

An *ex vivo* perfusion platform for the testing of cardiovascular interventional devices

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The development of cardiovascular interventional devices from drug eluting stents to drug coated balloons (DCBs), is hindered by a crucial bottleneck in the preclinical development pathway. The arteries of small animal models do not reflect the size and physiology of human arteries, thus often requiring device miniaturization that limits device performance. Large animal models, which are more anatomically relevant to humans, are costly and logistically demanding, making them suboptimal for the rapid, iterative prototyping required in early-stage device development. As a result, the transition of promising devices from benchtop characterization to *in vivo* testing remains inefficient owing to a long-standing gap in physiologically relevant, predictive preclinical testbeds. A system that mimics key features of coronary physiology outside the living system could help overcome this gap.

Our research team have developed a perfusion platform that recapitulates fundamental haemodynamic features of the human coronary circulation within a controlled flow and pressure environment. Flow and pressure are driven by a peristaltic pump operated in either steady or pulsatile modes, and temperature is maintained by a heated water reservoir. The circuit can run with buffer solutions or whole blood and includes vessel segments prepared from pig or human *ex vivo* arteries or from synthetic constructs. Crucially, this platform is not a static bath test, but is equipped with a haemostatic valve and a tortuous tracking fixture, forcing the interventional device to navigate a realistic path before reaching the target vessel. This platform allows the simulation of the sequence of interventional devices, from insertion and tracking to inflation and withdrawal, under tightly controlled, yet biologically relevant conditions. After device implantation, vessel tissue can be harvested for downstream analysis (for example, drug retention and cellular responses). The collection of overflow perfusate allows the evaluation of drug or coating constituents lost during passage through the circuit, shedding light on device behaviour beyond simple inflation outcomes.

Although the platform is broadly applicable for interventional device testing, we have optimized the system particularly for the evaluation of DCBs. The system is designed to meet key regulatory requirements, including the American Society for Testing and Materials (ASTM) standards F2394, which governs stent retention and fixation on delivery systems, and F3320, which outlines the characterization of DCB coatings for durability, uniformity and particulate release during simulated use. The platform facilitates the inflation and withdrawal of DCBs under controlled conditions, allowing for the direct measurement of coating durability, particulate release and drug transfer to tissue. This preclinical, predictive analysis minimizes the risks associated with device development, accelerates iterative design optimization and establishes a foundation for future *in vivo* testing.

This approach provides a controlled testbed to study mechanisms of device-vessel interaction. In our studies, we have used the system to compare prototype DCB formulations, relating coating design and inflation parameters to crucial determinants of both efficacy and safety, such as drug loss during delivery, drug transfer efficiency and particulate release. The same approach can be extended to address broader questions, such as how lesion morphology or repeated inflations influence

particulate release and local drug release from the device. Insights derived from these experiments could help elucidate key mechanisms of device–vessel interactions and guide rational device iteration to create a more efficient and targeted preclinical pathway. The platform provides a controlled yet physiologically complex environment, moving beyond simple performance testing to gain the necessary mechanistic insights for the design of the next generation of cardiovascular interventional devices.

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Acknowledgements

T.T. acknowledges support from a British Heart Foundation (BHF) Fellowship (FS/ATA/21/20015), the BHF Centre of Research Excellence, the University of Oxford (BHF RE/24/130024) and a Wellcome Trust award (312718/Z/24/Z). The authors thank Keith Channon (University of Oxford, UK) for valuable discussions.

Competing interests

T.A.T is the principal inventor on a UK patent application entitled “NO generating material” (application no. 2319023.4 filed by Oxford University Innovation), which relates to nitric oxide - generating vascular stent coatings. This patent is not directly related to the drug-coated balloon work or the perfusion platform described in this article. T.F. declares no competing interests.

