REVIEW ARTICLE

Woven Endobridge embolization: Indications and innovation

Ashley M. Carter¹, Bethsabe Romero¹, Harrison Dai¹, Simran Phuyal¹, Danxun Li¹, and Brandon Lucke-Wold² *

¹Eastern Virginia Medical School, Norfolk, Virginia, USA
²Department of Neurosurgery, University of Florida, Gainesville, Florida, USA

Abstract

The treatment of intracranial aneurysms has seen incredible advancements over the last few decades. Long-term occlusion of wide-neck bifurcation aneurysms remains technically challenging. The Woven Endobridge (WEB) embolization device is innovative in its construction and uses. The design of the device has evolved over the last decade. Pre-clinical and clinical trials are ongoing and continue to inform the development of intrasaccular flow-diverting devices. The WEB device is currently approved by the U.S. Food and Drug Administration (FDA) for treating wide-neck aneurysms. The safety and efficacy of the WEB device have yielded promising clinical results that may have additional indications. This review aims to discuss the development of the WEB device and the current state of the WEB device in the treatment of wide-neck aneurysms. We also summarize ongoing clinical studies and potential innovative uses.

Keywords: Woven Endobridge embolization device; Aneurysms; Wide-neck aneurysms; Posterior communicating artery aneurysms; Sidewall aneurysms; Flow-diverting device; Intrasaccular embolization

1. Overview of the WEB embolization devices and current treatment approaches

The American Association for Neurological Surgeons (AANS) recommends three broad treatment approaches for brain aneurysms: Endovascular therapy or coiling with or without adjunctive devices, medical intervention, and surgical therapy or clipping[1]. Endovascular strategies for treating aneurysms have demonstrated great success with embolization coils. Despite this, long-term occlusion of wide-neck and wide-neck bifurcation aneurysms remains technically challenging[2]. Balloon-assisted and stent-assisted coiling have demonstrated safe and effective treatment of these aneurysms without increased thromboembolic or iatrogenic rupture events[3,4]. However, the balloon-assisted technique risks temporary occlusion of the parent artery[5]. Stent-assisted coils eliminate the need for temporary luminal occlusion. Although they are effective for wide-neck aneurysms, they do not adequately treat bifurcation aneurysms as the second branch vessel is often left unprotected and thus risks coil herniation. Various shapes have been developed to address this issue, such as the Y-stent and waffle-cone techniques, which generally provide better coverage[6,7]; though, the introduction of a stent requires prolonged use of dual antiplatelet therapy[8].
Flow diversion emerged as a paradigm shift in treating wide-neck and bifurcation aneurysms. Rather than direct intrasaccular embolization, flow diversion aimed to divert flow away from the aneurysm resulting in delayed thrombosis and endothelialization of the parent vessel wall. Devices such as the Pipeline Flex embolization device (PED) achieve flow diversion with lower porosity and approximately 30% higher metal coverage. The Honeycomb Microporous Covered Stent features a stent covered by a polyurethane film that allows for greater flow-diverting properties than a traditional stent. While these devices are promising, dual antiplatelet therapy is still required.

The Woven Endobridge (WEB) embolization device is an intrasaccular flow diverter designed to divert flow at the interface between the aneurysm neck and the parent artery. The device deploys a double-layer (DL) braided oblate nitinol mesh within the aneurysm sac, which self-expands to conform to the aneurysm wall and span the aneurysm neck. As the therapy focuses on stabilization and coverage of the aneurysm neck, the device is designed for both wide-neck and bifurcation aneurysms. The device may also be a single layer (SL) or a single-layer sphere (SLS). The inner and outer layers of the mesh are held together by radiopaque markers, which allow direct visualization of the device within the aneurysm with X-ray-based techniques. The thrombogenicity of the WEB device is comparable to that of intrasaccular coils, but the radiopaque marker at the luminal surface of the mesh is not thrombogenic, except where an endoluminal construct is indicated for better support. Long-term antiplatelet therapy is usually unnecessary in most patients.

The WEB embolization device mesh is advanced up to the aneurysm using a VIA catheter, usually with a transfemoral approach. The microcatheter containing the mesh is positioned within the fundus of the aneurysm dome and deployed within the aneurysm. An angiogram is performed immediately after deployment. If positioning is favorable, the device can be detached and remains within the aneurysm. If not, the device can be resheathed and repositioned. Serial control angiograms are performed following the deployment, demonstrating progressively rapid cessation of blood flow within the aneurysm, starting distally and progressing toward the aneurysm neck. Complete cessation of intra-aneurysmal blood flow is noted within minutes of placement, and complete occlusion of an aneurysm can be confirmed at 8 weeks. Endothelialization of the parent vessel by the growth of neo-endothelium within the recessed concavity of the embolization device has been noted. Thus, the WEB embolization device combines stent-assisted coiling and flow diversion features while minimizing the need for long-term antiplatelet therapy.

2. Clinical trials and ongoing investigations

The WEB embolization device has demonstrated success in pre-clinical trials. Several ongoing clinical trials are investigating the device’s effectiveness and safety, while exploring its suitability to various types of intracranial aneurysms. A total of 11 trials using the device have been registered (National Library of Medicine), of which six have been completed (Table 1). Of these six trials, five have results available, while one does not have results available currently. Of the remaining five registered studies, one was withdrawn, one was terminated, one is under recruiting phase, one is not currently recruiting, and one is under unknown status. A summary of clinical trials and their current statuses are found in Table 1.

A prospective, multicenter, and observational study conducted with ten French neurointerventional centers, collectively called French Observatory (NCT01975233), primarily looked at the post-procedure occlusion durability of the aneurysms treated with WEB devices (Table 2). The WEBCAST study (NCT01778322) evaluated the safety and efficacy of WEB devices in wide-neck bifurcation aneurysms, mostly unruptured (Table 2). A cumulative population study was performed with the patients from the French Observatory trial (NCT01975233) and the WEBCAST trial (NCT01778322). In the cumulative study, treatment with WEB was successfully performed in 96.5%. At 1 year, complete aneurysm occlusion was observed in 56.0%, neck remnant in 26.0%, and an aneurysm remnant in 18.0%, of which 2.0% worsened since the procedure. At 1 year, mortality was 3.9%, with three deaths unrelated to an aneurysm or treatment and one related to a partially thrombosed aneurysm.

The WEBCAST-2 was later designed to corroborate further the high degree of safety and efficacy demonstrated by WEBCAST and French Observatory studies. The study had a comparable protocol to WEBCAST, with a few changes. At 1 year, complete occlusion was achieved.

**Figure 1.** Angiogram of anterior communicating artery aneurysm. (A) Placement of WEB device in aneurysm with early stasis. (B) Final positioning of WEB device in aneurysm dome. Abbreviation: WEB: Woven Endobridge.
Table 1. Registered trials and their current statuses

<table>
<thead>
<tr>
<th>Study</th>
<th>Title</th>
<th>Status</th>
<th>Population</th>
<th>References</th>
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<tbody>
<tr>
<td>NCT04621552 (France)</td>
<td>Virtual Simulation for Woven EndoBridge Device Sizing</td>
<td>Completed, results available</td>
<td>Sample size: 186; Inclusion criteria: Patients &gt;18 years treated with WEB for intracranial aneurysms</td>
<td>[64]</td>
</tr>
<tr>
<td>NCT01975233 (France)</td>
<td>WEB French Observatory of the WEB Aneurysm Embolization System</td>
<td>Completed, results available</td>
<td>Sample size: 62; Inclusion criteria: Patients &gt;18 years; independent use of WEB device prior to inclusion in French Observatory; Aneurysm characteristic: morphology, saccular, located in BA, MCA bifur, ICA terminus, ACom, or ACA; appropriate diameter and width of aneurysm to be treated with WEB device, and Dome-to-Neck ratio ≥1.0</td>
<td>[65]</td>
</tr>
<tr>
<td>NCT01778322 (Denmark, France, Germany, Hungary)</td>
<td>WEB Clinical Assessment of Intrasaccular Aneurysm Therapy (WEBCAST)</td>
<td>Completed, results available</td>
<td>Sample size: 51; Inclusion criteria: Patient ≥18 years of age; must sign informed consent form prior to study</td>
<td>[66]</td>
</tr>
<tr>
<td>NCT02687607 (France)</td>
<td>Clinical Assessment of WEB Device in Ruptured Aneurysms (CLARYS)</td>
<td>Completed, results available</td>
<td>Sample size: 60; Inclusion criteria: independent use of WEB device prior to inclusion in CLARYS; patient ≥18 years and ≤80 years; Hunt &amp; Hess score of I, II, or III; Aneurysm characteristic: morphology, saccular, located in BA, MCA bifurcation, ICA terminus, ACom, PCom, or ACA; appropriate diameter, height, and maximum width of 10 mm of aneurysm to be treated with WEB device; patient must be followed up by the physician; patient must comply with all aspects of the study; patient or their legal team must be informed about data collection and its protection, and must sign for consent when mandatory</td>
<td>[67]</td>
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<tr>
<td>NCT03844334 (France, Germany, Hungary)</td>
<td>Clinical Evaluation of WEB 0.017 Device in Intracranial Aneurysms (CLEVER)</td>
<td>Completed, results not yet available</td>
<td>Sample size: 163; Inclusion criteria: Patient ≥18 years and &lt;80 years of age; patient must have an intracranial aneurysm; must sign informed consent form prior to any data collection; Hunt &amp; Hess score &lt;III</td>
<td>[68]</td>
</tr>
<tr>
<td>NCT02191618 (Canada, Denmark, Germany, Hungary, Turkey, United States)</td>
<td>The WEB-IT Clinical Study</td>
<td>Completed, results available</td>
<td>Sample size: 150; Inclusion criteria: Patient ≥18 years and &lt;75 years of age; patient must have a single IA requiring treatment; patient must sign an informed consent form</td>
<td>[69]</td>
</tr>
<tr>
<td>NCT03936647 (Canada)</td>
<td>The RISE Trial: A Randomized Trial on Intra-Saccular Endobridge Devices</td>
<td>Currently recruiting</td>
<td>Estimated enrollment: 250; Inclusion criteria: Patient with intracranial aneurysm where WEB device is considered appropriate for treatment; aneurysm diameter of 4–11 mm; can include saccular bifurcation aneurysms of MCA, BA, carotid terminus, or ACom; ruptured aneurysms with WFNS ≤3</td>
<td>[70]</td>
</tr>
<tr>
<td>NCT03312725 (Belgium)</td>
<td>Mid-term Data Collection of the Treatment of Intracranial Aneurysms with the WEB aneurysm Embolization System</td>
<td>Terminated</td>
<td>-</td>
<td>[71]</td>
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(Cont'd...)
in 54.0% of the aneurysms, neck remnant in 26.0%, and an aneurysm remnant in 20.0%. Adequate occlusion was reported in 80.0%. More recently, data have been published with a cumulative trial population of WEBCAST and WEBCAST-2 at 3 years\(^2\) and 5-year analysis\(^3\) that shows long-term aneurysm stability and occlusion rate in aneurysms treated with the WEB devices.

The WEB Intrasaccular Therapy (WEB-IT) study (NCT02191618) also aimed to validate further the WEB system’s safety and effectiveness for treatment of wide-neck bifurcation aneurysms (Table 2)\(^4\). Mortality remained 0.0% throughout the entire 12-month study period\(^5\). In the case-controlled and multicenter study (NCT04621552), investigators compared a virtual simulation with conventional sizing to determine the appropriate WEB device size for an aneurysm. The results demonstrated fulfillment of the primary outcome measure by shortening the intervention time, lowering the radiation dose, and lowering the number of WEB devices not
deployed (Table 2)\[^{26}\]. Finally, the most recently published independent trial is the CLARYS (NCT02687607), which assessed the utility of the WEB embolization specifically in patients with recently ruptured intracranial aneurysms (Table 2)\[^{26}\].

### 3. Outcomes and proposed grading scale for aneurysm recurrence

The most feared complication of intracranial aneurysms is a rupture causing a subarachnoid hemorrhage (SAH), posing a significant risk of morbidity and mortality\[^{1,27}\]. Medical intervention, without surgery, is the preferred treatment approach to un-ruptured intracranial aneurysms. Nevertheless, unruptured aneurysms may need surgical intervention, requiring a personalized approach\[^{4}\]. The mainstay approach to managing unruptured cerebral aneurysms involves blood pressure control and smoking cessation to prevent further aneurysm development\[^{27}\]. Conversely, surgical and endovascular approaches aim to repair aneurysms.

Numerous studies in the literature have demonstrated safety and efficacy in the treatment options for intracranial aneurysms\[^{28-30}\]. There are currently several criteria that evaluate the stage, structural morphology, and severity of intracerebral aneurysms, such as the Hunt and Hess classification or Yasagril Grading Scales. However, there remain significant gaps in data examining the long-term recurrence of aneurysms that have been surgically or medically treated\[^{28-30}\]. Each modality used to treat intracerebral aneurysms individually estimates re-occurrence rates and outcomes\[^{28-30}\]. Evaluating aneurysm re-occurrence remains a highly controversial and active area of research in neurological surgery and neuroradiology.

Several criteria have been proposed to evaluate the future reoccurrence of intracranial aneurysms. Of the criteria that exist, the Raymond-Roy occlusion classification system (RROC) has shown promise. The RROC grades the occlusion of endovascularly-treated aneurysms in an angiographic classification system (Figure 2). Although initially created to assess an aneurysm’s occlusion class, the RROC has been modified to predict aneurysmal occurrence after surgical intervention, whereby Mascitelli et al. (2015) proposed their modified RROC scale (Figure 2)\[^{31,33}\]. The modified scale includes further divided class III to signify progression to occlusion\[^{31}\]. A follow-up study in 2015 validated the modified RROC, which demonstrated that specific categories of aneurysms are more likely to reoccur than others\[^{32,33}\]. A subsequent 2016 meta-analysis examining the predictiveness of the RROC on aneurysm coiling consisting of 4587 patients found that the RROC provided a considerable predictive value in reoccurrence for more severe aneurysms treated with coiling\[^{34}\].

### 3.1. Association of WEB device with recurrence and rupture of aneurysm

The recurrence and rupture of wide-neck intracranial aneurysms following treatment with the WEB device are not abundantly reported in the literature\[^{35,36}\]. Peterson and Cord (2021) are among the first to focus on the recurrent and residual aneurysms post-WEB that required treatment\[^{10}\]. Their meta-analysis included 16 studies and 901 WEB cases and found that 18.7 ± 11.5% cases of either recurrent or residual aneurysms post-initial WEB device; while 10.7 ± 11% of cases had to undergo some form of retreatment\[^{35}\]. A meta-analysis by Zhang et al. that focused on the efficacy of the WEB device in treating wide-neck intracranial aneurysms (36 studies, 1759 patients with 1749 aneurysms) found that the recanalization rate was 9% and intraoperative rupture rate was 3%\[^{36}\]. Factors leading to a higher recanalization rate were older-generation WEB devices, posterior circulation, and rupture status\[^{36}\]. Thus far, the most likely treatment for the recurrence of an aneurysm following an operation with the WEB device is stent-assisted coiling (SAC). Some other techniques used include flow diversions, additional coiling, clipping, and additional WEB devices, and all have shown success\[^{35,37}\]. Further investigation into long-term association of recurrence and rupture rates of wide-neck intracranial aneurysms post-treatment with the WEB devices would provide value to the literature. The ability to keep up with the rapid pace of WEB device innovations within the literature as it relates to the recurrence and rupture rate of each new generation can also provide value for clinicians.

### 4. Discuss how pre-clinical studies are seeking to improve the devices

The WEB device has been in clinical use for over 10 years\[^{38}\]. The first pre-clinical study evaluated the short-term performance of the WEB II device\[^{12}\]. The WEB II device was improved by adding more than a single layer of nitinol mesh. The device was implanted in two patients to assess occlusion’s short-term performance and durability. One patient had an unruptured middle cerebral artery (MCA) trifurcation aneurysm, while the other had a basilar tip aneurysm. The device was successfully implanted in both patients without complications of hemorrhage or peri or post-procedural thromboembolism. Complete aneurysm occlusion was achieved within minutes of device placement. Eight weeks later, angiography confirmed stable occlusion in both patients\[^{12}\].

A stable construct across the neck of the aneurysm is critical for achieving durable occlusion\[^{39}\]. Failure of
the WEB II device was documented in a case study of a patient who presented with regrowth of an unruptured MCA aneurysm 9 months after implantation\cite{40}. During the patient’s 6-month follow-up, the magnetic resonance imaging (MRI) showed continued progression of aneurysm neck filling, pushing the device distally. Balloon-assisted coiling was used to treat the regrown aneurysm according to standard neurointerventional approaches\cite{41,42}. Although not desired, device failure can reveal deficiencies that lead to improvement of subsequent device models.

Pre-clinical studies continue to inform the modification and development of these devices. Several changes have been made to the device since its introduction in 2011\cite{12,43}. The current devices, the WEB SLS and WEB SL model, are spheroid and cylindrical shaped devices composed of single layers of braided nitinol\cite{24}. Another change was incorporation of platinum into nitinol strands to enhance visualization in the WEB SLS EV and WEB SL models\cite{49}. In the U.S., 27 cylindrical and eight spheroid devices are available, differing in diameters and heights\cite{44}. These improvements have expanded European treatment indications to treat distal and sidewall aneurysms and wide-neck bifurcation aneurysms\cite{44,45}.

5. Discuss novel innovations for wide-neck aneurysms

Decades of research and development have been invested to make endovascular treatments the standard of care for intrasaccular aneurysms. However, treating wide-neck aneurysms can be technically challenging as they have a higher risk of recanalization\cite{46,47}. It has been demonstrated that coil embolization can successfully treat aneurysm but is limited by several factors, including neck size and the dome-to-neck ratio\cite{48-51}. In addition, the instability of coils can lead to herniation of the parent artery, and herniated coils may migrate or lead to thromboembolism and incomplete occlusion\cite{12}.

Over the past decade, a paradigm shift has occurred in the treatment of wide-neck aneurysms. A new treatment model emerged in 2011 when the FDA approved the first flow-diverting device\cite{12,44}. Conventionally, endovascular treatment involves direct intrasaccular embolization, followed by immediate protection\cite{39}. On the contrary, flow-diverting devices delay aneurysm occlusion, an approach different from the traditional treatment model. The device diverts blood flow away from the aneurysm, allowing for thrombosis to occur. Over time, endothelialization of the device takes place in the aneurysm’s parent vessel wall\cite{38,52}.

Several flow-diverting devices are under clinical trials, and the FDA has approved various devices for treating wide-neck aneurysms (Table 3)\cite{31,39,43,58}. The WEB aneurysm embolization system (MicroVention Terumo, Aliso Viejo, CA, USA) is a flow-diverting device that differs from traditional flow diverters\cite{3,5,38,39}. Rather than occupying the parent vessel’s lumen, the WEB device is intrasaccular and composed of nitinol-based braided wire\cite{38}. The device is not limited by the use of dual antiplatelet therapy and can be used to treat both ruptured and unruptured aneurysms\cite{38,39}.

6. Discussion

The WEB device is unique in its innovation and indications, yet further research and development is warranted in several areas. At present, the proposed grading scale, the RROC, with its modifications by Mascielli et al., should be additionally classified based on the treatment used\cite{31}. It would be advantageous to assess the rate of complications with WEB devices versus stents or clipping. Pre-clinical studies are crucial to advancing the WEB device to its fullest potential. Accurate WEB device size selection is imperative to a safe and effective procedure; automated volumetric software and digital subtraction angiography (DSA) are actively being studied to improve this aspect of the device\cite{60}. The need for guidelines for successful implantation could
also prove beneficial as it may decrease waste and provide efficiency in practice. As novel innovations for wide-neck aneurysms continue to be investigated, it is essential to continue to evaluate the effectiveness and indications of the WEB embolization device.

In recent years, novel advancements in neurological surgery, such as the WEB device, have broadened surgical and endovascular aneurysm management\[30\]. The WEB device can treat anatomically complex bifurcation aneurysms, and the treatment is safer and more effective than the traditional approach. Conventionally, the placement of stent-assisted coiling would require antiplatelet therapy, which has the risk of hemorrhagic complications\[24\]. Some of the advantages of the WEB device treatment are that it does not require dual antiplatelet therapy, and the procedure can be performed within a shorter timeframe, resulting in improved cost-effectiveness and decreased anesthesia exposure\[61\]. The WEB device is currently only FDA approved to treat wide-neck bifurcation aneurysms\[24\]; however, several ongoing clinical trials are investigating the device's suitability in various intracranial aneurysms. As the results from these clinical studies emerge, the device and its applications will likely evolve.

Recently, a multicenter study evaluated the use of the WEB device in both sidewall and bifurcation intracranial aneurysms\[62\]. When 91 pairs of aneurysms were compared, outcomes were not significantly different between the two groups. In particular occlusion status, device deployment success and complication rates were not significantly different — indicating that the WEB device may be used off-label for sidewall aneurysms. A small cohort study of 15 patients was also performed to evaluate the use of the WEB device in posterior communicating artery (PComA) aneurysms\[97\]. The authors reported complete and adequate occlusion. Retreatment was required for two patients and no intraoperative ruptures occurred. Considering the common occurrence of aneurysms in the PComA and their rates of rupture, the off-label use of the WEB device is a promising alternative for PComA aneurysms.

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The authors declare that they have no competing interests.

### Author contributions
Conceptualization: Brandon Lucke-Wold, Ashley M. Carter, Bethsabe Romero
Writing – original draft: All authors
Writing – review & editing: Brandon Lucke-Wold, Ashley M. Carter, Bethsabe Romero, Simran Phuyal

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### Consent for publication
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### Availability of data
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### References
   https://doi.org/10.1136/neurintsurg-2017-013448

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**Table 3. Wide-neck aneurysm treatment devices with FDA approval**

<table>
<thead>
<tr>
<th>Year of approval</th>
<th>Wide-neck aneurysm treatment devices</th>
<th>Manufacturer</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>Barrel Vascular Reconstruction Device</td>
<td>Reverse Medical Corporation (Irvine, CA, USA)</td>
<td>[56,74]</td>
</tr>
<tr>
<td>2019</td>
<td>Comaneci Device</td>
<td>Rapid Medical, (Yokneam, Israel)</td>
<td>[55,56]</td>
</tr>
<tr>
<td>2015</td>
<td>eCLIPS Device</td>
<td>EVASC Neurovascular Enterprises (Vancouver, BC, Canada)</td>
<td>[54,56]</td>
</tr>
<tr>
<td>2017</td>
<td>PulseRider Aneurysm Neck Reconstruction Device</td>
<td>Pulsar Vascular Inc., (Los Gatos, CA, USA)</td>
<td>[53,56]</td>
</tr>
<tr>
<td>2011</td>
<td>Woven EndoBridge</td>
<td>MicroVention Terumo (Aliso Viejo, CA, USA)</td>
<td>[12,24,43,56]</td>
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</table>

All treatment devices names are as listed. Abbreviation: FDA: Food and drug administration.


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