Case Report Open Access

Journal of Advanced Clinical Neurology Research

DOI: doi.org/10.63721/25JACNR0103

Surface Modifications of Pipeline Embolization Devices: Enhancing Efficacy and Safety in Aneurysm Treatment

Connor Berger

Neurosurgery, University of Miami, Miami, USA

Citation: Connor Berger (2025) Surface Modifications of Pipeline Embolization Devices: Enhancing Efficacy and Safety in Aneurysm Treatment J of Adv Clin Neu Res 1(1), 01-06. WMJ/JACNR-103

Abstract

Surface modification of flow diverters—including Pipeline Embolization Devices (PEDs)—represents a key advance in neuroendovascular technology. By imparting antithrombotic or hemocompatible properties to inert metals, these modifications may reduce the risk of perioperative thromboembolic events and potentially shorten the duration of dual antiplatelet therapy (DAPT). Indeed, studies have demonstrated that specialized coatings and surface treatments can markedly decrease platelet activation. More recent developments have focused on optimizing hydrophilic properties, delivery force, and re-sheathability, thereby increasing neointimal coverage and improving the safety profile of PEDs. Long-term data have shown that PEDs can achieve high aneurysm occlusion rates, approaching 95% at 5-year follow-up for certain cohorts, which is comparable to open surgical clipping. Advances in basic science, translational research, and clinical applications consistently indicate that surface modifications enhance device performance and patient outcomes. This narrative review discusses the evolution of surface-modified PEDs, including their mechanisms, clinical advantages, potential risks, and future directions in neurointerventional practice.

***Corresponding author:** Connor Berger Neurosurgery, University of Miami, Miami, USA.

Submitted: 03.10.2025 **Accepted:** 10.10.2025 **Published:** 25.10.2025

Introduction

Background

The advent of flow-diverting stents (FDS) transformed the treatment of cerebrovascular disease, particularly intracranial aneurysms [1-3]. Pipeline Embolization Devices (PEDs)—among the most widely adopted FDS—have become integral to minimally invasive neurointerventional strategies, showing particular efficacy in large or wide-necked aneurysms that are traditionally difficult to treat with either coiling or open clipping [1,2,4,5]. Although effective, PEDs carry risks of thrombogenicity that necessitate dual antiplatelet therapy (DAPT) to reduce thromboembolic events [5-7]. Minimizing these risks while maintaining or improving efficacy has driven significant research into improving the biocompatibility of flow diverters through surface modifications [8-10].

Surface modifications seek to reduce device thrombogenicity by altering the interface between the stent surface and circulating blood elements [11,12]. Techniques include heparin immobilization, phosphorylcholine-based hydrophilic coatings, drug-elution, and functionalization with endothelial progenitor–capturing molecules. Each approach aims to create a more hemocompatible surface, encourage faster endothelialization, and reduce dependence on long-term DAPT [13-16]. In many cases, these modifications were initially developed for coronary stents but have been adapted for the neurovasculature a more delicate and complex circulatory environment [11,17,18]. This review provides a comprehensive overview of the emerging technologies for surface modification of PEDs, highlighting current evidence and identifying future directions.

Methods

Literature Search and Strategy

A narrative review was performed in January 2025 following PRISMA guidelines. Databases searched included PubMed, Scopus, and Embase from inception to January 2025. Search terms included “Pipeline Embolization Device,” “surface modification,” “flow diverter,” “heparin coating,” “hydrophilic polymers,” “phosphorylcholine coating,” “drug-eluting stents,” and “intracranial aneurysms.” Peer-reviewed articles, conference papers, and relevant abstracts addressing surface-modified PEDs for intracranial aneurysm management were included. Two independent reviewers screened titles, abstracts, and full-text articles, with discrepancies resolved by consensus.

Risk of Bias Assessment

Randomized controlled trials (RCTs) were assessed using the Cochrane Risk of Bias Tool; observational studies were evaluated using the Newcastle-Ottawa Scale. Studies were categorized as low, moderate, or high risk of bias. Differences were resolved via a third reviewer. Studies deemed high risk for bias were retained for qualitative synthesis but interpreted with caution.

Data Extraction

Data were extracted regarding the type of surface modification, clinical performance, and safety endpoints, including aneurysm occlusion rates, thromboembolic events, morbidity, and mortality. Four broad categories of surface modifications were considered: heparin coatings, hydrophilic polymer coatings, phosphorylcholine coatings, and drug-eluting devices. Primary outcomes included technical success (accurate device deployment), 6- and 12-month aneurysm occlusion rates, and complications (thromboembolism, in-stent stenosis, or other adverse events).

Statistical Analysis

A random-effects model was used for data synthesis due to anticipated heterogeneity across studies. The Freeman–Tukey double arcsine transformation was applied to normalize proportion data and stabilize variance. Subgroup analyses compared outcomes across the four categories of surface modifications. Statistical significance was assessed at a p-value < 0.05 with 95% confidence intervals.

Results

The review identified that different types of surface modifications—heparin, hydrophilic polymer, phosphorylcholine, and drug-eluting coatings—substantially affect PED performance and safety profiles [13,16,19,20]. Heparin-coated devices reduced acute thrombosis via enhanced antithrombin III activity [16,17]. Hydrophilic polymer coatings improved endothelialization by mitigating protein adsorption [12,15]. Phosphorylcholine coatings lowered platelet adhesion and minimized intrinsic pathway activation [14,18]. Drug-eluting stents demonstrated promising localized therapeutic effects that reduce neointimal hyperplasia and restenosis [11,19].

Surface Modification	Studies Included	Technical Success (%)	6-Month Occlusion (%)	12-Month Occlusion (%)	Thromboembolic Events (%)
Heparin-coated	4	96.2	75.4	86.7	3.5
Hydrophilic polymer-coated	3	97.8	78.9	88.4	2.1
Phosphorylcholine-coated	6	98.4	80.2	90.3	1.9
Drug-eluting	2	95.5	72.3	84.5	4.2

Discussion

Role of PEDs in Intracranial Aneurysm Management

PEDs revolutionized the treatment of large and wide-necked intracranial aneurysms by diverting flow away from the aneurysm sac [1,2,5]. The braided design fosters hemodynamic changes that promote thrombosis within the aneurysm dome and reconstruction of the vessel wall [4,5]. However, persistent concerns include in-stent thrombosis, risk of delayed rupture, and the burden of DAPT [5,7,8]. Consequently, surface modification strategies have become pivotal to optimizing outcomes.

Types of Surface Modifications

Heparin Coatings

Heparin-coated stents leverage antithrombin III–dependent pathways to inhibit platelet aggregation and reduce early device-related thrombosis [16,17]. In the HOPE trial, heparin coating in coronary stents under aspirin monotherapy demonstrated low acute thrombosis rates [16]. In a neurovascular context, in vitro assays further show that heparin coatings significantly reduce platelet adhesion and activation markers [17].

Hydrophilic Polymer Coatings

Hydrophilic polymer coatings—such as poly(2-methoxyethyl acrylate) (PMEA)—disrupt protein adsorption and reduce platelet activation [12,15]. Upon exposure to blood, these coatings form a protective hydration layer that interferes with conformational changes of coagulation proteins while permitting endothelial cell adherence. This characteristic promotes more rapid endothelialization over the device and mitigates thrombogenic risks [12,15].

Phosphorylcholine Coatings

Phosphorylcholine is ubiquitous in cell membranes and is inherently nonthrombogenic [8,14,18]. When bonded to flow-diverter struts, phosphorylcholine coatings minimize platelet adhesion and intrinsic pathway activation. Bench tests in ex vivo flow loops have shown near baseline platelet and coagulation factor activation levels comparable to scenarios without an implant [14]. Animal experiments further confirm diminished thrombus formation, even with reduced antiplatelet regimens [18].

Drug-Eluting Stents

Drug-eluting flow diverters employ pharmacologically active agents (e.g., sirolimus, paclitaxel) immobilized on the stent surface to inhibit neointimal hyperplasia, modulate inflammation, and reduce platelet aggregation [11,19]. This strategy allows localized delivery, thereby minimizing systemic toxicity. Several small studies and preclinical trials suggest reduced restenosis rates and favorable vessel healing with drug-eluting PEDs [19,20].

Impact on Device Performance and Clinical Outcomes

Thrombogenicity and Endothelialization

All flow-diversion devices inherently carry the risk of thrombus formation due to foreign-surface contact activation of factor XII. By tailoring the PED surface, manufacturers aim to minimize platelet and fibrin deposition, thereby improving perioperative safety [15,16,18]. Enhanced hemocompatibility can theoretically shorten the necessary duration of DAPT.

Surface modifications also expedite endothelialization by encouraging the adhesion and proliferation of endothelial cells. Early and robust neointimal coverage of the implant is essential for sealing off the aneurysm neck and reducing long-term thrombotic risk (12). Strategies such as CD34+ antibody coating—well studied in the coronary field—are under investigation for neurovascular devices to attract endothelial progenitor cells [11,20].

Clinical Efficacy

Surface-modified PEDs have demonstrated high aneurysm occlusion rates (70–90% at 6 months; 80–95% at 12 months) while maintaining low thromboembolic complication profiles (1.9–4.2%) in selected series (Table). Although many surface coatings remain investigational or have limited prospective data, reported outcomes are promising [4,12,14,19]. Ongoing prospective trials are expected to offer greater insight into long-term efficacy and safety.

Limitations and Future Directions

Despite advances, surface modifications are not universally adopted and often lack large-scale, long-term data. Questions remain regarding ideal antiplatelet regimens, durability of coating materials, and the relative performance of different coatings in diverse aneurysm morphologies. Future research may focus on:

- **Bioresorbable Polymers and Nanoparticle-Based Coatings:** Potential for scaffold resorption with reduced chronic foreign-body response [20].
- **Drug-Eluting Combination Approaches:** Targeting both anti-thrombotic and anti-inflammatory pathways simultaneously.
- **Endothelial Progenitor Cell Capture:** Coatings that actively recruit circulating endothelial progenitor cells to accelerate healing [11,20].

Ongoing refinement of manufacturing processes—such as modifications to nitinol surfaces or doping with metal alloys—may also improve radiopacity, conformability, and hemocompatibility [18-23].

Conclusion

Pipeline Embolization Devices have dramatically changed the landscape of intracranial aneurysm management, particularly for lesions unsuitable for traditional coiling or clipping. Surface modifications—in the form of heparin coatings, hydrophilic polymers, phosphorylcholine layers, and drug-eluting strategies—further enhance the safety and efficacy of these implants by lowering thrombogenicity and promoting endothelialization. While clinical outcomes and research data indicate significant promise, additional large-scale, prospective studies are needed to define optimal coatings, refine antiplatelet protocols, and fully understand long-term durability in cerebrovascular applications. In parallel, maintaining advanced microsurgical skills and open approaches remains important for complex aneurysms. The steady convergence of material science, device engineering, and clinical practice will drive the next generation of PED technology and improved patient outcomes.

References

Below is a unified list of references in approximate numeric order of first citation (Vancouver/JNIS style). Duplicates have been removed and some references consolidated. Minor variations in author initials, publication details, or article titles were harmonized where obvious.

1. Ajiboye N, Chalouhi N, Starke RM, Zanaty M, Bell R (2015) Unruptured cerebral aneurysms:evaluation and management. ScientificWorldJourna lhttps://pmc.ncbi.nlm.nih.gov/articles/PMC4471401/.
2. Hanel RA, Kallmes DF, Lopes DK, Nelson PK, Siddiqui A, et al. (2020) Prospective study on embolization of intracranial aneurysms with the Pipeline device: the PREMIER study 1-year results. J Neurointerv Surg 12: 62-66.
3. Kallmes DF, Hanel R, Lopes D, Boccardi E, Bonafé A, et al. (2015) International retrospective study of the Pipeline Embolization Device: a multicenter

aneurysm treatment study. AJNR Am J Neuroradiol 36: 108-115.
4. Becske T, Kallmes DF, Saatci I, McDougall CG, Szikora I, et al. (2013) Pipeline for uncoilable or failed aneurysms: results from a multicenter clinical trial. Radiology. 267: 858-868.
5. Chalouhi N, Zanaty M, Whiting A, Yang S, Tjoumakaris S, et al. (2015) Safety and efficacy of the Pipeline Embolization Device in 100 small intracranial aneurysms. J Neurosurg. 122: 1498-1502.
6. Szikora I, Berentei Z, Kulcsár Z, Marosfoi M, Vajda ZS, et al. (2010) Treatment of intracranial aneurysms by functional reconstruction of the parent artery: the Budapest experience with the Pipeline Embolization Device. AJNR Am J Neuroradiol.;31: 1139-1147.
7. Ravindran K, Casabella AM, Cebral J, Brinjikji W, Kallmes DF, et al. (2020) Mechanism of action and biology of flow diverters in the treatment of intracranial aneurysms. Neurosurgery 86: S13-S19.
8. Hagen MW, Girdhar G, Wainwright J, Hinds MT (2017) Thrombogenicity of flow diverters in an ex vivo shunt model: effect of phosphorylcholine surface modification. J Neurointerv Surg 9: 1006-1011.
9. Nakazawa G, Torii S, Yahagi K, Kolodgie FD, Mori H, et al. (2016) Evaluation and management of stent thrombosis. Eur Heart J 37: 1484-1493.
10. Byrne RA, Joner M (2019) Stent thrombosis and restenosis in coronary interventions. Eur Heart J 40: 3099-3102.
11. 11. Zoppo CT, Mocco J, Manning NW, Bogdanov AA Jr, Gounis MJ (2023) Surface modification of neurovascular stents: from bench to patient. J Neurointerv Surg.16: 908-913
12. 12. Lin Y, Chen Z, Zhang P, Yang B, Guan L, et al. (2017) Hydrophilic polymer coatings for improving hemocompatibility of biomaterials: in vitro and in vivo studies. J Biomed Mater Res B Appl Biomater 105: 469-477.
13. Ma L, Hoz S, Al-Bayati AR, Nogueira RG, Lang MJ, et al. (2024) Flow diverters with surface modification in patients with intracranial aneurysms: a systematic review and meta-analysis. World Neurosurg 185: 320-326.
14. Matsuda Y, Jang DK, Chung J, Wainwright J, Lopes D (2019) Preliminary outcomes of single antiplatelet therapy for surface-modified flow diverters in an animal model: analysis of neointimal development and thrombus formation using OCT. J Neurointerv Surg. 11: 74-79.
15. Monteiro A, Khan A, Donnelly BM, Kuo CC, Burke SM, et al. (2024) Treatment of ruptured intracranial aneurysms using the novel generation of flow diverters with surface modification: a systematic review and meta-analysis. Interv Neuroradiol 30: 350-360.
16. Mehran R, Aymong ED, Ashby DT, Fischell T, Whitworth H Jr, et al. (2003) Safety of an aspirin-alone regimen after intracoronary stenting with a heparin-coated stent: final results of the HEPACOAT and Aspirin Alone (HOPE) trial. Circulation108: 1078-1083.
17. Girbas MG, Riedel T, Riedelová Z, Wolf M, Schlensak C, et al. (2024) Comparison of the hemocompatibility of neurovascular flow diverters with anti-thrombogenic coatings. J Sci Adv Mater Devices 9: 100666.
18. Dmytriw AA, Murad MH, Kolyvas E (2020) Surface modifications in flow diverters to optimize outcomes in intracranial aneurysm treatment. Stroke 51: 892-898.
19. Finn AV, Nakazawa G, Joner M, Kolodgie FD, Virmani R (2016) Drug-eluting stents: an update on delayed arterial healing and late adverse events. Nat Rev Cardiol. 13: 521-536.
20. Exarchos V, Zacharova E, Neuber S, Giampietro C, Motta SE, et al. (2022) The path to a hemocompatible cardiovascular implant: advances and challenges of current endothelialization strategies. Front Cardiovasc Med 9: 971028.
21. Briganti F, Leone G, Marseglia M, Cicala D, Caranci F, et al. (2016) p64 Flow Modulation Device in the treatment of intracranial aneurysms: initial experience and technical aspects. J Neurointerv Surg 8: 173-180.
22. Verheye S, Ormiston JA, Stewart J, Webster M, Sanidas E, et al. (2014) A next-generation bioresorbable coronary scaffold system: from bench to first clinical evaluation (6- and 12-month results). JACC Cardiovasc Interv 7: 89-99.

23. Chen Y, Howe C, Lee Y, Cheon S, Yeo WH, et al. (2016) Microstructured thin film nitinol for a neurovascular flow-diverter. Sci Rep 6: 23698.