SmartReactors

ADVANCEMENTS IN **NEUROVASCULAR INTERVENTIONS**:

THE ROLE OF **CAMOUFLAGE™** COATING FOR NEUROVASCULAR DEVICES

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1 Introduction

Neurovascular devices such as flow diverters and intracranial stents, play a vital role in treating conditions such as intracranial aneurysms and atherosclerotic disease. These life-saving technologies help restore normal blood flow and prevent severe complications, but their effectiveness is often hindered by challenges such as thrombosis and delayed endothelialization.

Surface interactions between these devices and circulating blood can trigger unwanted immune responses, increasing the risk of clot formation, inflammation, and device failure. Addressing these challenges requires advanced surface modifications that enhance hemocompatibility and promote seamless integration into the vascular system.

Camouflage™ coating technology offers an innovative biocompatible solution that minimizes immune response, reduces clot formation, and accelerates endothelial healing. By leveraging a unique combination of a synthetic polymer and a non-inflammatory protein, Camouflage™ transforms the way neurovascular devices interact with blood, ensuring safer and more reliable treatment outcomes.

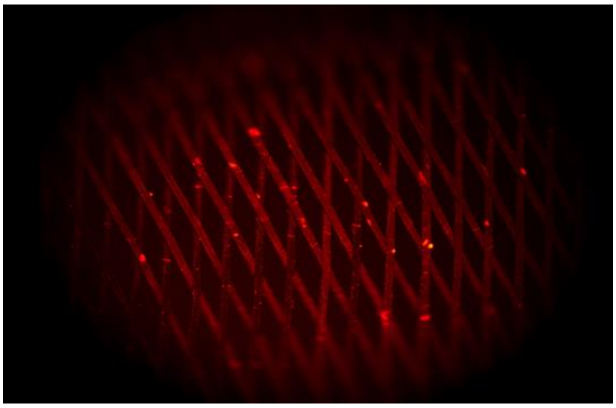

Fig 1 Fluorescent Image of Camouflage™ Coated Flow Diverter

This article explores the key challenges facing neurovascular implants and demonstrates how Camouflage™ coating technology enhances device performance, ultimately improving patient safety and long-term success.

2 Challenges Facing Current Neurovascular Devices

Neurovascular devices such as flow diverters and intracranial stents have revolutionized the treatment of complex cerebrovascular conditions. However, despite their clinical benefits these devices face significant challenges that impact their safety, effectiveness, and long-term performance. Two primary concerns are thrombogenic risks and delayed endothelialization, both of which can compromise patient outcomes.

2.1 Thrombogenic Risks - The Threat of Clot Formation

One of the most critical challenges with neurovascular implants is their interaction with circulating blood. When a foreign material is introduced into the bloodstream, it can trigger an immediate response from platelets and coagulation factors leading to clot formation (thrombosis). This complication can result in device occlusion, increased stroke risk, and the need for prolonged dual antiplatelet therapy (DAPT), which carries additional bleeding risks.

The surface properties of neurovascular devices play a crucial role in thrombogenicity. Hydrophobic or poorly hemocompatible materials can activate platelets and initiate the coagulation cascade. A biocompatible surface is essential to reducing thrombosis while maintaining effective blood flow through the device.

2.2 Insufficient Endothelialization - A Barrier to Long-Term Success

Endothelialization is the process where endothelial cells grow over an implanted device. This process is critical for the long-term integration and function of the device. Slow or incomplete endothelialization increases the risk of clotting and device instability. Until the device is fully covered with endothelial cells, it remains exposed to blood, which raises the likelihood of thrombosis and requires extended use of antiplatelet therapy.

Many conventional neurovascular implants have bare metal surfaces that do not promote endothelial cell attachment and growth. Without proper endothelial coverage, the body may respond with neointimal hyperplasia. This occurs when smooth muscle cells grow excessively and deposit extracellular matrix on the device surface, leading to vessel narrowing and a higher risk of restenosis. These complications can reduce long-term device success. Coatings that support faster endothelialization are essential for improving device performance and reducing risks.

2.3 The Need for Advanced Coating Solutions

Overcoming the challenges faced by neurovascular devices requires innovative surface modifications that improve hemocompatibility and promote rapid endothelialization. These advancements must address issues such as thrombogenic risks, delayed healing, immune response and restenosis, which can compromise device functionality and patient outcomes.

3 Solution: Camouflage™ Coating Technology

Camouflage™ coating technology, developed by Smart Reactors, is an advanced coating technology that improves blood-contacting medical device performance and safety by directly addressing the issues of hemocompatibility, endothelialization and inflammation which current neurovascular devices face.

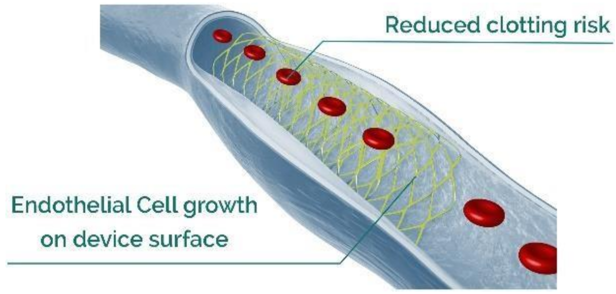

Fig 2 Camouflage™ coating reducing clotting risk and promoting endothelialization

3.1 How Camouflage™ Works

Camouflage™ is an advanced coating designed for blood-contacting medical devices. It works by concealing the device's surface from circulating blood by incorporating non-inflammatory proteins into the coating. These proteins, combined with a synthetic polymer, regulate how blood interacts with the device, helping to prevent thrombosis, or blood clot formation. The coating also encourages endothelial cell attachment, promoting faster healing. By masking the device surface and reducing the immune response, Camouflage™ effectively addresses hemocompatibility issues, accelerates endothelialization, and minimizes inflammation in neurovascular devices.

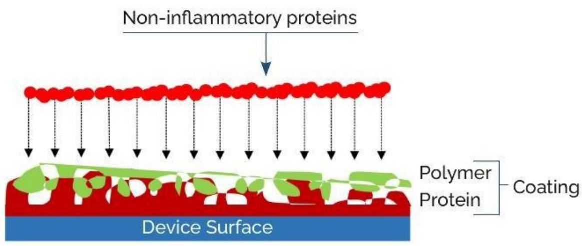

Fig 3 Camouflage™ Coating

3.2 Camouflage™ Key Properties

- **Hemocompatible** – Camouflage™ is designed to seamlessly interact with blood, minimizing unwanted biological responses. 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.
- **Enhanced Endothelialization** – The coating promotes rapid attachment and controlled proliferation of endothelial cells, ensuring faster integration of the device with the vascular system. This accelerated healing process reduces exposure time to circulating blood, decreasing the reliance on long-term antiplatelet therapy and improving overall device safety.
- **Anti-Inflammatory** – Camouflage™ minimizes immune system activation by masking the device surface from inflammatory cells. By reducing leukocyte adhesion and suppressing inflammatory responses, the coating helps maintain vascular stability and prevents complications associated with chronic inflammation and restenosis.

3.3 Manufacturing Benefits

One of Camouflage's greatest advantages is its seamless integration into existing device manufacturing processes. Unlike many coatings that require extensive surface preparation or functionalization, Camouflage™ adheres to virtually any substrate without additional modifications. This simplifies production while maintaining the device's structural integrity and performance.

As a non-pharmaceutical solution, Camouflage™ offers a more straightforward regulatory pathway, making it easier to integrate into existing medical device approvals. By optimizing hemocompatibility and accelerating vascular healing, Camouflage™ represents a transformative advancement in neurovascular device technology.

4 Camouflage™ Coating Data

Smart Reactors have performed detailed evaluations of Camouflage™ to demonstrate its performance for neurovascular implantable devices. After 1 hour of blood circulation in a dynamic blood flow model at 37 °C, Camouflage™ coating demonstrated minimal thrombus formation on nitinol flow diverters, in contrast to uncoated nitinol flow diverters, which were extensively covered with thrombi (Fig 4).

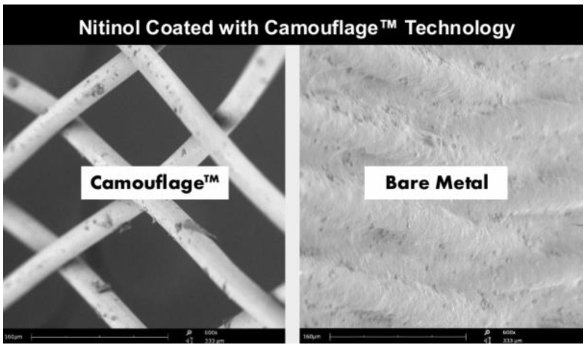

Fig 4 SEM Analysis 600x of nitinol coated flow diverter with Camouflage™ coating vs. uncoated after blood circulation.

4.1 Hemocompatibility

Smart Reactors Camouflage™ coating was evaluated using several biomarkers to assess its blood compatbility. β-thromboglobulin (BTG), is released from activated platelets and serves as an indicator of platelet activation. Nitinol coated with Smart Reactors Camouflage™ coating showed markedly lower BTG levels compared to uncoated nitinol, demonstrating the coating's effectiveness in suppressing platelet activation and thereby reducing thrombus formation (Fig 5).

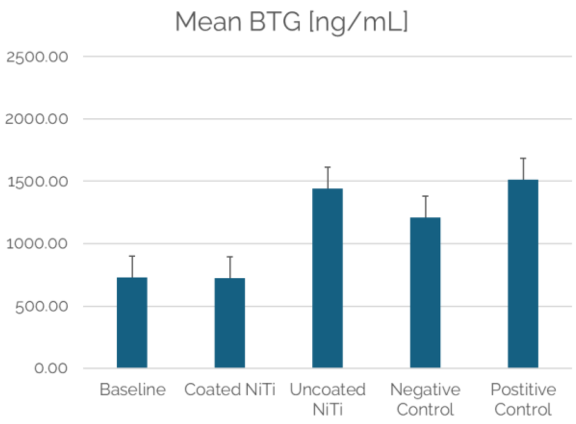

Fig 5 Mean BTG levels on Coated and Uncoated nitinol

Platelet binding was determined by the amount of acid phosphatase (platelet release enzyme) present on the sample surface. The Camouflage™ coated nitinol group showed the lowest platelet binding levels, demonstrating a significantly more hemocompatible surface when treated with Camouflage™ (Fig 6).

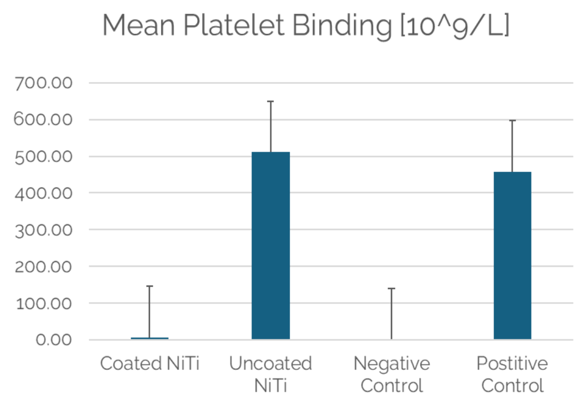

Fig 6 Mean Platelet Binding levels on Coated and Uncoated nitinol

Fibrin binding was determined by the amount of labelled anti-fibrin antibodies that adhered to the surface. Nitinol coated with Camouflage™ indicated a lower level of fibrin binding than uncoated nitinol.

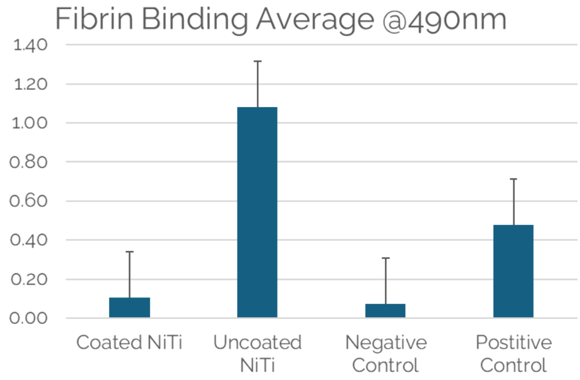

Fig 7 Fibrin Binding Levels of Coated and Uncoated Nitinol

4.2 Endothelialization

Camouflage™ coating on Nitinol surfaces promote endothelial cell proliferation when compared to uncoated stents, thereby reducing the device exposure time to circulating blood. The uptake of HUVEC cells is greater on coated verses uncoated nitinol stents after a 29-hour incubation period (Fig 8).

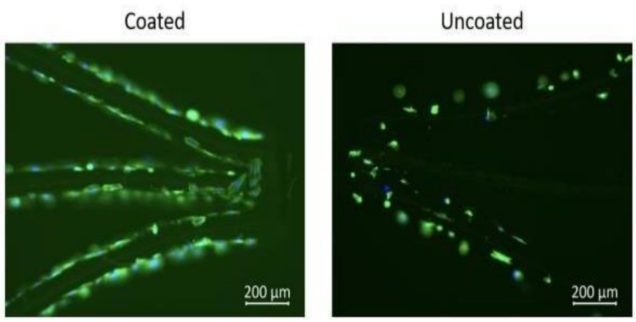

Fig 8 Endothelial cell attachment after 29-hour dynamic incubation

4.3 Anti-Inflammatory

Camouflage™ coating minimizes the interaction with white blood cells and reduces the inflammatory response. Data demonstrates white blood cells exhibiting minimal adhesion to the surface, with elastase activity remaining at low levels with suppressed inflammatory response (Fig 9 & 10)

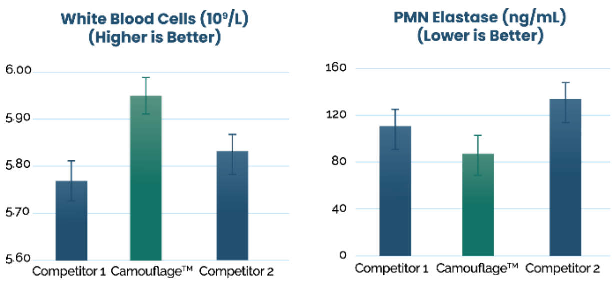

Fig 9

5 Flow Diverters in Treating Intracranial Aneurysm

Flow diverters have transformed the treatment of complex intracranial aneurysms, offering a minimally invasive approach to redirect blood flow and promote aneurysm healing. However, the effectiveness of these devices depends heavily on their surface properties. Specialized coatings are becoming essential for addressing clinical challenges, improving patient outcomes, and enhancing the safety and durability of these neurovascular devices.

Flow diverters are typically crafted from durable alloys like cobalt-chromium or Nitinol and are designed to be placed across the neck of an aneurysm. By diverting blood flow away from the aneurysm sac, these devices facilitate vessel remodeling, gradually closing the aneurysm and promoting natural healing. However, bare metal flow diverters face several critical issues: without proper surface treatment, they are prone to thrombosis, delayed endothelialization, and inflammation.

These limitations often necessitate prolonged dual antiplatelet therapy (DAPT) to prevent clotting, which adds complexity to treatment and limits patient eligibility. These challenges have driven the need for advanced coatings that optimize device biocompatibility and performance in neurovascular applications. Implanted flow diverters undergo three primary phases of integration into the body with different risks to the patient during each phase.

Acute Phase (0–30 days): During the critical early days post-implantation, coatings provide immediate protection against thrombosis, reducing the risk of clot formation.

Subacute Phase (1–3 months): Coatings maintain stability as blood flow remodeling occurs, allowing endothelial cells to attach and cover the device.

Chronic Phase (3+ months): Advanced coatings continue to support ongoing endothelialization and device integration, ensuring long-term stability and compatibility with the vascular tissue.

Camouflage™ is designed to overcome the current challenges in flow diverter technology by providing a stable, durable coating that minimizes thrombosis, enhances endothelialization, and reduces inflammation, resulting in a fully integrated and long-lasting flow diverter.

6 Stents in Managing Intracranial Atherosclerotic Disease (ICAD)

Intracranial Atherosclerotic Disease (ICAD) is a progressive condition where arteries in the brain become narrowed due to the buildup of plaque, consisting of lipids, inflammatory cells, and fibrous tissue. This narrowing restricts blood flow, significantly increasing the risk of ischemic stroke. As the disease progresses, reduced blood flow can cause transient ischemic attack or full stroke, making ICAD one of the leading causes of stroke-related disability and death. While medical therapy such as antiplatelet drugs and lifestyle changes can help manage the condition, patients with severe stenosis often require endovascular interventions like intracranial stenting to restore blood flow. Stents address ICAD by mechanically reopening the narrowed vessel and providing structural support to keep the artery open. When deployed, they push plaque against the vessel wall, increasing the lumen for blood to pass through. However, stenting introduces risks including thrombosis and restenosis due to neointimal hyperplasia.

Thrombosis can occur when platelets recognize the stent as a foreign body and begin forming clots. Restenosis happens as excessive smooth muscle cell proliferation leads to tissue growth inside the stent causing the artery to narrow again. Inflammation results from the body's immune response to the stent material further contributing to restenosis and impairing long-term stent function.

To mitigate these issues, drug-eluting stents have been developed. These stents are coated with antiproliferative drugs like sirolimus or paclitaxel which prevent smooth muscle cell overgrowth and reduce neointimal hyperplasia. While effective at limiting restenosis, drug-eluting stents also slow endothelialization, leaving the stent surface exposed to circulating blood for longer, increasing the risk of thrombosis. Consequently, patients often require long-term dual antiplatelet therapy, which carries a higher risk of bleeding complications.

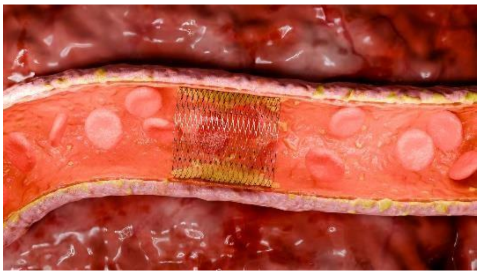

Fig 10 Image of a stent implanted into the neurovasculature

Camouflage™ provides a non-pharmaceutical solution to optimize intracranial stent performance. By retaining non-inflammatory proteins from the blood on the stent's surface, it reduces platelet activation and minimizes thrombosis formation. The coating also promotes endothelialization, allowing for faster integration of the stent into the vessel wall, which enhances healing and long-term stability. Additionally, by reducing immune recognition of the stent, Camouflage™ reduces inflammation and the likelihood of restenosis. Without relying on drug-eluting agents, Camouflage™ enables a safer, more predictable healing process, leading to a fully integrated, stable stent that remains free from restenosis, inflammation and thrombosis, ultimately improving patient outcomes.

7 Clinical and Industry Benefits of Camouflage

For Device Manufacturers: As a non-pharmaceutical solution, Camouflage™ offers a more straightforward regulatory pathway, making it easier to integrate into existing medical device approvals.

For Clinicians: The coating minimizes thrombosis and inflammatory responses, leading to improved patient safety and better procedural outcomes with reduced dependency on long-term antiplatelet therapy.

For Patients: Camouflage™ promotes faster healing, reduces complications, and enhances long-term vascular integration, leading to quicker recovery times and improved quality of life.

8 Future Directions

Camouflage™ is expanding to coat a wider range of blood-contacting medical devices. Smart Reactors is actively collaborating with medical device manufacturers and academic institutions to optimize the performance of Camouflage™ and validate its benefits. Through ongoing research and partnerships, Camouflage™ continues to advance biomaterial coatings for improved device integration, reduced thrombosis, and enhanced healing.

9 Conclusion

There is a clear clinical need to improve flow diverter and ICAD stent technology to enhance patient outcomes. Addressing challenges such as thrombosis, endothelialization, and inflammation is critical for long-term device success. Camouflage™ offers an effective solution providing a durable, non-pharmaceutical coating that improves hemocompatibility, promotes endothelial healing, and reduces inflammation, making it a valuable advancement in neurovascular device technology.

10 About Us

Smart Reactors delivers cutting-edge hemocompatible coating technologies for medical devices. Services include coating selection, regulatory support, and commercialization. Founded in 2019 by industry experts with over 50 years of combined experience, Smart Reactors excel in creating advanced biomaterial solutions and providing superb customer service.

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