

One Year Patency and Remodeling of Biorestorative Polymeric Coronary Bypass Grafts in an Ovine Model

Masafumi Ono, Xinlei Wu, Mohammed El-Kurdi, Jochen Reinöhl,
Renu Virmani, Martijn Cox, Yoshinobu Onuma, and Patrick W. Serruys
*On behalf of Xeltis, Eindhoven, the Netherlands, and Academic Team in
CORRIB Core Lab, National University of Ireland Galway (NUIG), Ireland*

Disclosure Statement of Financial Interest

I, **Masafumi Ono**, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

Background

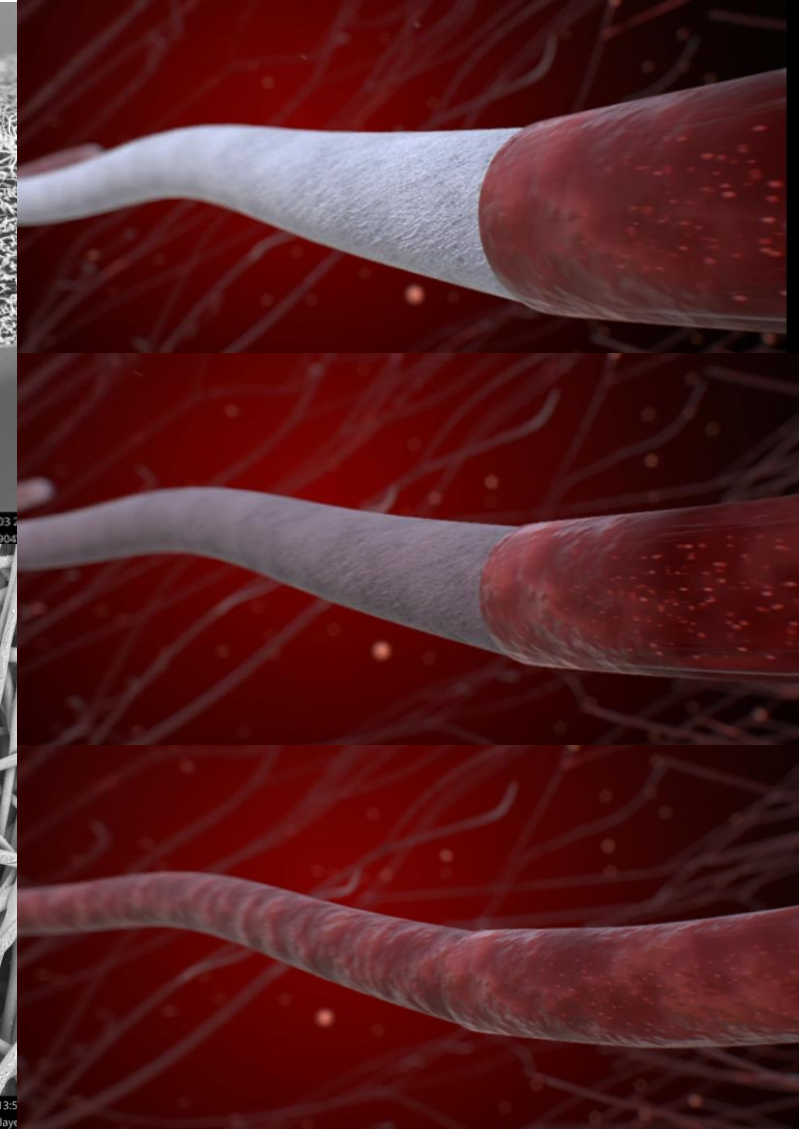
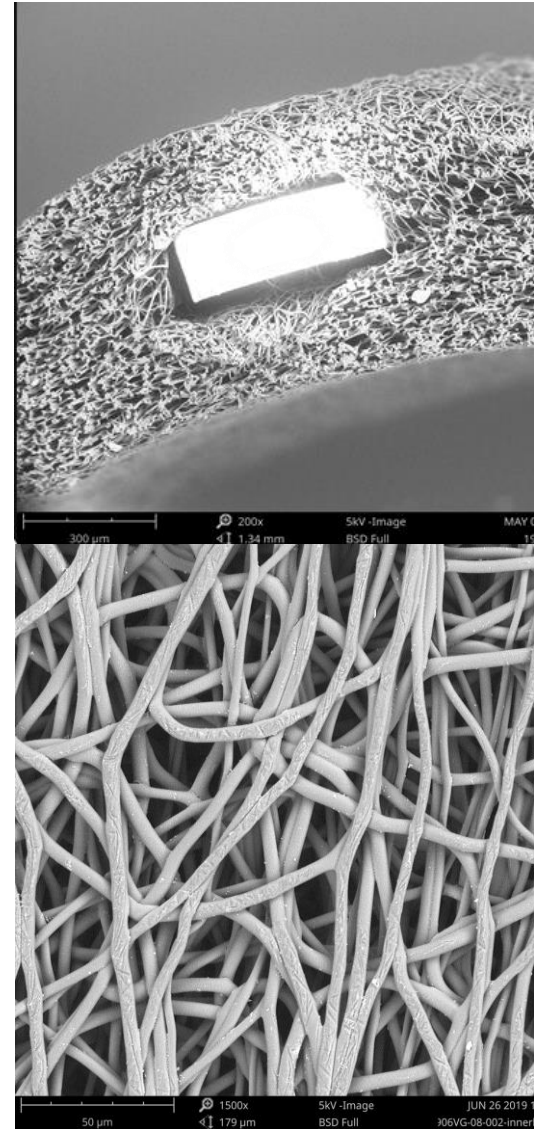
- Saphenous vein grafts (SVGs) are being used in 80% of coronary artery bypass graft (CABG) surgeries despite limitations including **painful SVG harvesting**, and **poor chronic patency** due to dilation-induced hemodynamic disturbances resulting in neointimal hyperplasia
- Synthetic CABG could eliminate the need for SVG harvesting, but thus far have failed to perform sufficiently, and are not in clinical use.
- The novel restorative vascular graft (RVG) is based on bioabsorbable supramolecular polymer technology, and is scalable in length, and diameter, and can be available off the shelf.

Study Objective

- The primary goal of our preclinical work was to assess the technical feasibility of the RVG device, and to demonstrate the performance over time via serial angiographic assessments.

Methods 1 - Devices/ Animal models

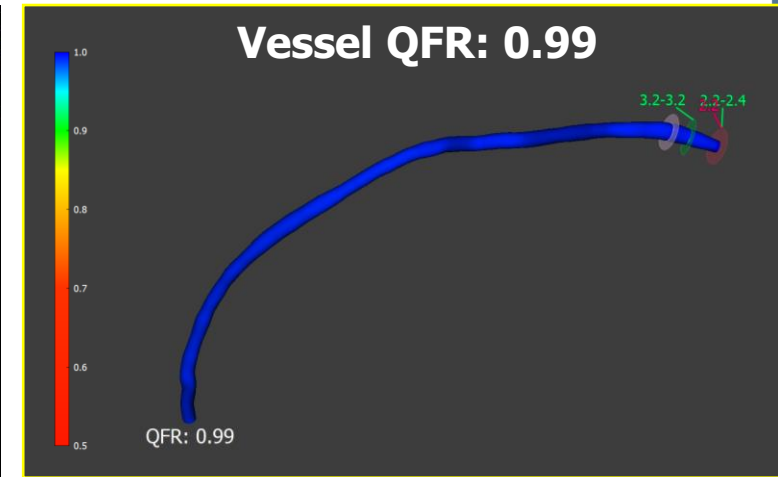
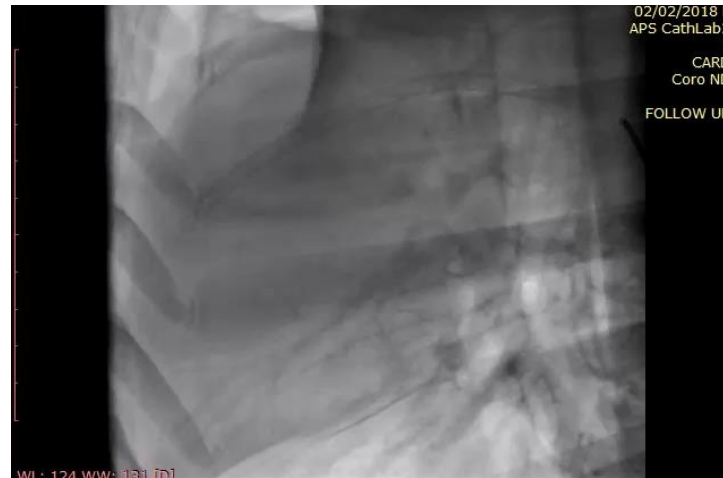
- The RVB is composed of an electrospun supramolecular polymer fiber matrix encapsulating a nitinol microskeleton for kink resistance
- Fifteen sheep underwent CABG surgery, either with **RVGs** (ϕ 4mm/ 15cm long, $n=12$) or **SVGs** ($n=3$) and were followed up up to 1 year
- RVGs or SVGs (one graft per animal) were implanted from the descending aorta to the left anterior descending artery (LAD), which was ligated upstream of the distal anastomosis, simulating a CTO of the LAD.
- The study was conducted in accordance with the Guide for Care and Use of Laboratory Animals and was approved by the local Institutional Animal Care and Use Committee.



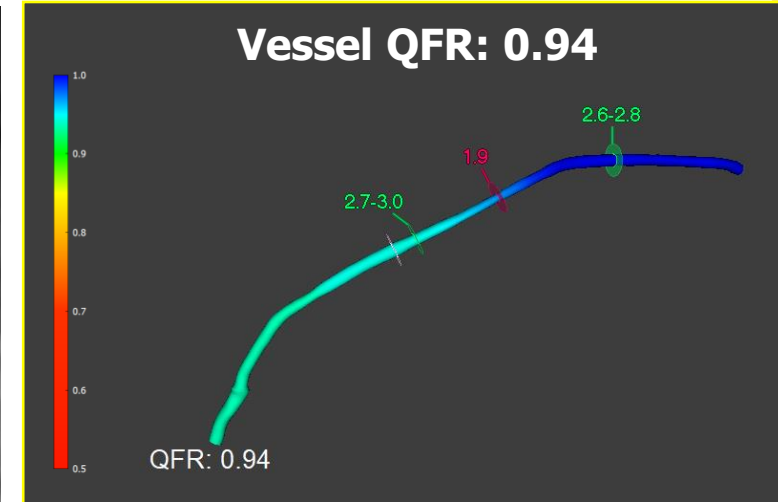
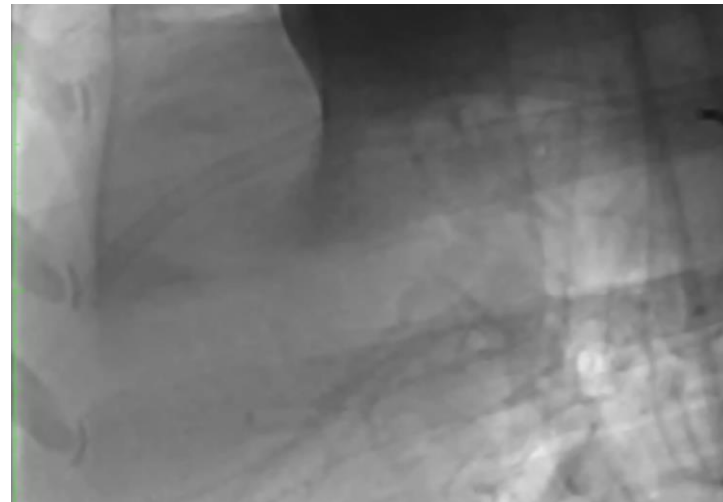
Methods 2 – Patency evaluation

1-month follow-up angiography

- Serial angiography was performed at baseline, 1, 3, 6, 9, and 12 months.
- The patency and hemodynamic performance were evaluated by angiography providing a combination of anatomic (QCA and flow speed) and a simulated physiological parameter (QFR) derived from two- and three-dimensional (3D) angiography reconstruction.



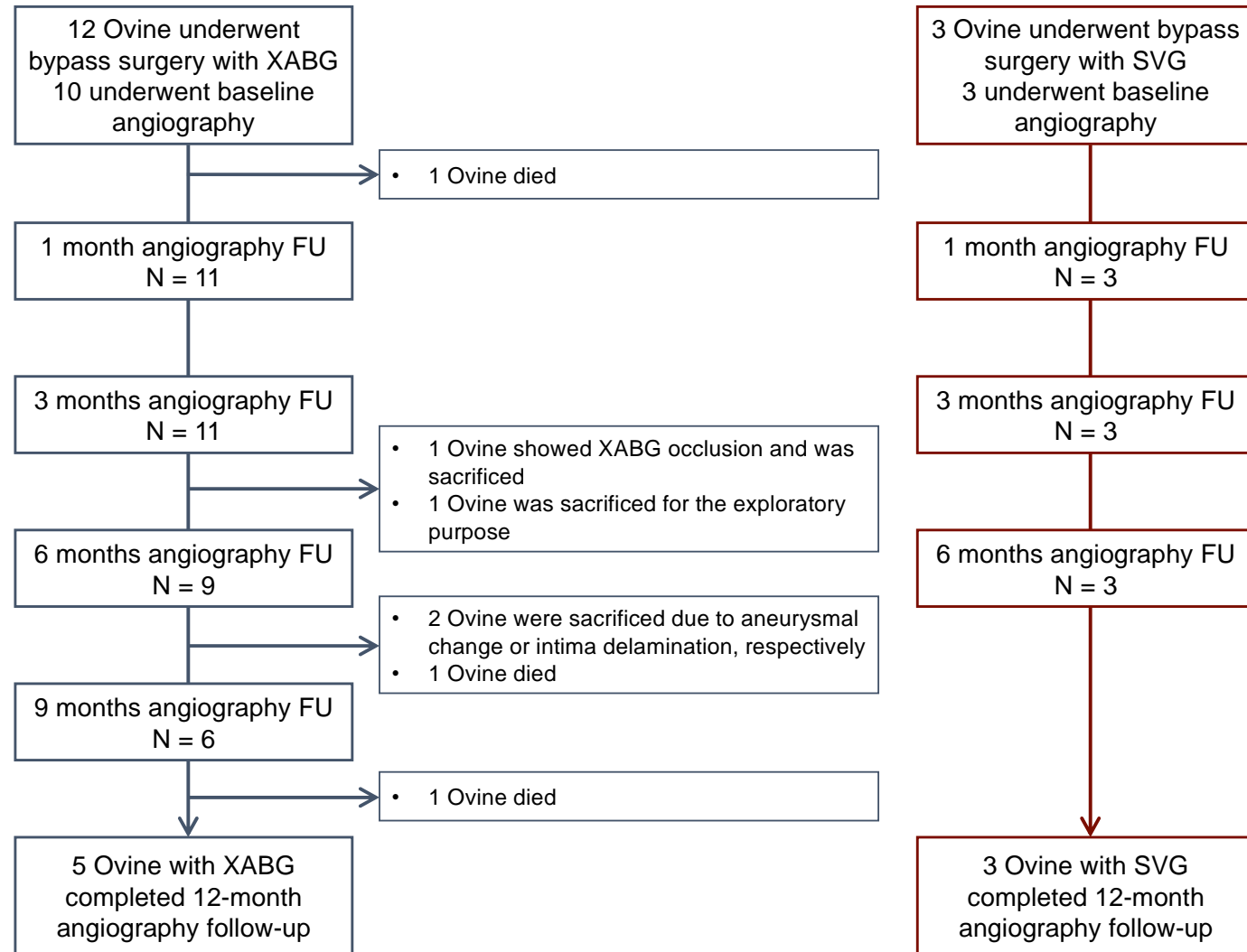
12-months follow-up angiography



Results 1

- One sheep in the RVG arm died at the time of bypass surgery due to surgical error, and two sheep with RVG died prematurely, between 6 – 12 months
- Four sheep with RVGs were sacrificed early for examination purposes.
 - One of them presented a total occlusion of the graft at 3 months
 - One presented with distal narrowing at 3 months.
 - One exhibited an aneurysm at 6 months
 - One showed intimal delamination potentially due to OCT

Flowchart

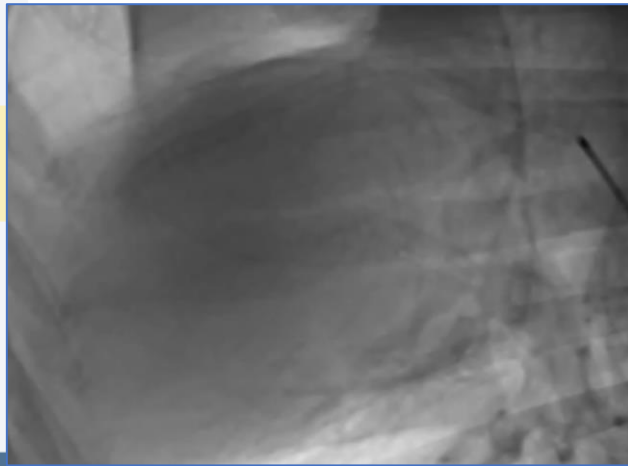


Results 2

- Chronically, 10/11 RVGs and 3/3 SVGs were patent up to 6m follow-up
- 5 RVG and 3 SVG sheep were kept alive until 12-month follow-up
- **RVG** at 12mo showed uniform lumen along graft length with acceptable flow speed of **14.0 cm/s** and QFR value of **0.93** on average
- **SVG** showed **diffuse dilation** with considerably slower flow velocity of **3.4 cm/s** with signs of **distal anastomosis narrowing**, with relatively lower QFR value of **0.87** on average.

RVG Angiography at 12 months

SVG Angiography at 12 months

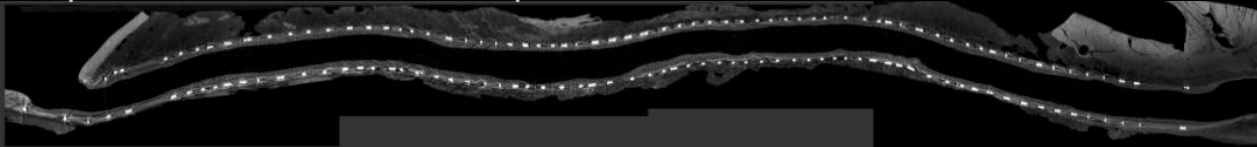


RVG 12mo f-up		
	Flow speed [cm/s]	QFR
Case 1	5.0	0.94
Case 2	13.9	0.83
Case 3	19.6	0.99
Case 4	14.3	1.00
Case 5	17.4	0.87
Mean	14.0±5.6	0.93±0.07

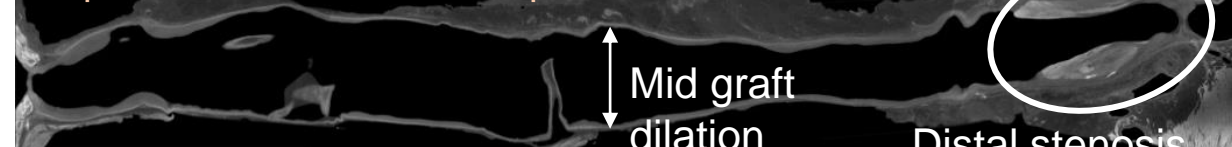
SVG 12mo f-up		
	Flow speed [cm/s]	QFR
Case 1	1.8	0.99
Case 2	3.7	0.81
Case 3	4.7	0.81
Mean	3.4±1.5	0.87±0.10



Representative 12m RVG explant microCT



Representative 12m SVG explant microCT



Conclusion

- **The RVG demonstrated acceptable patency and performance at 6 and 12 months in a challenging ovine CABG model with uniform graft diameters at 12 months follow-up**
- **Vein graft controls demonstrated good patency until 12 months but with diffuse dilation resulting in significantly slower flow velocity with relatively lower QFR than RVG.**
- **Further studies including clinical trials in human are warranted to demonstrate the clinical feasibility and performance of the novel RVG bypass graft.**