




## PRECLINICAL EVALUATION OF CAMOUFLAGE™ COATED STENTS IN A RABBIT CAROTID MODEL

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## 1 Executive Summary

Intravascular devices such as stents and flow diverters have significantly advanced the treatment of cardiovascular and neurovascular disease, but they continue to face limitations related to thrombosis, delayed healing, and dependence on dual antiplatelet therapy (DAPT). While drug-eluting coatings help reduce neointimal hyperplasia, they have limited functional lifespan due to complete drug elution over time.

Camouflage™ is an innovative, drug-free, nanoscale coating developed by Smart Reactors to address these challenges. By adsorbing non-inflammatory proteins from the blood, the coating effectively conceals the device from the surrounding blood and reduces the risk of clot formation. Camouflage™ produces a surface that promotes endothelial cell attachment, all while preserving the mechanical performance of the device.

A preclinical rabbit study was conducted to assess the safety and performance of Camouflage™ coated stents compared to uncoated controls. Coated stents showed early tissue deposition within 24 hours, complete endothelialization by 14 to 90 days, and no visible signs of thrombus formation, inflammation, or foreign body reaction.

These findings provide strong support for the safety and effectiveness of Camouflage™ coating technology. The consistent absence of thrombus, early tissue coverage, and full endothelialization highlight its potential to improve the healing process of intravascular implants.

## 2 Background & Rationale

### 2.1 Current Coating Technology Limitations

Intravascular devices, such as stents and flow diverters, have transformed the treatment of cardiovascular and neurovascular diseases. However, despite decades of innovation, these implants continue to face critical challenges in achieving optimal biocompatibility, particularly in relation to thrombus formation, delayed endothelialization, and neointimal hyperplasia.

One of the most immediate concerns following device implantation is thrombogenicity. The foreign surface of an implant can activate platelets and the coagulation cascade when in contact with blood, leading to the formation of thrombi. Thrombus formation on intravascular implants poses a serious risk to patients' health as clots can obstruct local blood flow. Blood clots can also dislodge and form emboli, potentially leading to stroke, myocardial infarction, or other life-threatening complications. To mitigate these risks, patients are routinely placed on dual antiplatelet therapy (DAPT), typically a combination of aspirin and a P2Y<sub>12</sub> inhibitor (e.g. clopidogrel). Patients may require DAPT for extended periods post-implantation. While DAPT is effective in reducing thrombotic risk, it also introduces new complications. These include increased bleeding risk, patient non-compliance, and limited treatment

options for patients with contraindications to antiplatelet therapy. The reliance on pharmacological intervention highlights the inherent thrombogenicity of existing device surfaces.

Another challenge facing current intravascular devices is incomplete or delayed endothelialization, which can prolong the thrombotic risk period and impair vessel healing. A functional endothelial layer is critical not only for restoring vascular homeostasis but also for preventing thrombosis and restenosis. However, current device surfaces often fail to actively promote rapid and spatially controlled endothelial growth.

To combat neointimal hyperplasia, drug-eluting stents (DES) have become standard in many clinical settings. These devices release anti-proliferative agents such as sirolimus or paclitaxel to inhibit smooth muscle cell growth and reduce restenosis. While effective in this regard, DES come with significant trade-offs. DES have limited drug stability, which can reduce their long-term effectiveness. DES coatings are microns thick which may affect stent flexibility and delivery, and in some cases, cause inflammation or delayed healing.

Given these limitations, there is a clear need for a new generation of intravascular device coatings that can address these challenges simultaneously. An ultrathin, nanoscale surface coating that is non-thrombogenic, promotes controlled endothelialization, and maintains mechanical integrity offers a compelling solution. Ideally, such a coating would be drug-free, durable, and compatible with existing device substrates without altering their functional properties. By reducing or eliminating the dependence on DAPT, improving endothelial healing, and preventing thrombus formation without compromising device performance, this approach holds significant promise for improving clinical outcomes across a broad range of intravascular interventions.

### 2.2 Solution: Camouflage™ Coating Technology

Camouflage™ is an innovative coating technology developed by Smart Reactors, tailored for blood-contacting medical devices. The coating conceals the device's surface by adsorbing non-inflammatory proteins from the blood on to the coated surface. The combination of recombinant protein and synthetic polymer regulates protein adsorption, preventing thrombosis and providing a foundation for endothelial cell attachment. Camouflage™ provides the following key attributes:

**Hemocompatibility** – Camouflage™ is designed to seamlessly interact with blood, minimizing unwanted biological responses. The coating reduces platelet activation and prevents the initiation of the coagulation cascade, significantly lowering the risk of thrombosis.

**Enhanced Endothelialization** – The coating promotes the rapid attachment and 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.

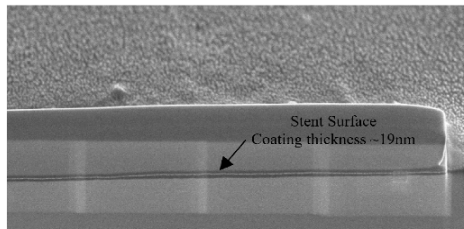


Fig 1 Camouflage™ coating thickness under FIB SEM

Camouflage™ is a drug-free, ultra-thin nanoscale coating designed to minimize thrombogenicity and promote endothelialization without the use of active pharmacologic agents. Unlike drug-eluting coatings, which may lose effectiveness once the drug supply is depleted, Camouflage™ coating maintains its functional performance indefinitely. Its minimal thickness ensures that the mechanical properties of the stent remain unaffected particularly during device implantation processes of crimping, expansion, and deployment. This property preserves medical devices' intended performance during and after implantation.

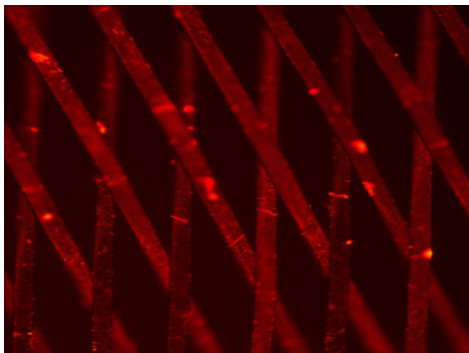


Fig 2 Uniformity of coverage of a Camouflage™ coated nitinol flow diverter by fluorescent microscopy.

### 3 Study Design & Methods

This preclinical study was conducted to evaluate the safety and endothelialization performance of Camouflage™ coated nitinol stents in comparison to uncoated control stents using a rabbit carotid artery model. Rabbits were selected for this study due to the suitable size of their arteries for small stent implantation and their well-established use in preclinical vascular device evaluation. This model provides translational relevance for early-phase assessment of vascular implants.

Implantation involved the placement of 2 stents into the left common carotid artery (LCCA) of each rabbit model, one Camouflage™ coated and one uncoated. This

enabled intra-animal comparisons while minimizing inter-animal variability.

Animals (N = 4) were sacrificed at three key time points to capture the early, mid, and late tissue response phases:

- 24 hours (n=1), to evaluate acute responses and immediate post-implantation effects
- 14 days (n=2), to assess early healing and endothelial coverage
- 90 days (n=1), to observe long-term vascular integration and any chronic inflammatory responses

At 24 hours and in one of the two rabbits evaluated at 14 days, no dual antiplatelet therapy (DAPT) was administered. The other rabbit at 14 days and the rabbit evaluated at 90 days received DAPT consisting of aspirin and clopidogrel. This distribution allowed for a preliminary assessment of the coating's performance under both pharmacologically supported and unsupported conditions.

At the designated endpoints, animals were euthanized and the stented vessel segments were explanted and fixed in formalin for 24 hours. Vessel segments were then longitudinally opened to expose the inner lumen and enable gross visual inspection, focusing on thrombus formation, neointimal coverage, and overall vessel patency.

### 4 Results

All animals remained healthy throughout the study period, with no adverse events or complications observed. No technical issues occurred during stent implantation, and all devices were successfully delivered and deployed.

Gross inspection of the stented vessel segments revealed visible differences in tissue coverage between Camouflage™ coated and uncoated stents at the acute time point. At 24 hours, the coated stent displayed early tissue deposition along the struts, whereas the uncoated stent appeared largely bare, with minimal visible surface coverage (Figure 3). No sign of thrombus was observed.

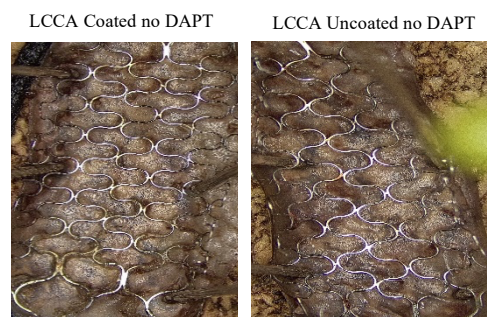


Fig 3 Gross Inspection of Stents Explanted 24 Hours Post-Implantation

By 14 days, all stents—both coated and uncoated, with and without DAPT—exhibited clear evidence of endothelialization, with no visible thrombus formation or abnormalities. The intima appeared healthy across all



groups. Notably, stents implanted under DAPT conditions demonstrated slightly greater endothelial coverage than their non-DAPT counterparts, regardless of coating (Figures 4 and 5).

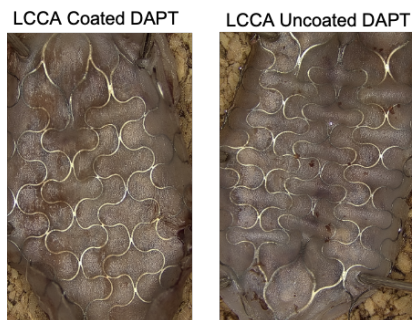


Fig 4 Gross Inspection of Stents Explanted 14 days Post-Implantation (with DAPT)

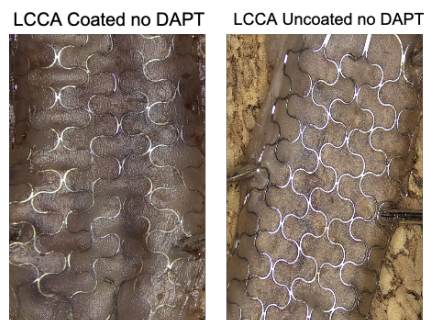


Fig 5 Gross Inspection of Stents Explanted 14 days Post-Implantation (with no DAPT)

At 90 days, both coated and uncoated implants were fully covered with endothelial cells. The coated implant had a thinner layer of endothelial cells compared to the uncoated. That suggests no progression towards neointimal hyperproliferation on the coated implant.

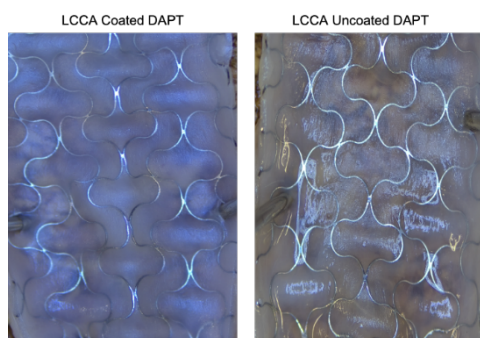


Fig 6 Gross Inspection of Stents Explanted 90 days Post-Implantation

(Figure 6) No signs of foreign body reaction, gross inflammation, or perivascular swelling were noted upon visual examination. All stents remained patent until the time of extraction.

## 5 Discussion

The findings from this preclinical rabbit study offer compelling evidence supporting the biocompatibility and efficacy of the Camouflage™ coating for blood-contacting vascular implants. All animals tolerated the implants well, with no adverse events or complications reported throughout the 90-day study period. The absence of technical challenges during stent deployment

highlights the practicality of the coating in real-world settings.

A key observation was the distinct acute tissue response evident at the 24-hour implantation observation. The Camouflage™ coated stents exhibited early tissue deposition along the struts, in contrast to the minimal surface coverage seen with uncoated stents. This rapid onset of tissue growth suggests that the coating promotes early endothelial cell attachment, a critical feature for reducing acute thrombogenic risk and accelerating healing.

By 14 days, all stents demonstrated progressive endothelialization, but the early advantage seen with the coated devices reinforces the coating's role in modulating early-phase tissue integration. The observation after 14 days that stents implanted under DAPT conditions showed slightly greater endothelial coverage than those without DAPT, regardless of coating, aligns with findings by Caroff et al. on neointimal hyperplasia. However, it contrasts with results from Forestier et al., who reported significantly higher neointimal growth in rabbits not receiving DAPT. Despite these differences, the present study consistently showed no thrombus formation in any group. This was true regardless of whether animals received DAPT. These findings reinforce the potential of the Camouflage™ coating to reduce thromboembolic risk and support endothelial healing, even under limited pharmacological support.

The complete endothelialization observed in all groups by day 90, without evidence of thrombosis, foreign body reaction, or inflammation, further validates the long-term compatibility of the Camouflage™ coating.

From a biomaterials perspective, Camouflage™ represents a significant advancement. Its ultrathin profile ensures that device deliverability and mechanical performance are not compromised, while its drug-free nature eliminates concerns related to pharmacological side effects or elution kinetics. The ability to achieve durable hemocompatibility and endothelial coverage without the need for drug loading positions Camouflage™ as a next-generation surface treatment for intravascular devices.

In conclusion, these results provide further evidence supporting the efficacy and safety of Camouflage™ coating technology. The observed rapid endothelialization, absence of thrombus, and overall biocompatibility underscore its potential to improve the healing profile of blood-contacting medical devices and reduce dependence on prolonged antiplatelet therapy.

## 6 References

- Caroff, J. et al. Phosphorylcholine surface modified flow diverter associated with reduced intimal hyperplasia. *Journal of NeuroInterventional Surgery* **10**, 1097–1101 (2018).
- Forestier, G. et al. Comparison of arterial wall integration of different flow diverters in rabbits: The CICAFLow study. *Journal of Neuroradiology* **51**, 236–241 (2023).