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Abstract

Cerebral aneurysms are treated in one of the two ways: a) Microsurgical clipping (+_ Bypass), b) Endovascular coiling (+_ balloon/stent), c) Flow diversion / Flow disruption. Treatment options vary depending on the age, comorbidities, location /morphology of aneurysm and finally patient preference and surgeon's expertise. A combination of microsurgical and endovascular techniques might be needed in management of complex cerebral aneurysms. The technological advancements in coil properties with novel interventional techniques are improving long term occlusion rates of cerebral aneurysms. In this review, we discuss recent advances in endovascular management of cerebral aneurysms with respect to evolving hardware and various endovascular techniques.

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INTRODUCTION

The history of neurointervention is short as our field is still in its puberty. The 1970s was the time when the pioneers of the field boldly went where no one had gone before. We have to particularly recognize the tremendous input of Pierre Lasjaunias in the very precise description of vascular anatomy of skull base and Fedor Serbinenko who developed a technique to treat cerebral aneurysms with a detachable latex balloon.^[1]

In 1990, Guglielmi detachable coil was used for the first time in a patient with carotid artery aneurysm. This was considered to be a breakthrough in the field of neurointerventional surgery and by the end of 1990s endovascular coiling became an established treatment option for ruptured and unruptured aneurysms.^[2] Various neck bridging techniques for the treatment of complex cerebral aneurysms soon became a reality with subsequent procedural and engineering innovations.^[3]

The early steps towards evidence based medicine was made in 2000s when the first major randomised trial ISAT : the International Subarachnoid aneurysm Trial was published which showed a clear benefit of endovascular coiling over surgical clipping for the management of cerebral aneurysms.^[4] The advanced techniques such as balloon assisted coiling, stent assisted coiling, flow diversion along with varying shapes and stiffness of coils were subsequently developed which resulted in

further increase in endovascular management of cerebral aneurysms.^[5]

The use of braided mesh devices in neuroendovascular surgery for treatment of cerebral aneurysms has quickly evolved since the initial introduction of flow diverter technology in 2007. At present PED, Surpass (2018) and FRED (2019), Derivo (2019) are the only commercial devices approved by FDA in United states. The technique of flow diversion has expanded with success into small aneurysms, posterior circulation aneurysms and distal intracranial aneurysms beyond ICA.

Pipeline embolisation device was introduced in 2008 and Pipeline Flex in 2014 with stiffer delivery wire and PTFE polytetrafluoroethylene sleeves instead of capture coil. PUFs (Pipeline for uncoilable or failed aneurysms) study reported 93.4% and 95.2% complete aneurysm occlusion at end of 3, 5 yrs respectively with good clinical outcome in 96.3% of patients.^[6]

The pipeline shield technology is a modification of device in which a synthetic phosphorylcholine polymer is bonded to pipeline braid to reduce thrombogenicity.^[7]

The Surpass, Silk, Silk +, are similarly used for treating complex aneurysms over past 3 yrs. The latest in silk line of devices is Silk vista baby (SVB) which is specifically designed for small parent vessels. It is the only FD capable of being delivered via 0.017 in microcatheter.^[8]

Liu-Jm in 2018 has published a case series about parent artery reconstruction for large /giant

aneurysms using Turbridge flow diverter trial evaluating the safety, efficacy of the same.^[9]

The DERIVO (Acandis) embolisation device was introduced as second generation flow diverter for treating intracranial aneurysms with improved flexibility, better visibility and higher aneurysmal occlusion rates relative to its prototype flow diverter. This device is approved by FDA for clinical applications since 2019. D. Ley et al has evaluated its efficacy in an elastase induced aneurysm model and has concluded that Derivo embolisation device meets the requirements for being a promising alternative in treating cerebral aneurysms.^[10]

The Acclino (Acandis) stent is a new self expanding nitinol microstent used for wide neck aneurysms. Kabbasch et al has demonstrated the safety and efficacy of the stent in a case series and concluded a promising rate of immediate ,midterm complete occlusion for stent assisted coil embolisation.^[11]

FRED Jr. (Microvention) and p48-Phenox are recently introduced low profile delivery systems which are compatible with small diameter microcatheters (021) that allow easy navigation into small distal arteries.^[12]

With the advent of sophisticated hardware in the recent past, more and more techniques have been developed for the mangement of cerebral aneurysms. Double balloon remodelling techique is one such technique used in bifurcation aneurysms and in wide neck aneurysms distal to circle of willis. Two compliant balloons can be placed across the neck in two branches of artery to cover the entire neck and prevent coil prolapse.^[13] Double stent technique is used in fusiform ,wide neck aneurysms wherein two overlapping stents help in vascular remodelling with stent endothelialisation and thrombosis of aneurysm.^[14]

Another unique technique ,stent assisted coil embolisation of ultrawide necked circumferential aneurysm via a spring shaped microcatheter on down the barrel view was described by Hyo et al in 2018.Here a microcatheter was steamed into a spring shape which was delivered to distal portion of aneurysm sac. Then one another microcatheter was positioned distal to aneurysm and low profile stent(LVIS) was deployed across the neck of aneurysm. Coiling was then performed by pulling spring microcatheter litle by little and so moving to proximal portion of sac rotating naturally around the stent. Hyo et al has proposed this novel technique for treating ultrawide neck or fusiform aneurysms.^[15]

Igor et al in 2019 have concluded in their case series that the results of “T” technique {A1 to ipsilateral A2} of Acom aneurysm embolisation are better with H1 configuration of anterior cerebral artery relative to other categories (H1-A1 equal diameters either side;H2-<50% of diameter difference in both A1;H3->50% of diameter difference both A1).^[16]

3D Vascular Simulation models for preprocedure planning:

3D printing of artificial vascular models for pretreatment simulation holds promise for guiding the treatment of intracranial aneurysms. Data from CT,MRA or rotational angiography can be used to generate a printable vascular model tailored to patients unique anatomy, further processed with addition of liquid silicon coat, smoothing out of artificial vessels and attachment to peristaltic pump to allow simulation with endovascular devices. Kaneko et al utilised similar 3D models to plan and treat two wide neck aneurysms (A3, Basilar-SCA) with NEUROFORM ATLAS over LVIS Jr.^[17]

Different computational methods have been described in the past to model endovascular devices. Hector Fernandez et al has recently proposed one such novel method to calculate the length of braided device when released inside parent vessel. The method effectively calculates the final length of a braided stent inside a vessel within computing times of seconds showing an accurate matching for the case studied. Neurointerventionist thus can plan, select a device specific to anatomy of the vessel being treated and so preventing intraoperative mishaps.^[17]

Optical coherence tomography (OCT) is an ultra-high resolution real time intravascular imaging method that is gaining interest in cerebrovascular applications. Frederik et al has conducted studies in animal models and have concluded that OCT was more sensitive than conventional angiography for the assessment of aneurysms and their recurrence at 28 days after FD implantation.^[18]

Following the evolution of flow diverters and its associated techniques, the neuroendovascular space has continued to iterate with additional flow modulation devices such as the intrasaccular flow disrupter.

Flow Disrupters

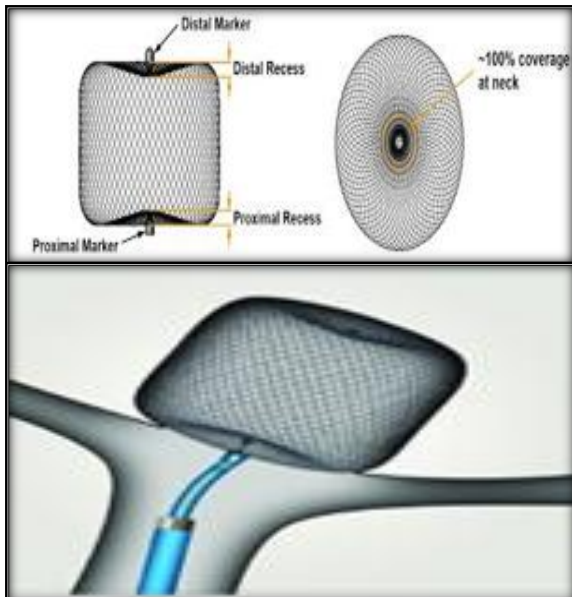
Intrasaccular flow diversion devices or flow disrupters are developed to overcome the limitation of thromboembolic complications and side branch occlusion for wide neck bifurcation aneurysms. These devices enable reconstruction of anatomy at the neck while providing a robust scaffolding to the coil mass .They are placed within the aneurysm and are responsible for progressive thrombosis and occlusion of aneurysm.

Overview of Flow Disrupters

Device	Retrievable	Compatible microcatheter
WEB (sequent medical, Inc)	Yes	0.027 in ID
LUNA (Nfocus Neuromedical)	Yes	0.027 in ID
Medina (Medtronic)	Yes	0.027 in ID

WEB (Woven endobridge) was introduced in 2011 as first intrasaccular device for treatment of bifurcation aneurysms. It comes in two configurations: standard SL (single layer), DL (double layer), spherical SLS (single layer sphere).

The WEB SL-EV (Enhanced visualisation) is the latest version of these devices and is delivered through 0.017-in ID microcatheter. In 2016, the WEBCAST study reported successful treatment outcomes in 85% of patients. Metaanalysis of all available series showed complete or near complete occlusion in 80% of aneurysms at the end of 1 year.^[19]



WEB SL, SLS are products of improvisations in basic WEB design and have an added advantage of resheathability and repositioning even after complete deployment.^[19]

Cristian et al,^[20] has proposed a novel technique, balloon remodelling assisted Woven endobridge technique for aneurysms with complex shape or orientation. They have concluded that this technique is advantageous over conventional stent assisted coiling of aneurysms. Further Zaid et al (39) has described a snare salvage technique for deformed WEB device after deployment.

The LUNA AES (aneurysm embolisation system) is a self-expanding double layer nitinol mesh with platinum markers. The study conducted by Piotin et al showed 77% rate of complete or near complete aneurysm occlusion at end of 1 year.^[21]

The MEDINA embolisation device is a 3D coil made from shape set core wire with outer filaments forming petals. The 3D petals constitute broader coil loops. This coil loop allows for stable anchoring of coil mass within aneurysm sac. Lobulated aneurysms can be affectively treated with Medina and coils combination to avoid recurrences.^[22]

CONTOUR system and NEQSTENT (Coil assisted flow diverter) are next generation flow disrupters recently introduced yet to be subjected for RCTs.^[22]

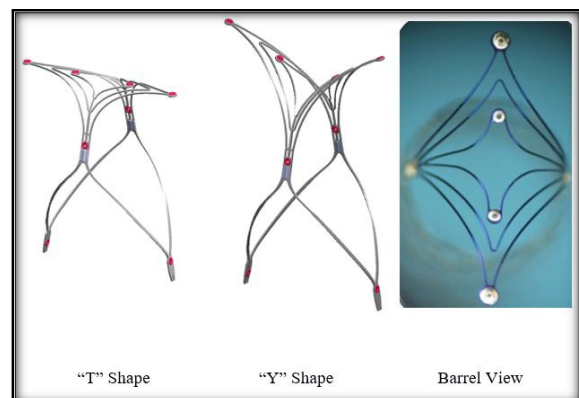
Bifurcation Support Devices

Most of the bifurcation devices developed previously were only for the support of coil mass during aneurysm treatment. Bifurcation support

devices are new devices which offer support for coil mass as well as neck reconstruction of the aneurysm.

1.pCONus (Phenox GmbH) is a stent like device with four petals at the distal end that rests on inner wall of the sac. The meshwork at the petal base prevents coil prolapse. The aneurysm sac can be catheterised through the mesh at base of petals via a standard 0.021in (ID) microcatheter. A retrospective study conducted by Lubicz et al showed 75% occlusion rate at 1 year with two embolic complications directly related to device.^[23] pCONus 2 is a latter generation device that has six petals to provide a better scaffold at the level of neck.

2.Pulse Rider (Pulse Vascular, Inc, Los Gatos, California, USA) is a self-expanding nitinol implant available in “T” and “Y” configurations intended to fit geometry of daughter vessels arising at bifurcation. It was first approved for use in USA by FDA on 19, June 2017. The key benefit of device is that the daughter branches need not be accessed to deploy the device. The petals of device offer neck protection regardless of their position within the sac or daughter branches. A prospective nonrandomised clinical trial showed near complete occlusion in 87.9% patients at 6months.^[24]



Low Profile Braided Stents

LVIS (Low profile visualised intraluminal systems), LVIS Jr (Microvention), LeoPlus, Leo Plus Baby are self-expandable nitinol stents with closed cell construction. They are approved for treating wide neck aneurysms by FDA on 30 May 2018. LVIS and Leo Plus are recommended for larger vessels(>2mm) whereas LVIS Jr and Baby Leo are for smaller vessel upto 2mm diameter. In view of braided construct, these devices allow to create an effective scaffold across the aneurysm neck (“Shelving” technique) thus reducing the complication rates. Poncyjusz et al have demonstrated 82% occlusion rates with LVIS, Leo Plus in 78 patients at 6 month follow up period.^[24]

LVIS EVO (Enhanced visualisation) stents were introduced with various sizes (2.5-4mm) and are compatible with 017 microcatheters and supercompliant balloon systems.They have an

advantage of resheathability upto 80% after deployment.^[25]

LVIS EVO X, FRED X, FRED Jr X are desirable versions of the basic low-profile stents which eliminates the need for dual antiplatelets in view of their polymer coating to braided nitinol meshwork. Accero (Acandys) is yet another novel, fully visible low profile braided stent with platinum-nitinol composite wire technology recently approved for treatment of intracranial aneurysms.^[26]

Vascular Reconstruction Devices (VRD)

Neuroform Atlas (Stryker) has a unique hybrid combination of closed cell design at proximal end and open cell design at distal end. This offers a better conformability-vessel wall apposition, easy delivery, precise stent placement and easy microcatheter (0.017in) access to aneurysm sac. The stent has been approved by FDA on 16 May 2019 for the treatment of wide neck intracranial saccular aneurysms.

Barrel VRD

The barrel VRD (Medtronic/ covidien, Irvine, CA, USA) is a novel, fully retrievable, self-expanding, laser cut, nitinol stent designed for treating wide neck bifurcation aneurysms. It is delivered via 0.021 in microcatheter and has greater aneurysmal neck coverage in view of its bulging centre. It is yet to obtain FDA approval for market use.

Compliant and supercompliant balloons:

More compliant balloons such as Hyperform, Hyperglide (single lumen), Transform (single lumen), Scepter (dual lumen) were introduced for treating aneurysms with balloon assisted coiling.

The Transform occlusion balloon catheter (Stryker neurovascular, Fremont, california, USA) is the latest single lumen balloon catheter using 0.014 inch microwires with compliant, supercompliant versions. It has micromachined hypotube design with multiple slits for rapid inflation, deflation with increased visibility and reduced procedural times. In study conducted by Quadri et al 78% occlusion rates were documented with no serious complications.^[27]

Hyperglide is an oblong, compliant single lumen balloon catheter used with 0.010 in microwire for wide necked side wall aneurysms like internal carotid and vertebral arteries. The more compliant hyperform is a round balloon preferred for wide neck as well as small arteries like PICA, PCA, Acom artery.^[28]

Double Lumen Balloon Catheters

The development of double lumen balloon catheters with 0.014 -in microwire compatibility has provided better wire torquability thereby helping catheterisation of appropriate branches near aneurysm neck. Ability to deploy low profile stent in case of bail out options, injection of liquid embolics (if required), simultaneous mechanical and chemical angioplasty of severe vasospasm in SAH

are distinct advantages offered by double lumen balloon catheters.^[29]

Scepter (Microvention, Irvine, california, USA) is a dual lumen balloon microcatheter approved by FDA in 2012. The compliant and supercompliant version of the same are scepter-c and scepter-XC which are frequently used for bifurcation aneurysms.

Technical details of double lumen catheters:^[29]

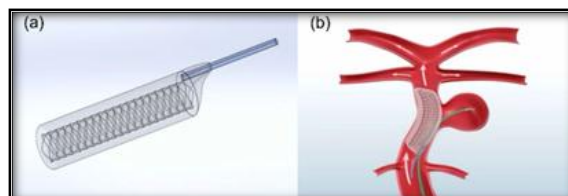
Balloon	Guidewire (in)	Length balloon (mm)	Diameter balloon (mm)
Ascent (DePuy)	0.014	7.9,10,15	4,6
Scepter (Microven)	0.014	10,15,20/11	4
Eclipse 2L(Balt)	0.014	7/9,12,20	6

Scepter mini occlusion balloon catheters

First microballoon designed to occlude blood flow and achieve controlled delivery of coils/liquid embolics. Small profile and soft balloon allows navigation to distal target vessels for embolisation of aneurysms with smaller diameters. The double lumen technology provides instant flow arrest for a controlled embolisation. These devices are compatible with 0.08in microwire.^[29]

Stent-Balloon Device

A novel stent - balloon device is recently introduced by Asgari et al (2020) which has an advantage of safer delivery of coils into aneurysm sac while being protected by a stent (patent parent vessel) and balloon (prevents coil prolapse) simultaneously. The stent is delivered via large lumen while balloon is inflated via smaller secondary lumen of a double lumen catheter.^[30]



a – Stent Balloon Device, Double lumen catheter b – Balloon inflated around stent while deploying coils

Temporary Bridging Devices

In recent years, novel stents and stent like devices have been designed to serve as adjunctive treatments for endovascular coiling of wide neck aneurysms. These include Cascade, Comaneci, pCANvas and Eclips.

The Cascade and Comaneci devices provide support during coiling and do not require antiplatelet therapy as they are not permanently deployed. Whereas pCANvas and Eclips have flow modifying properties that decrease blood flow into aneurysm thus decreasing the risk of recanalisation and recurrence.

The Comaneci (Rapid Medical) device includes a compliant radioopaque mesh which temporarily bridges the aneurysm neck to support coil mass

without compromising flow in the parent artery. It comes in 3 different sizes -Basic design (32 mm length,4.5 mm expansion), Comaneci Petit (24 mm length,3.5mm expansion), Comenaci 17 (22 mm length,3mm expansion). Fischer et al have demonstrated stable occlusion of 14/18 patients using this device.^[31]

Cascade (Perflow medical, Israel) is a retrievable, neck bridging device which has similar advantage of providing patency of parent vessel during coil embolisation. Compatible with 0.017 in micro cath it is more suitable for tortuous vessels relative to Comaneci device.

The pCANvas is a third generation device to its predecessors, pCONus 1,pCONus 2 and is used to treat wide neck intracranial aneurysms. It is currently approved by FDA for use in Europe.Lylyk et al in 2019 published the earliest clinical data on use of pCANvas.^[32]

The second generation eCLIPS is novel, selfexpanding, fully retrievable, nitinol, stent like device with flow diverter properties and successor to original Eclips device first described in 2008.It is neither balloon mounted nor circumferential unlike its predecessor and so prevents jailing of branch or parent vessel.81% patients had complete occlusion rates with this device in a study conducted by Chiu et al.^[33]

10 Coil Systems

Manufacturers now offer coil lines with varying degrees of stiffness from frame building (Target 3D-Stryker, cerenovus, Irvine) filling with soft to supersoft coils and finishing with nanos (Target Nano), Axiom AX (Medtronic), Galaxy G3 Mini (Cerenovus). Recently developed ultra –small diameter coils like hypersoft helical,3D Coils especially with 1-1.5mm diameter achieve higher packing density in small aneurysms. These soft platinum coils offer neurointerventionist to fill smaller spaces and allow for improved packing in smaller aneurysms.^[34]

The second generation Hydroframe and hydrosoft 3D coils were introduced (microvention) with an advantage of usage without steaming. Hydrogel polymer based softer coils with softer primary wind would eliminate the working time to deploy the coils. The German -french Randomized Endovascular Aneurysm Trial has recommended use of second generation hydrogel coils over bare platinum coils in view of ease of deployment and lesser complications.^[35]

20 Coil systems: To address larger aneurysms, larger coil diameters combined with significantly increased coil lengths as long as 50-60 cm are developed (Target XL-Stryker) and Penumbra Coil (PC) 400. They have an advantage of achieving early aneurysmal packing, less hardware manipulations reducing the operative time and complication rate.

Future of Endovascular Neurosurgery

There are few desirable developments that would likely or desirable to happen in the field of endovascular neurosurgery in the near future.

1. Several prehospital imaging tools including the vessel wall imaging techniques are currently in development that could allow us to identify various cerebrovascular pathologies prior to hospital arrival.^[36]
2. Device surfaces might experience significant advancements. The ongoing trend among the manufacturers is to develop antithrombogenic coatings for stents and flow diverters to obviate the need for dual antiplatelet regimens.^[37]
3. Simulator training and Robotic endovascular neurosurgery: Current simulator training for interventions lack adequate haptic feedback and are restricted to narrow repertoire of devices and patient specific anatomy cannot be routinely simulated. The substantial advancements in the existing technology gives us a hope that within the next decade sophisticated simulators will improve the human performances reducing the negative outliers. Mendes Periera et al,^[38] have reported first case series of successful robotic assisted elective neuroendovascular procedures. Presently the degree of autonomy of current robotic systems is very low and further limited stability of network infrastructures, imaging transfer protocols have to be overcome in order to tap the full potential of robotics and cost of course would be a major stumbling block.^[39]
4. Remote mentoring is another highly desirable development that will probably soon find its way into clinical routine partly because one-one person teaching has become very challenging during the COVID pandemic. This has led to dramatic increase in demand for online teaching resources and virtual discussion forums.^[40]

CONCLUSIONS

Endovascular techniques have continued to evolve since the invention of Guglielmi detachable coils in the 1990s.Advancements in vascular reconstruction intracranial stents now provide low profile alternatives with delivery via small 0.017inch microcatheters. Improvements in balloon microcatheters now provide supercompliant conformable balloons designed for treatment of wide neck aneurysms with dual lumen capabilities and improved navigation via 0.014inch microwires. Recently introduced temporary bridging devices and stents with semiflow diverting properties aim to broaden the efficacy of coiling techniques.The fate of coiling and adjunctive devices is yet to be seen with advent and adoption of flow modulation braided devices like WEB. Finally 3D-printed vascular simulation flow models are gaining popularity for preprocedure planning to assist with appropriate device selection and sizing.

The endovascular field continues to evolve and advance with innovative devices further raising the bar for safety and efficacy of cerebral aneurysm treatments.

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