



# The Evolution of Endovascular Therapy for Intracranial Aneurysms: Historical Perspective and Next Frontiers

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**ABSTRACT:** The history of cerebral aneurysm treatment has a rich and storied past with multiple notable luminaries contributing insights. The modern era has transitioned from primarily clip ligation to increasing use of endovascular therapy. Even more recently, the use of intrasaccular flow diverters has been introduced for the treatment of wide necked aneurysms. The field is continuing to transform, and bioactive coils and stents have resurfaced as promising adjuvants to promote aneurysm healing. Advanced imaging modalities are being developed that could further advance the endovascular arsenal and allow for porous memory polymer devices to enter the field. This focused review highlights notable historic contributions and advances to the point of futuristic technology that is actively being developed.

**KEYWORDS:** Cerebral aneurysm, vascular neurosurgery, endovascular surgery, coil, bioactive stents, flow diversion

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## Introduction: A Brief History of Open and Endovascular Therapies

Technological advancements have revolutionized vascular neurosurgery over the past century. Sir Thomas Willis' *Cerebri anatome* (1664) is widely credited for the first anatomical description of the skull base arteries.<sup>1</sup> The first open surgical treatment of an intracranial aneurysm was reportedly performed in 1931 by Norman Dott utilizing wrapping, followed shortly thereafter by the first application of an aneurysm clip in 1937 by Walter Dandy.<sup>2</sup> Over the latter half of the 20<sup>th</sup> century, additional technical advances in vascular neurosurgery were largely the purview of the neurosurgical luminaries including Vinko Dolenc, M. Gazi Yasargil, Thoralf Sundt Jr., and Charles G. Drake.<sup>3–9</sup> Many of their tools and techniques are still relied upon today by cerebrovascular surgeons treating complex aneurysms and vascular malformations best addressed through an open approach. Still, the field sought less invasive options to improve patient survival and reduce morbidity.

The origins of endovascular neurosurgery are traced back to the Portuguese neurologist Egas Moniz (1874–1955) with the first successful intravascular contrast administration to visualize cerebral architecture with X-ray beams.<sup>10</sup> Leveraging such early advances in angiography, it wasn't until 1964 that Luessenhop and Velasquez performed the first successful micro-catheterization of the cerebral vessels for temporary balloon occlusion of a posterior communicating artery aneurysm.<sup>11</sup> In 1974, Hilal et al and colleagues then reported a 120 patient series on the percutaneous catheterization of cerebral vessels using magnetic catheters, a practice that was abandoned

shortly thereafter.<sup>12</sup> Detachable balloons were popularized by Serbinenko also in 1974, and these devices remained in vogue for the subsequent decade before eventually falling out of favor due to high rates of morbidity and mortality.<sup>13,14</sup>

The modern era of neurointervention was born at the end of the 20<sup>th</sup> century. In 1991, Guido Guglielmi et al—a young interventional neuroradiologist and neurosurgeon from Rome studying aneurysm treatments in swine models at the University of California, Los Angeles—published his pioneering work on the use of electrolytically detachable platinum coils to treat cerebral aneurysms.<sup>15,16</sup> This ushered in a new era for neuroendovascular surgery with technical modifications of balloon assisted coil embolization to treat wide-necked aneurysms and increase packing density.<sup>14,17</sup> Recent years have seen the maturation of neuroendovascular technique and device innovation to best treat aneurysms on a patient-specific basis owing to variant anatomy and comorbidities. In the early 2000s, large clinical trials demonstrated the safety and efficacy of coil embolization for the treatment of aneurysmal subarachnoid hemorrhage.<sup>18,19</sup> Given the recency of these developments, questions remain about the long-term durability of endovascular treatment.<sup>20,21</sup> Flow diversion for the treatment of complex aneurysms and bioactive coils to facilitate aneurysm healing have also been introduced and may modulate patient clinical outcome over time.<sup>22,23</sup>

## The Advent of Flow Diversion

The Pipeline for Uncoilable or Failed Aneurysms (PUFS) trial was the first major clinical trial demonstrating the safety



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and efficacy of flow diversion for the treatment of complex intracranial aneurysms located from the petrous to hypophyseal segments of the internal carotid artery.<sup>24</sup> Flow diversion represented a novel approach in which a low porosity, low profile stent is situated within the parent artery, extrinsic to the aneurysm, leading to vessel wall remodeling and aneurysm occlusion.<sup>24</sup> There have been many renditions of flow diversion devices, including the Pipeline embolization device (Covidien, Mansfield, MA, United States), the Silk (Balt Extrusion, Montmorency, France), the Flow Re-direction Endoluminal Device ("FRED," Microvention, Tustin, CA, United States), the p64 Flow-Modulation Device (phenox GmbH, Bochum, Germany) and the Surpass Flow-Diverter (Stryker Neurovascular, Fremont, CA, United States).<sup>25</sup> Such devices have extended the application of endovascular techniques to more complex cerebral aneurysms where traditional methods, such as clipping and coiling, are challenging or not possible.<sup>25</sup> Still, the treatment of posterior circulation aneurysms remains challenging, requiring a steep learning curve and necessitating the dissection and preservation of vital perforators for open surgical technique.<sup>26</sup> While intraluminal flow diverters have become increasingly used for the treatment of aneurysms located from the vertebral arteries, basilar trunk, and the basilar apex with moderate success, their use in such situations is tempered by the relatively high rates of morbidity and device occlusion.<sup>27,28</sup>

Intra-saccular flow diversion is an alternative technique in which the device is placed inside the aneurysm, thereby minimizing parent vessel metal coverage. The technique has emerged as potential mechanism to increase safety for the treatment of complex wide necked aneurysms.<sup>29</sup> The Woven EndoBridge or "WEB" (microvention, Tustin, CA, United States) remains the only FDA-approved intra-saccular flow diverter. While the device has been received with significant optimism by the neurointerventional community owing to its simple delivery system, its long-term aneurysm occlusion rates remain suboptimal.<sup>30,31</sup>

## Next Frontiers in Endovascular Management

### Bioactive devices

The creation of bioactive devices that serve to facilitate aneurysm healing dates to the early 2000s but has not yet yielded superior results relative to non-bioactive detachable stents and coils.<sup>14,22,32,33</sup> Laboratory research has provided insights into the aneurysm healing pathway to inform these advances, and will continue to serve as a scaffold for new device development.<sup>34</sup> Recent years have seen modifications of existing endovascular devices to incorporate bioactive polymers. For example, a surface modified version of the Pipeline device (Covidien, Mansfield, MA, United States) was recently introduced to include surface-bound phosphorylcholine due to decreased device thrombosis rate and increased patient safety.<sup>35</sup> Using a rabbit model of saccular aneurysm, Cortese et al<sup>36</sup> also improved

rates of parent vessel reconstruction, aneurysm occlusion, and reduced rates of stent occlusion after introducing a CD31 coated Silk Vista Baby (Balt Extrusion, Montmorency, France) flow diverting stent. In a mouse model of saccular aneurysm, monocyte chemoattractant protein 1 (MCP-1), osteopontin, and interleukin 10 (IL-10) have further demonstrated increased aneurysm healing when locally delivered using bioactive aneurysm coils.<sup>37-40</sup> Recently, Laurent et al published their results using dual coated aneurysm coils to target the inflammatory pathway of aneurysm healing.<sup>41</sup> As our understanding of the biology of aneurysm healing continues to advance, the creation of endovascularly deployable devices that leverage and potentiate natural aneurysm healing mechanisms will likely serve as next revolution in cerebrovascular disease.

### Increased visualization

Interventional cardiology has recently transitioned to the use of intravascular imaging for better lesion characterization.<sup>42</sup> Intravascular ultrasound and optical coherence tomography are adjunctive tools which provide axial resolution within the vessel of up to 40 or 15  $\mu\text{m}$  respectively.<sup>43</sup> Leveraging this technology allows interventional cardiologists to have certainty in choosing appropriate stent sizing and length, optimizing stent expansion and identifying acute complications.<sup>44</sup> In fact, the use of this technology is known to improve patient outcomes.<sup>45</sup> This has potential for neurovascular lesions identification as well. When the images are combined with intravascular photoacoustic imaging, increased accuracy is obtained.<sup>46</sup> Additionally, narrow-band endoscopic imaging is being developed for real time intravascular imaging.<sup>47</sup> For tortuous vessels or aneurysms with narrow openings, this would facilitate more direct navigation. It also opens the field to porous memory polymers.<sup>48</sup> These new embolic devices can develop shape memory and be fixed with infrared light once adequately placed. The potential for combination with bioactive particles is also much higher. Finally, mapping pulse wave coherence for arterial and venous phases offers added value for determining mismatch is arteriovenous coupling, thereby indicating patients that have transitioned into disequilibrium.<sup>49</sup>

## Conclusions

Since the advent of open vascular surgical therapies for intracranial aneurysms, the leaders of neurological surgery have focused on developing technologies and techniques to improve patient outcomes. The modern revolution in this field is in endovascular therapies, which continue to evolve to include optimized stent and coil designs which leverage underlying aneurysm biology and promote healing. While flow diversion has extended the application of endovascular techniques to more complex aneurysms, newer bioactive devices in combination with existing endovascular techniques should be studied to verify long-term benefit. Increased visualization with intra-arterial imaging could also enhance ability to treat complex


aneurysms and more readily appreciate the interplay of vascular connections.

## Previous presentations

The contents of this original manuscript have not been previously presented or published, in part or in full, in any medium.

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