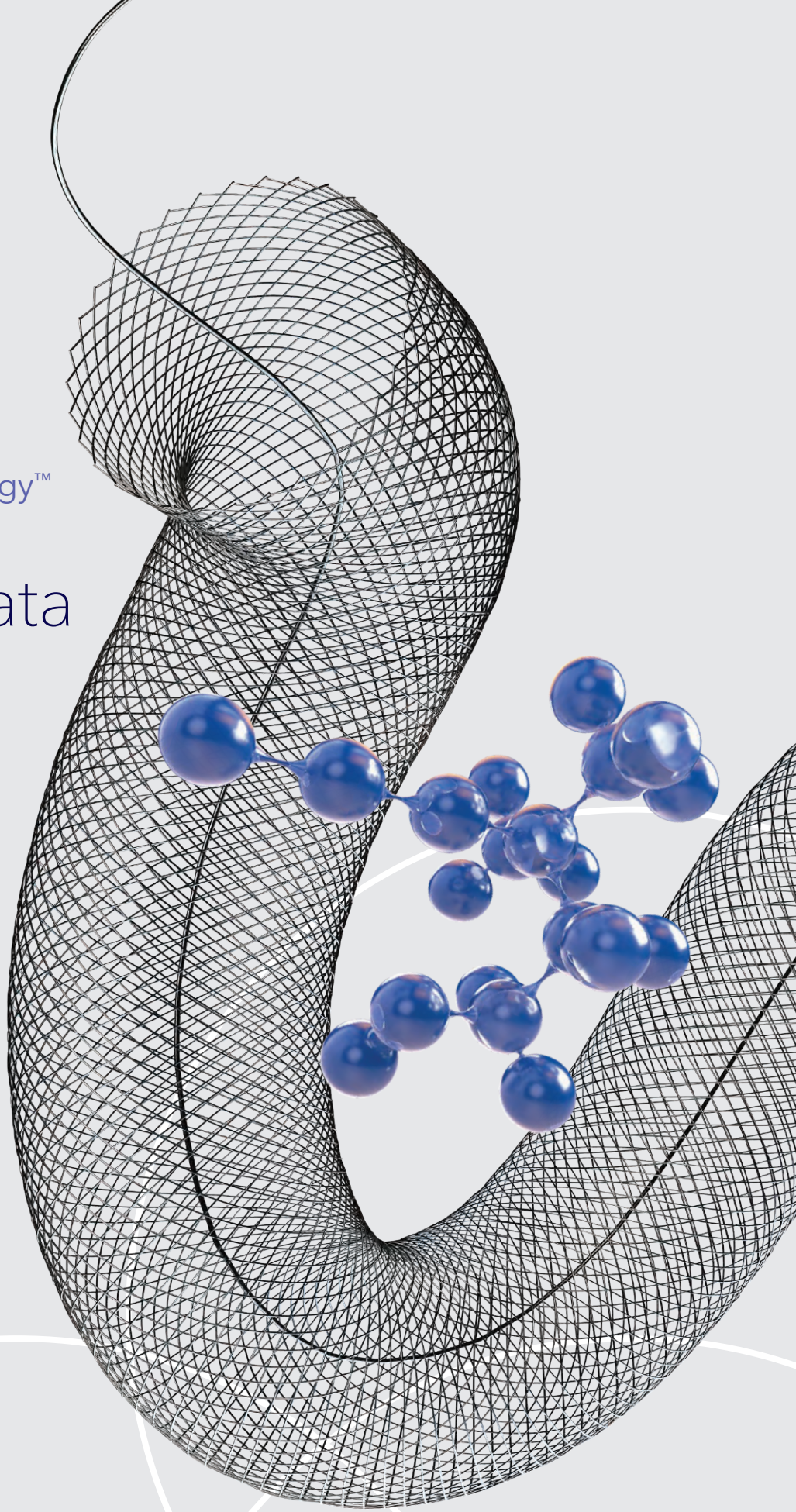
Medtronic
Neurovascular

Pipeline™ Flex
Embolization Device
& Pipeline™ Flex
Embolization Device
with Shield Technology™

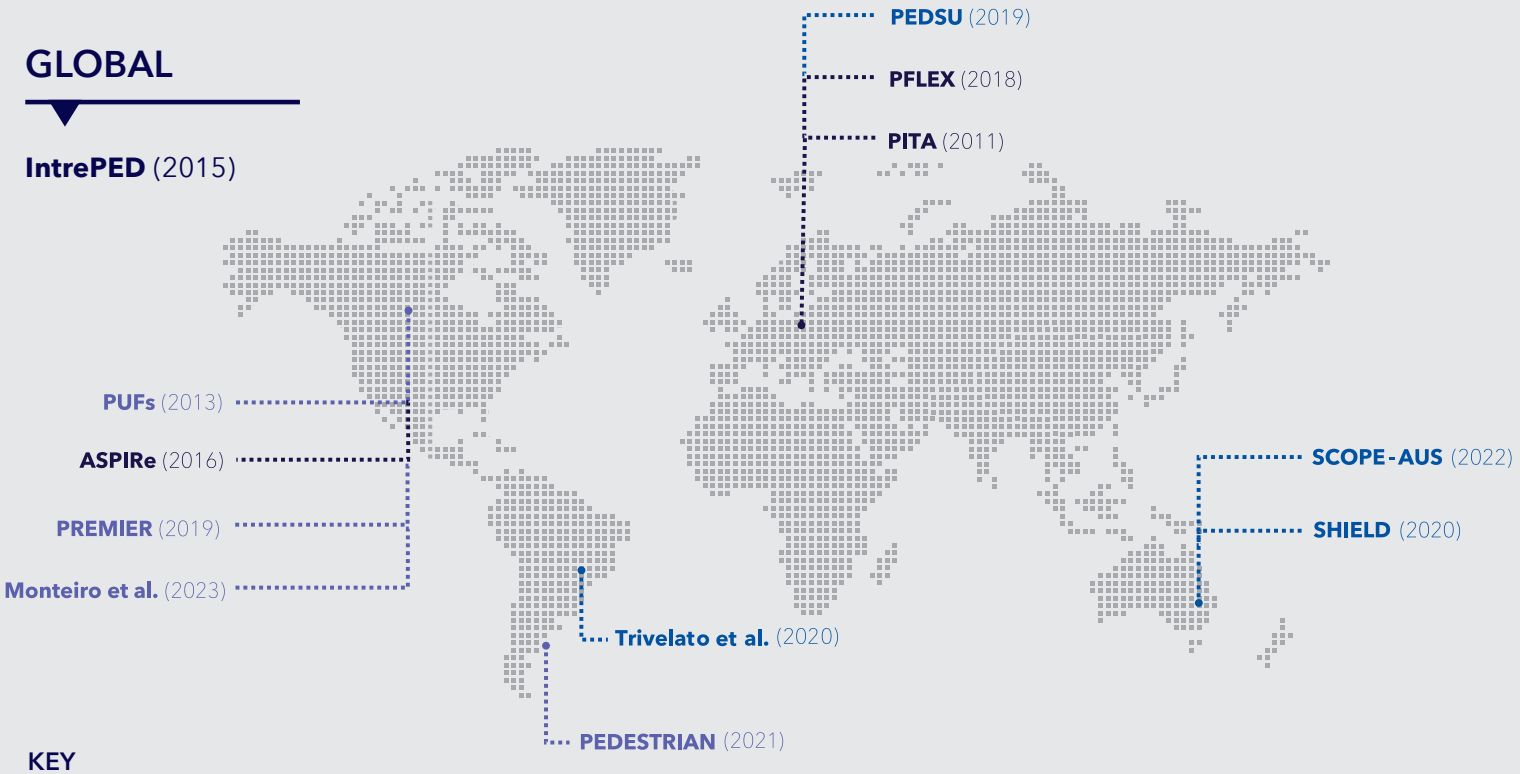
Clinical Data Summary



The Pipeline™ franchise has been studied in centers around the globe…

Pipeline™ is the most studied flow diverter worldwide*, with over **55,000 patients**† in **950 Pipeline™ only publications**.‡

GLOBAL



KEY

- Pipeline™ Flex Device
- Pipeline™ Flex Device with Shield Technology™
- Combination

This document presents data summaries for 12 of the key landmark publications in the Pipeline™ franchise. Please note that this represents **less than 3%** of the publications in the entire portfolio.

* At the time of publication in March 2025.
† Data on file; TR-NV11820 Rev U
‡ Medtronic Internal Report TR-NV11820

For a full list of references, please scan the QR code >

Index

Index *cont...*

1. PITA

The Pipeline Embolization Device for the Intracranial Treatment of Aneurysms Trial

P. K. Nelson, P. Lylyk, I. Szikora, S. G. Wetzel, I. Wanke, D. Fiorella

JAN 2011, AMERICAN JOURNAL OF NEURORADIOLOGY: 32 (1) 34-40.
DOI: 10.3174/ajnr.A2421

Background:

Endoluminal reconstruction with flow diverting devices represents a novel constructive technique for the treatment of cerebral aneurysms. The authors present the results of the first prospective multicenter trial of a flow-diverting construct for the treatment of intracranial aneurysms.

Methods:

Patients with unruptured aneurysms that were wide-necked (>4 mm), had unfavourable dome/neck ratios (<1.5), or had failed previous therapy were enrolled in the PITA trial between January and May 2007 at 4 (3 European and 1 South American) centres. Aneurysms were treated with the PED with or without adjunctive coil embolization. All patients underwent clinical evaluation at 30 and 180 days and conventional angiography 180 days after treatment. Angiographic results were adjudicated by an experienced neuroradiologist at a nonparticipating site.

Results:

Thirty-one patients with 31 intracranial aneurysms (6 men; 42–76 years of age; average age, 54.6 years) were treated during the study period. Twenty-eight aneurysms arose from the ICA (5 cavernous, 15 parophthalmic, 4 superior hypophyseal, and 4 posterior communicating segments), 1 from the MCA, 1 from the vertebral artery, and 1 from the vertebrobasilar junction. Mean aneurysm size was 11.5 mm, and mean neck size was 5.8 mm. Twelve (38.7%) aneurysms had failed (or recurred after) a previous endovascular treatment. PED placement was technically successful in 30 of 31 patients (96.8%). Most aneurysms were treated with either 1 (n = 18) or 2 (n = 11) PEDs. Fifteen aneurysms (48.4%) were treated with a PED alone, while 16 were treated with both PED and embolization coils. Two patients experienced major periprocedural stroke. Follow-up angiography demonstrated complete aneurysm occlusion in 28 (93.3%) of the 30 patients who underwent angiographic follow-up. No significant inconstruct stenosis (≥50%) was identified at follow-up angiography.

Conclusion:

Intracranial aneurysm treatment with the PED is technically feasible and can be achieved with a safety profile analogous to that reported for stent-supported coil embolization. PED treatment elicited a very high rate (93%) of complete angiographic occlusion at 6 months in a population of the most challenging anatomic subtypes of cerebral aneurysms.

*Please note this study represents some clinical cases that are off-label for the US market.

TABLE 1.1

Patient baseline and aneurysm characteristics

Characteristic	Summary (n=31)
Age (years)	
Mean (range)	54.6 (35-76 years)
Gender (% n)	
Female	80.6 (25/31)
Previously treated (% n)	38.7 (12/31)
Coils only	21.6 (8/31)
Stents only	6.5 (2/31)
Coils and stents	6.5 (2/31)
Target IA location (% n)	
Anterior	
Cavernous	16.1 (5/31)
Paraophthalmic	48.4 (15/31)
Superior hypophyseal	12.9 (4/31)
Posterior communicating	12.9 (4/31)
M1 segment	3.2 (1/31)
Posterior	
Distal pre-PICA vertebral	3.2 (1/31)
PICA vertebral	3.2 (1/31)
Neck ≥ 4mm	71 (22/31)

31 Aneurysms

1.52
Average PEDs per aneurysm

11.5mm
Mean aneurysm size

38.7%
Previously treated

51.6%
Adjunctive devices (coils)

5.8mm
Mean neck diameter

58.1%
Single PED in cases

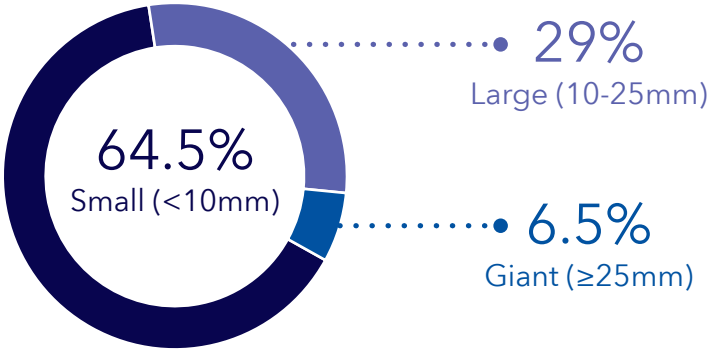
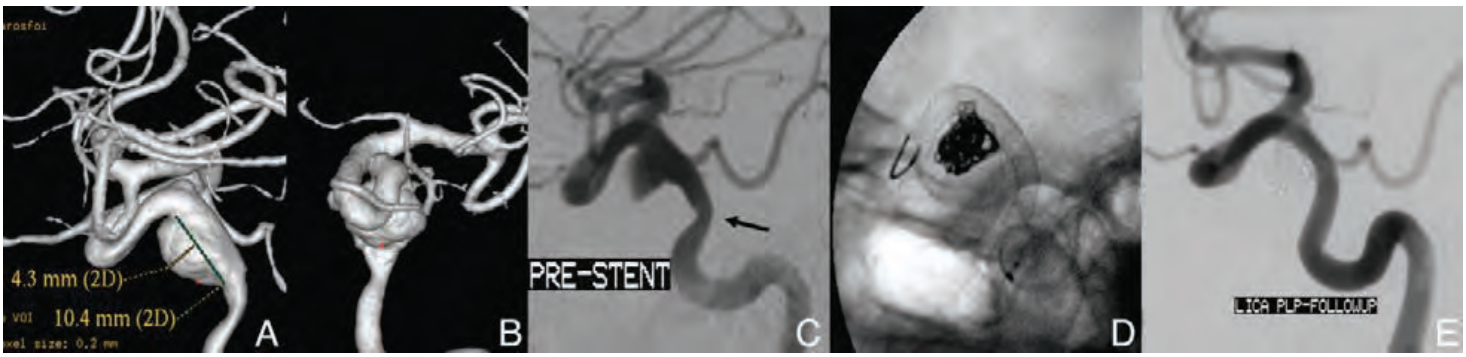


FIGURE 1.1



Dysplastic wide-neck partially thrombosed aneurysm arising from the proximal cavernous segment of the internal carotid artery. A and B, 3D images reconstructed from rotational angiographic source data demonstrate that the neck of the aneurysm incorporates >180° of the vessel circumference over a 10-mm segment of the carotid artery. C, Conventional angiography in the lateral working projection depicts the partially thrombosed wide--neck aneurysm arising from the circumferentially diseased segment. Just proximal to the aneurysmal segment is a mild focal stenosis (arrow). D, Native image in the lateral working-angle projection after treatment demonstrates the Pipeline construct in place across the aneurysm neck, with a loose packing of the aneurysm with embolization coils. E, Follow-up angiography at 180 days in the lateral working projection shows total occlusion of the aneurysm as well as complete anatomic remodeling of the diseased parent artery. The dysplastic aneurysmal vascular segment now has a smooth tubular configuration. The proximal stenosis has also completely remodeled and now is normal in caliber.

6.5%
Rate of periprocedural complications

96.7%
No device migration

93.3%
Aneurysm occlusion at 6 months

The images presented in Figure 1.1 are those of the authors from the referenced publication and not owned by Medtronic.
For Internal Medtronic and Health Care Professional Use Only, and should not be shared with patients or any other third parties.

2. IntrePED

International retrospective study of the Pipeline Embolization Device: a multicenter aneurysm treatment study

D. F. Kallmes, R. Hanel, D. Lopes, E. Boccardi, A. Bonafé, S. Cekirge, D. Fiorella, P. Jabbour, E. Levy, C.McDougall, A. Siddiqui, I. Szikora, H. Woo, F. Albuquerque, H. Bozorgchami, S. R. Dashti, J. E. Delgado, Almandoz, M. E. Kelly, R. Turner 4th, B. K. Woodward, W. Brinjikji, G. Lanzino, P. Lylyk

JAN 2015, AMERICAN JOURNAL OF NEURORADIOLOGY
DOI: 10.3174/AJNR.A4111

Background:

Flow diverters are increasingly used in the endovascular treatment of intracranial aneurysms. Our aim was to determine neurologic complication rates following Pipeline™ Embolization Device placement for intracranial aneurysm treatment in a real-world setting.

Methods:

The authors retrospectively evaluated all patients with intracranial aneurysms treated with the Pipeline™ Embolization Device between July 2008 and February 2013 in 17 centers worldwide. The authors defined 4 subgroups: internal carotid artery aneurysms of ≥10 mm, ICA aneurysms of <10 mm, other anterior circulation aneurysms, and posterior circulation aneurysms. Neurologic complications included spontaneous rupture, intracranial hemorrhage, ischemic stroke, permanent cranial neuropathy, and mortality. Comparisons were made with t tests or ANOVAs for continuous variables and the Pearson $\chi 2$ or Fisher exact test for categoric variables.

Results:

In total, 793 patients with 906 aneurysms were included. The neurologic morbidity and mortality rate was 8.4% (67/793), highest in the posterior circulation group (16.4%, 9/55) and lowest in the ICA <10mm group (4.8%, 14/294) (P = .01). The spontaneous rupture rate was 0.6% (5/793). The intracranial hemorrhage rate was 2.4% (19/793). Ischemic stroke rates were 4.7% (37/793), highest in patients with posterior circulation aneurysms (7.3%, 4/55) and lowest in the ICA <10-mm group (2.7%, 8/294) (P = .16). Neurologic mortality was 3.8% (30/793), highest in the posterior circulation group (10.9%, 6/55) and lowest in the anterior circulation ICA <10-mm group (1.4%, 4/294) (P < .01). The long-term neurologic morbidity and mortality rate was 8.4% (67/793) with a neurologic morbidity rate of 7.4% (59/793) and a neurologic mortality rate of 3.8% (30/793).

Conclusion:

Aneurysm treatment with the Pipeline™ Embolization Device is associated with the lowest complication rates when used to treat small ICA aneurysms. Procedure-related morbidity and mortality are higher in the treatment of posterior circulation and giant aneurysms.

*Please note this study represents some clinical cases that are off-label for the US market.

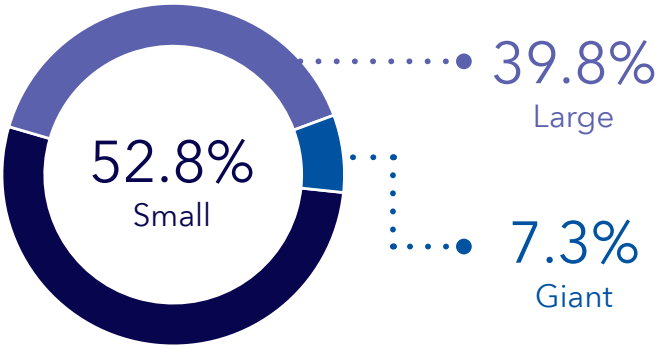
906 Aneurysms

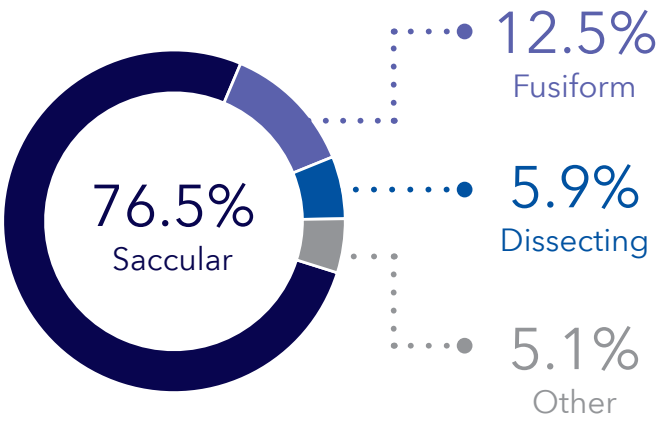
91%
Unruptured aneurysms

65.8%
Single PED in cases

10.7mm
Mean sac diameter

6.2mm
Mean neck diameter





7.4%
Combined morbidity

3.8%
Combined mortality

TABLE 2.1

Aneurysm characteristics

	Anterior ICA ≥10mm (*n*=311)	Anterior <10mm (*n*=349)	Posterior (*n*=59)	Other Anterior ≥10mm (*n*=178)	Total (*n*=896)[a]	P Value
Aneurysm size (mm)						
Mean ± SD	16.8 ± 6.2	5.2 ± 2.2	14.5 ± 9.0	9.8 ± 7.9	10.7 ± 7.7	< .001
Median, range	15.0, 10.0–42.0	5.0, 1.0–9.9	11.8, 1.7–45.0	7.2, 1.0–55.0	9.0, 1.0–55.0	
Aneurysm type						
Small	0	349/349 (100%)	19/58 (32.8%)	105/178 (59.0%)	473/897 (52.8%)	
Large	268/311 (86.2%)	0	29/58 (50.0%)	60/178 (33.7%)	357/897 (39.8%)	
Giant	43/311 (13.8%)	0	10/58 (17.2%)	13/178 (7.3%)	66/897 (7.3%)	
Aneurysm neck (mm)						
Mean ± SD	8.5 ± 5.1	4.1 ± 2.2	9.3 ± 8.4	5.3 ± 5.1	6.2 ± 4.9	< .001
Median, range	7.6, 0.9–50.0	4.0, 0.8–22.0	8.0, 1.7–53.0	4.0, 1.0–50.0	5.0, 0.8–53.0	
Aneurysm shape						
Fusiform	49/311 (15.8%)	17/349 (4.9%)	17/59 (28.8%)	29/178 (16.3%)	112/897 (12.5%)	< .001
Saccular	239/311 (76.9%)	305/349 (87.4%)	25/59 (42.4%)	118/178 (66.3%)	686/897 (76.5%)	
Dissecting	10/311 (3.2%)	8/349 (2.3%)	13/59 (22.0%)	22/178 (12.4%)	53/897 (5.9%)	
Other	13/311 (4.2%)	19/349 (5.4%)	4/59 (6.8%)	9/178 (5.1%)	46/897 (5.1%)	
Aneurysm location						
Internal carotid artery	311/311 (100%)	349/349 (100%)	0	0	660/897 (73.6%)	< .001
Middle cerebral artery	0	0	0	43/178 (24.2%)	43/897 (4.8%)	
Posterior cerebral artery	0	0	15/59 (25.4%)	0	15/897 (1.7%)	
Basilar artery	0	0	44/59 (74.6%)	0	44/897 (4.9%)	
Other	0	0	0	135/178 (75.8%)	135/897 (15.1%)	
Presented with ruptured aneurysm	12/311 (3.9%)	24/345 (7.0%)	4/59 (6.8%)	34/176 (19.3%)	74/891 (8.2%)	< .001
Multiple PEDs used	143/311 (46.0%)	97/347 (28.0%)	19/59 (32.2%)	47/178 (26.4%)	306/895 (34.2%)	<. 001

Note – *n* indicates the number of aneurysms
a. Aneurysm size was not reported for 10 aneurysms

3. ASPIRe

Aneurysm Study of Pipeline in an Observational Registry (ASPIRe)

D. F. Kallmes, W. Brinjikji, E. Boccardi, E. Ciceri, O.Diaz, R. Tawk, H. Woo, P. Jabbour, F. Al buquerque, R. Chapot, A. Bona fe, S. R. Dashti, J. E. D. Almandoz, C. Given II, M. E. Kelly, D. T. Cross III, G. Duckwiler, N. Razack, C. J. Powers, S. Fischer, D. Lopes, M. R. Harrigan, D. Huddle, R. Turner IV, O.O. Zaidat, L. Defreyne, V. M. Pereira, S. Cekirge, D. Fiorella, R. A. Hanel, P. Lylyk, C. McDougall, A. Siddiqui, I. Szikora, E. Levy

JUNE 2016, INTERVENTIONAL NEUROLOGY: 5(1-2):89-99
DOI: 10.1159/000446503

Background:

Few prospective studies exist evaluating the safety and efficacy of the Pipeline™ Embolization Device (PED) in the treatment of intracranial aneurysms. The Aneurysm Study of Pipeline In an observational Registry (ASPIRe) study prospectively analyzed rates of complete aneurysm occlusion and neurologic adverse events following PED treatment of intracranial aneurysms.

Methods:

The authors performed a multicentre study prospectively evaluating patients with unruptured intracranial aneurysms treated with PED. Primary outcomes included (1) spontaneous rupture of the Pipeline-treated aneurysm; (2) spontaneous non-aneurysmal intracranial haemorrhage (ICH); (3) acute ischemic stroke; (4) parent artery stenosis, and (5) permanent cranial neuropathy. Secondary endpoints were (1) treatment success and (2) morbidity and mortality at the 6-month follow-up. Vascular imaging was evaluated at an independent core laboratory.

Results:

One hundred and ninety-one patients with 207 treated aneurysms were included in this registry. The mean aneurysm size was 14.5 ± 6.9mm, and the median imaging follow-up was 7.8 months. Twenty-four aneurysms (11.6%) were small, 162 (78.3%) were large and 21 (10.1%) were giant. The median clinical follow-up time was 6.2 months. The neurological morbidity rate was 6.8% (13/191), and the neurological mortality rate was 1.6% (3/191). The combined neurological morbidity/mortality rate was 6.8% (13/191). The most common adverse events were ischemic stroke (4.7%, 9/191) and spontaneous ICH (3.7%, 7/191). The complete occlusion rate at the last follow-up was 74.8% (77/103).

Conclusion:

The authors prospective post market study confirms that PED treatment of aneurysms in a heterogeneous patient population is safe with low rates of neurological morbidity and mortality. Patients with angiographic follow-up had complete occlusion rates of 75% at 8 months.

*Please note this study represents some clinical cases that are off-label for the US market.

TABLE 3.1

Patient baseline characteristics

Characteristic	Summary (n=191)
Age (years)	
Mean ± SD	59.9 ± 12.5 (191)
Median (min, max)	60.0 (25.0, 89.0)
Gender	
Male	16.2 (31/191)
Female	83.8 (160/191)
Race	
White	86.7 (157/181)
Black or African American	7.2 (13/181)
Asian	1.7 (3/181)
American Indian or Alaska Native	0.6 (1/181)
Native Hawaiian or other Pacific Islander	0.6 (1/181)
Other	3.3 (6/181)
Ethnicity	Ethnicity
Hispanic or Latino	17.5 (28/160)
Hypertension	
Yes	53.9 (103/191)
Controlled	93.2 (96/103)
No	41.9 (80/191)
Unknown	4.2 (8/191)
Current or previous smoker	43.7 (80/183)

207 Aneurysms

100% Unruptured aneurysms

14.5mm Mean aneurysm size

95.2% Anterior circulation aneurysm location

17.3% Adjunctive devices (coils)

1.2 Average PEDs per aneurysm

7.1mm Mean neck diameter

66.5% Patients treated with PED alone

10.5% Adjunctive devices (balloons)

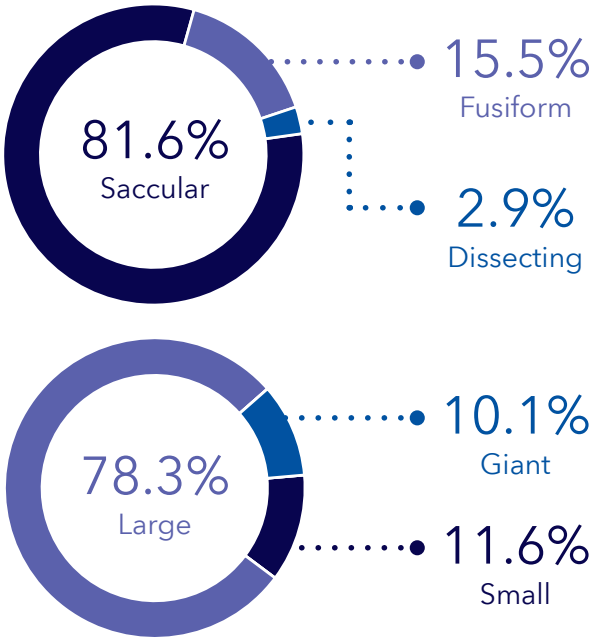


TABLE 3.2

Primary Endpoint: Incidence of primary adverse events of interest after PED placement

Adverse Event of Interest	Major[1]	Minor
Spontaneous rupture of the PED treated aneurysm	1.6% (3/191)	0% (0/191)
Intracranial haemorrhage (Ipsilateral or Contralateral)	3.7% (7/191)	0% (0/191)
Ischemic stroke	1.6% (3/191)	3.1% (6/191)
Symptomatic parent artery stenosis	0% (0/191)	0% (0/191)
Asymptomatic parent artery stenosis	0% (0/191)	1.6% (3/191)
Permanent cranial neuropathy	0% (0/191)	0% (0/191)
Total events	15	9
Patients with AE of Interest[3]	6.8% (13/191)	4.7% (9/191)

[1]Symptoms remain present after 7 days

[2]Symptoms resolved within 7 days with no clinical sequelae

[3]Some subjects had more than one event.

TABLE 3.3

Aneurysm location

Location	Summary
ICA	90.8 (188/207)
Anterior cerebral artery	0.5 (1/207)
Middle cerebral artery	1.4 (3/207)
Posterior cerebral artery	0.5 (1/207)
Basilar artery	2.9 (6/207)
Vertebral artery	1.4 (3/207)
Anterior communicating artery	2.4 (5/207)

6.8% Combined morbidity & mortality

5.8% Subjects requiring re-treatment

74.8% Aneurysm occlusion at last follow-up

79% Aneurysm occlusion at 12 months

4. PUFS

Long-Term Clinical and Angiographic Outcomes Following Pipeline Embolization Device Treatment of Complex Internal Carotid Artery Aneurysms: Five-Year Results of the Pipeline for Uncoilable or Failed Aneurysms Trial

Tibor Becske, Waleed Brinjikji, Matthew B Potts, David F Kallmes, Maksim Shapiro, Christopher J Moran, Elad I Levy, Cameron G McDougall, István Szikora, Giuseppe Lanzino, Henry H Woo, Demetrius K Lopes, Adnan H Siddiqui, Felipe C Albuquerque, David J Fiorella, Isil Saatci, Saruhan H Cekirge, Aaron L Berez, Daniel J Cher, Zsolt Berentei, Miklós Marosfoi, Peter K Nelson.

JANUARY 2017, NEUROSURGERY; 80(1):40-48
DOI: 10.1093/neuros/nyw014

Background:

Early and mid-term safety and efficacy of aneurysm treatment with the Pipeline™ Embolization Device (PED) has been well demonstrated in prior studies. The objective of this study was to present 5-yr follow-up for patients treated in the Pipeline for Uncoilable or Failed Aneurysms clinical trial.

Methods:

In the prospective, multicenter trial, 109 complex internal carotid artery (ICA) aneurysms in 107 subjects were treated with the PED. Patients were followed per a standardized protocol at 180 d and 1, 3, and 5 yr. Aneurysm occlusion, in-stent stenosis, modified Rankin Scale scores, and complications were recorded.

Results:

The primary endpoint of complete aneurysm occlusion at 180 d (73.6%) was previously reported. Aneurysm occlusion for those patients with angiographic follow-up progressively increased over time to 86.8% (79/91), 93.4% (71/76), and 95.2% (60/63) at 1, 3, and 5 yr, respectively. Six aneurysms (5.7%) were retreated. New serious device-related events at 1, 3, and 5 yr were noted in 1% (1/96), 3.5% (3/85), and 0% (0/81) of subjects. There were 4 (3.7%) reported deaths in the trial. Seventy-eight (96.3%) of 81 patients with 5-yr clinical follow-up had modified Rankin Scale scores ≤2. No delayed neurological deaths or haemorrhagic or ischemic cerebrovascular events were reported beyond 6 mo. No recanalization of a previously occluded aneurysm was observed.

Conclusion:

The authors 5-yr findings demonstrate that PED is a safe and effective treatment for large and giant wide-necked aneurysms of the intracranial ICA, with high rates of complete occlusion and low rates of delayed adverse events.

TABLE 4.1

Patient baseline characteristics

Characteristic	Value
Mean age (y) *	57.0 (11.3, 30.2-75.1)
Female sex	96 (88.9)
Race	
White	99 (91.7)
Black	6 (5.6)
Not reported	3 (2.8)
Medical History	
Remote subarachnoid haemorrhage	8 (7.4)
Stroke	7 (6.5)
Hypertension	60 (55.6)
History of smoking	
Never a smoker	46 (42.6)
Current smoker	31 (28.7)
Previous smoker	31 (28.7)
Prior treatments for target aneurysm	
Coil embolisation	6 (5.6)
Surgery	1 (0.9)
Other	1 (0.9)
mRS score	
0	60 (55.6)
1	34 (31.5)
2	9 (8.3)
3	2 (1.9)
4	1 (0.9)
Not performed	2 (1.9)
Mean maximum fundus diameter (mm)* 1	8.2 (6.4, 6.2†-36.1)
No. with neck measurement ≥ 6 mm	85 (78.7)
No. with neck measurement < 6 mm 2	2 (20.4)
Mean dome size (mm) *	14.6 (5.5, 4.4 – 29.5)
No. of target aneurysms partially thrombosed	17 (15.7)

Note – Numbers in parentheses are percentages unless otherwise noted.
* Numbers in parentheses are standard deviation and range.
† Patient with 6.2-mm aneurysm excluded from effectiveness cohort.

109 Aneurysms

18.2mm Mean aneurysm dome size

8.8mm Mean neck size

0.9% Adjunctive devices (coils)

5.7% Retreated aneurysms

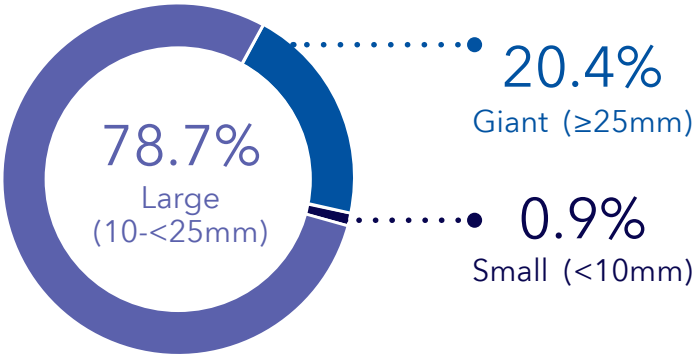


TABLE 4.2

Aneurysm characteristics

Aneurysm Location	#	%
Intra-Dural: (Paraopthalmic, Superior Hypophyseal, Supraclinoid, Carotid Cave, Lateral Clinoidal)	59	54%
Extra-Dural: (Caverous, Petrous)	48	45%
Off-Target Location: (Posterior Communicating) [a]	1	1%
Total	**108**	**100%**

a. Excluded from efficacy analysis

TABLE 4.3

Trial endpoints

Primary Effectiveness Endpoint: Index treatment success, defined as complete occlusion of intracranial aneurysms at 180-day angiography in the absence of major stenosis (>50%) or adjunctive use of complimentary embolic agent.
Secondary Effectiveness Endpoint: Complete occlusion of the target aneurysm at 1, 3, and 5 years.
Primary Safety Endpoint: Occurrence of ipsilateral major stroke or neurologic death by 180 days.
Secondary Safety Endpoint: Complete aneurysm occlusion, incidence of significant in stent stenosis (>50%), occurrence of delayed device-related adverse events, and functional outcomes based on the modified Rankin Scale.

TABLE 4.4

Dual anti-platelet regime

Pre-Treatment	Post Treatment
Aspirin 325 mg orally daily for 2 days prior and clopidogrel 75 mg daily for 7 days prior to treatment	Aspirin 325 mg daily for at least 6 months post treatment
OR /AND	
600 mg loading dose of clopidogrel 1 day prior to treatment	Clopidogrel 75 mg daily for at least 3 months post treatment

Angiographic Complete Occlusion Rates

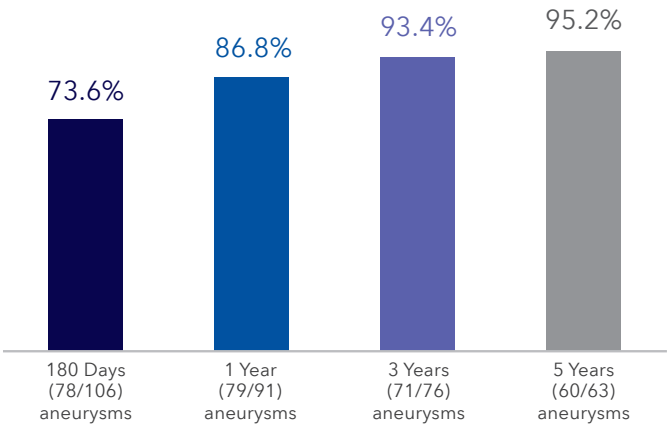


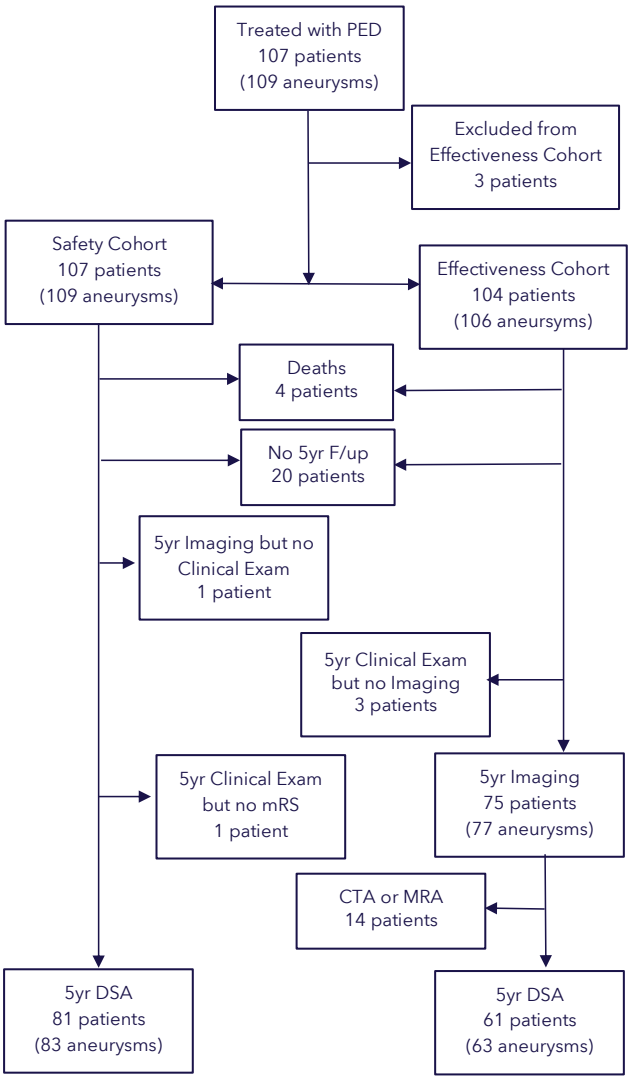
TABLE 4.5

Clinical Outcomes based on the Modified Rankin Scale (mRS)

mRS	3 yr	5 yr
0	60	62
1	19	14
2	2	2
3	1	2
4	2	1
5	0	0
6[a]	4	4
No mRS	19	22

a. mRS score of 6 assigned to subjects who had died (all deaths occurred within 2 yr).

FIGURE 4.1



Study limitations*:

1. Approximately 15% of patients did not complete formal long-term follow-up.
2. Single-arm study employing a historical control; therefore, direct comparison of PED treatment to parent vessel occlusion and endosaccular coiling is not possible.
3. Study was limited to aneurysms of the ICA from the petrous to superior hypophyseal segments, therefore, safety and efficacy results of this study may not be reflective of more distal anterior circulation or posterior circulation aneurysms.

Study strengths*:

1. Prospective study design.
2. Independent adjucation of imaging (Core Lab) and clinical (CEC) outcomes.

*As stated by the authors

0%

Recurrence of aneurysms after complete occlusion at 5 years**

95%

Occlusion at 5 years follow-up**

5.6%

Major stroke or neurologic death at 5 years

Other clinical outcomes:

Effectiveness: 73.3% (11/15) of aneurysms with remnants at 6-mo demonstrated subsequent complete closure. There were no delayed aneurysm recanalization or rupture. Overall, 5.5 % (6/109) of treated parent vessels occluded through 5-year; all occurring within 3-year post-treatment. At 5-yr clinical follow-up, 96.3% (78/81) of patients had mRS scores of 0-2.

Safety: There were no additional device-related serious adverse events between 3 and 5-yr; with 3 events occurring between 180-d and 3-yr post-treatment.

**For subjects with available imaging

5. PFLEX

Treatment of intracranial aneurysms using the Pipeline Flex Embolization Device with Shield Technology: angiographic and safety outcomes at 1-year follow-up

M. Martínez-Galdámez, S. M. Lamin, K. G. Lagios, T. Liebig, E. F. Ciceri, R. Chapot, L. Stock, S. Chavda, C. Kabbasch, G. Faragò, H. Nordmeyer, T. Boulanger, M. Piano, E. P. Boccardi

SEP 2018, JOURNAL OF NEUROINTERVENTIONAL SURGERY
DOI: 10.1136/NEURINTSURG-2018-014204

Background:

The Pipeline™ Embolization Device (PED) is a routine first-line treatment option for intracranial aneurysms (IAs). The Pipeline™ Flex Embolization Device with Shield Technology™ (Pipeline Shield) is an updated version of the PED which has been modified to include a surface phosphorylcholine biocompatible polymer. Its early technical success and safety have been reported previously. Here, the authors assessed the long-term safety and efficacy of the Pipeline Shield for the treatment of IAs.

Methods:

The Pipeline™ Flex Embolization Device with Shield Technology™ (PFLEX) study was a prospective, single-arm, multicenter study for the treatment of unruptured IAs using the Pipeline™ Shield. The primary endpoint was a major stroke in the territory supplied by the treated artery or neurologic death at 1-year post-procedure. Angiographic outcomes were also assessed by an independent radiology laboratory at 6 months and 1 year.

Results:

Fifty patients (mean age, 53 years; 82% female) with 50 unruptured IAs were treated. Mean aneurysm diameter was 8.82±6.15 mm. Of the target aneurysms, 38/50 (76%) were small (<10 mm), 11/50 (22%) were large (≥10 and<25 mm), and 1/50 (2%) was giant (≥25 mm). Forty-seven (94%) were located in the internal carotid artery and three (6%) in the vertebral artery. At 1-year post-procedure, no major strokes or neurologic deaths were reported, and complete occlusion was achieved in 27/33 (81.8%). There were no instances of aneurysm recurrence or retreatment.

Conclusion:

Our 1-year follow-up concerning angiographic and safety outcomes corroborate previous evidence that the Pipeline™ Shield is a safe and effective treatment for IAs.

*Please note this study represents some clinical cases that are off-label for the US market.

TABLE 5.1

Patient baseline characteristics and aneurysm characteristics

Characteristic	Summary (n=50)
Mean Age	53.0±13.01
Women	41 (82.0%)
Medical History	
Hypertension (controlled)	12 (24.0%)
Hyperlipidaemia	5 (10.0%)
Diabetes type 2	2 (4.0%)
Obesity	0
Atrial fibrillation	0
Coronary artery disease	0
Congestive artery disease	0
Subarachnoid haemorrhage	11 (22.0%)
Smoking history	50 (100.0%)
Never smoked or not smoked within last 10 days	19 (38.0%)
Not a current smoker but has smoked within past 10 years	15 (30.0%)
Current smoker, <1 pack per day	5 (10.0%)
Current smoker, ≥1 pack per day	4 (8.0%)
Unknown	7 (14.0%)

TABLE 5.2

Aneurysm occlusion and parent artery stenosis at 6-months and 1-year post-procedure

Aneurysm occlusion	6 months n/N (%)	1 year n/N (%)
Target aneurysm		
Complete occlusion	29/38 (76.3)	27/33 (81.8)
Residual neck	5/38 (13.2)	2/33 (6.1)
Residual aneurysm	4/38 (10.5)	4/33 (12.1)
Cannot determine*	1	1
All aneurysm		
Complete occlusion	31/40 (77.5)	27/33 (81.8)
Residual neck	5/40 (12.5)	2/33 (6.1)
Residual aneurysm	4/40 (10.0)	4/33 (21.1)
Cannot determine*	1	1
Parent artery stenosis		
0% - 25%	29/36 (80.6)	28/32 (87.5)
>25% - 50%	5/36 (13.9)	3/32 (9.4)
>50% - 75%	1/36 (2.8)	0
>75%	1/36 (2.8)	1/32 (3.1)
Cannot determine*	3	2

*Imaging was performed as per standard of care in 39 patients at 6 months, and in 34 patients at 1 year. Occlusion rate was indeterminate in one patient of 50.

50 Aneurysms

1.12
Average devices per subject

5.1mm
Mean neck diameter

92%
Patients with DAPT

12%
Previously ruptured aneurysms

8.8mm
Mean sac diameter

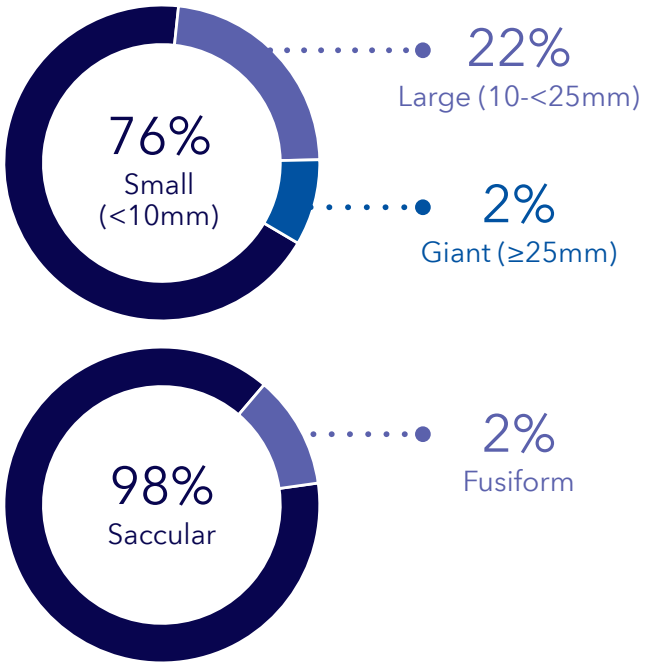


TABLE 5.3

Primary and secondary safety outcomes at 1-year post procedure

Endpoint	Event rate n/N (%) (95%%CI)
Major stroke in the territory supplied by the treated artery or neurological death	0/50 (0%) (0%, 5.8%)
Major stroke in the territory supplied by the treated artery	0/50 (0%) (0%, 5.8%)
Neurological death	0/50 (0%) (0%, 5.8%)
Pipeline Flex embolization device with shield technology-related neurologic adverse event rate	7/50 (14.0%) (5.8%, 26.7%)

76.3%
Aneurysm occlusion at 6 months

81.8%
Aneurysm occlusion at 12 months

0%
Target aneurysm recurrence or retreatment: 1 year follow-up

0%
Neurological death

6. PEDSU

Outcome Study of the Pipeline Embolization Device with Shield Technology in Unruptured Aneurysms (PEDSU)

D. Atasoy, N. Kandasamy, J. Hart, J. Lynch, S.-H. Yang, D. Walsh, C. Tolias and T.C. Booth

DEC 2019, AMERICAN JOURNAL OF NEURORADIOLOGY
DOI: 10.3174/AJNR.A6314

Background:

The recently introduced Pipeline™ Flex Embolization Device with Shield Technology™ (Pipeline Shield) is the third generation of Pipeline™ flow-diverter devices. It has a new stent-surface modification, which reduces thrombogenicity. The authors aimed to evaluate clinical and radiographic (safety and efficacy) outcomes of the Pipeline™ Shield.

Methods:

The 30-day and 1-year mortality and morbidity rates and the 6- and 18-month radiographic aneurysm occlusion outcomes for procedures performed between March 2016 and January 2018 were analyzed. 3D-TOF-MRA was used for follow-up.

Results:

Forty-four attempted Pipeline™ Shield procedures were performed for 41 patients with 44 target aneurysms (total of 52 aneurysms treated). A total of 88.5% of devices were inserted in the anterior circulation, and 11.5%, in the posterior circulation; 49/52 (94.2%) aneurysms were saccular; and 1/52 (1.9%) was fusiform. One (1.9%) aneurysm was an iatrogenic pseudoaneurysm, and 1 (1.9%) was a dissecting aneurysm. Seventy-one percent (35/49) of the saccular aneurysms were wide-neck (neck, >4 mm), 34.6% (18/52) were large (≥10 mm), and 3.8% (2/52) were giant (≥25 mm). The mean aneurysm sac maximal diameter was 9.0 mm, and the mean neck width was 5.0 mm. The cumulative mortality and morbidity rates were 2.3% and 6.8% at 1 year, respectively. The adequate occlusion rate was 78.8% at 6 months and 90.3% at 18 months.

Conclusion:

In this pragmatic and non-industry-sponsored study, the occlusion rates and safety outcomes were similar to those seen in previously published studies with flow-diverter devices and earlier generation Pipeline™ Embolization Devices.

*Please note this study represents some clinical cases that are off-label for the US market.

TABLE 6.1

Patient baseline and aneurysm characteristics

Characteristic	Summary (n=41)
Mean Age	56
Female	28 (68.3%)
Aneurysm Location	
Anterior circulation	46 (88.5%)
ICA cavernous segment	2 (3.8%)
ICA paraophthalmic segment	29 (55.7%)
ICA posterior communicating segment	12 (23.1%)
ICA Terminal segment	2 (3.8%)
M1 segment of MCA	1 (1.9%)
Posterior circulation	6(11.5%)
Basilar artery	3 (5.8%)
Vertebral artery	2 (3.8%)
Posterior cerebral artery	1 (1.9%)
Neck width (mm)	5.0 (1.0 – 21.0)
Maximum aneurysm sac diameter (mm)	9.0 (1.0 – 28.0)
<10	32 (60.8%)
10-25	18 (34.6%)
≥25	2 (3.8%)

44 Aneurysms

100% Unruptured aneurysms

32.6% Previously treated

9.0mm Mean sac diameter

5.0mm Mean neck diameter

1.02 Average devices per target aneurysm

28.8% Adjunctive devices

95% Single PED in cases

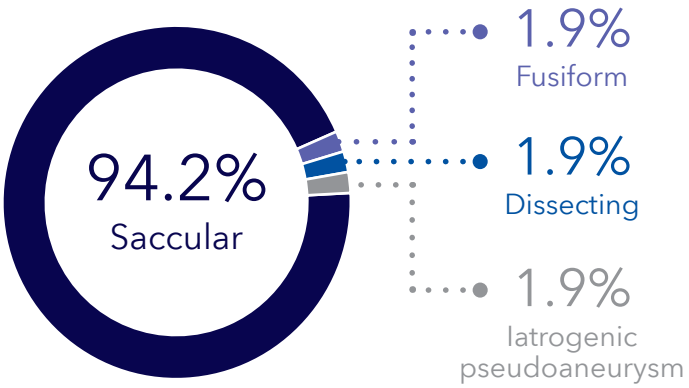


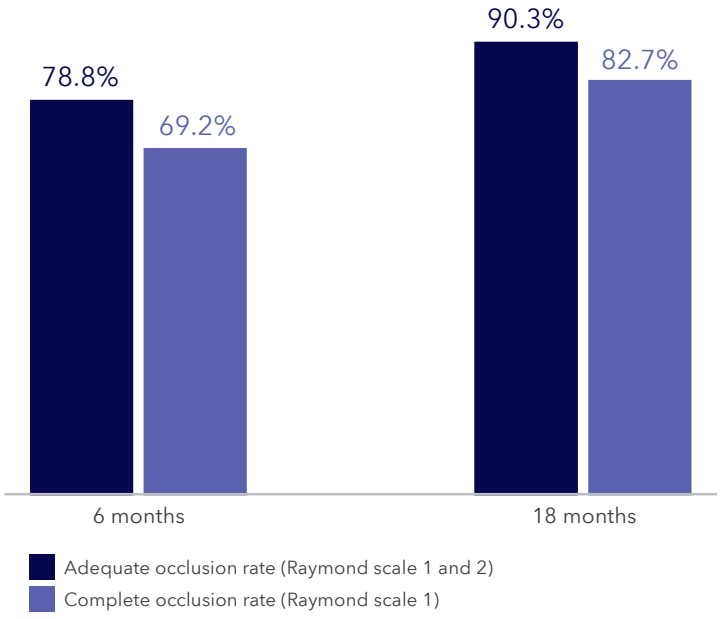
TABLE 6.2

Clinical outcomes

Outcome	Procedure No. (%)
Clinical outcomes	
Periprocedural outcomes (within 30 days)	
Major adverse events[1]	
Death from subdural haemorrhage	1 (2.3%)
Cranial nerve palsy[2]	1 (2.3%)
Minor adverse events	
Stroke/TIA	1 (2.3%)
Headache[2]	1 (2.3%)
Postprocedural outcomes (30 days to 1 year)	
Major adverse events[1]	
Pulsatile tinnitus (carotid cavernous fistula)	1 (2.3%)
Mass effect causing reduced visual acuity	1 (2.3%)

1. Ongoing clinical event at 7 days following the event
2. Same patient

MRA Occlusion Rates



6.8% Combined morbidity

2.3% Combined mortality

82.7% Complete occlusion at 18 months

7. PREMIER

Prospective study on embolization of intracranial aneurysms with the pipeline device (PREMIER study): 3-year results with the application of a flow diverter specific occlusion classification

Ricardo A Hanel, Gustavo M Cortez, Demetrius Klee Lopes, Peter Kim Nelson, Adnan H Siddiqui, Pascal Jabbour, Vitor Mendes Pereira, Istvan Szikora István, Osama O Zaidat, Chetan Bettegowda, Geoffrey P Colby, Maxim Mokin, Clemens M Schirmer, Frank R Hellinger, Curtis Given, Timo Krings, Philipp Taussky, Gabor Toth, Justin F Fraser, Michael Chen, Ryan Priest, Peter Kan, David Fiorella, Donald Frei, Beverly Aagaard-Kienitz, Orlando Diaz, Adel M Malek, C Michael Cawley, Ajit S Puri, David F Kallmes

JULY 2019, JOURNAL OF NEUROINTERVENTIONAL SURGERY; 12:62–66.
DOI: 10.1136/https://jnis.bmj.com/content/neurintsurg/early/2022/03/14/neurintsurg-2021-018501.full.pdf

Background:

The pipeline embolization device (PED; Medtronic) has presented as a safe and efficacious treatment for small- and medium-sized intracranial aneurysms. Independently adjudicated long-term results of the device in treating these lesions are still indeterminate. We present 3-year results, with additional application of a flow diverter specific occlusion scale.

Methods:

PREMIER (prospective study on embolization of intracranial aneurysms with pipeline embolization device) is a prospective, single-arm trial. Inclusion criteria were patients with unruptured wide-necked intracranial aneurysms ≤12mm. Primary effectiveness (complete aneurysm occlusion) and safety (major neurologic event) endpoints were independently monitored and adjudicated.

Results:

As per the protocol, of 141 patients treated with a PED, 25 (17.7%) required angiographic followup after the first year due to incomplete aneurysm occlusion. According to the Core Radiology Laboratory review, three (12%) of these patients progressed to complete occlusion, with an overall rate of complete aneurysm occlusion at 3 years of 83.3% (115/138). Further angiographic evaluation using the modified Cekirge–Saatci classification demonstrated that complete occlusion, neck residual, or aneurysm size reduction occurred in 97.1%. The overall combined safety endpoint at 3 years was 2.8% (4/141), with only one nondebilitating major event occurring after the first year. There was one case of aneurysm recurrence but no cases of delayed rupture in this series.

Conclusion:

The PED device presents as a safe and effective modality in treating small- and medium-sized intracranial aneurysms. The application of a flow diverter specific occlusion classification attested the long-term durability with higher rate of successful aneurysm occlusion and no documented aneurysm rupture

*Please note this study represents some clinical cases that are off-label for the US market.

TABLE 7.1

Patient baseline characteristics and aneurysm characteristics

Characteristic	Summary (n=141)
Age (years)	54.6±11.3
Female	124 (87.9%)
Comorbidities (n (%))	
Hypertension	72 (51.1%)
Hyperlipidemia	54 (38.3%)
Diabetes mellitus	16 (11.3%)
Obesity	24 (17.0%)
Cerebral atherosclerosis	1 (0.7%)
Atrial fibrillation	7 (5.0%)
Myocardial infarction	2 (1.4%)
Coronary artery disease	9 (6.4%)
Sleep Apnea	16 (11.3%)
Alcohol use	3 (2.1%)
Smoking history (n (%))	7 (3.4%)
Never smoked, or not within 10 years	79 (56.0%)
Not currently, but within 10 years	21 (14.9%)
Current smoker, <1 pack/day	27 (19.1%)
Current smoker, ≥1 pack/day	14 (9.9%)
Internal carotid artery	134 (95%)
Petrous (C2)	1 (0.7%)
Clinoid (C4)	11 (8.2%)
Cavernous (C5)	3 (2.2%)
Ophthalmic (C6)	100 (74.6%)
Communicating (C7)	19 (14.2%)
Vertebral artery	7 (5%)

141 Aneurysms

1.1
Average devices per subject

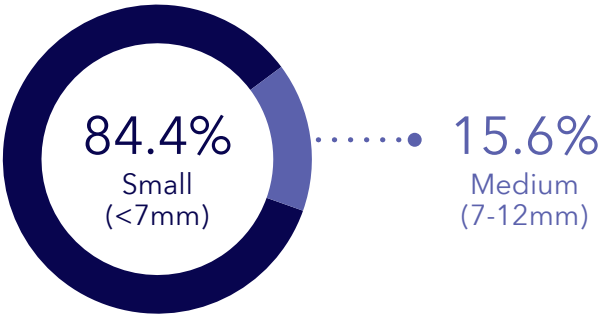
4.6mm
Mean sac diameter

3.5%
Adjunctive devices

55%
Treated with PED Flex

3.7mm
Mean neck diameter

92.9%
Single PED in cases



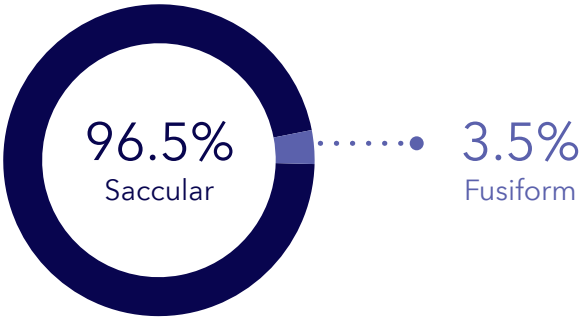


TABLE 7.2

Effectiveness, safety, & functional long-term outcomes (n=138)

	1-year follow-up	3-year follow-up†
Primary effectiveness outcome	106 (76.8%)	108 (78.3%)
Occlusion status: Raymond-Roy		
Complete occlusion (1)	113 (81.9%)	115 (83.3%)
Residual neck (2)	3 (2.2%)	7 (5.1%)
Residual aneurysm (3)	22 (15.9%)	16 (11.6%)
Occlusion status: mCSC		
Complete occlusion (1/1A/1B)	113 (81.9%)	118 (85.5%)
Residual neck (2)	3 (2.2%)	1 (0.7%)
Aneurysm size reduction (3A/5/5A)	-	15 (10.8%)
Residual aneurysm (3/3C)	22 (15.9%)	1 (0.7%)
No consecutive follow-up for classification	-	3 (0.9%)
Target aneurysm retreatment	4 (2.9%)	7 (5.0%)
Target aneurysm recurrence	0	1 (0.7%)
Stenosis >50%	4 (2.9%)	5 (3.6%)
Primary safety outcome*	3 (2.2%)	4 (2.9%)
Functional independence (mRS ≤2)	137/139 (98.6%)	127/130 (97.7%)

81.9%
Complete aneurysm occlusion at 1 year

83.3%
Complete aneurysm occlusion at 3 years

2.8%
Combined safety endpoint at 3 years

78.3%
Primary effectiveness endpoint at 3 years

Data are n (%) or n/N (%).
* Defined as major stroke in the supplied territory or neurologic death; three events occurred within the first year, and one within the second year.
† In cases where 3-year digital subtraction angiography (DSA) control was not available, last observation carried forward of 2-year DSA was used. The latest follow-up is used for the mCSC.
mCSC, modified Cekirge-Saatci classification; mRS, modified Rankin Scale.

8. SHIELD

Periprocedural to 1-year safety and efficacy outcomes with the Pipeline Embolization Device with Shield technology for intracranial aneurysms: a prospective, post-market, multi-center study

Hal Rice, Mario Martínez Galdámez, Markus Holtmannspötter, Laurent Spelle, Konstantinos Lagios, Maria Ruggiero, Pedro Vega, Hemant Sonwalkar, René Chapot, Saleh Lamin

JUNE 2020, JOURNAL OF NEUROINTERVENTIONAL SURGERY 12(11): DOI:10.1136/NEURINTSURG-2020-015943

Background:

The first and second generations of the Pipeline™ Embolization Device (PED) have been widely adopted for the treatment of intracranial aneurysms (IAs) due to their high associated occlusion rates and low morbidity and mortality. The objective of this study was to evaluate the safety and effectiveness of the third generation Pipeline™ Shield device (PED-Shield) for the treatment of IAs.

Methods:

The SHIELD study was a prospective, single arm, multicenter, post-market, observational study evaluating the PEDShield device for the treatment of IAs. The primary efficacy endpoint was complete aneurysm occlusion without significant parent artery stenosis or retreatment at 1-year post-procedure and the primary safety endpoint was major stroke in the territory supplied by the treated artery or neurological death.

Results:

Of 205 subjects who consented across 21 sites, 204 subjects with 204 target aneurysms were ultimately treated (mean age 54.8±12.81 years, 81.4% [166/204] female). Technical success (ie, deployment of the PED Shield) was achieved in 98.0% (200/204) of subjects with a mean number of 1.1±0.34 devices per subject and a single device used in 86.8% (177/204) of subjects. The primary effectiveness endpoint was met in 71.7% (143/200) of subjects while the primary safety endpoint occurred in six (2.9%) subjects, two (1.0%) of which led to neurological death.

Conclusion:

The findings of the SHIELD study support the safety and effectiveness of the PED-Shield for IA treatment, evidenced by high occlusion rates and low rates of neurological complications in the study population.

*Please note this study represents some clinical cases that are off-label for the US market.

TABLE 8.1

Patient baseline characteristics

Characteristic	Summary (n=204)
Age (mean±SD)	54.8±12.81
Female	166 (81.3%)
Cigarette smoking (n (%))	98 (48.0%)
Currently	45 (46.0%)
Previous	53 (54.1%)
Comorbidities (n (%))	
Family history of stroke/TIA	26 (12.7%)
Hypertension	89 (43.6%)
Controlled	85 (95.5%)
Uncontrolled	4 (4.5%)
Diabetes	15 (7.3%)
Type 1	1 (6.7%)
Type 2	14 (93.3%)
Hyperlipidaemia	44 (21.6%)
Atrial fibrillation	9 (4.4%)
Cardiovascular disease	7 (3.4%)
Coronary heart disease	8 (3.9%)
Subarachnoid haemorrhage (excl. rupture of target aneurysm)	19 (9.3%)
Multiple aneurysms present	51 (25.0%)
Additional aneurysms present in parent artery	25 (12.3%)

TABLE 8.2

Primary effectiveness endpoint through 1-year post-procedure by aneurysm location (FAS population with observed data)

Primary effectiveness endpoint	Rate	95% CI
All aneurysms	143/200 (71.7%)	(65.0% to 77.7%)
Intracranial ICA (C2-C7 including terminus)	109/144 (75.7%)	(67.9% to 82.4%)
Non-intracranial ICA	28/45 (62.2%)	(46.5% to 76.2%)
C1	1/2 (50%)	(1.3% to 98.7%)
Vertebral	8/13 (61.5%)	(31.6% to 86.1%)
MCA	7/13 (53.8%)	(25.1% to 80.8%)
ACA	6/8 (75.0%)	(34.9% to 96.8%)
AComm	6/9 (66.7%)	(29.9% to 92.5%)

204 Aneurysms

81.4% Unruptured aneurysms

8.5mm Mean aneurysm size

93.6% Anterior circulation aneurysm location

18.6% Adjunctive devices (coils)

1.1 Average PEDs per aneurysm

4.6mm Mean neck length

86.8% Single PED in cases

10.8% Adjunctive devices (balloons)

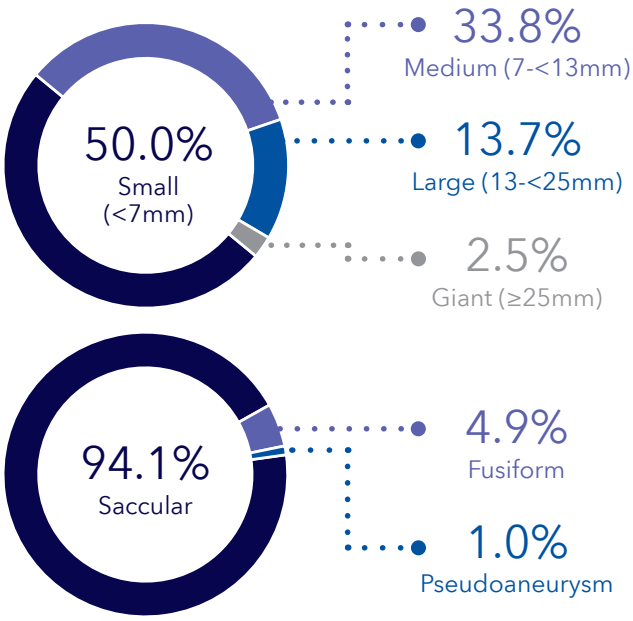


TABLE 8.3

Post procedure target aneurysm occlusion at 1 year and last follow-up post procedure (ITT population with observed data)

	6 months	12 months	Last follow up
Complete occlusion	92/130 (70.8%)	61/79 (77.2%)	141/188 (75.0%)
Residual neck	7/130 (5.4%)	4/79 (5.1%)	9/188 (4.8%)
Residual aneurysm	31/130 (23.8%)	14/79 (17.7%)	38/188 (20.2%)

70.8% Aneurysm occlusion at 6 months

2.9% Combined morbidity

0.05% Retreatment rate

71.7% Primary effectiveness endpoint

77.2% Aneurysm occlusion at 12 months

1.0% Combined mortality

75% Occlusion at last follow-up

9. Trivelato et al.

Safety and Effectiveness of the Pipeline Flex Embolization Device With Shield Technology for the Treatment of Intracranial Aneurysms: Midterm Results From a Multicenter Study

F.P. Trivelato, E. Wajnberg, M. T. S. Rezende, A. C. Ulhôa, R. L. Piske, T. G. Abud, L. H. de Castro-Afonso, C. G. C. Abath, G. S. Nakiri, J. F. Santoro Araújo, J. L. Júnior Silva, R. T. Tosello, J. R. Vanzin, L. B. Manzato, C. E. Baccin, B. A. Araújo da Mota, D. G. Abud

JULY 2020, JOURNAL OF NEUROSURGERY 1;87(1):104-11112
DOI: 10.1093/neuros/nyz356

Background:

The safety and efficacy of the first generation of the Pipeline™ Embolization Device (PED; Medtronic, Inc) have been proven in large case series. Ischemic events are one of the most common complications following treatment of aneurysms with flow diverters. The new PED Flex with Shield Technology™ (PED Shield; Medtronic Inc) was introduced to minimize the rate of complications.

Objective:

To evaluate the outcomes of patients harboring aneurysms treated with the PED Shield.

Methods:

This was an observational, prospective, single-arm multicenter study of patients treated with the PED Shield. The primary safety endpoint was the absence of major neurological complications and death. The secondary effectiveness endpoint was angiographic occlusion at 6 and 12 mo. Technical complications were also reported.

Results:

Between November 2017 and December 2018, 151 patients from 7 centers with 182 aneurysms were enrolled. The mean aneurysm size was 7.0 mm; 27 (14.8%) aneurysms were large, and 7 (3.8%) were giant. In 141 of 151 patients (93.4%), the primary endpoint was reached. The overall rate of periprocedural complications was 7.3%. Of the aneurysms, 79.7% met the study's secondary endpoint of complete occlusion at 6 months and 85.3% at 12 months.

Conclusion:

The PED Shield is a safe and effective treatment for intracranial aneurysms. The results regarding total occlusion and ischemic complications did not differ from those obtained in case series using previous versions of the PED. Long-term follow-up and comparative studies are required to provide stronger conclusions regarding the reduced thrombogenicity of this device.

*Please note this study represents some clinical cases that are off-label for the US market.

TABLE 9.1

Patient baseline and aneurysm characteristics

Characteristic	Summary (n=151)
Age (years)	
Mean ± SD	52.7 ± 14
Gender (% / n)	
Female	79.5 (120/151)
Comorbidities (% / n)	
Hypertension	41.7 (63/151)
Smoker	18.5 (28/151)
Aneurysm Location (% / n)	
ACA	6.5 (12/151)
Cavernous	11 (20/151)
Communicating	8.2 (15/151)
MCA	10.4 (19/151)
Paraophthalmic	53.8 (98/151)
Other	11.1 (18/151)
Circulation (%)	
Anterior	93.4 (170/182)
Posterior	6.6 (12/182)
Partially thrombosed	4.9 (9/182)
Ruptured	3.8 (7/182)
Branch arising from the sac	15.9 (29/182)
Mass effect	9.9 (18/182)
Cranial nerve palsy	9.9 (15/151)
Aneurysms previously treated	7.7 (14/182)

182 Aneurysms

96.2% Unruptured aneurysms

7.0mm Mean aneurysm size

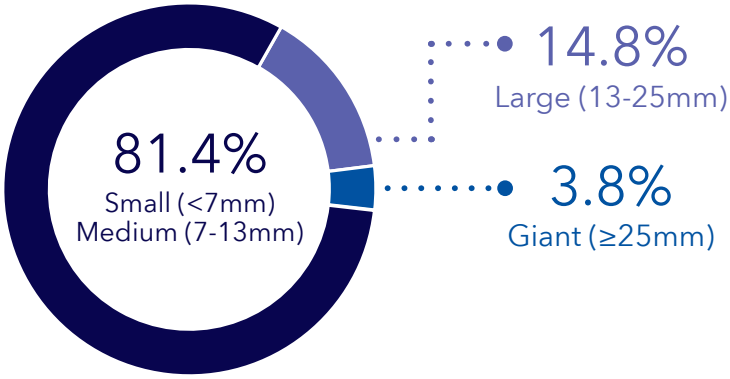
97.3% Single PED in cases

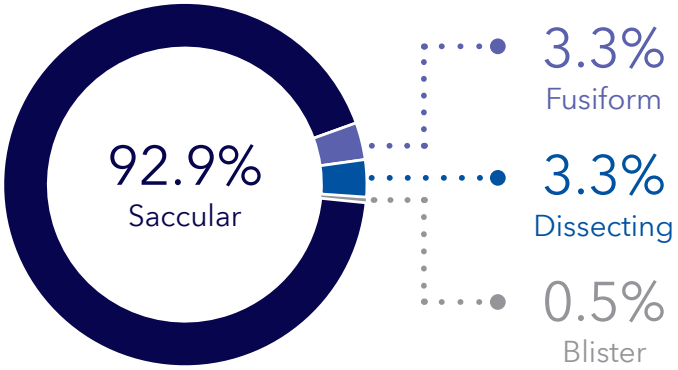
17% Adjunctive devices (coils)

7.7% Previously treated

4.1mm Mean neck length

11.5% Adjunctive devices (balloons)





7.3% Peri procedural complications

79.7% Complete occlusion at 6 months

85.3% Complete occlusion at 12 months

93.4% Primary safety endpoint

10. PEDESTRIAN

Pipeline Embolization Devices for the Treatment of Intracranial Aneurysms, Single-Center Registry: Long-Term Angiographic and Clinical Outcomes from 1000 Aneurysms

I. Lylyk, E. Scrivano, J. Lundquist, A. Ferrario, C. Bleise,
N. Perez, P. Nicolas Lylyk, R. Viso, R. Nella-Castro, P. Lylyk

AUG 2021, NEUROSURGERY, 89(3): 443-449
DOI: 10.1093/NEUROS/NYAB183

Background:

Prospective studies have established the safety and efficacy of the Pipeline™ Embolization Device (PED; Medtronic) for treatment of intracranial aneurysms (IA). The aim of this study was to investigate long-term outcomes from the Pipeline™ Embolization Devices for the Treatment of Intracranial Aneurysms (PEDESTRIAN) Registry.

Methods:

The PEDESTRIAN Registry data were retrospectively reviewed, which included patients (March 2006 to July 2019) with complex IAs treated with PED. Patients with unfavorable anatomy and/or recurrence following previous treatment were included and excluded those with acute subarachnoid hemorrhage. The primary angiographic endpoint was complete occlusion and long-term stability. Clinical and radiological follow-up was performed at 3 to 6 month, 12 month, and yearly thereafter.

Results:

A total of 835 patients (mean age 55.9±14.7 years; 80.0% female) with 1,000 aneurysms were included. Aneurysms varied in size: 64.6% were small (≤10 mm), 25.6% were large (11–24 mm), and 9.8% were giant (≥25 mm). A total of 1,214 PEDs were deployed. Follow-up angiography was available for 85.1% of patients with 776 aneurysms at 24.6±25.0 months (mean). Complete occlusion was demonstrated in 75.8% of aneurysms at 12-months, 92.9% at 2–4 years, and 96.4% at >5 years. During the post-procedural period, mRS remained stable or improved in 96.2% of patients, with stability or improvement in 99.1% of patients >5 years. The overall major morbidity and neurological mortality rate was 5.8%.

Conclusion:

This study demonstrated high rates of long-term complete aneurysm occlusion, stable or improved functional outcomes, and low rates of complications and mortality. Clinical and angiographic outcomes improved over longterm follow-up, demonstrating endovascular treatment of IA with PED is safe and effective.

*Please note this study represents some clinical cases that are off-label for the US market.

TABLE 10.1

Patient baseline characteristics and aneurysm characteristics

Characteristic	Summary (n=835)
Age (mean ± SD)	55.9 ± 14.7
Female	671 (80.4%)
Comorbities	
Hypertension	376 (45%)
Smoker	152 (18.2%)
Family history of aneurysm	56 (6.7%)
Multiple aneurysms	242 (29%)
Previously treated with PED	144 (17%)
Aneurysm location (No., %)	
Anterior circulation	910 (91%)
Posterior circulation	90 (9%)
ICA	867 (86.7%)
PCoA	199 (20%)
MCA	41 (4.1%)
PCA	10 (1%)
BA	37 (3.7%)
ACoA/ACA	14 (1.4%)
VA	29 (2.9%)
PICA	10 (1%)

1000 Aneurysms

1.21 Average devices per subject

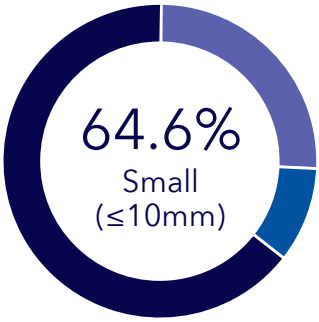
17% Previously treated

6.4mm Mean aneurysm diameter (saccular)

9.3% Adjunctive devices

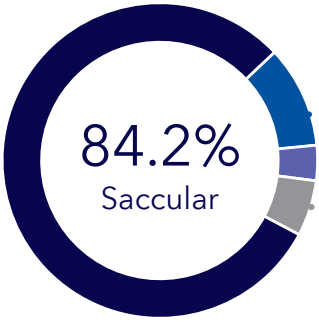
84.2% Single PED in cases

4.5mm Mean neck length (saccular)



25.6% Large (11-24mm)

9.8% Giant (≥25mm)



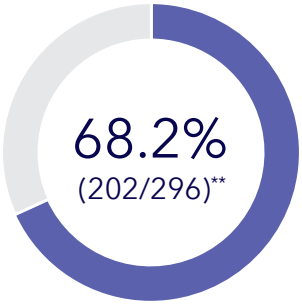
11% Dissection

3.8% Fusiform

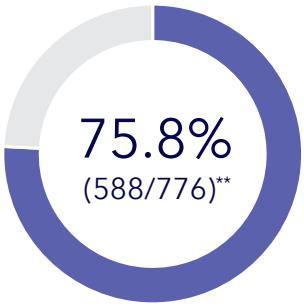
6% Blister

5.8%

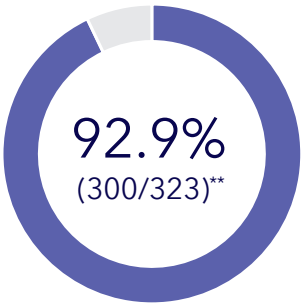
Combined major morbidity and neurological mortality over entire study period* (March 2006 – July 2019)



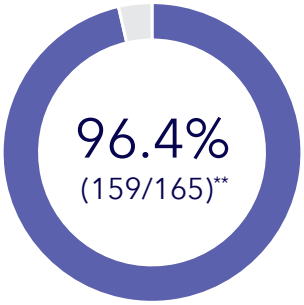
180 days
Complete Occlusion



1 year
Complete Occlusion



3 years
Complete Occlusion



5 years+
Complete Occlusion

* Includes Pipeline™ Embolization Device (no longer commercially distributed), Pipeline™ Flex Embolization Device & Pipeline™ Flex Embolization Device with Shield Technology™

** Patient numbers at follow-up.

11. SCOPE-AUS

Safety and Clinical Effectiveness of Pipeline Shield Device for Intracranial Aneurysms in an Australian Cohort (SCOPE-AUS)

Ghim Song Chia, Laetitia de Villiers, Vinicius Carraro do Nascimento, Cheryl Lee Rapier, Maame Amma Owusu, Fiona S. Lau, Alexander McQuinn, Cameron Williams, Justin Whitley, Andrew Cheung, Nathan W. Manning and Hal Rice.

SEPTEMBER 2022, STROKE VASC INTERV NEUROL. 2022;2:e000292.
DOI: 10.1161/SVIN.121.000292

Background:

The Pipeline™ Flex Embolization Device (PED) with Shield Technology™ (PED-Shield) is a third-generation flow diverting stents with surface modification designed to reduce platelet adhesion and thrombogenicity. The authors report the long-term safety and effectiveness of the PED-Shield in the treatment of unruptured intracranial aneurysms in an Australian cohort.

Methods:

SCOPE-AUS (Safety and Clinical Effectiveness Of Pipeline Shield Embolization Device for Treatment of Intracranial Aneurysms in Australia) is a multi-center, single-arm, retrospective study of patients with unruptured intracranial aneurysms treated with the PED-Shield flow diverting stents at 3 high-volume neurointervention centers in Australia between May 1, 2015, and June 30, 2018, evaluating safety and efficacy. The primary outcome was neurologic adverse event or neurologic-related death at 1 year, and the secondary outcome was long-term complete aneurysm occlusion.

Results:

A total of 238 patients (mean age 55.8±11.0 years, 73.1% [174/238] female) and 278 aneurysms were treated via 247 procedures. Two (0.7%) aneurysms were retreated during the 18-month follow-up. Overall occlusion rates at 18 months or at last follow-up imaging were 92.5% (233/252). There were 35 (14.7%) total primary end point events. The 12-month neurologic morbidity and mortality rates were 3.8% (9/238) and 1.3% (3/238), respectively. For the subgroup of internal carotid artery aneurysms, mortality (0.7%) and morbidity (2.0%) rates were low, and the complete occlusion rate was 92.5% (147/155).

Conclusion:

In this multi-center study, which includes a wide variety of both distal bifurcation and proximal unruptured intracranial aneurysms, the occlusion rates and safety outcomes of the PED-Shield flow diverting stent demonstrate a high proportion of complete aneurysm occlusion, extremely low re-treatment rates, and low complication rates.

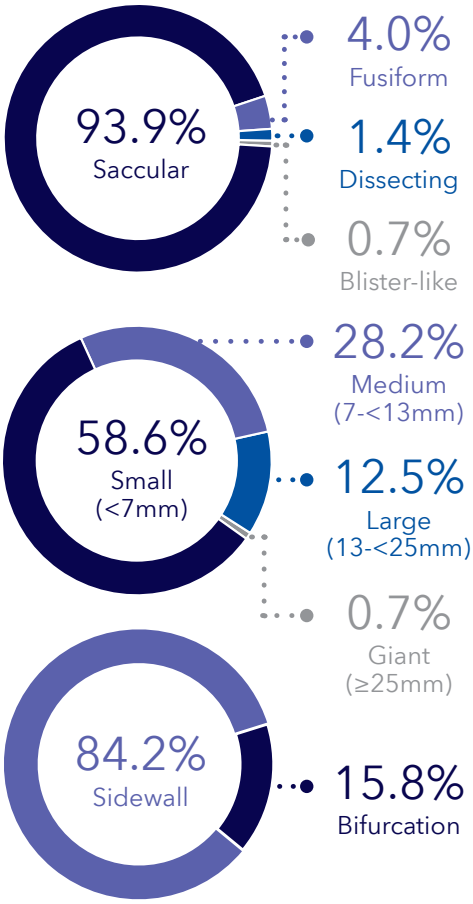
*Please note this study represents some clinical cases that are off-label for the US market.

TABLE 11.1

Baseline patient and aneurysm characteristics

Characteristic	Value (n=238)
Mean age (years)	55.8 ± 11.0
Female	174 (73.1%)
Family history of aneurysms	24 (10.1%)
Family history of hemorrhagic stroke/SAH	25 (10.5%)
Multiple aneurysms (≥ 2)	89 (41.4%)
Cigarette smoking	
Previous	77 (32.4%)
Current	68 (28.6%)
Alcohol consumption	122 (51.3%)
Comorbities	
Hypertension	127 (52.3%)
Hyperlipidemia	56 (23.0%)
Diabetes	23 (9.5%)
Atrial fibrillation	8 (3.3%)
Ischemic heart disease	16 (7.5%)
History of aneurysm rupture	63 (29.4%)
Characteristic	**Value (n=278)**
Aneurysm location	
Cavernous ICA	11 (4.0%)
Persistent trigeminal artery	1 (0.4%)
Paraophthalmic ICA	42 (15.1%)
Supraclinoid ICA	78 (28.1%)
Communicating ICA	47 (16.9%)
ICA T- Junction	4 (1.4%)
M1, M2, M3 MCA	12 (4.3%)
MCA bifurcation	28 (10.1%)
Anterior communicating artery	25 (9.0%)
Pericallosal ACA	7 (2.5%)
V4 vertebral artery/PICA	9 (3.2%)
Basilar artery/SCA	11 (4.0%)

238 Patients, 278 Aneurysms



1.23
Average devices per patient

97.3%
Technical success

1.05
Average devices per aneurysm

0.7%
Mortality rate of unruptured ICA aneurysms

2.0%
Morbidity rate of unruptured ICA aneurysms

The SCOPE-AUS multicenter study evaluating the use of the Pipeline Shield Embolization device in a real-world setting in Australia demonstrates excellent prolonged aneurysm occlusion rates (92.5%), low retreatment rates (0.7%), and robust safety outcomes.

SCOPE-AUS is the **largest** multicenter clinical study reported to date describing the safety, clinical outcomes, and effectiveness of the PED-Shield flow diverters.

TABLE 11.2

Primary and secondary outcomes

Effectiveness, safety and functional long-term outcomes 6	-month follow-up 1	-year follow-up	18-month or last follow-up
Primary Outcome (Safety): Neurologic death or adverse neurologic event occurring within 1 year of aneurysm treatment. Neurologic adverse events included neurologic death, ischemic stroke, intracranial hemorrhage, transient ischemic attack, visual deficits, cranial neuropathy, and seizure.			
Neurological adverse events		14.7% (35/238)	
Resolved neurological adverse events		65.7% (23/35)	
Neurologic morbidities 3		.8% (9/238)	
Neurologic mortalities		1.3% (3/238)	
Secondary Outcome (Effectiveness): Complete aneurysm occlusion on angiographic follow-up as defined by the O'Kelly Marotta grading scale, up to 18 months from treatment.			
Complete occlusion (OKM-D)	78.5% (193/246)	92.4% (207/224)	92.5% (233/252)
ICA aneurysm complete occlusion	75.5% (117/155)	90.8% (129/142)	92.5% (147/159)
Residual neck (OKM-C)			3.2% (8/252)
Residual aneurysm (OKM-B)			4.4% (11/252)
Target aneurysm retreatment			0.7% (2/252)
In-stent stenosis/intimal hyperplasia >50%			1.2% (3/252)

12. Monteiro et al.

The first decade of flow diversion for intracranial aneurysms with the Pipeline Embolization Device

Andre Monteiro, Jaims Lim, Manhal Siddiqi, Brianna M. Donnelly, Wasiq Khawar, Ammad Baig, RyanC. Turner, Mehdi Bouslama, Kunal P. Raygor, Pui Man Rosalind Lai, Steven B. Housley, Jason M. Davies, Kenneth V. Snyder, Adnan H. Siddiqui, and Elad I. Levy.

MAY 2023, NEUROSURG FOCUS, 54(5):E2
DOI: 10.3171/2023.2.FOCUS22646

Background:

Flow diverter devices have revolutionized the treatment of intracranial aneurysms (IAs) since their approval in 2011 and have continued to evolve. The devices have been widely adopted across institutions and centers over the past decade; however, long-term follow-up after treatment with the Pipeline™ embolization device (PED) is not well described in the literature. The authors' institution was among the first to begin using PEDs, allowing them to report their series of patients treated with flow diverters ≥ 10 years ago. In this study, the authors aimed to evaluate the long-term angiographic and clinical outcomes of these patients and review lessons learned along the way.

Methods:

The authors performed a retrospective review of their institution's IA database from January 2007 to July 2012. All patients with IAs treated with a PED prior to July 2012 were included. Clinical and angiographic characteristics were extracted. Available angiographic follow-up at 1, 3, 5, and 10 years was reported.

Results:

A total of 83 patients with 92 aneurysms treated with a PED ≥ 10 years ago were identified and included in the study. The mean aneurysm dome diameter was 9.2 (SD 5.7) mm, the mean aneurysm height was 10.4 (SD 6.8) mm, and the mean neck width was 4.1 (SD 2.4) mm. Only 1 (1.1%) aneurysm was ruptured at presentation. Eight (8.7%) aneurysms were recurrences of previous treatment modalities. The morphology was saccular in 77 (83.7%) aneurysms, fusiform in 14 (15.2%), and blister-like in 1 (1.1%). Among saccular aneurysms, 60 (77.9%) were widenecked. Seventy-five (81.5%) aneurysms were in the internal carotid artery, 12 (13.0%) were vertebrobasilar, 3 (3.3%) were in the middle cerebral artery, and 2 (2.2%) were in the posterior cerebral artery. Angiographic followup at 1, 3, 5, and 10 years was available for 75, 59, 50, and 15 patients, respectively. The complete occlusion rates at 1, 3, 5, and 10 years were 94.7%, 96.6%, 96.0%, and 100%, respectively. The re-treatment rates at 1, 3, 5, and 10 years were 8.0%, 6.8%, 8.0%, and 6.7%, respectively.

Conclusion:

The authors provide their single-institution series of IA patients treated with a PED ≥ 10 years ago, with the first report of 10-year follow-up clinical and angiographic outcomes for the available patients. Flow diversion is an effective treatment for wide-necked aneurysms with reliable long-term aneurysm occlusion and clinical outcomes.

*Please note this study represents some clinical cases that are off-label for the US market.

TABLE 12.1

Patient and aneurysm characteristics

Characteristic	Value (n=83)
Mean age (years)	58.9 ± 13.0
Female	66 (79.5%)
Comorbities	
Hypertension	33 (39.8%)
Hyperlipidemia	29 (34.9%)
Diabetes	15 (18.1%)
Other (noncardiovascular)	10 (12.0%)
Smoker status	
Active	16 (19.3%)
Former	30 (36.1%)
Never	37 (44.6%)
Ruptured status	1 (1.1%)
Recurrence of another treatment modality	
Coiling	4 (4.3%)
Stent-assisted coiling	2 (2.2%)
Clipping	2 (2.2%)
Aneurysm location	
ICA	75 (81.5%)
Vertebrobasilar	12 (13.0%)
MCA	3 (3.3%)
PCA	2 (2.2%)
No. of PEDs deployed	
1	60 (65.2%)
2	20 (21.7%)
≥ 3	12 (13.0%)
Adjunctive coiling	17 (18.5%)

83 Patients, **92** Aneurysms

10.4mm Mean aneurysm height

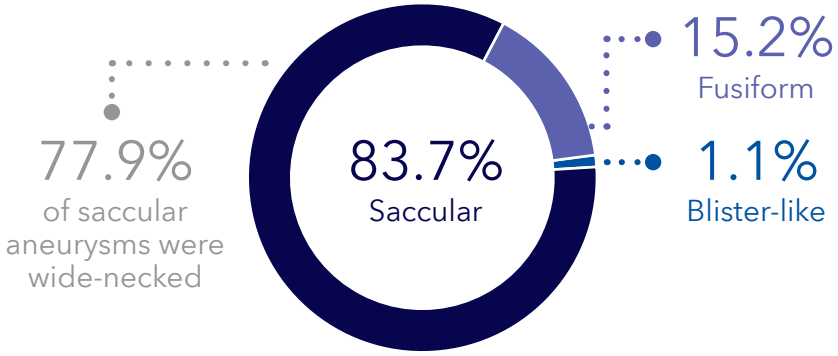
9.2mm Mean dome diameter

4.1mm Mean neck diameter

3.6% Nonfatal treatment-related complications

6.5% Retreatment

4.8% Mortality



"Within the subset of the 15 aneurysms that had ≥ 10 years of angiographic follow-up, all (100%) were completely occluded, with only 1 having required retreatment with a second PED. The data reported in our study represent the longest available follow-up for aneurysms treated with flow diverters." (May 2023)

Study strengths:

- First study to report 10-year follow-up for the available patients
- The longest angiographic and clinical follow-up data on flow diverters

Study limitations:

- Relatively small sample size of the population of interest, since the study reported data on patients treated ≥10 years ago at the beginning of the flow diversion era
- Retrospective study design
- Loss of patient data inherent to long-term follow-up in retrospective studies

Pipeline™ Flex Embolization Device essential prescribing information (EPI) statement

CAUTION: Federal (USA) law restricts this device to sale, distribution and use by or on the order of a physician. Indications, contraindications, warnings and instructions for use can be found in the product labeling supplied with each device. **Indications for Use:** The Pipeline™ Flex embolization device is indicated for the endovascular treatment of adults (22 years of age or older) with large or giant wide-necked intracranial aneurysms (IAs) in the internal carotid artery from the petrous to the superior hypophyseal segments. The Pipeline™ Flex embolization device is also indicated for use in the internal carotid artery up to the terminus for the endovascular treatment of adults (22 years of age or older) with small and medium wide-necked (neck width ≥ 4 mm or dome-to-neck ratio < 2) saccular or fusiform intracranial aneurysm (IAs) arising from a parent vessel with a diameter ≥ 2.0 mm and ≤ 5.0 mm. **Contraindications:** 1) Patients with active bacterial infection. 2) Patients in whom dual antiplatelet and/or anticoagulation therapy (aspirin and clopidogrel) is contraindicated. 3) Patients who have not received dual antiplatelet agents prior to the procedure. 4) Patients in whom a pre-existing stent is in place in the parent artery at the target aneurysm location. 5) Patients in whom the parent vessel size does not fall within the indicated range. **Warnings:** 1) Resheathing of the Pipeline™ Flex embolization device more than 2 full cycles may cause damage to the distal or proximal ends of the braid. 2) Persons with known allergy to platinum or cobalt/chromium alloy (including the major elements platinum, cobalt, chromium, nickel, molybdenum or tungsten) may suffer an allergic reaction to the Pipeline™ Flex embolization device implant. 3) Person with known allergy to tin, silver, stainless steel or silicone elastomer may suffer an allergic reaction to the Pipeline™ Flex embolization device delivery system. 4) Do not reprocess or resterilize. Reprocessing and resterilization increase the risk of patient infection and compromised device performance. 5) Post-procedural movement (migration and/or foreshortening) of the Pipeline™ Flex Embolization Device implant may occur following implantation and can result in serious adverse events and/or death. 6) Factors which may contribute to post procedural device movement include (but are not limited to) the following: Failure to adequately size the implant (I.e., under sizing), Failure to obtain adequate wall apposition during the implant deployment, Implant stretching, Vasospasm, Severe vessel tapering, Tortuous anatomy 7) Delayed rupture may occur with large and giant aneurysms. 8) Placement of multiple Pipeline™ Flex embolization devices may increase the risk of ischemic complications. 9) Use in anatomy with severe tortuosity, stenosis or parent vessel narrowing may result in difficulty or inability to deploy the Pipeline™ Flex Embolization Device and can lead to damage to the Pipeline™ Flex Embolization Device and microcatheter. Advancement or retraction of the Pipeline™ Flex embolization device against resistance may result in damage, including unintended device or component separation, fracture, or breakage of the delivery system due to inherent flexibility limits of device design. Device damage may result in patient injury or death. Refer to page 4 in the instructions for use for additional information. 10) Do not attempt to reposition the device after full deployment. 11) The benefits may not outweigh the risks of treatment of small and medium asymptomatic extradural intracranial aneurysms, including those located in the cavernous internal carotid artery. The risk of rupture for small and medium asymptomatic extradural intracranial aneurysms is very low if not negligible. 12) A decrease in the proportion of patients who achieve complete aneurysm occlusion without significant parent artery stenosis has been observed with the use of the device in the communicating segment (C7) of the internal carotid artery (47.4% (9/19 subjects in the PREMIER study at 1 year)), including those IAs fed by the posterior circulation or have retrograde filling. Ensure appropriate patient selection and weigh the benefits and risks of alternative treatments prior to use of this device for the treatment of intracranial aneurysms located in this region of the ICA. The following anatomical characteristics, associated with retrograde filling, should be carefully considered during procedural planning of C7 intracranial aneurysms: Observed PComm of fetal origin (A PCA of fetal origin is defined as a small, hypoplastic, or absent P1 segment of the PCA with the PComm artery supplying a majority of blood flow to the ICA); PComm overlapping with the aneurysm neck; and/or PComm branch arising from the dome of the aneurysm. 13) Pushing delivery wire without retracting the micro catheter at the same time will cause the open end braid to move distally in the vessel. This may cause damage to the braid or vessel. 14) Use in tortuous anatomy may result in difficulty or inability to deploy the Pipeline™ Flex Embolization Device and can lead to damage to the Pipeline™ Flex Embolization Device and microcatheter. To mitigate potential problems as a result of increased delivery forces, reduce the load in the system by: Unloading the microcatheter to the inner curves of vessel by pulling back on the system (i.e., the microcatheter and delivery wire together). Continue unloading the system until advancement of the device (inside the microcatheter is observed, while minimizing the distal tip movement prevent loss of position. Begin to re-advance the delivery wire while the device passes through tortuous area and the delivery force is decreased. 15) Resheathing the Pipeline™ Flex embolization device more than 2 full cycles may cause damage to the distal or proximal ends of the braid. **Precautions:** 1) The Pipeline™ Flex embolization device should be used only by physicians trained in percutaneous, intravascular techniques and procedures at medical facilities with the appropriate fluoroscopy equipment. 2) Physicians should undergo appropriate training prior to using the Pipeline™ Flex embolization device in patients. 3) The Pipeline™ Flex embolization device is provided sterile for single use only. Store in a cool, dry place. Carefully inspect the sterile package and device components prior to use to verify that they have not been damaged during shipping. Do not use kinked or damaged components. Do not use product if the sterile package is damaged. 4) Use the Pipeline™ Flex embolization device system prior to the "Use By" date printed on the package. 5) The appropriate anti-platelet and anti- coagulation therapy should be administered in accordance with standard medical practice. 6) A thrombosing aneurysm may aggravate pre-existing, or cause new, symptoms of mass effect and may require medical therapy. 7) Use of implants with labeled diameter larger than the parent vessel diameter may result in decreased effectiveness and additional safety risk due to incomplete foreshortening resulting in an implant longer than anticipated. 8) The Pipeline™ Flex embolization device may create local field inhomogeneity and susceptibility artifacts during magnetic resonance angiography (MRA), which may degrade the diagnostic quality to assess effective intracranial aneurysm treatment. 9) Take all necessary precautions to limit X-radiation doses to patients and themselves by using sufficient shielding, reducing fluoroscopy times, and modifying X-ray technical factors where possible. 10) Carefully weigh the benefits of treatment vs. the risks associated with treatment using the device for each individual patient based on their medical health status and risks factors for intracranial aneurysm rupture during their expected life time such as age, medical comorbidities, history of smoking, intracranial aneurysm size, location, and morphology, family history, history of prior asymptomatic subarachnoid hemorrhage (aSAH), documented growth of intracranial aneurysm on serial imaging, presence of multiple intracranial aneurysms, and presence of concurrent pathology. The benefits of device use may not outweigh the risks associated with the device in certain patients; therefore, judicious patient selection is recommended. 11) The safety and effectiveness of the device has not been established for treatment of fusiform IAs. 12) There may be a decrease in effectiveness and increase in safety events when the device is used in patients ≥ 60 years old. 13) The safety and effectiveness of the device has not been evaluated or demonstrated for ruptured aneurysms. **Potential Complications:** Potential complications of the device and the endovascular procedure, include, but are not limited to the following: Adverse reaction to antiplatelet/ anticoagulation agents, anesthesia, reactions due to radiation exposure (such as alopecia, burns ranging in severity from skin reddening to ulcers, cataracts, and delayed neoplasia) or contrast media, including organ failure; Vascular Complications like vasospasm, stenosis, dissection, perforation, rupture, fistula formation, pseudo aneurysm, occlusion , thromboembolic complications including ischemia (to unintended territory); Device complications like fracture, breakage (including unintended device or component separation), misplacement, migration / delayed foreshortening or reaction to device materials may occur; Systemic Complications like: Infection, Pain, fever, allergic reactions, organ failure, nerve damage; Bleeding/ hemorrhagic complication including retroperitoneal hemorrhage; Neurological Deficits or dysfunctions including Stroke, Infarction, Loss of vision, Seizures, TIA, Headache, Cranial Nerve Palsies, Confusion, Coma; Decreased therapeutic response including need for target aneurysm retreatment; Risks associated with visual symptoms include Amaurosisfugax/transient blindness, Blindness, Diplopia, Reduced visual acuity/field, Retinal artery occlusion, Retinal ischemia, Retinal infarction, Vision impairment including scintillations, blurred vision, eye floaters; Intra-Cranial Hemorrhage (including from Aneurysm Rupture) Brain Edema, Hydrocephalus, Mass Effect; Death. **Complete indications, Contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.**

Pipeline™ Flex with Embolization Device with Shield Technology™ essential prescribing information (EPI) statement

CAUTION: Federal (USA) law restricts this device to sale, distribution and use by or on the order of a physician. Indications, contraindications, warnings and instructions for use for the Pipeline™ Flex Embolization Device with Shield Technology™ can be viewed at https://www.medtronic.com/manuals. **Indications for Use:** The Pipeline™ Flex Embolization Device with Shield Technology™ is indicated for the endovascular treatment of adults (22 years of age or older) with large or giant wide-necked intracranial aneurysms (IAs) in the internal carotid artery from the petrous to the superior hypophyseal segments. The Pipeline™ Flex Embolization Device with Shield Technology™ is also indicated for use in the internal carotid artery up to the terminus for the endovascular treatment of adults (22 years of age or older) with small and medium wide-necked (neck width ≥ 4 mm or dome-to-neck ratio < 2) saccular or fusiform intracranial aneurysm (IAs) arising from a parent vessel with a diameter ≥ 2.0 mm and ≤ 5.0 mm. **Contraindications:** 1) Patients with active bacterial infection. 2) Patients in whom dual antiplatelet and/or anticoagulation therapy (aspirin and clopidogrel) is contraindicated. 3) Patients who have not received dual antiplatelet agents prior to the procedure. 4) Patients in whom a pre-existing stent is in place in the parent artery at the target aneurysm location. 5) Patients in whom the parent vessel size does not fall within the indicated range. **Warnings:** 1) Pushing delivery wire without retracting the micro catheter at the same time will cause the open end braid to move distally in the vessel. This may cause damage to the braid or vessel. 2) Use in tortuous anatomy may result in difficulty or inability to deploy the Pipeline™ Flex Embolization Device with Shield Technology™ and can lead to damage to the Pipeline™ Flex Embolization Device with Shield Technology™ and microcatheter. To mitigate potential problems as a result of increased delivery forces, reduce the load in the system by: Unloading the microcatheter to the inner curves of vessel by pulling back on the system (i.e., the microcatheter and delivery wire together). Continue unloading the system until advancement of the device (inside the microcatheter) is observed, while minimizing the distal tip movement to prevent loss of position. Begin to re-advance the delivery wire while maintaining reduced load in the microcatheter. This process should be repeated until the device passes through tortuous area and the delivery force is decreased. 3) Resheathing of the Pipeline™ Flex Embolization Device with Shield Technology™ more than 2 full cycles may cause damage to the distal or proximal ends of the braid. 4) Persons with known allergy to platinum or cobalt/chromium alloy (including the major elements platinum, cobalt, chromium, nickel, molybdenum or tungsten) may suffer an allergic reaction to the Pipeline™ Flex Embolization Device with Shield Technology™ implant. 5) Person with known allergy to tin, silver, stainless steel, or silicone elastomer may suffer an allergic reaction to the Pipeline™ Flex Embolization Device with Shield Technology™ delivery system. 6) Do not reprocess or resterilize. Reprocessing and resterilization increase the risk of patient infection and compromised device performance. 7) Post-procedural movement (migration and/or foreshortening) of the Pipeline™ Flex Embolization Device with Shield Technology™ implant may occur following implantation and can result in serious adverse events and/or death. 8) Factors which may contribute to post procedural device movement include (but are not limited to) the following: Failure to adequately size the implant (i.e., under sizing), Failure to obtain adequate wall apposition during the implant deployment, Implant stretching, Vasospasm, Severe vessel tapering, Tortuous anatomy 9) Delayed rupture may occur with large and giant aneurysms. 10) Placement of multiple Pipeline™ Flex Embolization Device with Shield Technology™ may increase the risk of ischemic complications. 11) Use in anatomy with severe tortuosity, stenosis or parent vessel narrowing may result in difficulty or inability to deploy the Pipeline™ Flex Embolization Device with Shield Technology™ and can lead to damage to the Pipeline™ Flex Embolization Device with Shield Technology™ and microcatheter. Advancement or retraction of the Pipeline™ Flex Embolization Device with Shield Technology™ against resistance may result in damage, including unintended device or component separation, fracture, or breakage of the delivery system due to inherent flexibility limits of device design. Device damage may result in patient injury or death. Refer to page 4 in the instructions for use for additional information. 12) Do not attempt to reposition the device after full deployment. 13) The benefits may not outweigh the risks of treatment of small and medium asymptomatic extradural intracranial aneurysms, including those located in the cavernous internal carotid artery. The risk of rupture for small and medium asymptomatic extradural intracranial aneurysms is very low if not negligible. 14) A decrease in the proportion of patients who achieve complete aneurysm occlusion without significant parent artery stenosis has been observed with the use of the device in the communicating segment (C7) of the internal carotid artery (47.4% (9/19 subjects in the PREMIER study at 1 year)), including those IAs fed by the posterior circulation or have retrograde filling. Ensure appropriate patient selection and weigh the benefits and risks of alternative treatments prior to use of this device for the treatment of intracranial aneurysms located in this region of the ICA. The following anatomical characteristics, associated with retrograde filling, should be carefully considered during procedural planning of C7 intracranial aneurysms: PComm of fetal origin (A PCA of fetal origin is defined as a small, hypoplastic, or absent P1 segment of the PCA with the PComm artery supplying a majority of blood flow to the ICA); PComm overlapping with the aneurysm neck; and/or PComm branch arising from the dome of the aneurysm. 15) The safety and effectiveness of this device for radial neurovasculature access in direct comparison to a transfemoral approach has not been demonstrated. The risks and benefits for radial access against a transfemoral approach should be carefully weighed and considered for each patient. **Precautions:** 1) The Pipeline™ Flex Embolization Device with Shield Technology™ should be used only by physicians trained in percutaneous, intravascular techniques, and procedures at medical facilities with the appropriate fluoroscopy equipment. 2) Physicians should undergo appropriate training prior to using the Pipeline™ Flex Embolization Device with Shield Technology™ in patients. 3) The Pipeline™Flex Embolization Device with Shield Technology™ is intended for single use only. Store in a cool, dry place. Carefully inspect the sterile package and device components prior to use to verify that they have not been damaged during shipping. Do not use kinked or damaged components. Do not use product if the sterile package is damaged. 4) Use the Pipeline™ Flex Embolization Device with Shield Technology™ system prior to the "Use By" date printed on the package. 5) The appropriate anti-platelet and anti-coagulation therapy should be administered in accordance with standard medical practice. 6) A thrombosing aneurysm may aggravate pre-existing, or cause new, symptoms of mass effect and may require medical therapy. 7) Use of implants with labeled diameter larger than the parent vessel diameter may result in decreased effectiveness and additional safety risk due to incomplete foreshortening resulting in an implant longer than anticipated. 8) The Pipeline™ Flex Embolization Device with Shield Technology™ may create local field inhomogeneity and susceptibility artifacts during magnetic resonance angiography (MRA), which may degrade the diagnostic quality to assess effective intracranial aneurysm treatment. 9) Take all necessary precautions to limit X-radiation doses to patients and themselves by using sufficient shielding, reducing fluoroscopy times, and modifying X-ray technical factors where possible. 10) Carefully weigh the benefits of treatment vs. the risks associated with treatment using the device for each individual patient based on their medical health status and risks factors for intracranial aneurysm rupture during their expected life time such as age, medical comorbidities, history of smoking, intracranial aneurysm size, location, and morphology, family history, history of prior asymptomatic subarachnoid hemorrhage (aSAH), documented growth of intracranial aneurysm on serial imaging, presence of multiple intracranial aneurysms, and presence of concurrent pathology. The benefits of device use may not outweigh the risks associated with the device in certain patients; therefore, judicious patient selection is recommended. 11) The safety and effectiveness of the device has not been established for treatment of fusiform IAs. 12) There may be a decrease in effectiveness and increase in safety events when the device is used in patients ≥ 60 years old. 13) The safety and effective-ness of the device has not been evaluated or demonstrated for ruptured aneurysms. 14) If using radial artery access, perform a screening examination of the radial artery per institutional practices to ensure that radial access is appropriate for the patient. **Potential Complications:** Potential complications of the device and the endovascular procedure include, but are not limited to, the following: Access site complications like hematoma, inflammation, infection, necrosis, pain and tenderness, granuloma; Adverse reaction to anti-platelet/anticoagulation agents,anesthesia, reactions due to radiation exposure (such as alopecia, burns ranging in severity from skin reddening to ulcers, cataracts and delayed neoplasia) or contrast media, including organ failure; Vascular Complications like vasospasm, stenosis, dissection, perforation, rupture, fistula formation, pseudo aneurysm, occlusion, thromboembolic complications including ischemia (to unintended territory); Device complications like fracture, breakage (including unintended device or component separation), misplacement, migration/delayed foreshortening or reaction to device materials may occur; Systemic Complications like: Infection, Pain, fever, allergic reactions, organ failure, nerve damage; Bleeding/hemorrhagic complication including retroperitoneal hemorrhage; Neurological Deficits or dysfunctions including Stroke, Infarction, Loss of vision, Seizures, TIA, Headache, Cranial Nerve Palsies, Confusion, Coma, Hand Dysfunction; Decreased therapeutic response including need for target aneurysm retreatment; Risks associated with visual symptoms include Amaurosis Fugax/transient blindness, Blindness, Diplopia, Reduced visual acuity/field, Retinal artery occlusion, Retinal ischemia, Retinal infarction, Vision impairment including scintillations, blurred vision, eye floaters; Intracranial Hemorrhage (including from Aneurysm Rupture) Brain Edema, Hydrocephalus, Mass Effect; Death. **Complete indications, Contraindications, warnings and instructions for use can be found in the product labeling supplied with each device.**

References:

1. Nelson, P. K., Lylyk, P., Szikora, I., Wetzel, S. G., Wanke, I., & Fiorella, D. (2011). The pipeline embolization device for the intracranial treatment of aneurysms trial. AJNR. American journal of neuroradiology, 32(1), 34–40. https://doi.org/10.3174/ajnr.A2421. The PITA trial was sponsored, funded, and conducted by Chestnut Medical Technologies.

2. Kallmes, D. F., Hanel, R., Lopes, D., Boccardi, E., Bonafé, A., Cekirge, S., Fiorella, D., Jabbour, P., Levy, E., McDougall, C., Siddiqui, A., Szikora, I., Woo, H.,Albuquerque, F., Bozorgchami, H., Dashti, S. R., Delgado Almandoz, J. E., Kelly, M. E., Turner, R., 4th, Woodward, B. K., … Lylyk, P. (2015). International retrospective study of the pipeline embolization device: a multicenter aneurysm treatment study. AJNR. American journal of neuroradiology, 36(1), 108–115. https://doi.org/10.3174/ajnr.A4111. This study was funded by ev3/ Covidien.

3. Kallmes, D. F., Brinjikji, W., Boccardi, E., Ciceri, E., Diaz, O., Tawk, R., Woo, H., Jabbour, P., Albuquerque, F., Chapot, R., Bonafe, A., Dashti, S. R., Delgado Almandoz, J. E., Given, C., 2nd, Kelly, M. E., Cross, D. T., 3rd, Duckwiler, G., Razack, N., Powers, C. J., Fischer, S., … Levy, E. (2016). Aneurysm Study of Pipeline in an Observational Registry (ASPIRe). Interventional neurology, 5(1-2), 89–99. https://doi.org/10.1159/000446503. This observational registry was funded and supported by Covidien, with scientific oversight of the study steering committee members. This study was funded by Medtronic, and D.F.K. receives research funding from Medtronic.

4. Becske, T., Brinjikji, W., Potts, M. B., Kallmes, D. F., Shapiro, M., Moran, C. J., Levy, E. I., McDougall, C. G., Szikora, I., Lanzino, G., Woo, H. H., Lopes, D. K., Siddiqui, A. H., Albuquerque, F. C., Fiorella, D. J., Saatci, I., Cekirge, S. H., Berez, A. L., Cher, D. J., Berentei, Z., … Nelson, P. K. (2017). Long-Term Clinical and Angiographic Outcomes Following Pipeline Embolization Device Treatment of Complex Internal Carotid Artery Aneurysms: Five-Year Results of the Pipeline for Uncoilable or Failed Aneurysms Trial. Neurosurgery, 80(1), 40–48. https://doi.org/10.1093/neuros/nyw014. This study was funded by Chestnut Medical and ev3/Covidien (Irvine, California). The PUFS trial was supported and funded by Chestnut Medical and eV3/Covidien.

5. Martínez-Galdámez, M., Lamin, S. M., Lagios, K. G., Liebig, T., Ciceri, E. F., Chapot, R., Stockx, L., Chavda, S., Kabbasch, C., Faragò, G., Nordmeyer, H., Boulanger, T., Piano, M., & Boccardi, E. P. (2019). Treatment of intracranial aneurysms using the pipeline flex embolization device with shield technology: angiographic and safety outcomes at 1-year follow-up. Journal of neurointerventional surgery, 11(4), 396–399. https://doi.org/10.1136/ neurintsurg-2018-014204. This study was funded by Medtronic.

6. Atasoy, D., Kandasamy, N., Hart, J., Lynch, J., Yang, S. H., Walsh, D., Tolias, C., & Booth, T. C. (2019). Outcome Study of the Pipeline Embolization Device with Shield Technology in Unruptured Aneurysms (PEDSU). AJNR. American journal of neuroradiology, 40(12), 2094–2101. https://doi.org/10.3174/ajnr.A6314

7. Hanel RA, Cortez GM, Lopes DK, et al. Prospective study on embolization of intracranial aneurysms with the pipeline device (PREMIER study): 3-year results with the application of a flow diverter specific occlusion classificationJournal of NeuroInterventional Surgery 2023;15:248-254.

8. Rice, H., Martínez Galdámez, M., Holtmannspötter, M., Spelle, L., Lagios, K., Ruggiero, M., Vega, P., Sonwalkar, H., Chapot, R., & Lamin, S. (2020). Periprocedural to 1-year safety and efficacy outcomes with the Pipeline Embolization Device with Shield technology for intracranial aneurysms: a prospective, post-market, multi-center study. Journal of NeuroInterventional Surgery, 12:1107-1112. https://doi.org/10.1136/neurintsurg-2020-015943. This study was sponsored by Medtronic, Inc.

9. Trivelato, F. P., Wajnberg, E., Rezende, M. T. S., Ulhôa, A. C., Piske, R. L., Abud, T. G., de Castro-Afonso, L. H., Abath, C. G. C., Nakiri, G. S., Araújo, J. F. S., Silva, J. L. J., Tosello, R. T., Vanzin, J. R., Manzato, L. B., Baccin, C. E., da Mota, B. A. A., & Abud, D. G. (2020). Safety and Effectiveness of the Pipeline Flex Embolization Device With Shield Technology for the Treatment of Intracranial Aneurysms: Mid-term Results From a Multicenter Study. Neurosurgery, 87(1), 104–111. https://doi.org/10.1093/neuros/nyz356

10. Lylyk, I., Scrivano, E., Lundquist, J., Ferrario, A., Bleise, C., Perez, N., Lylyk, P. N., Viso, R., Nella-Castro, R., & Lylyk, P. (2021). Pipeline Embolization Devices for the Treatment of Intracranial Aneurysms, Single-Center Registry: Long-Term Angiographic and Clinical Outcomes from 1000 Aneurysms. Neurosurgery, 89(3), 443–449. https://doi.org/10.1093/neuros/nyab183. This project was supported by Medtronic through an unrestricted research grant.

11. Chia, G. S., de Villiers, L., Carraro do Nascimento, V., Rapier, C. L., Owusu, M. A., Lau, F. S., McQuinn, A., Williams, Cameron., Whitley, J., Cheung, A., Manning, N. W., & Rice, H. (2022). Safety and Clinical Effectiveness of Pipeline Shield Device for Intracranial Aneurysms in an Australian Cohort (SCOPE-AUS). Stroke: Vascular and Interventional Neurology, 2(5), e000292. https://doi.org/10.1161/SVIN.121.000292. This study was supported by Medtronic, Inc.

12. Monteiro, A., Lim, J., Siddiqi, M., Donnelly, B. M., Khawar, W., Baig, A., Turner, R. C., Bouslama, M., Raygor, K. P., Lai, P. M. R., Housley, S. B., Davies, J. M., Snyder, K. V., Siddiqui, A. H., & Levy, E. I. (2023). The first decade of flow diversion for intracranial aneurysms with the Pipeline embolization device.Neurosurgical focus, 54(5), E2. https://doi.org/10.3171/2023.2.FOCUS22646

NOTES:

CONNECTIONS FOR LIFE

Bringing people and technology together for life-changing Neurovascular care

Medtronic
Neurovascular

9775 Toledo Way
Irvine, CA 92618
USA
Tel 800-716-6700
Fax 763-526-7888

medtronic.com