE study analysis at 1 year confirms the excellent safety profile of the FRED device for aneurysm treatment, with low morbidity and mortality rates (2.9% and 1.9%, respectively) and demonstrates its efficacy (adequate occlusion in 73/90 (81.1%)).

management of intracranial aneurysms.[1–3] The Pipeline flow diverter (Medtronic, Minneapolis, Minnesota, USA) was the first device to be systematically evaluated in the Pipeline for Uncoilable or Failed Aneurysms (PUFS) study, dedicated to internal

ruptured aneurysms are limited.

Besides the usual periprocedural complications (thromboembolic events, intraoperative rupture), more specific complications are seen after flow diversion: occlusion of collateral branches covered by the flow diverter, in-stent thrombosis or stenosis, delayed aneurysm rupture, or delayed remote hematomas.[10 11]

The Flow Direction Endoluminal Device (FRED) is a double-layer flow diverter with a stent-like outer layer and a flow diverter part inside the stent. This design enhances the navigability of the device, especially in tortuous anatomy and apposition of the device to the arterial wall, a key point in achieving aneurysm occlusion. According to the specific design of different flow diverters, these devices require careful evaluation for assessment of

CASE SERIES

Periprocedural outcomes and early safety with the use of the Pipeline Flex Embolization Device with Shield Technology for unruptured intracranial aneurysms: preliminary results from a prospective clinical study

Mario Martínez-Galdámez,[1] Saleh M Lamin,[2] Konstantinos G Lagios,[3] Thomas Liebig,[4] Elisa F Ciceri,[5,6] Rene Chapot,[7] Luc Stockx,[8] Swarupsinh Chavda,[2] Christoph Kabbasch,[4] Giuseppe Farago,[5] Hannes Nordmeyer,[7] Thierry Boulanger,[8] Mariangela Piano,[9] Edoardo P Boccardi[9]

ABSTRACT

Background and purpose The Pipeline Embolization Device (PED) has become a routine first-line option for treatment of intracranial aneurysms (IAs). We assessed the early safety and technical success of a new version of PED, Pipeline Flex Embolization Device with Shield Technology (Pipeline Shield), which has the same design and configuration but has been modified to include a surface synthetic biocompatible polymer.

with IAs.[1 3] The first-generation PED device, used for the embolization of cerebral aneurysms, received European CE mark approval in 2008 and US FDA approval in 2011.[4] Its safety and efficacy have been demonstrated in numerous clinical studies, such as the Pipeline for Uncoilable and Failed Aneurysms (PUFS) trial,[5] the International Retrospective Study of PED (IntrePED),[6] the Aneurysm Study of Pipeline in an Observational Registry (ASPIRe) study,[7] and

PROCEDURAL CHARACTERISTICS

CHARACTERISTICS	n (%) (N=50)
Successful device deployment to target site	53/56 (94.6%)
Procedure time (min)	77.3 ± 36.51
Number of Pipeline™ Shield devices implanted per subject	1.06 ± 0.24 (n=50)
Balloon used	9 (18%)
Adjunctive Devices Used (per imaging core lab)	
Coils	7 (14%)
None	43 (86%)
Complete wall apposition (per imaging core lab)	48 (96%)
Entire neck covered by Pipeline™ Shield device	50 (100%)

PRIMARY ENDPOINT OUTCOMES
AT 1 YEAR POST-PROCEDURE

No major stroke in the territory supplied by the treated artery

No neurological death

SECONDARY ENDPOINT OUTCOMES
AT 1 YEAR POST-PROCEDURE

14% (n=7) Pipeline™ Shield related neurologic adverse events

- 6 in-stent stenosis; all asymptomatic.
- ICA thrombosis; asymptomatic, resulted in no clinical sequelae

SERIOUS ADVERSE EVENTS OF INTEREST

1 device-related serious adverse event

- ICA thrombosis (secondary endpoint); asymptomatic, resulted in no clinical sequelae
  - Occurred during endovascular treatment of non-target aneurysm 63 days after Pipeline™ Shield implanted

3 procedure-related serious adverse events

- Headache; resolved in outcome
- Diplopia; resolved in outcome
- Retroperitoneal hemorrhage; resolved in outcome

ANEURYSM OCCLUSION
AT 1 YEAR POST-PROCEDURE

ANEURYSM OCCLUSION [a]	n (%) (N=33)
Complete occlusion	27 (81.8%)
Residual neck	2 (6.1%)
Residual aneurysm	4 (12.1%)

[a] Raymond-Roy Occlusion Scale[1]

0% target aneurysm recurrence

0% target aneurysm retreatment

[1] Roy D, Milot G, Raymond J. Endovascular treatment of unruptured aneurysms. *Stroke.* Sep 2001;32(9):1998-2004.

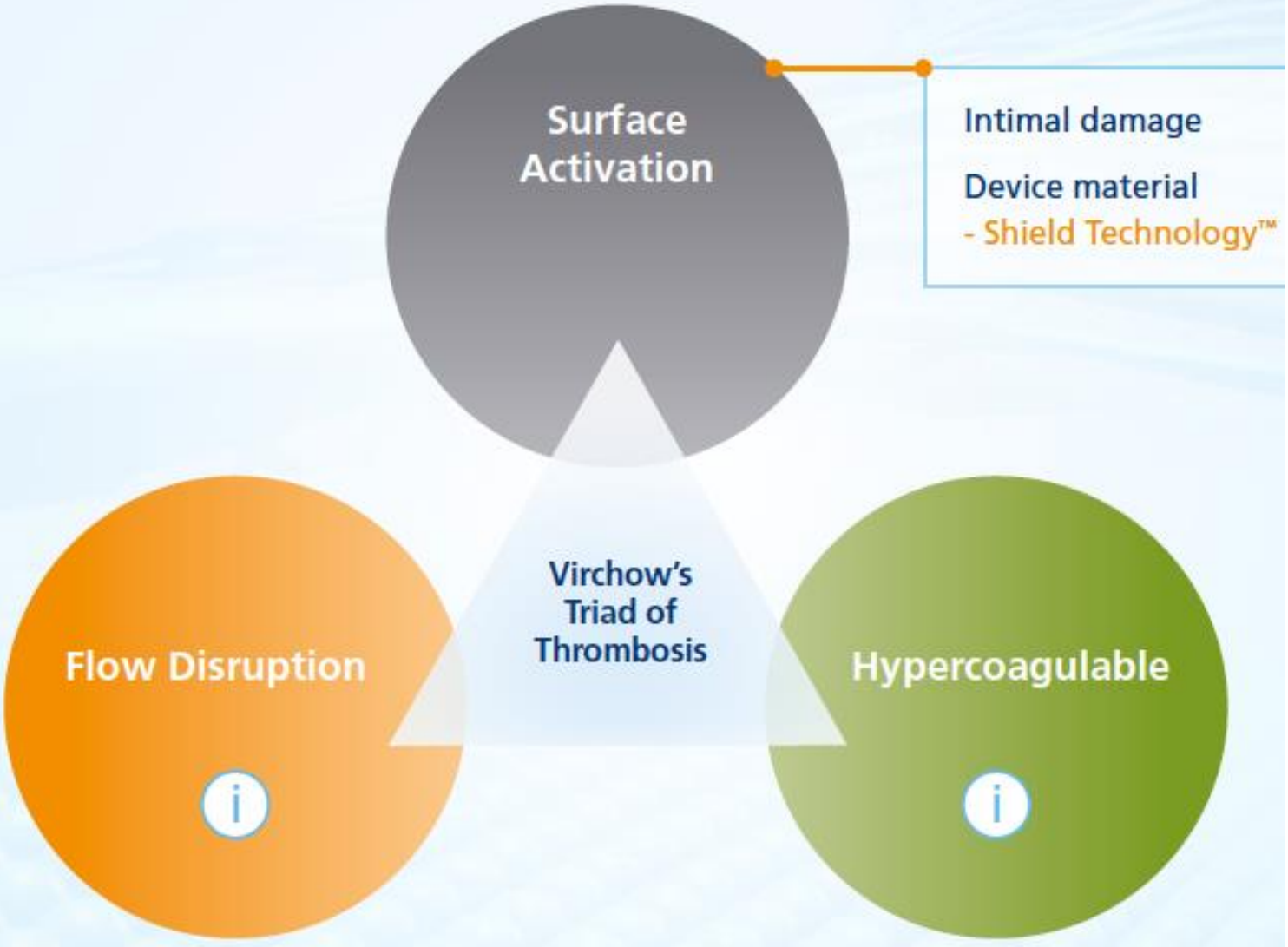
FD Complications

- Ischemic Complications

1 in situ parent vessel (construct) thrombosis, emboli, or

2 delayed ischemia resulting from device-related stenosis

What Causes **Thrombosis?**



Haemorrhagic Complications

- Haemorrhagic complications are observed in 2–3% of cases and include

1 iatrogenic or spontaneous intraparenchymal bleeds and

2 subarachnoid haemorrhage due to acute or delayed aneurysmal rupture.

Why coil large aneurysms?

Delayed Aneurysm Rupture

“Mural instability after Flow Diversion”

Incidence of Delayed Rupture

- PUFS 0.9% (1/107)
  - 1 spontaneous CCF
    - 3 weeks after treatment
  - NO delayed hemorrhagic complications between 6M-3Y (n=76)

Beske et al., 2014, 2015

Incidence of Delayed Rupture

- INTREPED: 5/793 (0.6%)
  - 2 of 5 with CCF
  - 4 of 5 within 30 days
  - Risk corresponded to aneurysm size ($p < 0.001$)
    - **Giant: 4.5% (3/66)**
    - Large: 0.6% (2/357)
    - Small: 0% (0/473)

Kallmes et al., AJNR 2015

Incidence of Delayed Rupture

- ASPIRE: 3/191 (1.6%)
  - All Anterior Circulation
  - All Large (> 10 mm)
  - All within 4 days
  - One was also coiled

Kallmes et al., Int Neuro 2016

Histopathologic features Kallmes et al AJNR Jul 2009

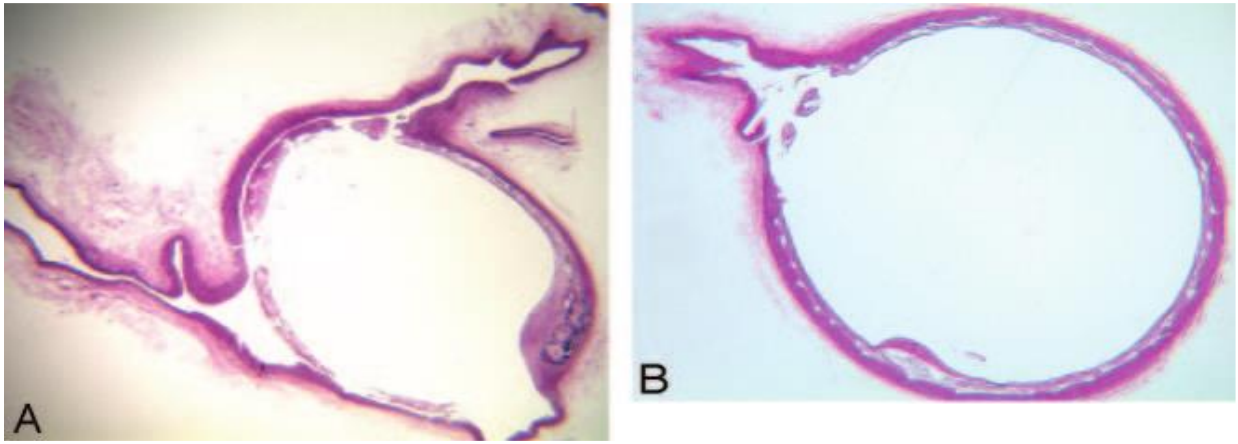


Fig 3. *A*, Photomicrograph (H&E; magnification, ×20) of the vertebral artery. *B*, Photomicrograph (H&E; magnification, ×25) of a lumbar artery. Both the vertebral and lumbar arteries had a device placed across their ostia. The vessels remained patent. The neointima across the origin of each vessel is discontinuous.

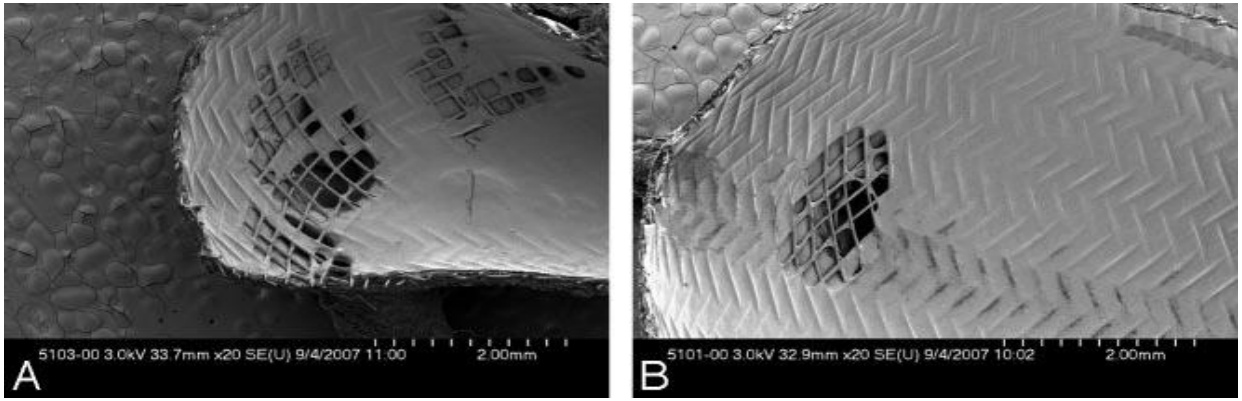


Fig 4. *A*, SEM photograph (magnification, ×20) of the vertebral artery. *B*, An SEM of the ostium of the lumbar artery (magnification, ×20). Both the vertebral and lumbar arteries had a device placed across their ostia. The vessels remained patent. The tissue covering the stents at the origins of branch vessels is continuous with that covering or on the devices at the aorta and parent artery.

Vessel occlusion

- 30 Ophthalmic arteries covered with PED in 29 patients with 6 months follow up.
- 17 patients had 24 months FU

Aneurysm Location

- P.Comm – 8
- ICA – Supraclinoid – 3
- Paraophthalmic – 16
- Cavernous – 2
- Complex cavernous Paraophthalmic - 1

Results 6-12 months

- Immediate post deployment ophthalmic occlusion– 0%
- Complete OphA occlusion on 6-12 months angio – 0%
- Readily noticeable change in OphA calibre – 4/30 = 13.3% .

Results 24 months

- OphA Patency rate = 14/17 = 82.3%
- OphA Occlusion rate = 3/17= 17.6%
- OphA Noticeable change in calibre = 1/17
- No visual symptoms recorded on follow up.

Acute FD

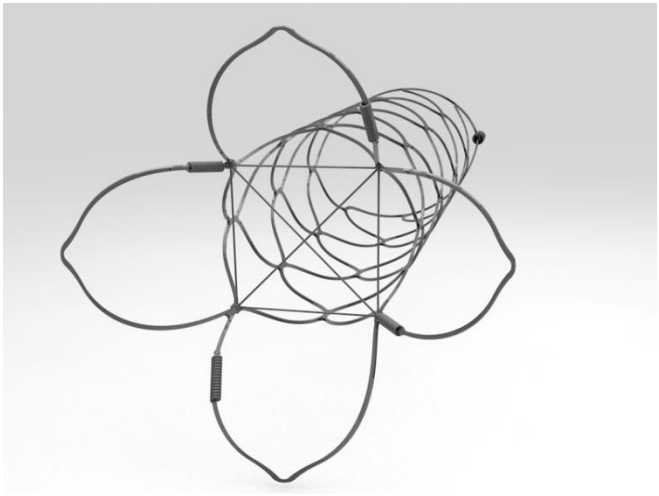
Antiplatelet management

- Integrilin prior to stent placement.
- DAPT when the patient wakes up
- In large vessels we use the shield device with Prasugrel/Ticagrelol only.

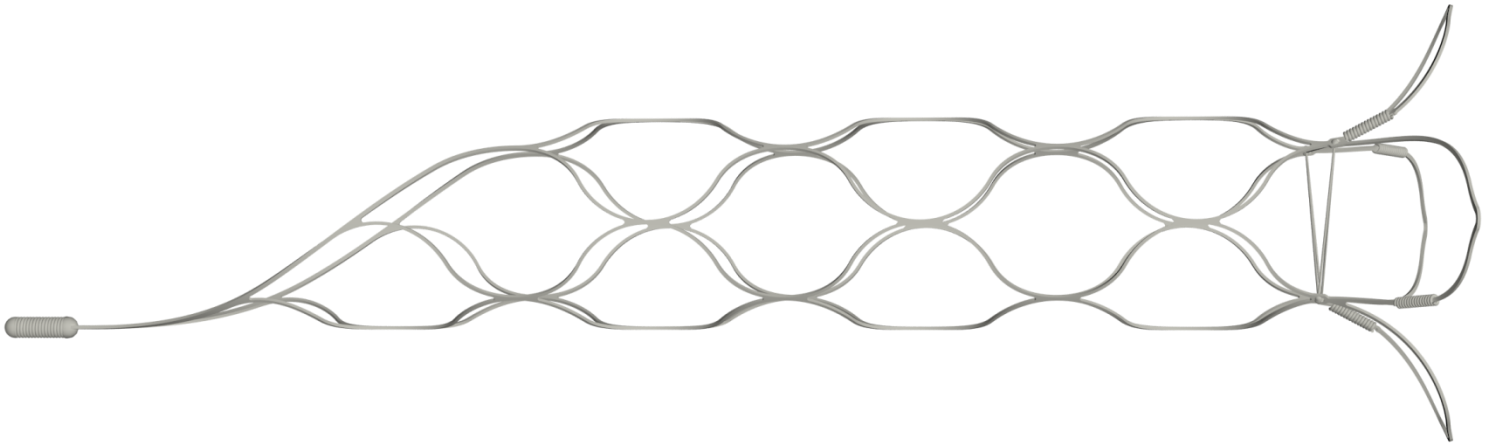
NECK BRIDGING DEVICES

- PCONUS
- PULSRIDER
- NEQSTENT
- Barrel stent
- WEB

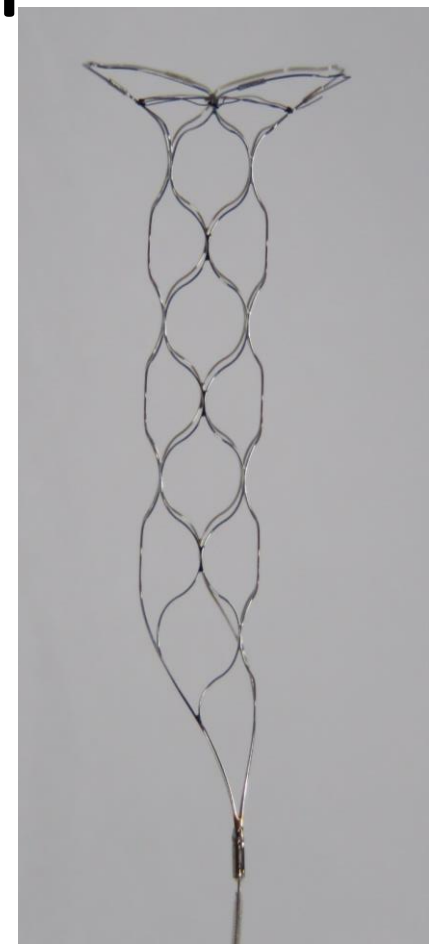
pCONUS
Bifurcation Aneurysm Implant



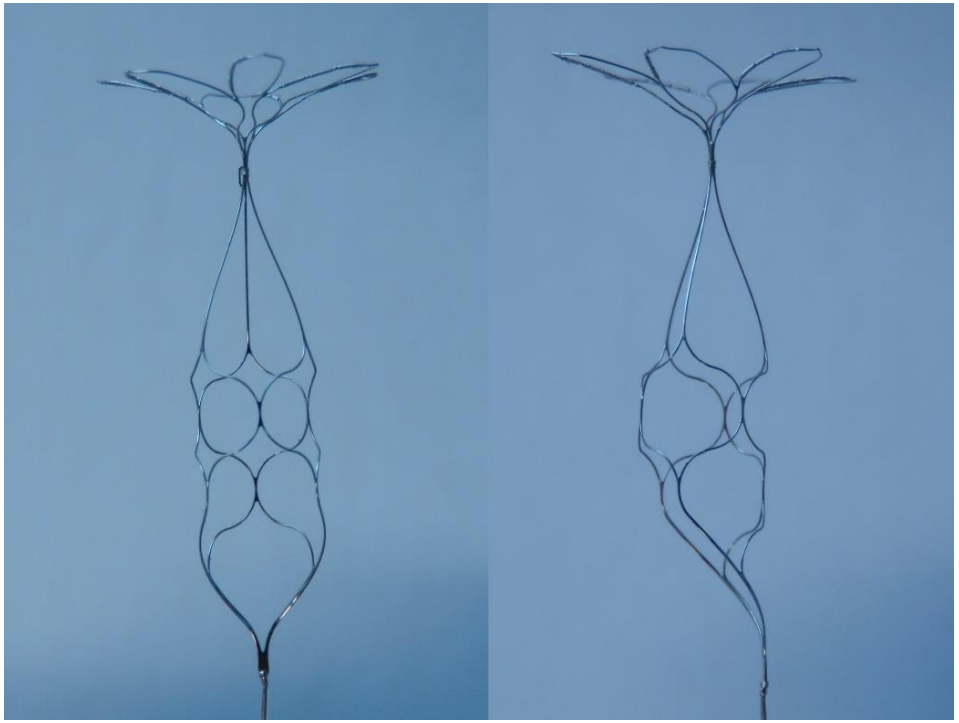
pCONUS provides a stent-like, self-expanding structure with distal petals and a border at the base of the crown made of Polymer fibers (to prevent coils from falling back into the parent vessel).



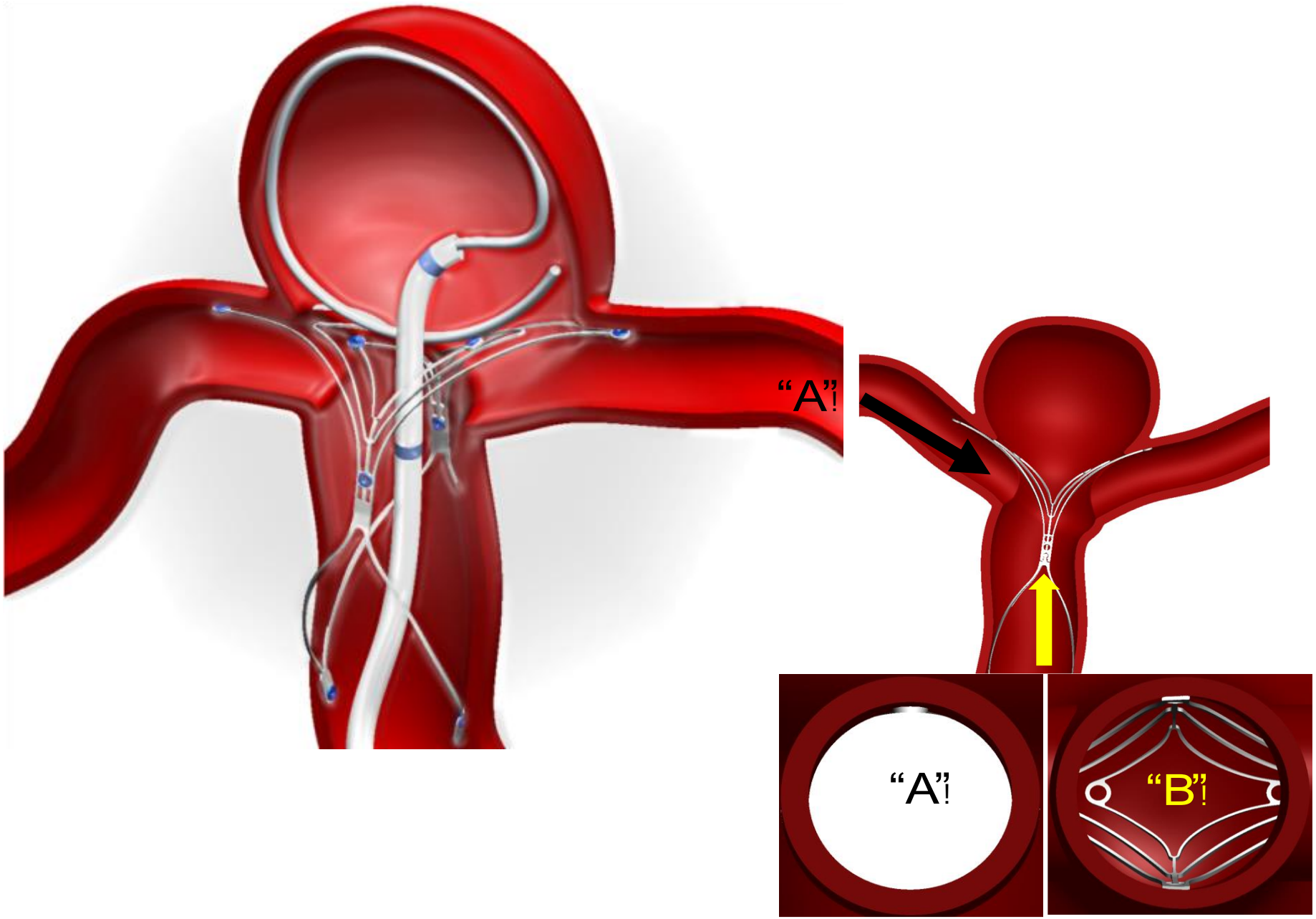
pCONUS vs. pCONUS 2



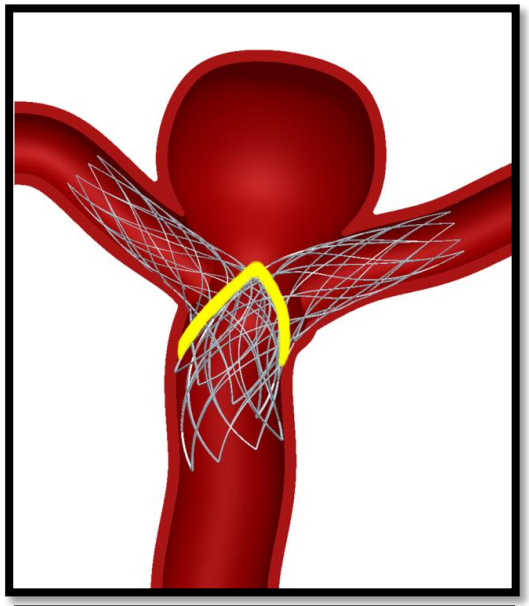
pCONUS (1. Gen.)

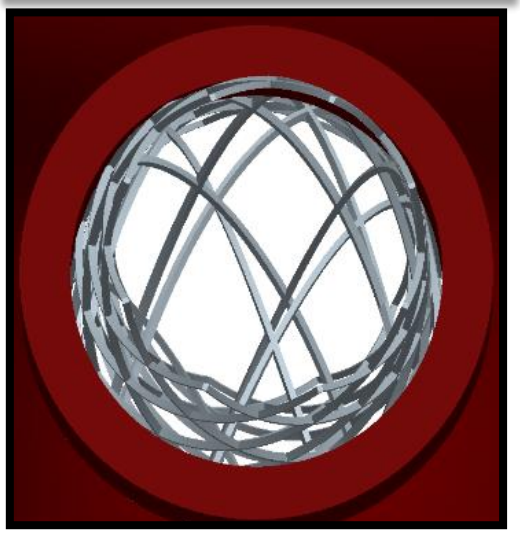


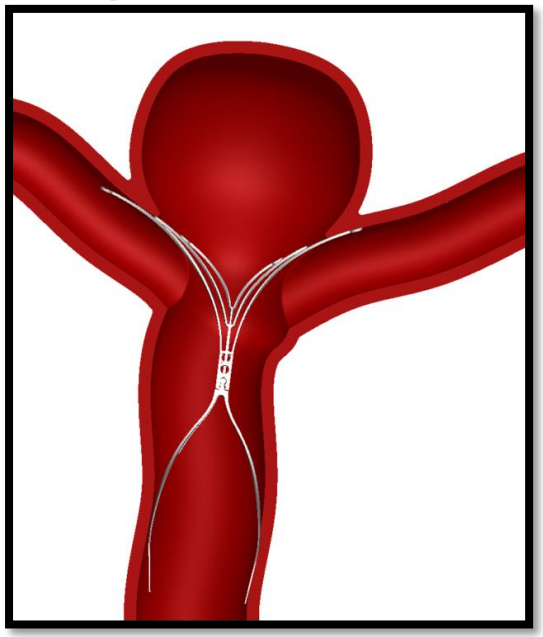
pCONUS **2**

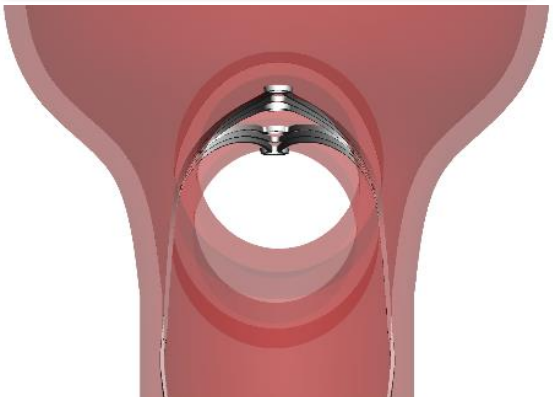

“A”
“A”
“B”

Pulse Rider vs Y stenting









Conclusion

- FD is a very valuable tool in managing complex aneurysms
- Thromboembolic complications remain the main problem with flow diversion in general.
- Shield and pHPC technology are promising steps forwards towards reducing thromboembolic complications.
- Haemorrhagic complications are rare but important to consider when treating large and giant aneurysms.

saleh.lamin@uhb.nhs.uk