The Evolving Endovascular Therapy Toolkit: Real-World and Clinical Experiences with Pipeline Flex and Vantage with Shield Technology and Solitaire X 3 mm

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Summary

Drs Szikora and Rautio presented their experiences with new flow diverters at a Symposium Sponsored by Medtronic that took place on Thursday, 9th September 2021 and was part of the 13th Congress of the European Society of Minimally Invasive Neurological Therapy (ESMINT), in Nice, France. Dr Szikora presented the analysis of the first 400-patient cohort treated with the Pipeline Flex with Shield technology from the INSPIRE registry. Dr Rautio shared her clinical experience with Pipeline Vantage with Shield technology through case studies. Dr Siddiqui presented his preliminary clinical experience with the next generation of Solitaire X, the smallest diameter revascularisation device made with the ability to deploy in smaller blood vessels.

KEYWORDS: FLOW DIVERTER, PIPELINE FLEX, PIPELINE VANTAGE, REVASCULARISATION DEVICE, SOLITAIRE X

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Introduction

Endovascular techniques for the minimally invasive treatment of aneurysms and strokes have evolved rapidly. Flow-modifying mesh-based tubular implants or flow diversion devices facilitate the safe treatment of aneurysms with challenging morphology and locations.[1] These devices are effective and have complication rates similar to other traditional techniques either alone or together with coil embolisation.[2] Pipeline devices came to market in Europe in 2008, followed by Pipeline Flex. The redesigned Pipeline Flex with Shield technology became available in 2015 hoping to reduce ischaemic complications.[3] The latest addition to this family of devices is Pipeline Vantage with higher pore density and thinner structure.[4] In the context of ischaemic stroke, prompt recanalisation with tissue plasminogen activator and mechanical thrombectomy have transformed management of acute ischaemic stroke. The initial studies proved effectiveness up to 6 hours and subsequently to 16 hours with improved outcomes and decreased mortality.[5] The 1st generation Solitaire FR revascularisation device was launched in Europe in 2012. During the last decade these devices have been improved with development of the latest generation in the form of Solitaire X. The most recent version of this device is Solitaire X 3 mm which broadens treatment to vessels as narrow as 1.5 mm. The effectiveness of this procedure now beckons beyond the large vessels to medium and distal vessels. Investigator initiated studies are already formally investigating these questions.

INSPIRE Registry – results from a 400-cohort treated with Pipeline Flex with Shield technology

*Istvan Szikora**

INSPIRE is a post-market, prospective, observational, single-arm, multi-centre patient registry to evaluate the effectiveness and safety of Medtronic neurovascular products, including Pipeline Flex with Shield technology, for treating intracranial aneurysms and acute ischaemic strokes in real-life.[6] The primary outcomes of this study are complete occlusion of the target aneurysm without retreatment or significant artery stenosis (≤50%) at 1 year and functional independence (modified Rankin scores (mRS) ≤2) at 90 days. The primary safety endpoint is major stroke in treated vascular territory or neurological death.[6]

Pipeline Flex with Shield technology is a second-generation flow diverter for treating aneurysms that is easier to deploy, and can be re-sheathed to optimise its placement and expansion. The device is made out of a braid of cobalt chromium alloy and platinum wires with a synthetic phosphorylcholine (PC) polymer coating.[7,8] This surface has biomimetic and non-thrombogenic qualities that improve the haemocompatibility of the device.[7] Pre-clinical data show that this coating reduces thrombin generation, platelet activation,[7] and neointimal hyperplasia.[9]

Dr Szikora presented the analysis of the first 400-patient cohort treated with Pipeline Flex with Shield technology in INSPIRE with core lab adjudicated procedure data (n=371), complete clinical follow up (safety cohort, n=376), and core lab adjudicated imaging follow up through 1 year (efficacy cohort, n=328). The patients in this cohort had a mean age of 53.5 years (±12.7) and 77.3% were female. Risk factors included hypertension (51.5%), cigarette smoking (36.8%), and hyperlipidaemia (15.2%).

Most aneurysms were proximal (84.7%) including the vertebral, basilar, and internal carotid artery. Others (15.5%) were located more distally such as the anterior

* On behalf of the INSPIRE Steering Committee: Istvan Szikora, Jens Fiehler, Mario Martínez-Galdámez, Markus Holtmannspötter, Saleh Lamin, Laurent Spelle, Francis Turjman.

communicating, middle cerebral, and posterior cerebral arteries. Most were saccular (88.4%), a few were fusiform (10.2%), and very few were classified as pseudo aneurysms (1.4%). Almost half of them were small (<7 mm, 46.1%), over a quarter were medium (7–13 mm, 26.7%), one in five were large (13–25 mm, 18.3%); and few were giant (≥25 mm, 5.9%). Most aneurysms had never ruptured (78.2%), some had preclinically ruptured (19.1%), and very few had acutely ruptured (2.7%).

The operators implanted 428 devices in 376 patients with a 97.7% success rate. Among these, 20 target aneurysms were treated with two Pipeline Flex with Shield technology devices, and three were treated with three devices. In addition to the flow diverter, adjunctive coiling was used in 11.3% of patients. Overall, the total procedure time was 61 minutes (±41), total microcatheter time was 15 minutes (±18), and cumulative fluoroscopy time was 27 minutes (±19).

Core lab adjudicated complete aneurysm occlusion was achieved in 79% of patients, and complete occlusion without significant parent artery stenosis and without retreatment was achieved in 77% of patients. The rate of complete occlusion was comparable across all aneurysm sizes, although higher in proximal (81%) vs distal (70%) locations, and higher in saccular (79%) vs fusiform (69%) aneurysms.

Retreatment due to incomplete occlusion was performed in three patients (0.9%). Significant stenosis (>50%) was detected in four patients (1.2%) and in 15 patients the grade of stenosis could not be properly determined. Regarding functional independence, 75.5% of patients had mRS 0 at baseline, increasing to 82.6% at 1 year, and at the latest follow up 97.3% of patients had mRS 0–2. Of the 3.7% (14/376) of patients with stroke, 1.3% had a disabling stroke.

Device and/or procedure-related serious adverse events occurred in 8% of patients, of which 5.3% were device-related and 5.6% were procedure-related. Neurological events of interest within 1 year per the clinical event committee were major stroke in treated vascular territory or neurological death (2.7%), neurological death (1.1%), and major stroke in treated vascular territories (2.1%), including intracerebral haemorrhage (ICH, 1.9%).

These data indicate that the safety and effectiveness of Pipeline Flex with Shield technology is consistent when treating more complex aneurysms (sizes and locations) and heterogeneous patient populations over time. They are also consistent in comparison with previous results using the Pipeline device. The rate of complete occlusion varies between 72% and 77% between Pipeline Flex,[10] the earlier study with Pipeline Shield (a clinical study),[3] and this real-life INSPIRE registry. There was no significant difference (3.3 vs 2.7%) regarding stroke or neurological death in the Shield and INSPIRE studies. The efficacy of this device reducing antiplatelet treatment use could not be determined because the antiplatelet was selected by the operators and in most cases, it included double antiplatelet. The device will be compared with others in the registry once the necessary data are available.

Pipeline Flow Diversion Reimagined: early clinical experience with the fourth generation Pipeline Vantage flow diverter with Shield technology

Riitta Rautio

Dr. Rautio presented seven of the cases that she and her team have treated with Pipeline Vantage with Shield technology at Turku University Hospital.

The Pipeline Vantage embolisation device with Shield technology has either 48 or 64 cobalt chromium wires with platinum cores. The wires are of a smaller diameter than in Pipeline Flex resulting in a lower overall thickness that could favour endothelial growth. The Vantage implant has a higher pore density (64 wire implants) than Flex in the same diameter range but with comparable metal coverage. This is hypothesised to improve aneurysm occlusion rates due to reduced inflow and improved flow stagnation in the aneurysm.[4] The Shield technology is the same as described by Dr Szikora.

Rist was the radial artery access system used in many of these procedures. It consists of a 5 French catheter and a 079 interventional guide catheter of variable lengths and with transitions to optimise tracking.[11] The Rist guide catheter works well with the Rist diagnostic catheters, even in tortuous anatomy. Due to the device qualities, radial access is no longer viewed as an alternative, but is now the first choice of operators at Turku University Hospital and favoured by patients.

For all case studies presented, the Pipeline Vantage sizing to be used in the procedures was based on arterial measurements acquired from 3D rotational angiography data. In addition, virtual sizing with Sim&Size simulation was

performed. The antiplatelet therapy for elective Vantage patients was prasugrel 5 mg and aspirin 100 mg, started 5 days pre-procedure. Platelet function was evaluated by Multiplate analyser and if there was low response, prasugrel dosing was increased. During the procedure, activated clotting time (ACT) was doubled by administering a heparin bolus and ACT was controlled at 30–45-minute intervals. After the procedure, heparinisation was neither antagonised nor maintained. Prasugrel and aspirin were continued for at least 3 months, until the first digital subtraction angiography (DSA) control. At that point, a decision to continue prasugrel or only aspirin was made.

Case 1

39-year-old patient with small left paraophthalmic internal carotid artery aneurysm, previously clipped due to subarachnoid haemorrhage (SAH) from pericallosal aneurysm. The patient was treated through radial access with Terumo Slender 6F, Penumbra Benchmark 6F 95 cm, Phenom 027 microcatheter, Synchro 014 microwire, and Pipeline Vantage 4x20 mm. The device opened very nicely in the tight curve of the vessel, wall apposition was exact, and contrast stagnation in the aneurysm was observed. At the 3-month DSA control the aneurysm was occluded but there was intimal hyperplasia and distal stent tapering. The patient had no symptoms, was prescribed to continue clopidogrel and aspirin, and told to undergo another DSA control in 3 months.

Case 2

66-year-old patient with an incidental right paraophthalmic internal carotid artery aneurysm. The patient was treated through radial access with Terumo Slender 7F 10 cm, Terumo 035 180 cm, Rist SIM2 5.5F 130 cm, Rist 079 guide catheter 100 cm, Phenom 027 150 cm, Synchro 014 200 cm, and Pipeline Vantage 4 x16 mm. This was the first patient treated with the Rist guiding catheter. Exact wall apposition with Vantage was achieved. At the 3-month DSA control, remarkable contrast stagnation was observed in the aneurysm, but no shrinkage. The patient continued on aspirin only and instructed to undergo another DSA control in 3 months.

Case 3

66-year-old patient with two middle cerebral artery aneurysms. The proximal aneurysm was treated via radial access with Glidesheath Slender 7F 10 cm, Terumo 180 cm, Rist SIM2 130cm, Rist guide 079 105 cm, Phenom Plus Catheter 120 cm for distal access, Synchro 014 200 cm, Phenom 021 catheter 150 cm, and Pipeline Vantage 3.5x14 mm. The vessel was straight and there were no issues opening the device. At the 3-month DSA control, no intima hyperplasia nor shrinkage of the aneurysm were observed. The patient continued on aspirin only.

Case 4

35-year-old patient with an incidental right posterior communicating artery aneurysm. Retreatment was necessary after intrasaccular device malposition. The patient was treated via femoral access with Infinity 6F 80 cm, Navien 072, Phenom 027 + Synchro 014, and Pipeline Vantage 4.5x14 mm. Despite a deep curve in the vessel, the device opened perfectly. The patient experienced visual disturbances after the procedure. In the MRI performed on the day of the procedure, two spotlike fresh infarcts were observed. The patient was discharged on the third postoperative day without symptoms. At the 3-month DSA control, the aneurysm was smaller, and some intima hyperplasia was observed. The patient was instructed to continue with double antiplatelet treatment.

Case 5

53-year-old patient with two aneurysms. Previously, the middle cerebral artery aneurysm was successfully clipped, but the basilar tip aneurysm treated with an intrasaccular device required retreatment due to recanalisation. The patient was treated through radial access with Terumo Slender 7f 10 cm, Rist BER 5.5F 130 cm, Rist 5.5f SIM2 130 cm, Rist 079 95 cm, Phenom 21 150 cm, Microvention Sofia EX 5F 155 cm, Synchro 014, and Pipeline Vantage 3.25x4 mm. The device was oversized to achieve full coverage of the lesion (proximal vessel width, 2.8 mm; Vantage device, 3.25x14 mm), delivery of the device was very smooth, and there was contrast stagnation in the aneurysm. The patient continued to receive prasugrel and aspirin. DSA control data are not available.

Case 6

36-year-old patient with an incidental supraophthalmic aneurysm. The patient was treated via radial access with Terumo 7f 10 cm, Rist 079 guide, Rist SIM2 130 cm, Navien 058 115 cm, Phenom 027 + Synchro 014, and Pipeline Vantage 4x14 mm. The device opened smoothly, and post-deployment contrast stagnation was observed in the

aneurysm. No control imaging performed yet.

Case 7

69-year-old patient with CT and CTA (computed tomography and computed tomography angiography) due to left side hemiparesis. The next day, the patient was symptomatic but with no SAH nor hemiparesis and was in good clinical condition. The MRI showed a partly thrombosed middle cerebral artery aneurysm with remarkable swelling around it. The patient was treated through femoral access with Cordis 8f sheath 11 cm, Terumo 035 180 cm, AXS Infinity 90 cm, Cordis 4f hh 125 cm, Sofia EX 115 cm, Phenom 21, Synchro 014, and Pipeline Vantage 3.5–20 mm. The device opened nicely and contrast stagnation in the aneurysm was observed after the procedure. The DSA control showed only the non-thrombosed part of the aneurysm. The patient continued on apixaban 5 mg and prasugrel 10 mg.

Dr. Rautio and her team have treated more than 10 cases to date with Pipeline Vantage with Shield technology. Through their experience, they found that they were able to start at the desired position (no need to start distally), that the distal opening was fast and reliable, and the device does not 'drop down' (other devices might fall from the desired distal positioning despite visible wall apposition while the operator opens the rest of the device). Additionally, less force and manipulation were needed when opening the device and re-sheathing was smooth. The distal 'bumper' is smaller, so it was not mandatory to go through the device to pick it up with the microcatheter. The 0.21 lumen microcatheters enabled endovascular aneurysm treatment in previously distal and untreatable anatomic locations, aneurysms otherwise difficult to treat with conventional endovascular techniques, and difficult to treat surgically. Radial access with Rist guiding catheter worked well but it needed distal support. Visibility remained unchanged relative to previous versions of the device.

New Frontiers in Neurointervention: Solitaire 3 mm

Adnan Siddiqui

The Solitaire X revascularisation device is the newest model of a family of stent retrievers that have been pivotal in the transition of stroke intervention from medical to endovascular therapy. It is a smaller device (3 mm diameter) designed to reach and treat smaller blood vessels and potentially more distal locations. It is similar to the previous versions in its parametric design, platinum marker visibility along its length, push wire length of 200 cm, microcatheter compatibility (Phenom 21/27, Rebar 18, Marksman), and STAT compatibility (React 68/71 catheter, Riptide aspiration system). The features unique to the new 3x20 version are that it is approved to treat vessels as small as 1.5 mm and up to 3 mm, it can be delivered through a .017" microcatheter (compatibility with Trevo Pro 14, Headway 17, VIA 17), the .0155" push wire diameter makes it compatible with smaller microcatheters, it has a tapered introducer sheath, and a fluorosafe marker design. The standard length is 20 mm; anything longer becomes problematic in the distal vessels as they tend to be considerably tortuous. This device increases procedural versatility because it is designed for a lower clot crossing profile with .017" microcatheters and lower delivery force with greater diameter .027" microcatheters.

Remarkably, vessel movement during retrieval is minimised enabling the treatment of distal occlusions out to M2. This is important because distal vessels are much more flexible and fragile; therefore, the distortion caused by a stent retriever being pulled out could potentially cause haemorrhagic complications. As demonstrated by in vitro tests, the deformation of blood vessels during Solitaire X retrieval is diminished, possibly due to its parametric design and reduced radial force. This significantly reduces the risk of adverse events such as asymptomatic subarachnoid haemorrhage or ICH in these particularly distal locations.

Clinical cases[1]

Case 1

The patient presented with left hemiparesis, confusion, and facial droop. On imaging, the patient had multiple clearly embolic infarcts and had distal anterior and middle cerebral artery occlusions with favourable perfusion, preserved volume, and decreased flow. The patient received tPA and had a National Institute of Health Score (NIHSS)=14.

The setup for the case included: Sofia 5F catheter (125 cm), Phenom 21 catheter/Synchro-2 Guidewire (x2), Solitaire X revascularisation device 3x20 mm, and Riptide aspiration

[1] Local research approval from the hospital was obtained. The need for informed consent was waived by the respective research committee because of the retrospective nature of the study (T011/014/18).

tubing. The 3 mm device allowed for fast and effective clot retrieval in distal locations.

The next day MRI showed a very small infarction, and the patient had an NIHSS total of 2 on discharge.

Case 2

The patient presented with right hemiparesis and aphasia. On imaging, the patient was found to have L M1 occlusion with a small core, favourable perfusion, but large territory at risk. The patient was outside the tPA window and NIHSS=9.

The setup for the case included: zoom 88-T/VTK Reperfusion catheter, Sim-select 6F/035, Zoom 71 Reperfusion catheter, Velocity delivery microcatheter/Synchro-2 Standard Guidewire, Solitaire X revascularisation device 6x40 mm, Riptide aspiration tubing, Penumbra RED reperfusion catheter, Phenom-27 catheter/Chikai-18 Neurovascular guidewire, and Solitaire X revascularisation device 3x20 mm. The larger devices removed the larger M1 clot but revealed an M3 clot where the 3x20 was effective in achieving complete revascularisation.

The postoperative NIHSS=6, pending rehabilitation. A CAT scan a week later showed no infarction.

Dr Siddiqui explains that these cases exemplify the value of having a small device for stent retrieval either because lesions are primarily in distal vessels causing significant clinical deficit, or distal clots are caused or found during thrombectomy for larger clots in more proximal vessels. Endovascular stroke treatment requires a toolkit and having a small stent retriever that can be delivered safely through smaller microcatheters in distal vessels is an invaluable tool.

Conclusion

The data and cases presented demonstrate how the latest generation flow diversion and revascularisation devices help treat challenging lesions safely and effectively. Although these are useful additions to the armamentarium of endovascular interventionists, more studies are needed to further evaluate their use and cost-effectiveness. In this regard, several prospective studies are recruiting or ongoing. ELEVATE,[12] INSPIRE Pipeline (start date, October 2021),[13] and ADVANCE[14] seek real-world data on the use of Pipeline devices with Shield technology (including Flex and Vantage) in ruptured and non-ruptured intracranial aneurysms. Similarly, studies are beginning to systematically evaluate the value of mechanical thrombectomy in medium and distal vessels.

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