


ENHANCING INTRASACCULAR DEVICES WITH **CAMOUFLAGE™** COATING



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1 Introduction

Intracascular flow-disruption devices are pivotal in the endovascular management of intracranial aneurysms – localized, pathological dilations of cerebral arteries resulting from vessel wall weakening. Aneurysms commonly develop at sites of turbulent blood flow, such as arterial bifurcations and present a risk of rupture. Intracascular devices are employed for the treatment of both ruptured and unruptured saccular aneurysms, including wide-neck bifurcation and side-wall configurations where traditional interventions may be limited. While these devices are designed to promote intra-aneurysmal thrombosis and exclude the aneurysm from circulation, effectively sealing it off, their long-term efficacy may be compromised by complications such as unintended thrombosis, inflammation and delayed endothelialisation.

Smart Reactors Camouflage™ coating technology offers an innovative hemocompatible solution to address these challenges. By integrating a synthetic polymer matrix with a non-inflammatory proteinaceous based layer, Camouflage™ reduces the risk of inflammation, minimizes thrombogenicity and facilitates accelerated endothelial healing. This advanced surface coating enhances the hemocompatibility and integration of intracascular devices, supporting safer aneurysm treatment.

This paper examines the crucial role of intracascular flow disruption devices in the treatment of intracranial aneurysms, outlines the limitations of current intracascular devices and demonstrates how Camouflage™ coating technology offers a novel surface solution that improves overall intracascular device performance.

1.1 Understanding Intracranial Aneurysms

Intracranial aneurysms are clinically significant vascular abnormalities, impacting approximately 3-5% of the U.S. [1]. Aneurysms are characterized by a bulge or ballooning of the arterial wall caused by structural weakening. Although aneurysms can form throughout the vascular system, they most frequently occur within intracranial circulation particularly at the Circle of Willis, where they pose a substantial risk of rupture and life-threatening subarachnoid hemorrhagic stroke. This anastomotic ring of arteries is located at the base of the brain within the subarachnoid space, encircling the optic chiasm infundibulum and hypothalamus (Fig. 1). It provides a redundant collateral circulation pathway between the anterior and posterior cerebral circulations. This configuration allows for cerebral

perfusion to be preserved in the event of proximal vessel stenosis or occlusion. Anteriorly, it is bounded by the anterior communicating artery (Acom) approximately 0.3-3mm in length, which connects to the A1 segments of the bilateral anterior cerebral arteries (ACA). Intracranial aneurysms most frequently arise within the anterior circulation, at common sites including the internal carotid artery and posterior communication artery (ICA-PCom) junction, the ACom and the middle cerebral artery (MCA) [2]. In the posterior circulation, aneurysms typically occur basilar artery bifurcation or at the vertebral artery-posterior inferior artery (VA-PICA). The posterior communicating arteries (PCom), which connect the internal carotid arteries to the ipsilateral posterior cerebral arteries (PCA), complete the circle posteriorly and are relevant to both anterior and posterior circulation pathology.

Circle of Willis

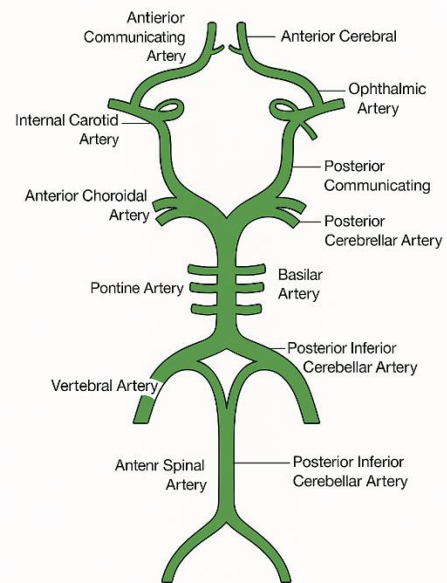


Fig 1: Posterior Spinal Artery Circle of Willis

Based on their morphology, intracranial aneurysms are commonly categorized as saccular, fusiform and pseudoaneurysms. Saccular aneurysms, the most common type, have a sac-like shape with a defined neck and are often found at arterial bifurcations. Fusiform aneurysms, a less common type involve a circumferential dilation of the vessel without a distinct neck and are more common in the posterior circulation (Fig. 2). Pseudoaneurysms result from a complete disruption of the arterial wall, with blood contained by surrounding tissues rather than the vessel itself. These are often linked to trauma, infection, or surgical intervention (Fig. 2). A

particularly challenging subtype is the wide neck-aneurysm, typically defined by having a neck diameter of ≥ 4 mm or a dome-to-neck ratio of < 2.0 . These morphological features can complicate endovascular treatment by increasing the risk of coil prolapse into the parent vessel. Wide-neck bifurcation aneurysms (WNBAs), which arise at vessel branch points such as the basilar apex, internal carotid artery terminus, middle cerebral artery bifurcation and the anterior communicating artery (A1-2 junction) present additional challenges [3]. Their complex geometry and wide-neck configuration often limit the efficacy of both surgical clipping and conventional endovascular approaches.

Aneurysms present a significant risk of thrombosis at their neck due to altered hemodynamics within the aneurysm sac, where stagnant blood flow promotes clot formation. Factors such as aneurysm size and configuration influence the likelihood of thrombosis occurring. Larger aneurysms or those with a narrow neck are especially prone to thrombus development. Endothelization across the aneurysm neck plays a crucial role in ensuring durable aneurysm occlusion, preventing recurrence, stabilizing the device, reducing thrombotic risk and facilitating vessel healing.

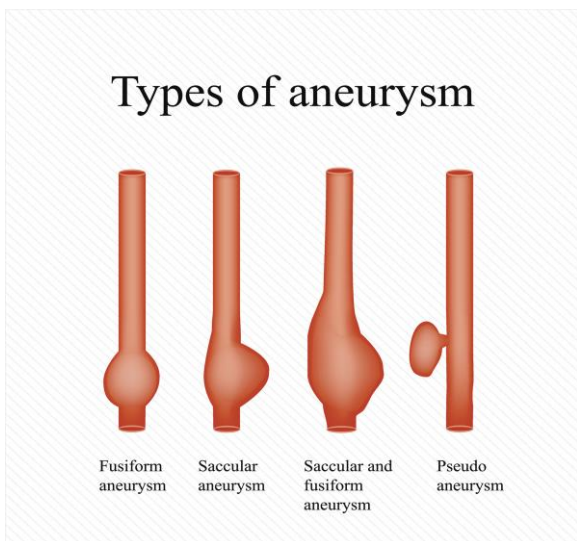


Fig 2: Different Classifications of Aneurysms

1.2 Key Design Features of Current Intracascular Flow Disruption Devices

Intracascular flow disruption devices designed for the treatment of intracranial aneurysms, are engineered with several critical features to optimize aneurysm occlusion while preserving physiological blood flow within the parent artery. These devices typically consist of a flexible, mesh-like structure that

promotes intracascular thrombosis by disrupting intra-aneurysmal blood flow, thereby enabling progressive clot formation and aneurysm exclusion. Radiopaque markers are incorporated to enable precise visualization and deployment under fluoroscopy or angiographic guidance. Their low-profile configuration and self-expanding designs allow for navigability through complex cerebrovascular anatomy and effective deployment at bifurcation points. Notable examples of intracascular flow disruption devices include the Woven Endobridge (WEB) device by Terumo, featuring a braided nitinol mesh designed to assume a stable, globular shape within the aneurysm sac (Fig. 3) [4]. The Artisse intracascular device by Medtronic features a braided, dual-layer mesh construction composed of high-density platinum core and nitinol drawn-filled tubing wires. This design allows the device to conform to the unique shape and neck of the aneurysm, ensuring secure placement. The devices' structure enhances stability with the aneurysm sac, promoting effective flow disruption.

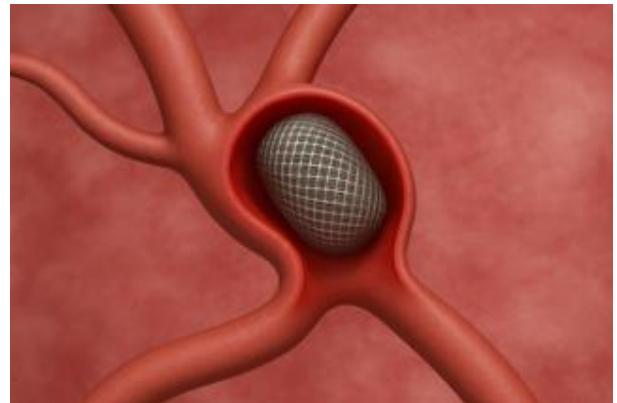


Fig 3: WEB device inserted into an aneurysm sac.

1.3 Historical Evolution of Aneurysm Treatment

The treatment of intracranial aneurysms has evolved substantially over the past century, progressing from open surgical approaches to advancements in diagnostic imaging, minimally invasive endovascular therapies and advanced biocompatible coatings. The first open surgical treatment of an intracranial aneurysm was reported in 1931 by Norman Dott who employed a wrapping technique to reinforce the aneurysm wall. This was followed in 1937 by Walter Dandy's introduction of the aneurysm clip [5]. In 1991, Guido Guglielmi revolutionized aneurysm treatment, with the first successful use of electrolytically detachable platinum coils for the endovascular treatment of cerebral aneurysms. Acknowledging the limitations of traditional methods such as coil compaction, recurrence and incomplete

aneurysm occlusion, attention increasingly turned towards the treatment of aneurysms by the sac directly. This shift led to the emergence of intracranial flow disruption devices with the WEB device marking a pivotal advancement in aneurysm treatment in 2010. Intracranial devices such as WEB are deployed within the aneurysm sac itself and redirect blood flow away from the sac thereby promoting rapid thrombosis. In contrast, stent-like flow diverters which have also gained prominence in the treatment of intracranial aneurysms in recent years direct blood flow through a bridge at the neck of the aneurysm thereby slowing intra-aneurysmal flow causing stasis, thrombosis and triggering an inflammatory response. While intracranial devices are particularly suited for bifurcation aneurysms and ruptured cases, stent-like flow diverters are often preferred for wide-neck or fusiform aneurysm along sidewall segments of cerebral arteries.

However, challenges such as incomplete occlusion, thrombosis and delayed healing have driven innovation beyond conventional mechanical methods. This has spurred the development of advanced surface modifications achieving durable and long-term aneurysm occlusion amongst intracranial devices. Camouflage™ coating technology presents a promising solution to address these issues thereby enhancing hemocompatibility and intracranial device integration, ultimately improving long-term durability and reducing patient complications.

2 Current Treatment Modalities for Intracranial Aneurysms

Current therapeutic options for intracranial aneurysms encompass a variety of surgical and endovascular techniques, selected based on the aneurysm size, shape, location and rupture status. The primary goal of these interventions is to isolate the aneurysm from circulation and prevent potentially fatal rupture which can lead to severe hemorrhaging and neurological damage. Microsurgical clipping remains a gold-standard surgical method, involving the placement of a clip at the aneurysm neck to exclude it from blood flow. This technique is more commonly used for aneurysms that are accessible via a direct surgical approach.

The wrapping and clipping technique applied to ruptured aneurysms occurs where a lesion is wrapped with tissue or absorbable material to reconstruct the integrity of the vessel wall before clipping [5]. Endovascular techniques, which are less invasive, have advanced significantly and are now preferred for many aneurysms. These options include

simple coiling, balloon- or stent-assisted coiling and intracranial flow disruption devices. Simple coiling involves advancing a microcatheter to the aneurysm dome, where detachable platinum is placed and packed. Balloon-assisted and stent-assisted coiling methods utilize one or multiple non-detachable balloons or stents to block the aneurysmal neck during coil placement [6].

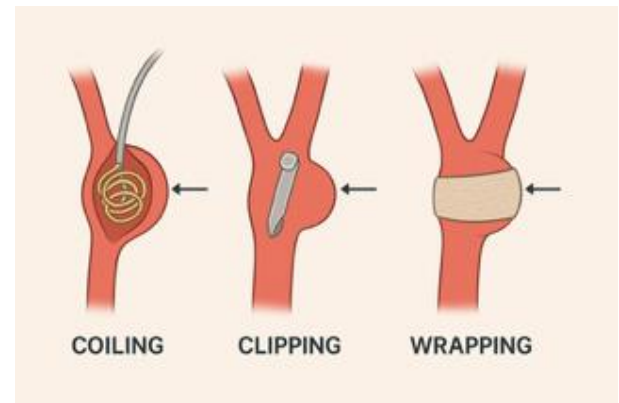


Fig 4: Image of Coiling, Clipping and Wrapping technique for aneurysm treatment

While these various current approaches in aneurysm treatment have been successful, limitations have driven interest in how advanced coatings such as Camouflage™ may enhance their overall performance.

2.1 Limitations of Current Intracranial Devices

While current intracranial devices offer significant clinical advantages, they still present notable limitations. Incomplete aneurysm occlusion remains a major concern, particularly in wide-neck aneurysms. Some devices may fail to conform optimally to irregular aneurysm geometries, leading to suboptimal wall apposition and residual blood flow. Additionally, the lack of biologically active surfaces limits their ability to promote endothelial healing and increases the risk of thromboembolic complications. As intracranial technologies continue to advance, there is an increasing interest in the application of surface coatings to address these challenges. Such limitations of intracranial devices have driven innovation in overall device design and surface modification technologies. To improve patient outcomes, next generation intracranial devices must overcome both mechanical and biological challenges. Smart Reactors Camouflage™ coating represents a hemocompatible solution that minimizes thrombogenicity on the portion of the intracranial device exposed to the parent artery, supports endothelial healing and reduces

inflammation. By integrating synthetic polymers with non-inflammatory proteins, Camouflage™ creates a biologically inert surface that enhances the performance of intracascular devices.

3 Camouflage™ Coating Technology: A Surface Engineered Solution

Camouflage™ coating technology offers a transformative solution to the limitations of current intracascular devices. By providing a biocompatible surface that reduces thrombogenicity and promotes rapid endothelialization, Camouflage™ enhances device integration within the vascular environment. It is designed to reduce the occurrence of thromboembolic events and accelerate the natural healing process offering a significant advancement over conventional intracascular flow disruption devices.

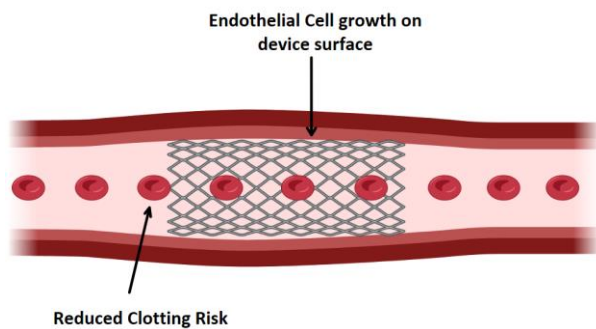


Fig5: Camouflage™ Coating over implant indicating endothelial cell growth on the device surface and reduced risk of blood clotting

3.1 The Mechanism of Camouflage™ Coating

Camouflage™ is a cutting-edge coating technology specifically tailored for blood-contacting medical devices. The coating technology effectively conceals the surface of the device from the surrounding circulating blood. This layer “camouflages” the device, reducing its interaction with blood components such as platelets which could initiate clot formation and trigger an inflammatory response. By providing a smooth, non-thrombogenic surface, Camouflage™ minimizes platelet adhesion and activation while promoting the proliferation and integration of endothelial cells.

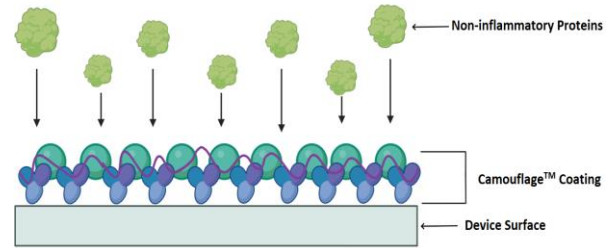


Fig 6: Camouflage™ Mechanism of Action

3.2 Camouflage™ Key Properties

Accelerated Endothelialization – The integration of Camouflage™ addresses medical device complications by enhancing endothelialization. This is accomplished by facilitating the adhesion of the patients’ own endothelial cells to the coated surface, providing a stable substrate for cellular attachment. Once endothelial cells adhere to the Camouflage™ coating, it stimulates their proliferation and migration, supporting the maturation of a functional endothelial layer.

Hemocompatibility – Devices that come into contact with blood must function seamlessly, without triggering complications like blood clotting. Camouflage™ is designed to dramatically improve the hemocompatibility of medical devices. By selectively adsorbing non-inflammatory proteins, the coating reduces platelet activation and prevents the initiation of the coagulation cascade, significantly lowering the risk of thrombosis.

Anti-Inflammatory – Camouflage™ mitigates immune system activation by effectively concealing the device surface from inflammatory cells. By reducing leukocyte adhesion and attenuating inflammatory responses, Camouflage™ plays a crucial role in maintaining vascular stability and preventing complications associated with chronic inflammation and restenosis. This targeted regulation of immune responses not only enhances healing but also minimizes the risk of adverse outcomes.

Heparin-Free – Camouflage™ is a passive, non-heparin, coating that employs a gentle water-based chemistry. It forms a robust bond with all medical-grade materials without the requirement for UV or thermal crosslinking ensuring seamless integration across a wide range of devices. The heparin-free nature of Camouflage™ eliminates the risk of heparin-induced thrombocytopenia (HIT).

3.3 Hemocompatibility

Activation of the clotting system was assessed by measuring thrombin–antithrombin III complex (TAT) in Smart Reactors Camouflage™ Coating. Compared to uncoated nitinol, Camouflage™ coating on nitinol material significantly reduced TAT levels, indicating minimal clotting activity and demonstrating its superior effectiveness in preventing thrombus formation (Fig. 7).

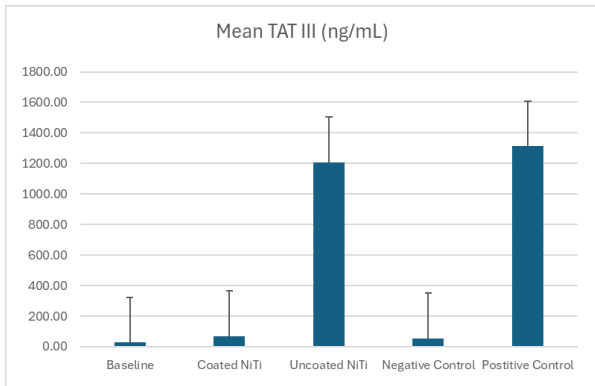


Fig 7: Mean TAT levels in Smart Reactors Camouflage™ coated nitinol

Fibrinopeptide A (FpA) was also measured as a direct indicator of thrombin activity. Nitinol coated with Smart Reactors Camouflage™ coating exhibited FpA levels comparable to the negative control (empty circuit) indicating reduced thrombin activation. In contrast, uncoated nitinol showed elevated FpA concentrations, indicating greater thrombin activity (Fig. 8).

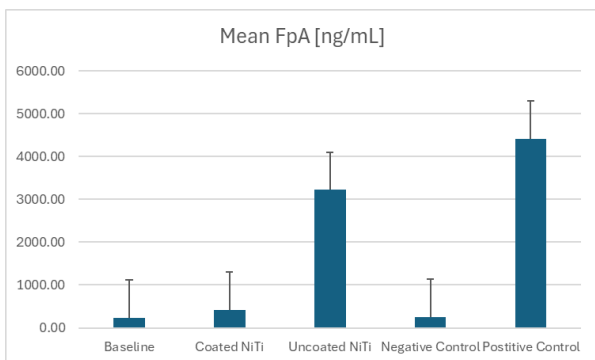


Fig 8: Mean FpA levels in Smart Reactors Camouflage™ coated nitinol

Endothelialization

Camouflage™ coating applied to nitinol surfaces significantly enhances endothelial cell proliferation when compared to uncoated nitinol. This effectively

reduces the duration of device exposure to circulating blood. After a 29-hour incubation period, human umbilical vein endothelial cells (HUVECs) exhibited a markedly higher uptake on Camouflage-coated nitinol surfaces than on uncoated counterparts (Fig. 9), indicating improved cellular compatibility and potential for accelerated endothelialization.

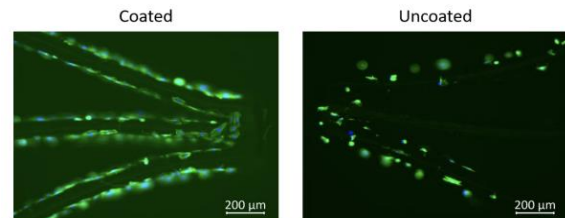


Fig 9: Fluorescence microscopy images of coated and uncoated stents after 29hr of static incubation

3.4 Anti-Inflammatory

Camouflage™ coating minimizes the interaction with white blood cells and reduces the inflammatory response. Camouflage™ exhibits minimal white blood cell (WBC) adhesion, effectively preserving overall WBC levels. In contrast, coatings such as Phosphoryl choline (PC) result in a significant reduction in WBC levels due to excessive cell attachment (Fig. 10). The lower levels of PMN elastase observed with Smart Reactors Camouflage™ indicate a decreased likelihood of eliciting inflammatory responses when compared to PC and Albumin coatings (Fig. 11).

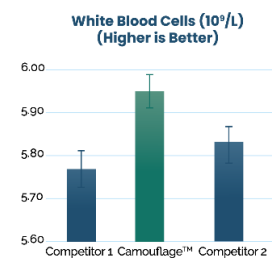


Fig 10: White Blood Cell Levels

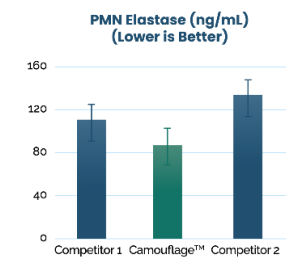


Fig 11: PMN Elastase Levels

4 Animal Model Evaluation

This preclinical study was conducted to assess the safety and endothelialization performance of Camouflage™ -coated nitinol stents compared to uncoated control stents using a rabbit carotid artery model. Rabbits were chosen for their anatomically suitable vessel size and widespread acceptance in vascular implant research. This model offers translational relevance for early-phase assessment of vascular implant devices in-vivo. Gross inspection of the stented vessel segments revealed clear differences in tissue coverage between

Camouflage™ -coated and uncoated stents at the acute time point. At 24 hours, the coated stent exhibited early tissue deposition along the struts indicating a more rapid healing response. In contrast, the uncoated stent remained largely bare, with minimal visible surface coverage. Notably, no thrombus formation was observed on either device (Fig. 12).

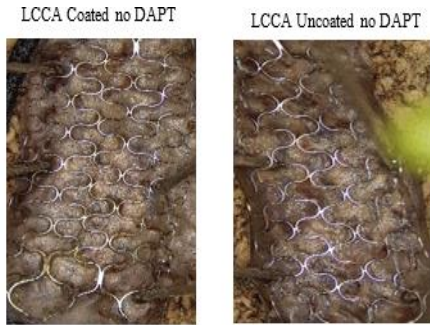


Fig 12: Gross Inspection of Stents Explanted 24 Hours Post-Implantation

By 14 days, all stents—coated and uncoated, with or without Dual Antiplatelet Therapy (DAPT) exhibited clear endothelialization, with no thrombus formation or abnormalities. Notably, stents implanted under DAPT conditions demonstrated slightly greater endothelial coverage than non-DAPT, regardless of coating (Fig.13 &14).

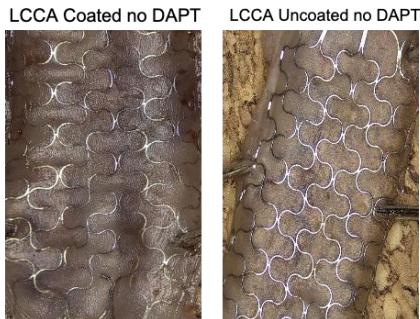


Fig 13: Gross Inspection of Stents Explanted 14 days Post-Implantation (with DAPT)

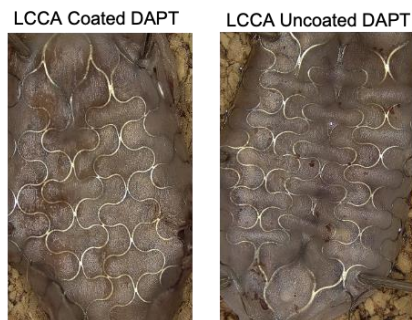


Fig 14: Gross Inspection of Stents Explanted 14 days Post-Implantation (with no DAPT)

At 90 days, both coated and uncoated implants exhibited complete endothelial coverage. However, Camouflage™ -coated stent demonstrated a thinner endothelial layer compared to the uncoated control, suggesting a reduced propensity for neointimal hyperplasia and favorable long-term healing response.

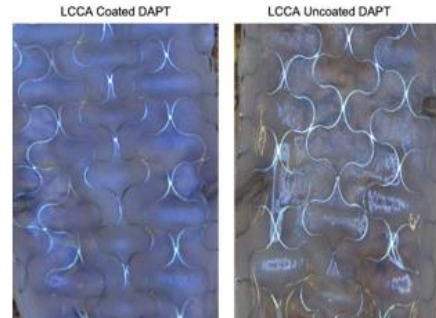


Fig 15: Gross Inspection of Stents Explanted 90 days post-implantation

5 Future Prospects

The future of intracranial flow disruption will largely hinge on the refinement and advancement of currently available technologies. Camouflage™ is currently being evaluated in a range of blood-contacting medical devices. Smart Reactors is actively partnering with leading medical device manufacturers and academic institutions to optimize the coatings' performance and validate its clinical benefits. Through sustained collaboration and innovation, Camouflage™ is driving the development of a novel biocompatible coating that enhances device integration, minimizes the risk of thrombosis and accelerates the healing process. These ongoing efforts hold the potential to significantly improve the efficacy and safety of aneurysm treatments, paving the way for more effective therapeutic solutions.

6 Conclusion

The development of intracranial flow disruption devices has marked a significant advancement in the treatment of intracranial aneurysms offering promising solutions to enhance patient outcomes. The modern field of endovascular therapies is undergoing a revolutionary transformation, continuously evolving to incorporate optimized designs that leverage aneurysm biology and promote healing.

The integration of Smart Reactors Camouflage™ represents an exciting frontier in this field, providing critical advantages in terms of biocompatibility and improved device integration within the aneurysmal sac. By reducing the risk of thrombosis and promoting endothelial healing, Camouflage™ has the

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ability to optimize intrasaccular device performance and improve long-term efficacy. As research progresses, it is evident that this coating can play a pivotal role in the success of aneurysm treatments. Addressing persistent challenges such as thrombosis and poor endothelialization, remains essential for the long-term success of intrasaccular devices. Camouflage™ offers an effective solution, providing a durable, non-pharmaceutical coating that enhances hemocompatibility, promotes healing, and mitigates inflammatory responses. Camouflage™ stands at the forefront of a new generation of bioengineered coatings thereby bridging the gap between innovation and long-term patient care.

7 References

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