Tissue Engineered Blood Vessels For Dialysis Access and Vascular Surgery

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Disclosure Information

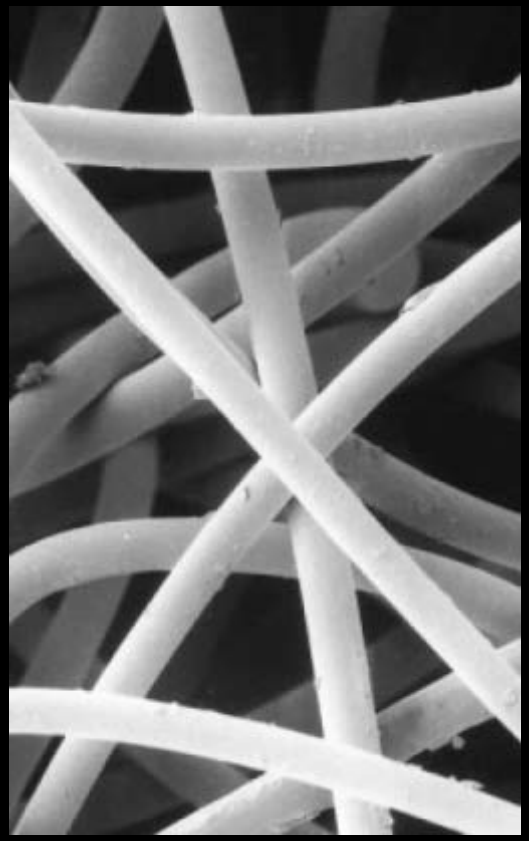
Lawson JH,

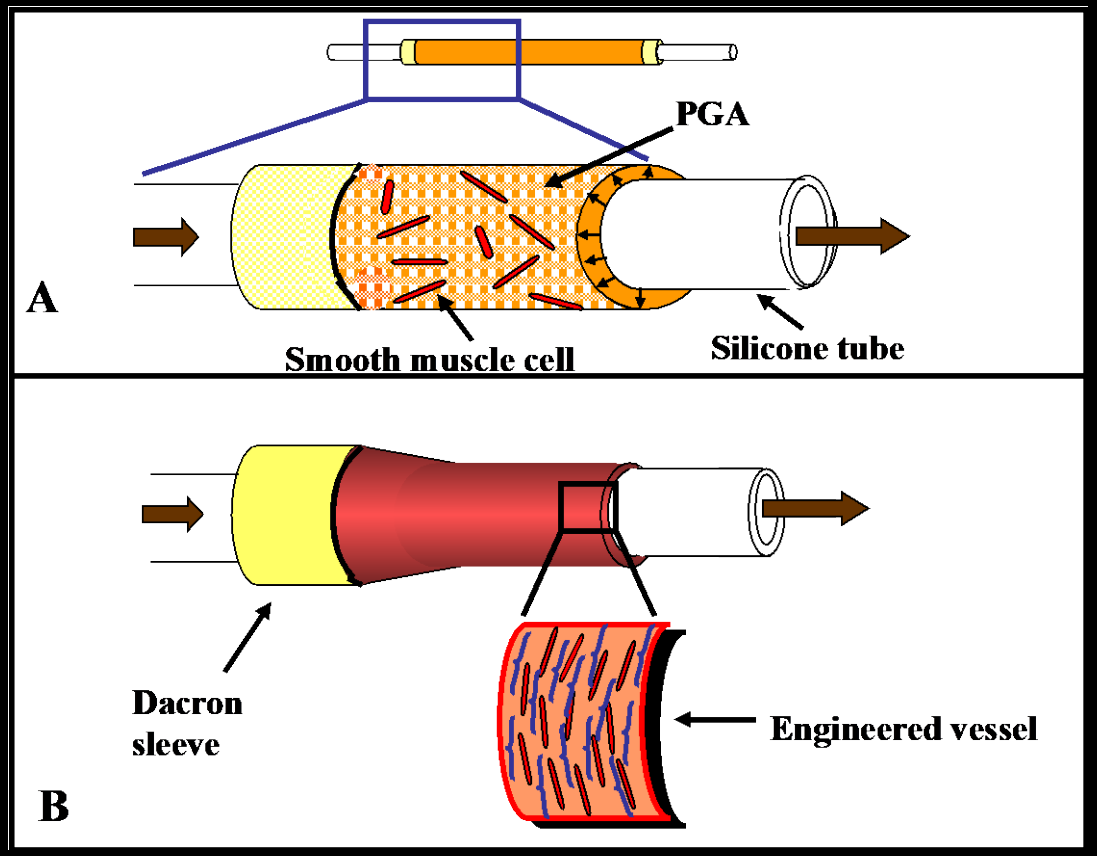
FINANCIAL DISCLOSURE:

Chief Medical Officer; Humacyte, Inc.

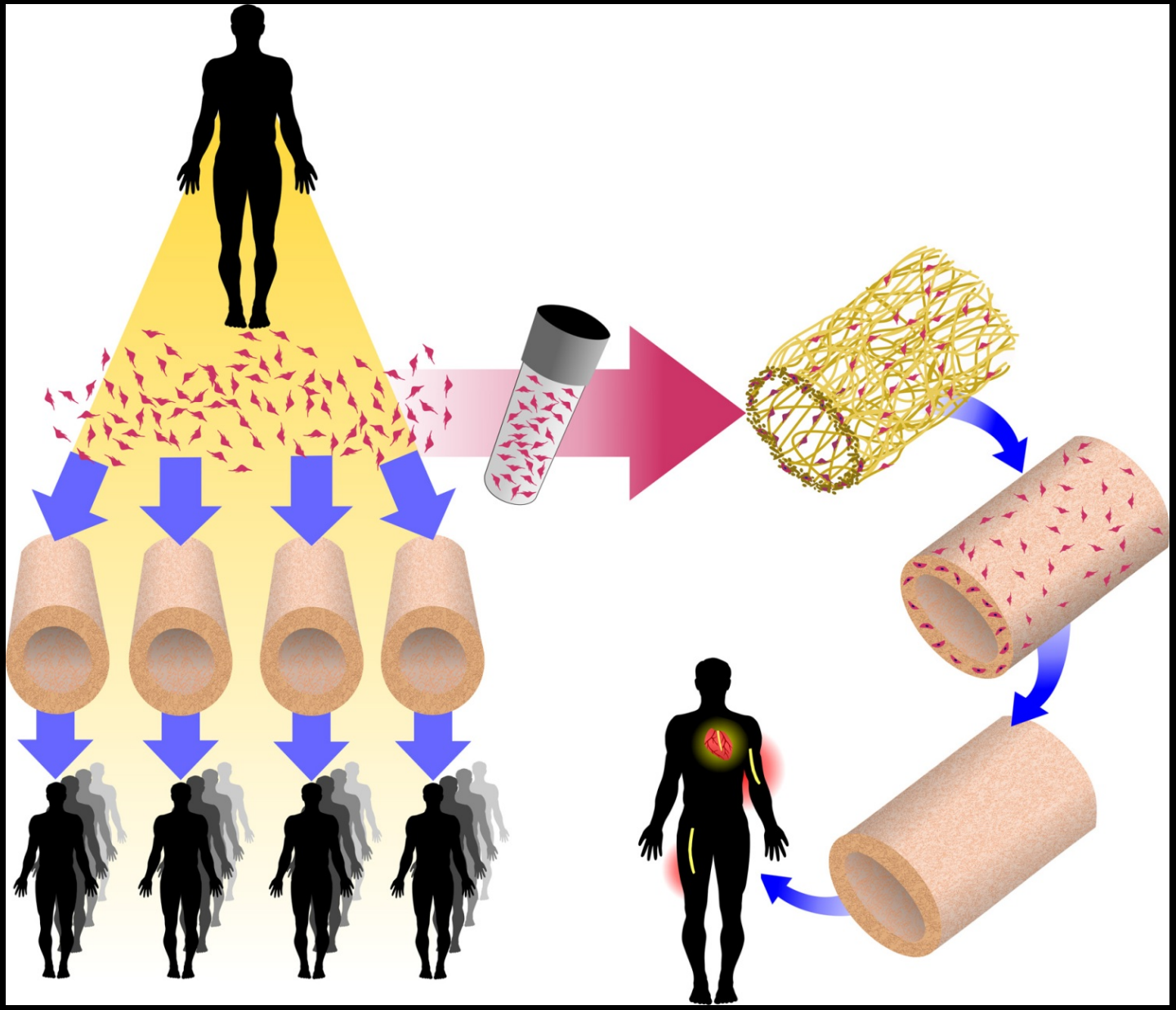
None of the data presented in this lecture is intended to be perceived as “claims” for the potential clinical use of the vascular grafts discussed today.

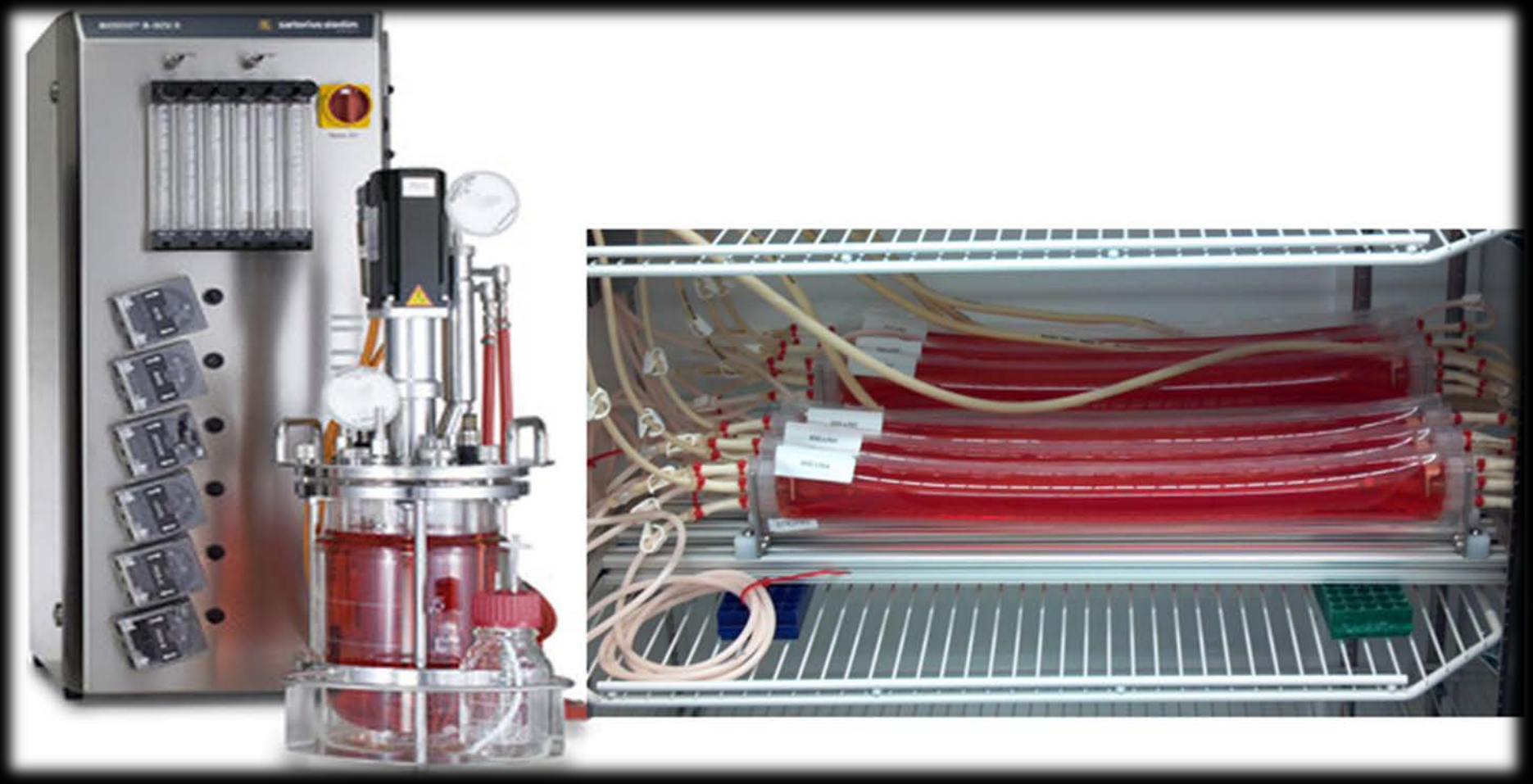
Polymer scaffold is designed to guide tissue shape ...

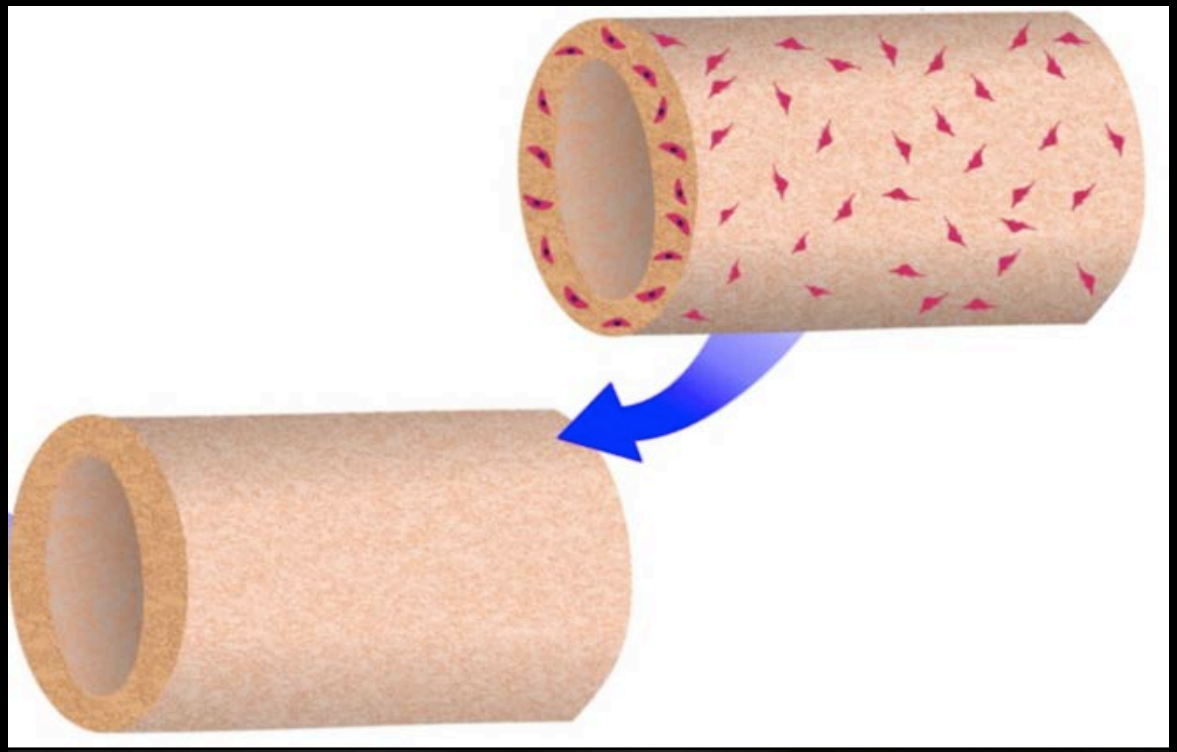


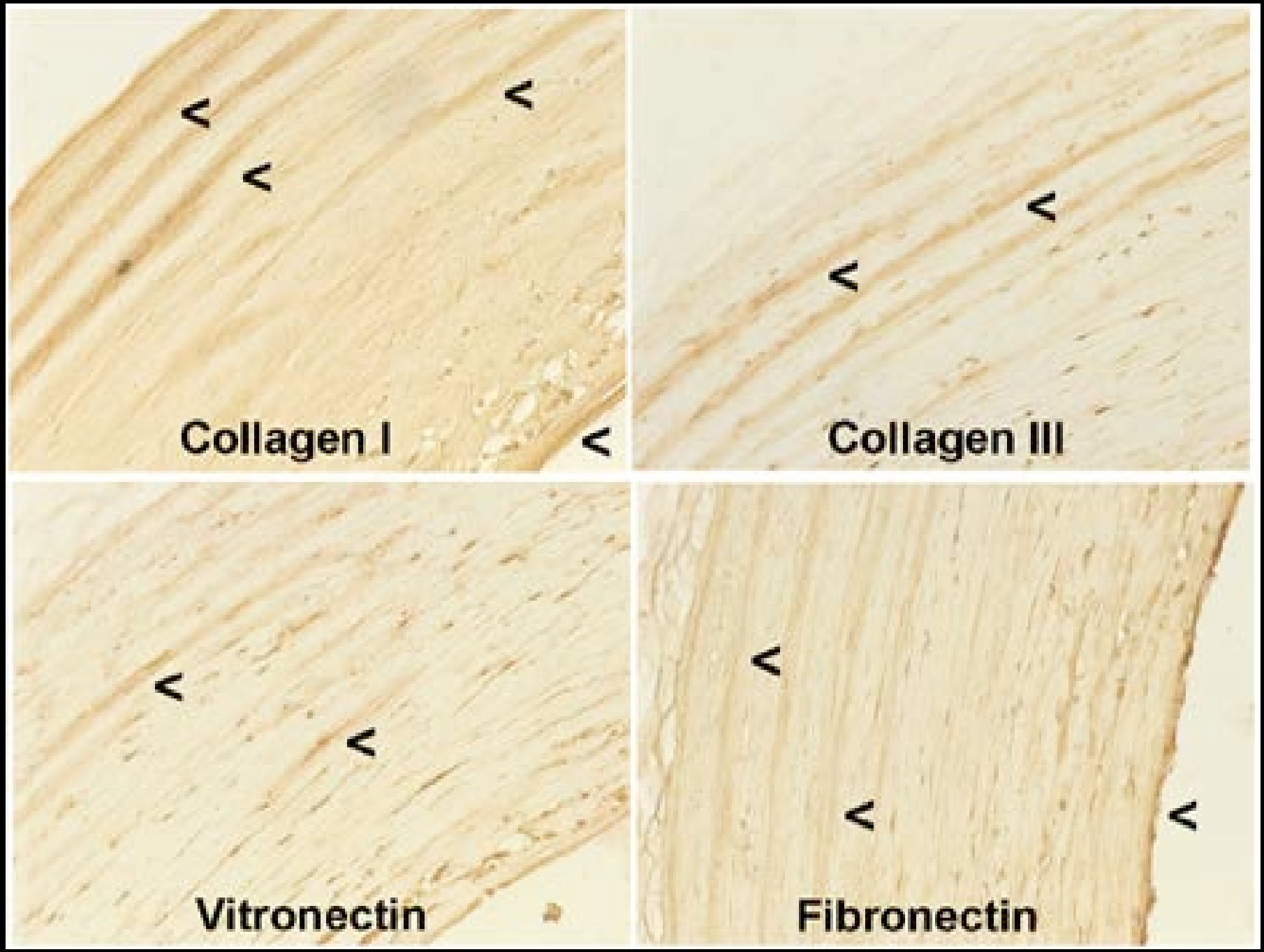


... and designed to degrade ...



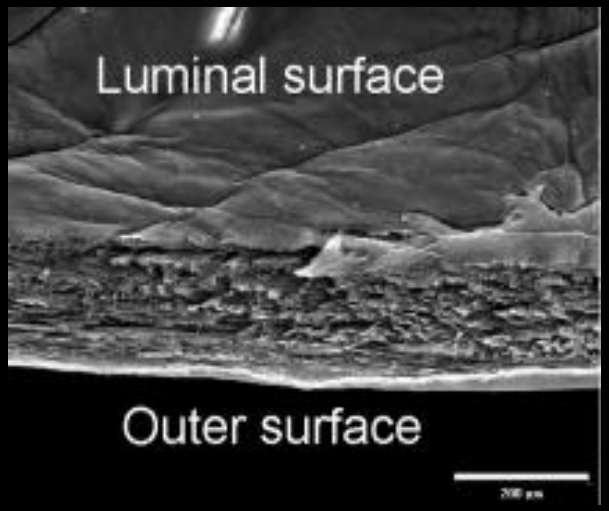


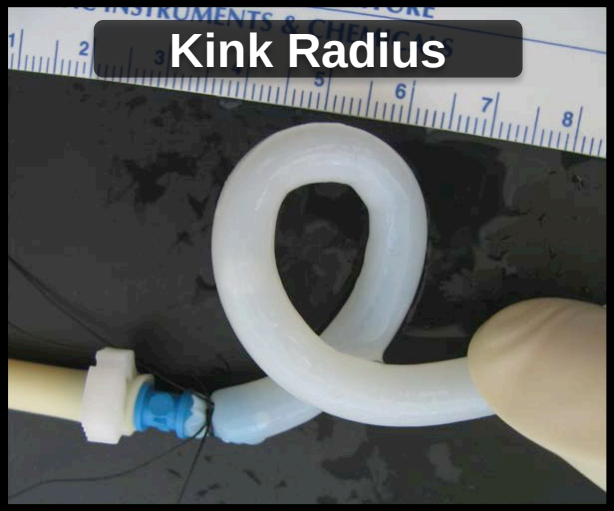


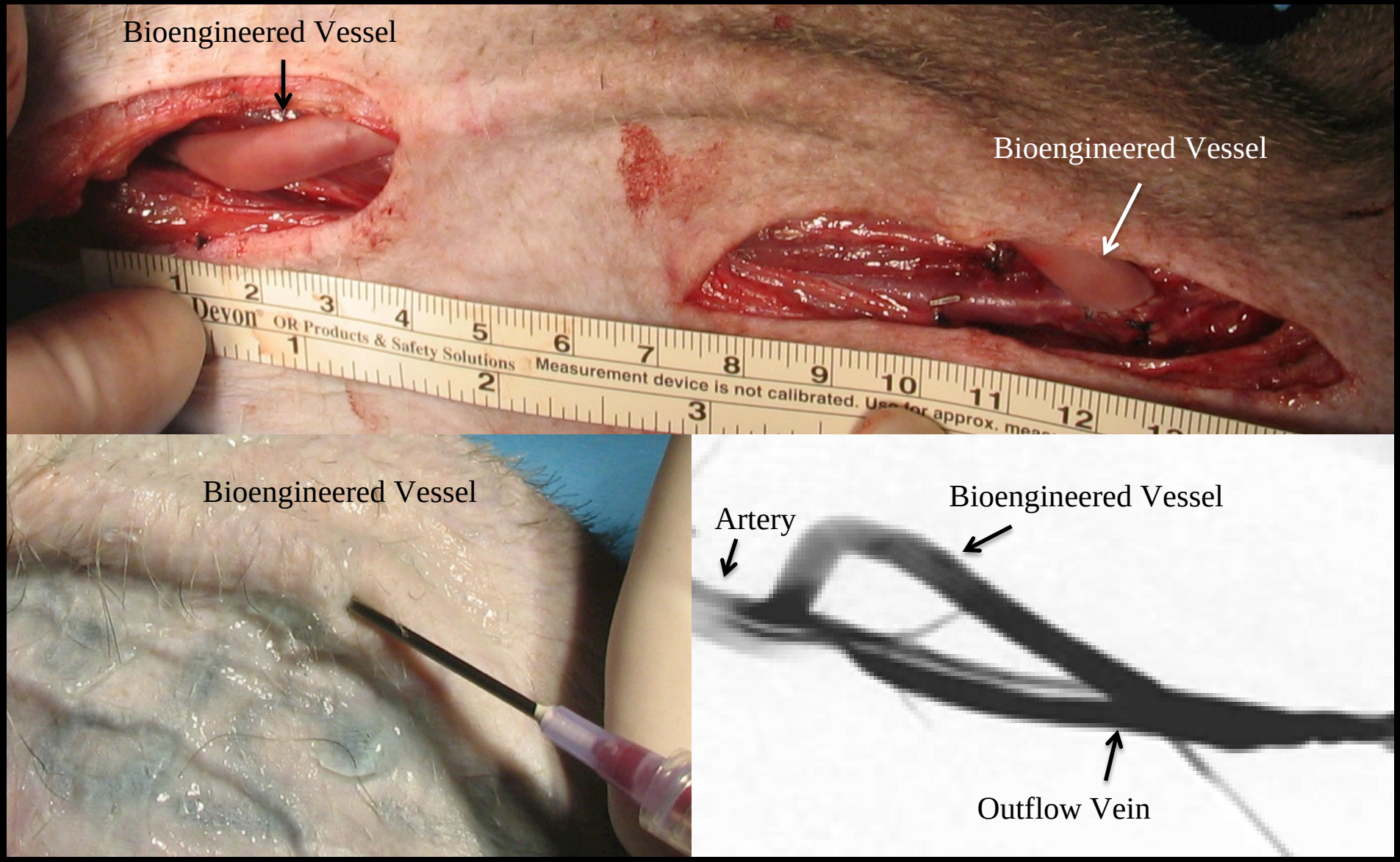

Collagen I
Collagen III
Vitronectin
Fibronectin

6mm diameter, 40cm length

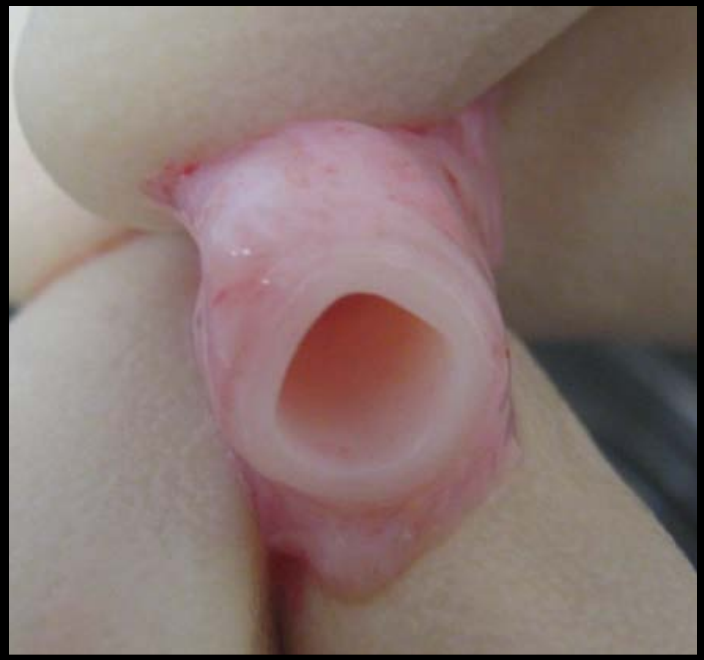
	Suture Strength (g)	Burst Pressure (mmHg)
HAVG	181 ± 18 (16)	3337 ± 343 (10)
Human saphenous vein	196 ± 29 (7)	1599 ± 877 (7)
Human internal mammary artery	138 ± 50 (6)	3196 ± 1264 (16)

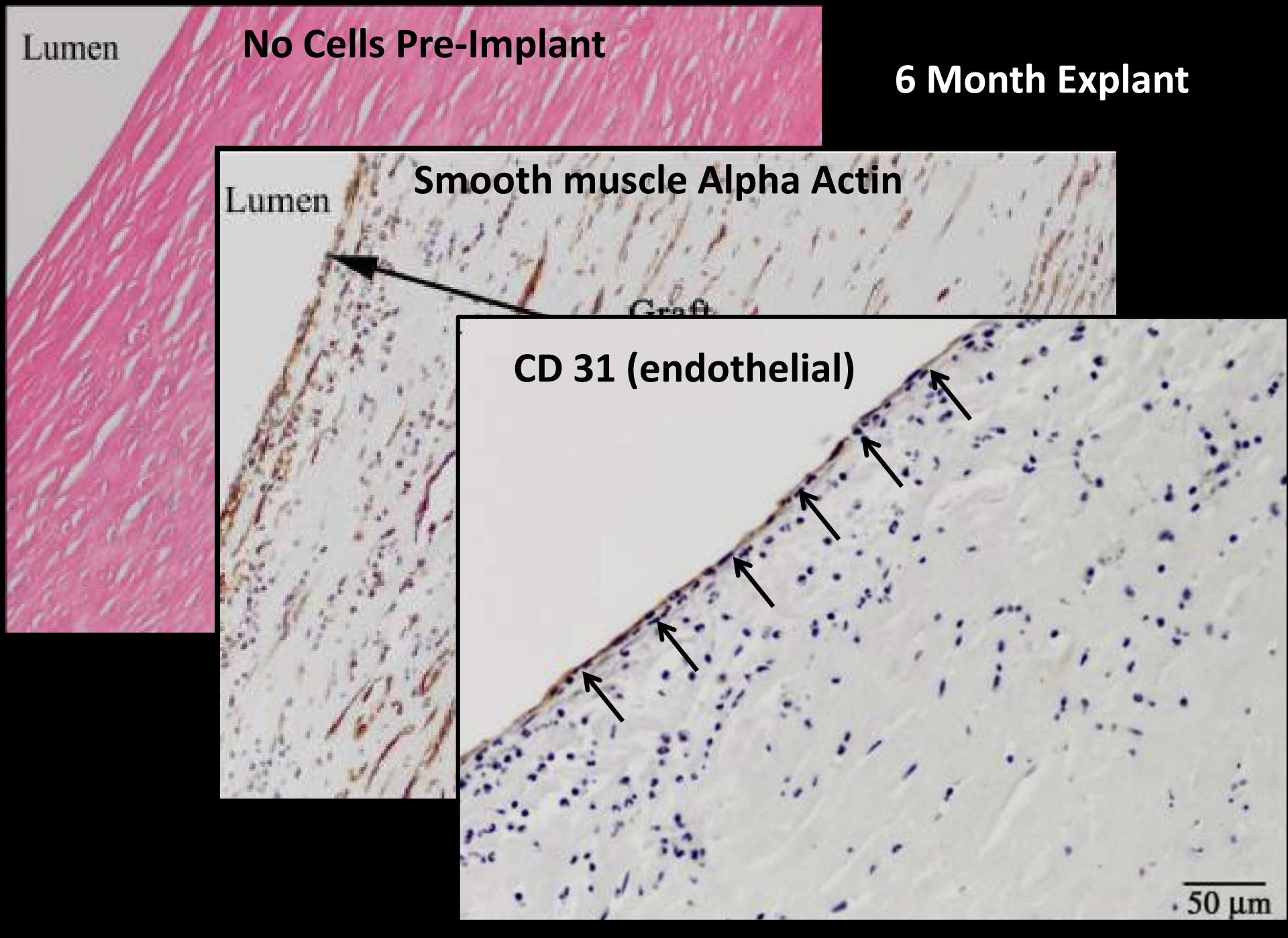


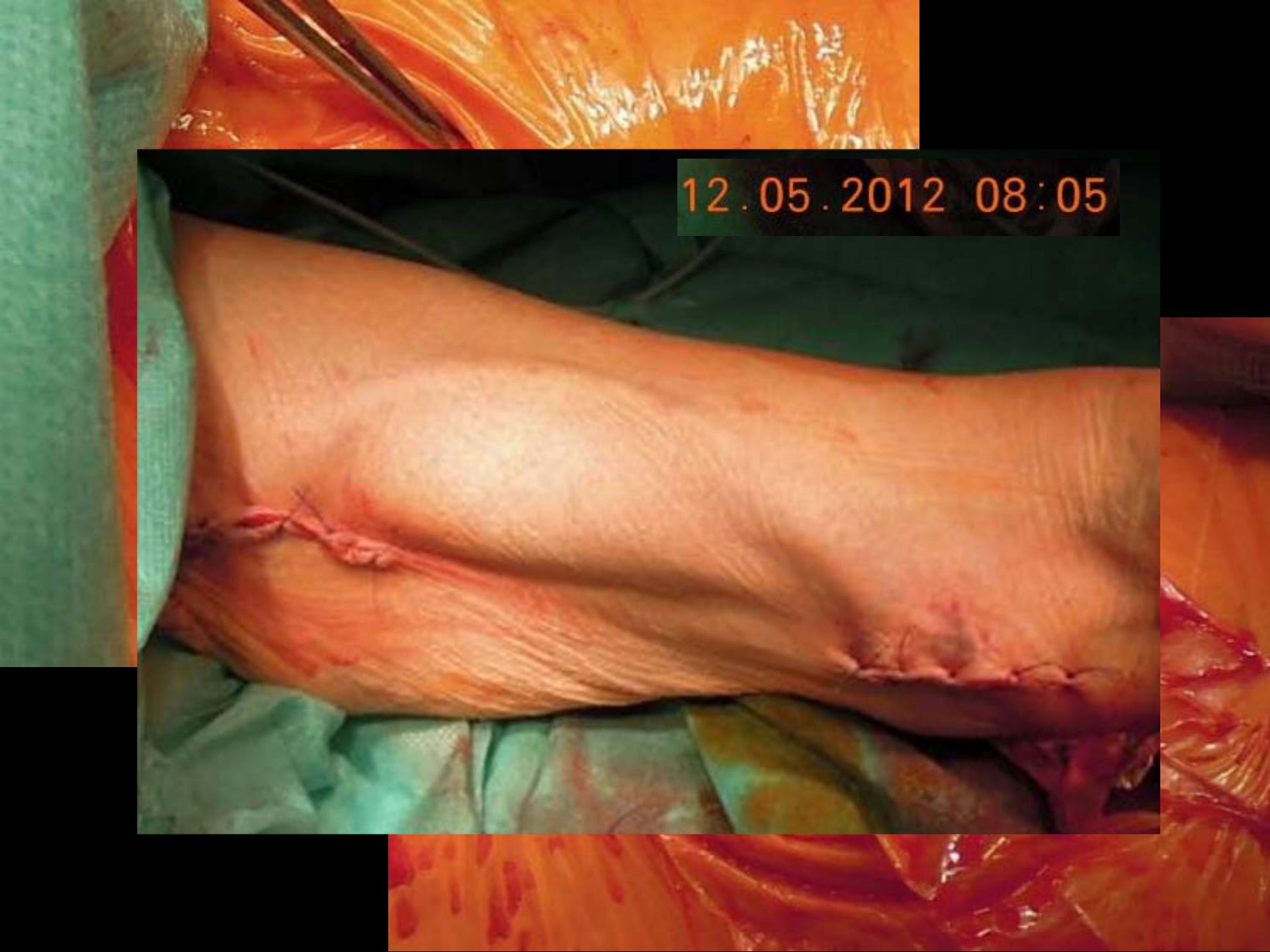




Dahl et al., *Sci Transl Med*, 2011, 68ra9.




Lumen
No Cells Pre-Implant
6 Month Explant
Lumen
Smooth muscle Alpha Actin
Graft
CD 31 (endothelial)
50 µm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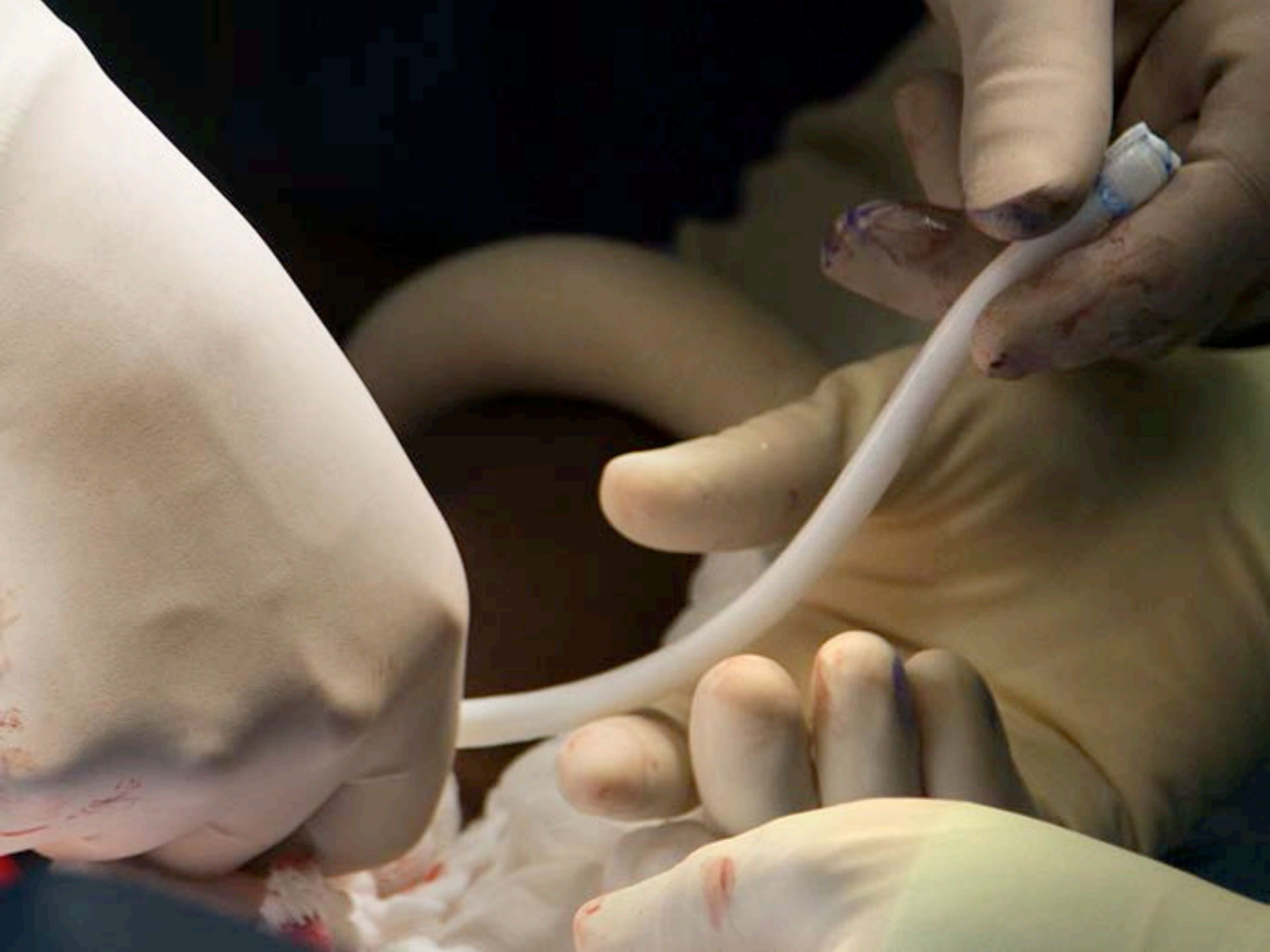

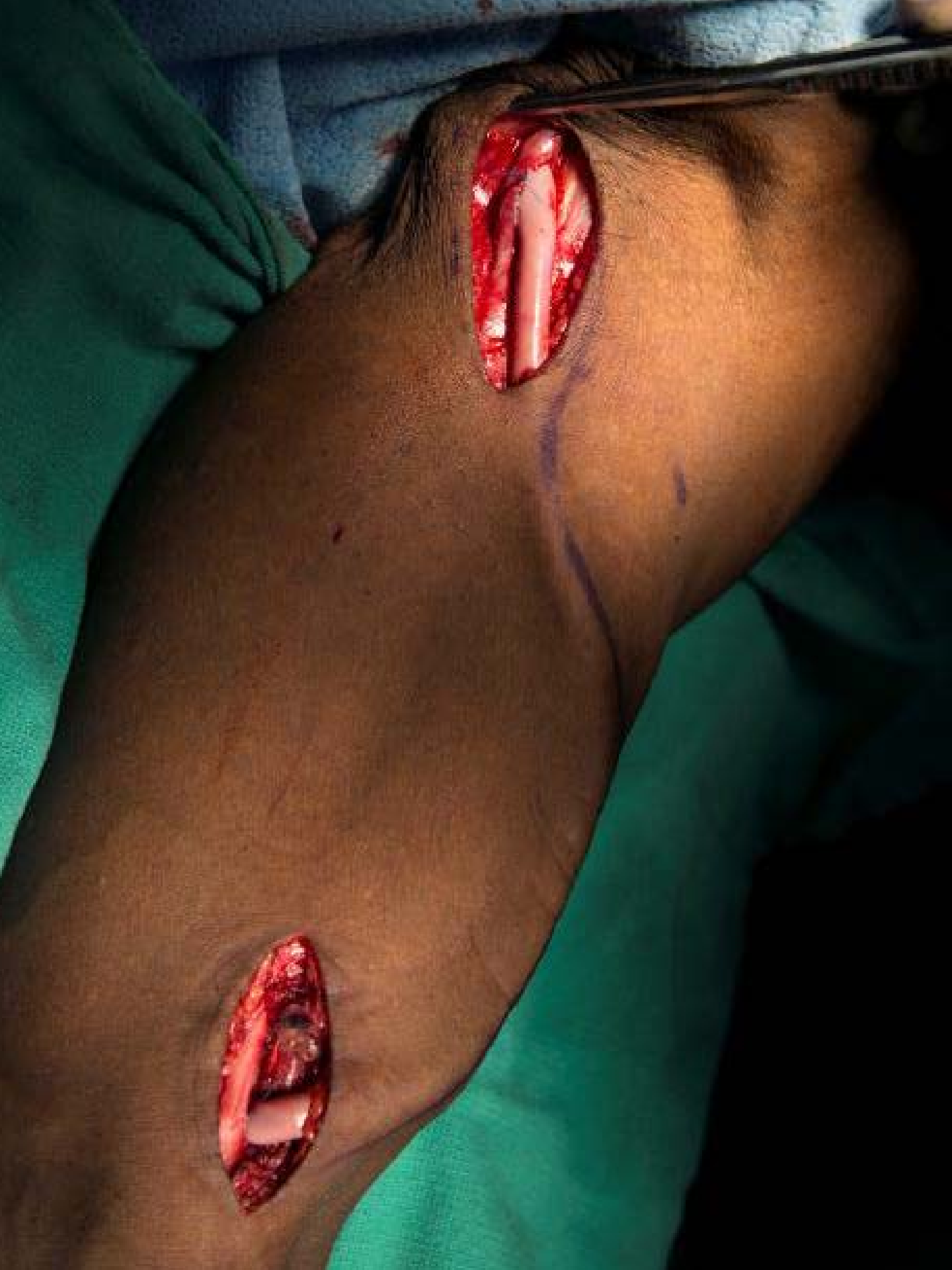

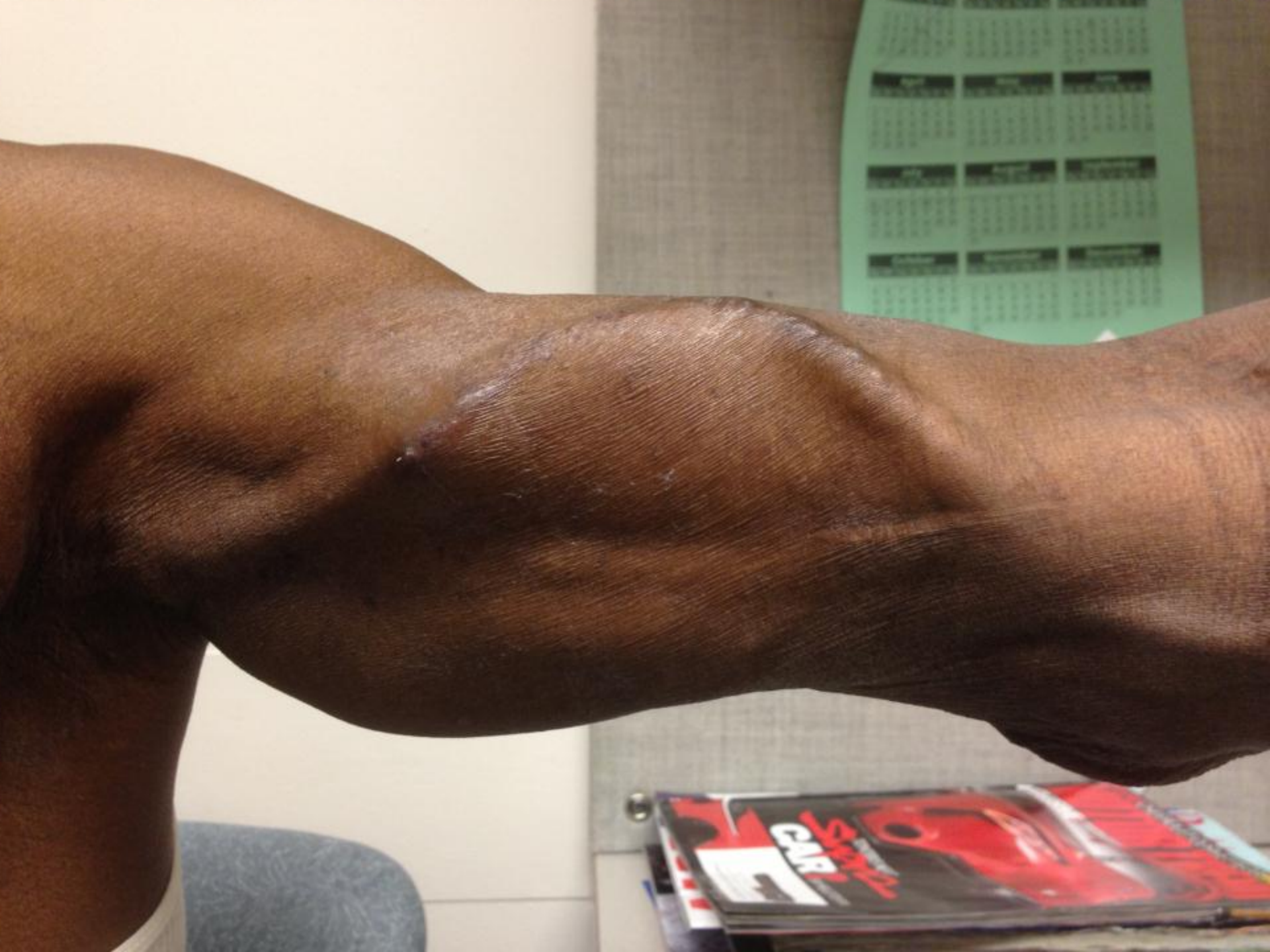
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Lancet Publication – May 2016

Bioengineered human acellular vessels for dialysis access in patients with end-stage renal disease: two phase 2 single-arm trials

Jeffrey H Lawson, Marc H Glickman, Marek Ilzecki, Tomasz Jakimowicz, Andrzej Jaroszynski, Eric K Peden, Alison J Pilgrim, Heather L Prichard, Malgorzata Guziewicz, Stanisław Przywara, Jacek Szmidt, Jakub Turek, Wojciech Witkiewicz, Norbert Zapotoczny, Tomasz Zubilewicz, Laura E Niklason

Lancet 2016; 387: 2026–34
See Editorial page 1969 and 1970
See Comment page 1976

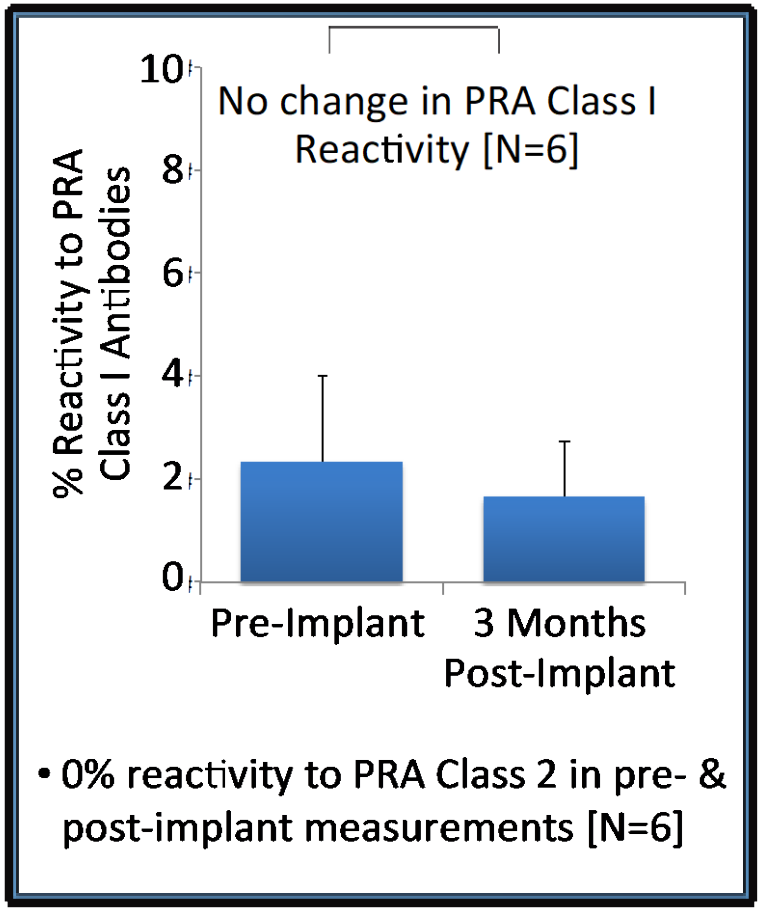
Humacyte, Durham, NC, USA
(J H Lawson MD PhD, H L Prichard PhD,

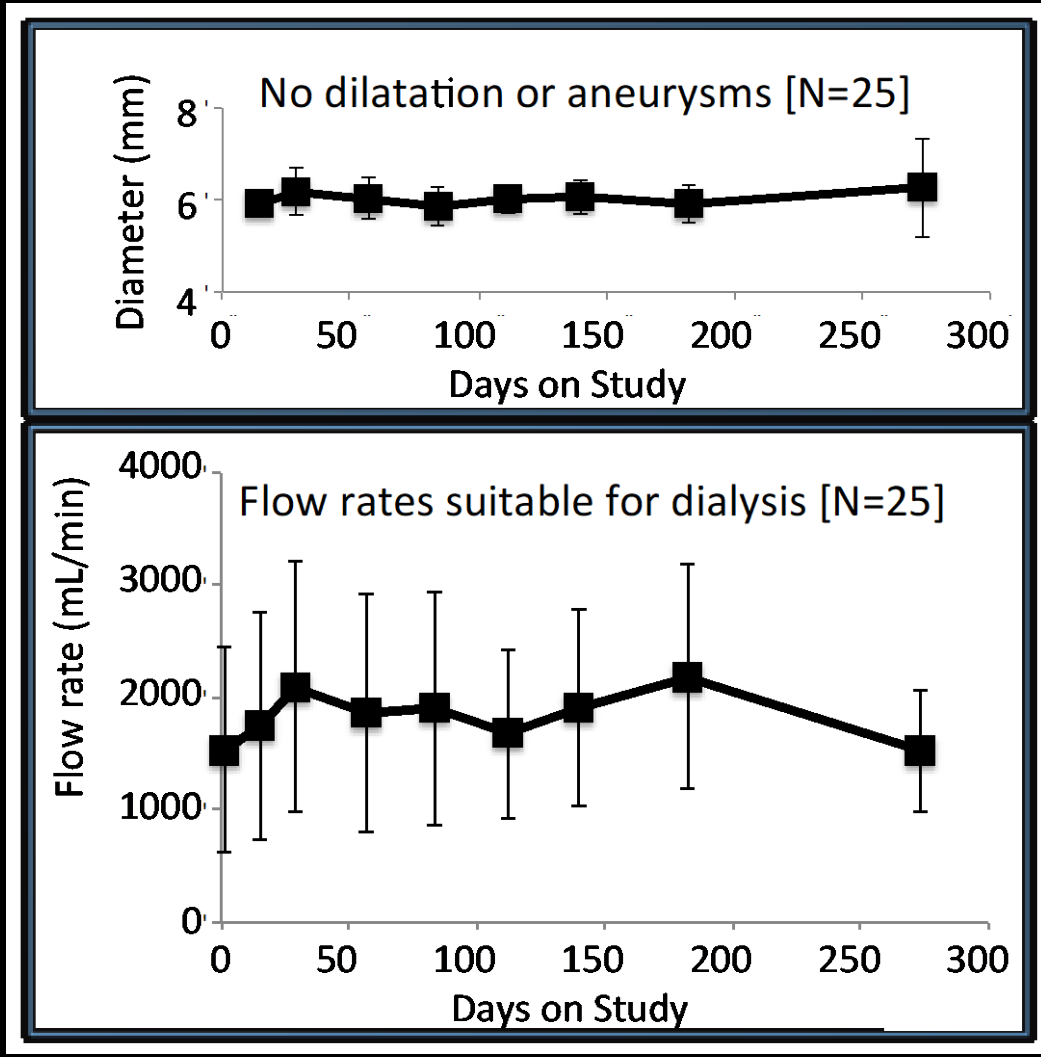
Summary

Background For patients with end-stage renal disease who are not candidates for fistula, dialysis access grafts are the best option for chronic haemodialysis. However, polytetrafluoroethylene arteriovenous grafts are prone to thrombosis, infection, and intimal hyperplasia at the venous anastomosis. We developed and tested a bioengineered human acellular vessel as a potential solution to these limitations in dialysis access.

Initial Clinical Outcomes of First-in-Man Human Implants (6 months)

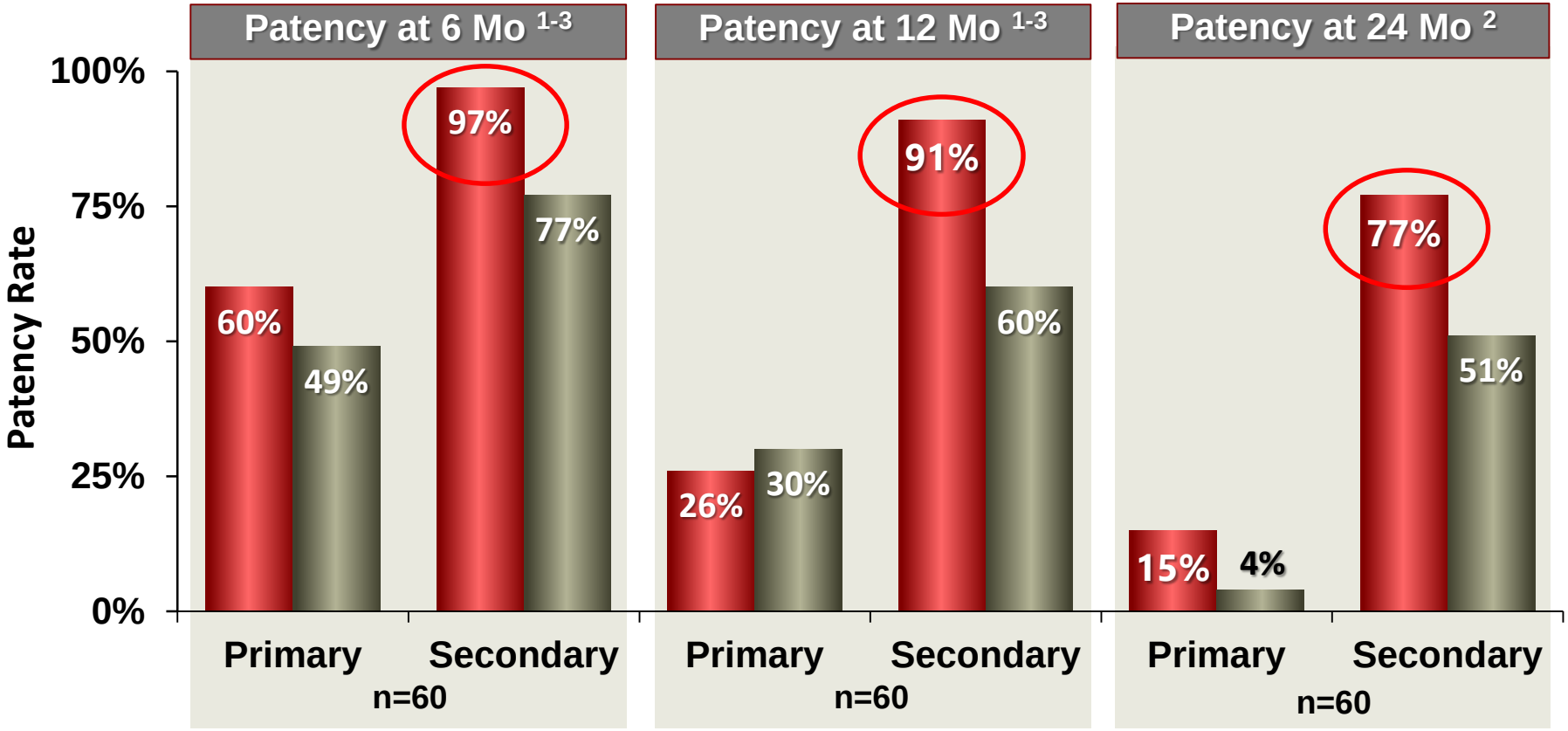
No indication of immune response





Lawson et al., *American Heart Association Meeting, Dallas TX* , 2013

Durable Patency



HAV Phase II Data vs Estimated Historical ePTFE Data

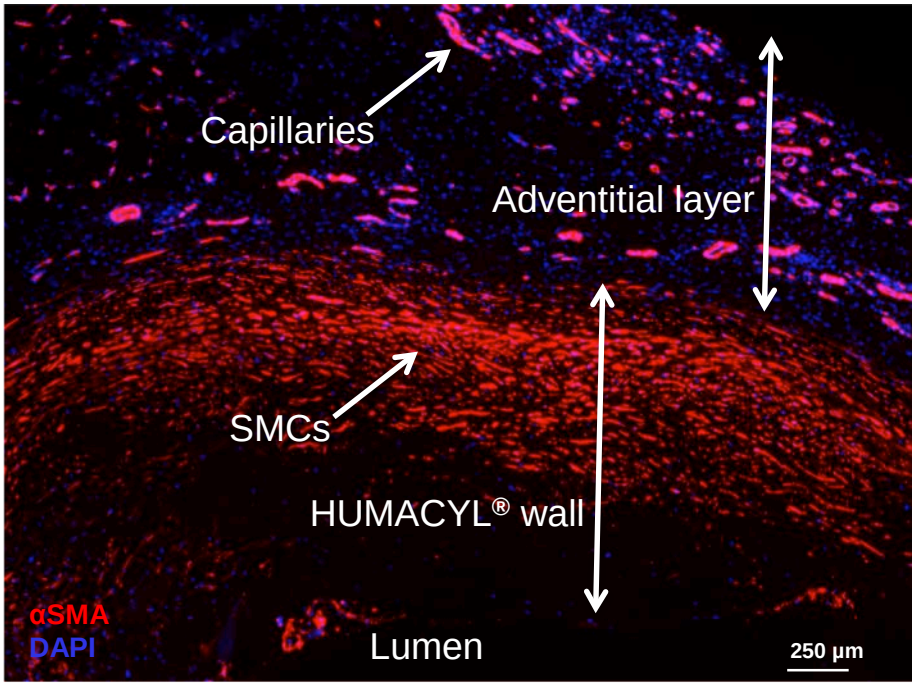
[1] Huber *Sem in Dial*, 2004,17:3.
[2] Miller *Am J Kid Dis, 2000,36:68.*
[3] Dixon, BS., *et al. NEJM,* 2009,5/21; 360(21), 2191-2201.

[4] Humacyte Phase II data, All pooled patients Poland and USA, CSR, as of May 2016.

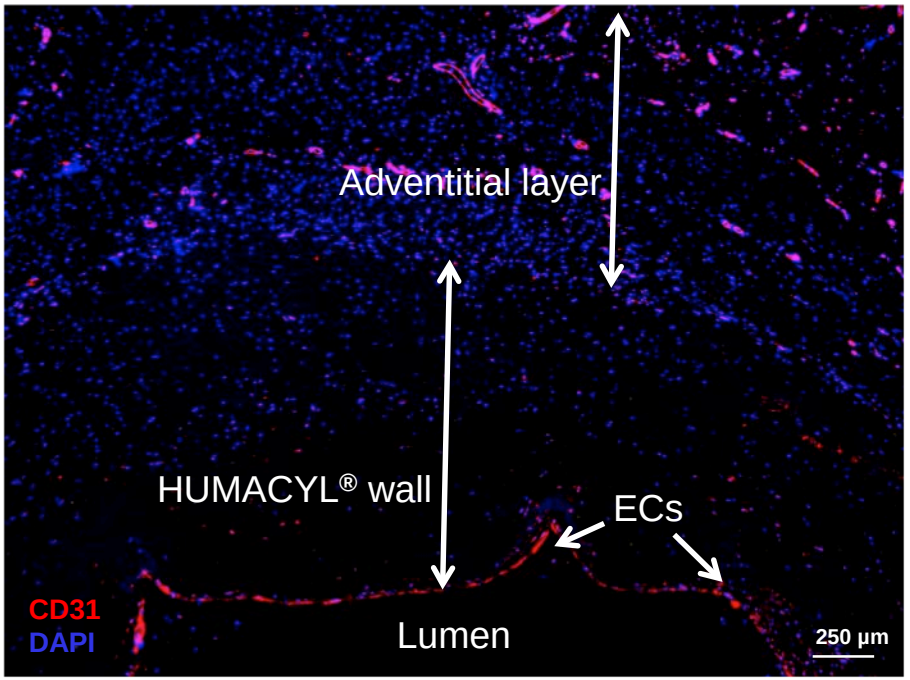
Clinical Evidence

- **Clinical data suggests that HUMACYL® becomes a living blood vessel:**

Smooth Muscle Cells (Red) Prominent in HUMACYL® Wall (44 wks); Adventitial Layer with Capillaries[3]



Endothelial Cells (Red) Line the HUMACYL® Lumen (44 wks)[3]



HUMACYL® repopulates with the patients own cells, angiogenesis enables self-maintenance, and the living blood vessel heals itself in response to injury

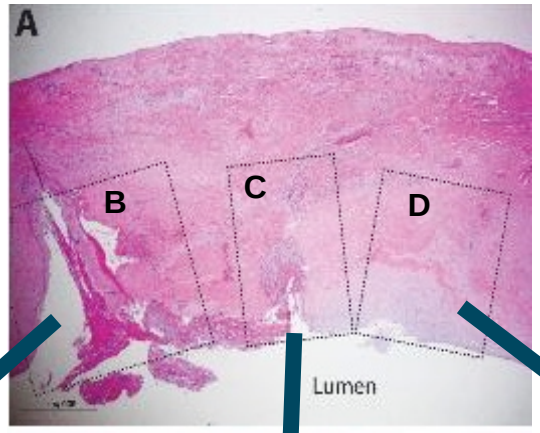
[1] Samples were assessed at 16, 18, 22, 27, 37, 44, 55, 97, 100, 121, and 200 weeks.
[2] No evidence of chronic inflammation
[3] Explant from 01-001-V003, 44 weeks after implantation.

HUMACYTE

Clinical Evidence of Healing

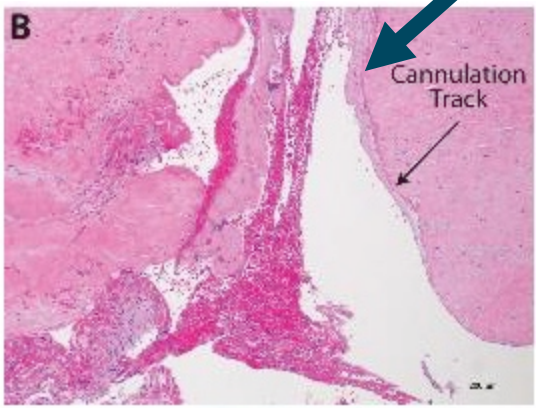
- **Clinical data suggests that HUMACYL® heals after cannulation injury[1]**

Low mag of 3 cannulation sites

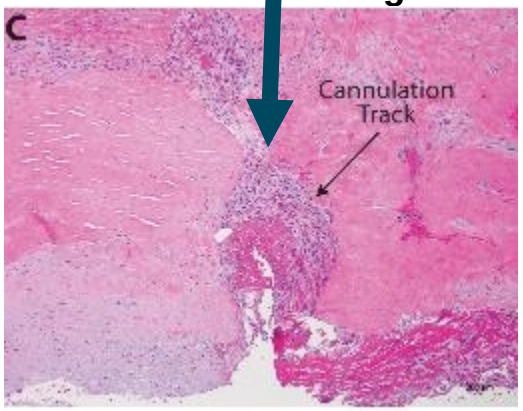


After cannulation, HUMACYL® heals to close the cannulation injury site; in contrast, PTFE has permanent cannulation injury with no healing benefit

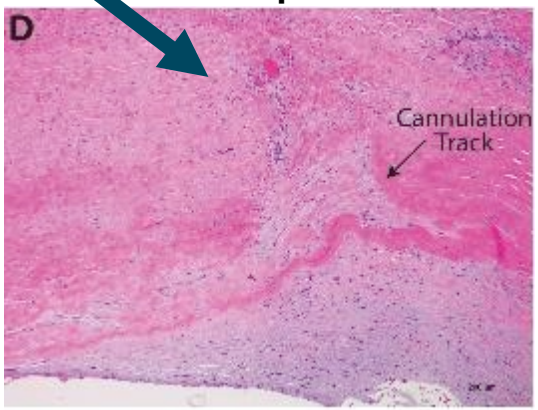
Fresh cannulation site



Cannulation site during healing



Cannulation site repaired



Repopulation with host vascular cells and angiogenesis enable healing

PTFE (Explanted)

[1] HUMACYL® Patient CLN-PRO-V003 01-001 histology Phase II trial, 2014. unpublished data. A section of an implanted Humacyte graft removed at 11 months. All images are Hematoxylin & Eosin stain (H&E) (n=1)

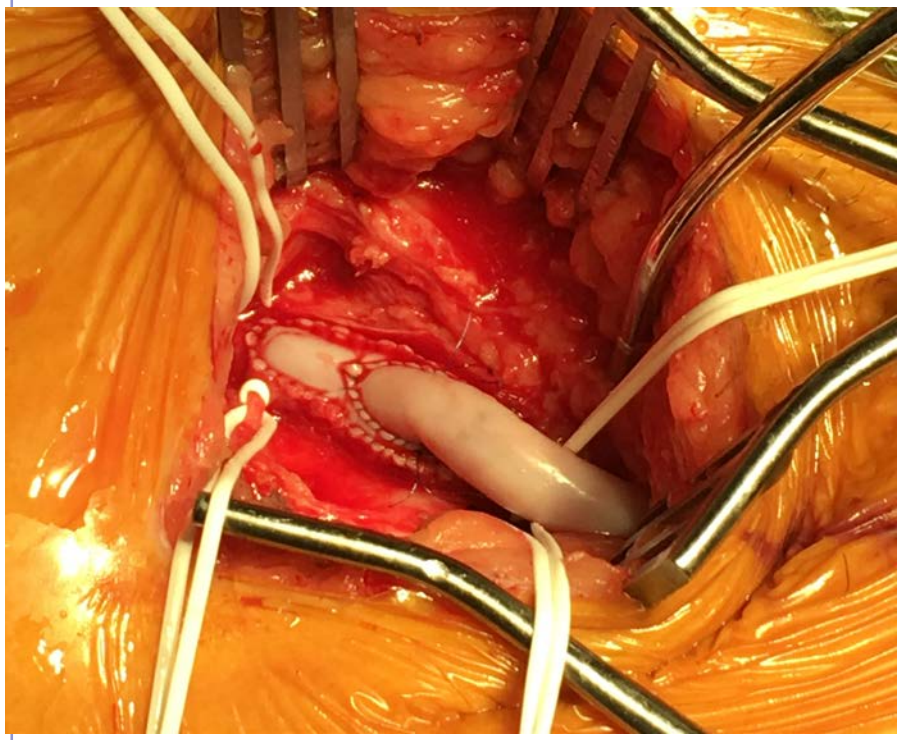
Ongoing Phase 3 Study (HUMANITY Trial)

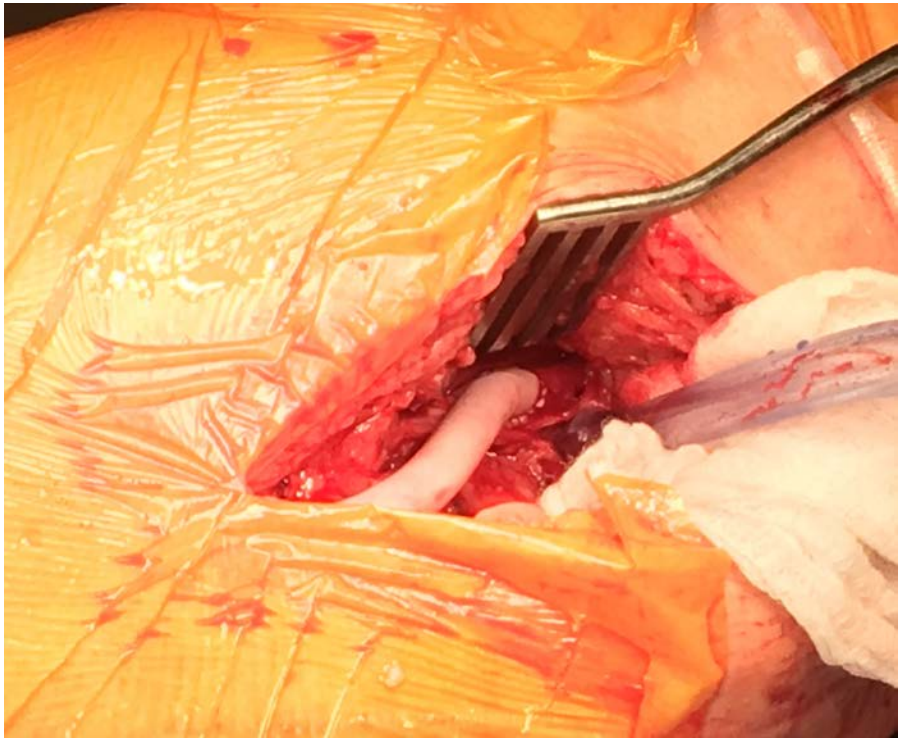
- **Clinical Study**
  - 350 patients – head to head vs. ePTFE
  - 6 countries, ~ 40 sites
  - 2 year follow up
  - Primary end point – secondary (enduring) patency
  - Secondary end points – infection and intervention rates

- **Global Status**
  - US, UK, Israel, Poland, Germany and Portugal are all approved and enrolled clinical subjects

- **Operations**
  - Successful vessel manufacturing, quality assurance and vessel release
  - Successful vessel distribution to US, European and Israeli sites
  - First patient enrolled 24 May 2016.
  - Last patient (**355)** enrolled September of 2017

Phase 2 Studies for Arterial Bypass

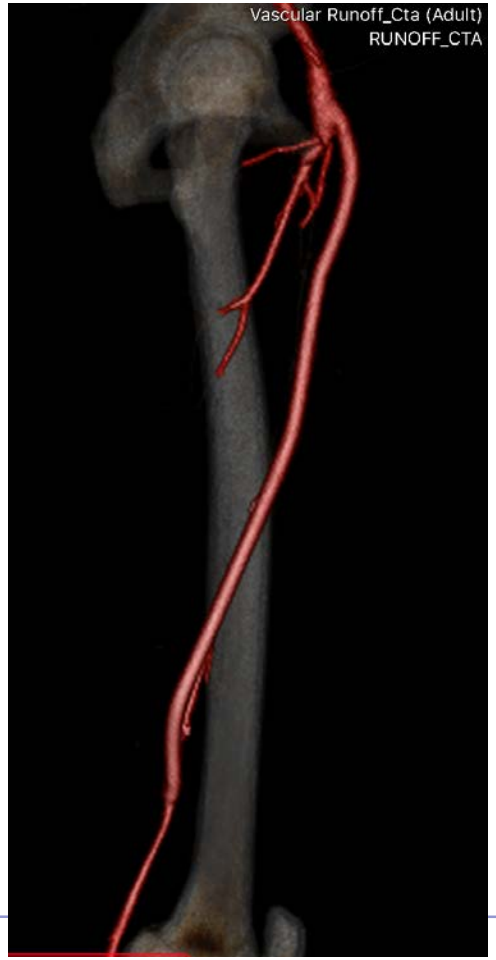




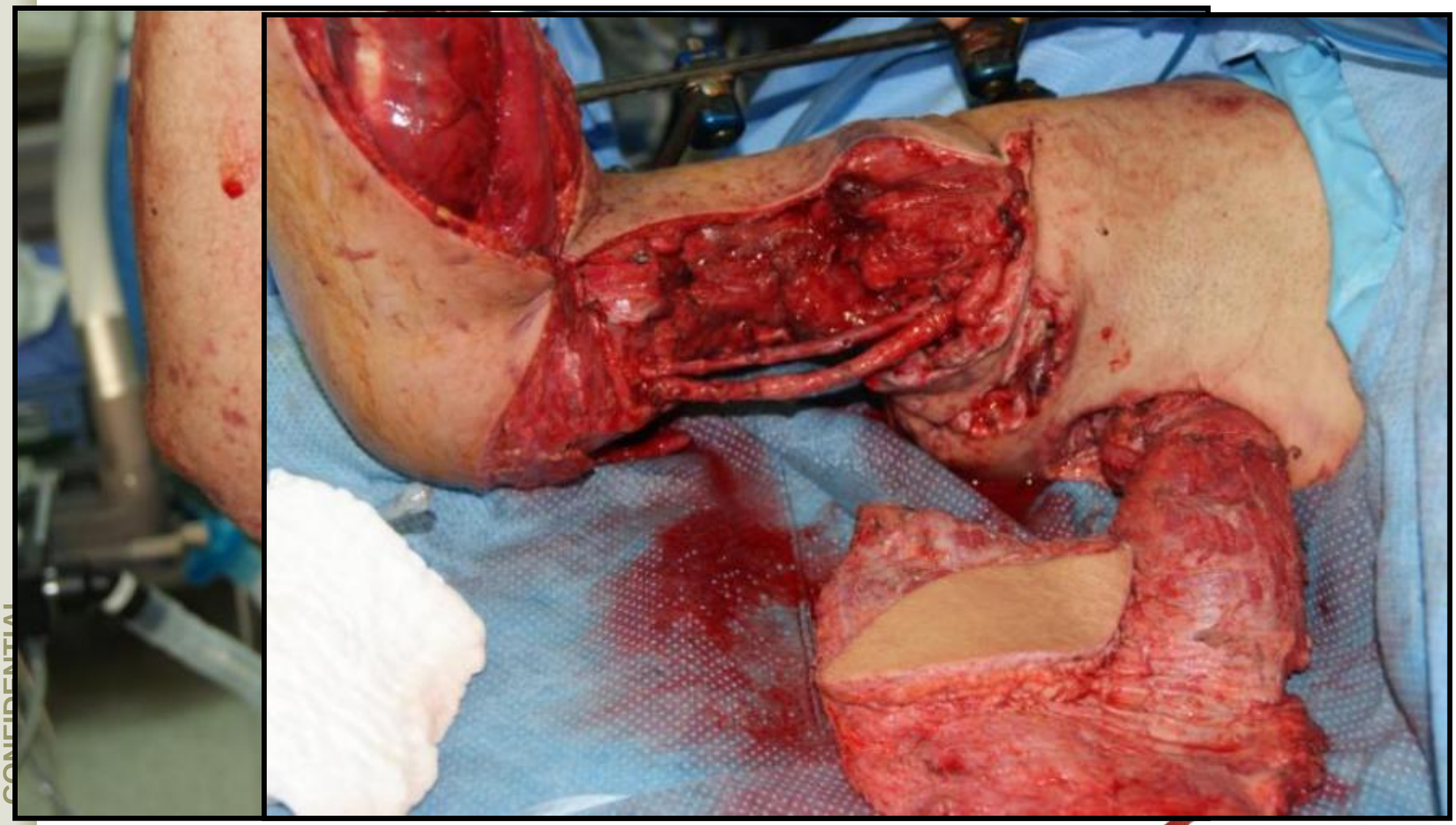
Phase 2 Study for Arterial Bypass

28 days

6 months



Vascular Trauma



Summary

- Off-the-shelf bioengineered vascular tissues are possible
- Non immunogenic, integrate with native tissue, repopulate and remodel
- Post implant vessels with increased strength and appear to have little intimal hyperplasia
- Phase II clinical trial are complete for hemodialysis and ongoing for PAD and vascular trauma
- Global Phase III clinical trial in hemodialysis access has completed enrollment and a number of additional clinical cardiovascular programs are in development