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BIOMECHANICS GROUP

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Advanced culture systems for ex-vivo vascular tissue conditioning

Gianfranco B. Fiore

Standard procedure with
aortic/pulmonary
homografts

Explantation

Cryopreservation

Thawing

Implantation



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*Banca dei tessuti
cardiovascolari*

HOMO project
(never completed...)

Thawing

Decellularization

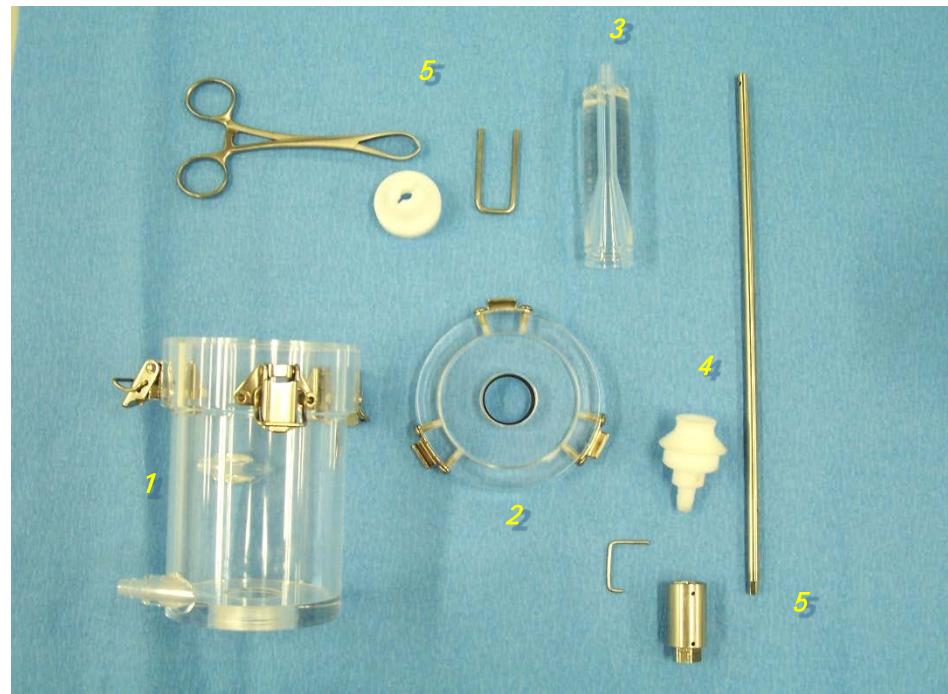
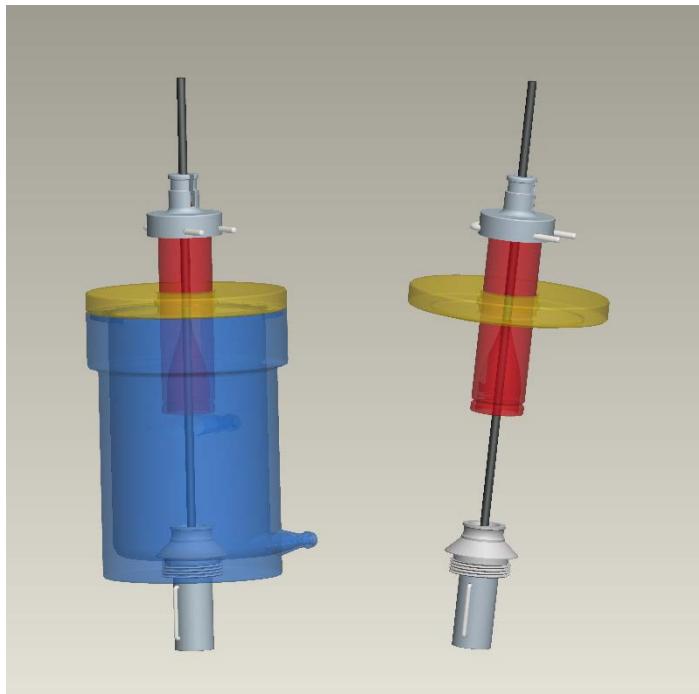
Recellularization
with the recipient's cells

In vitro culture

Implantation

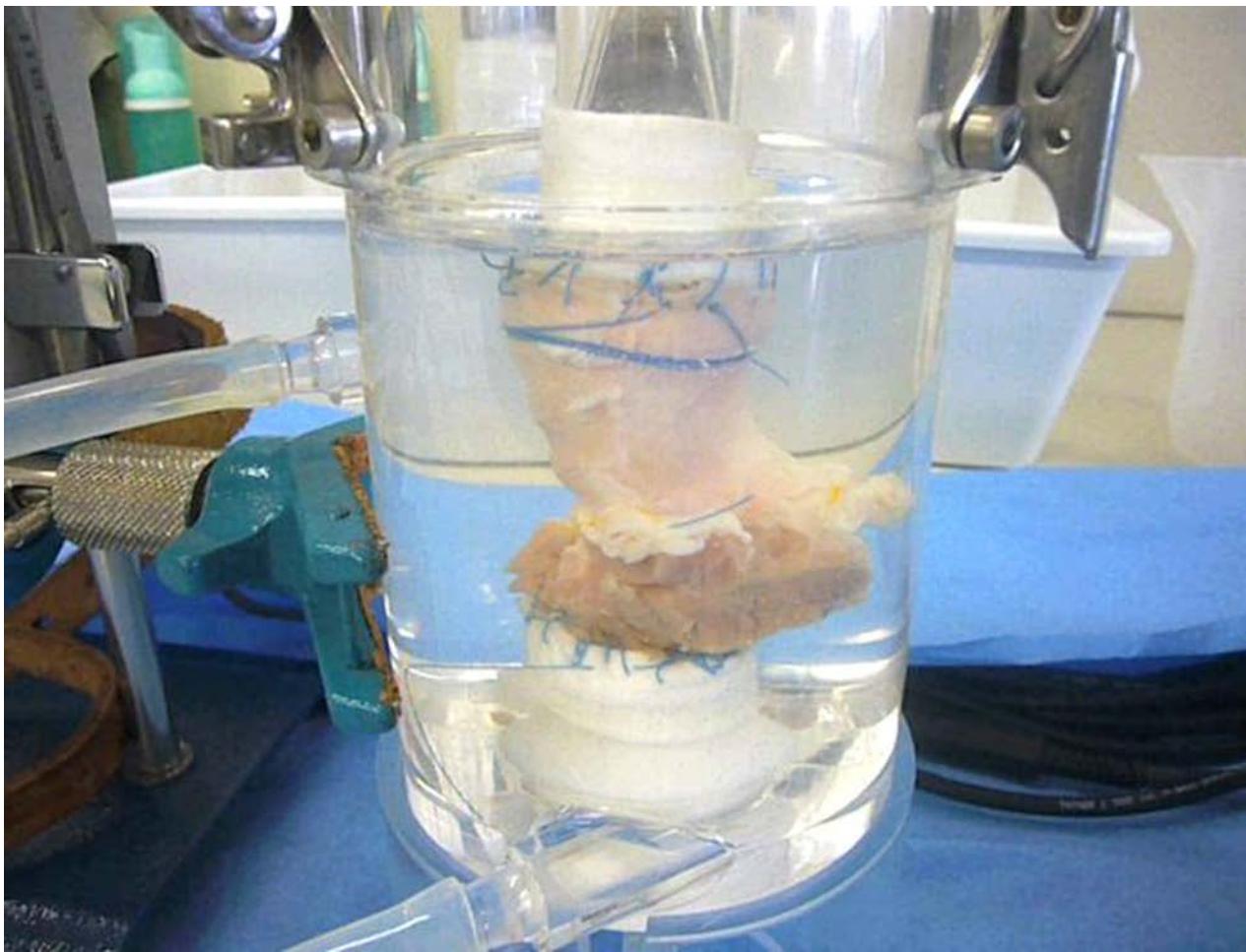


Dynamic culture
system (bioreactor)

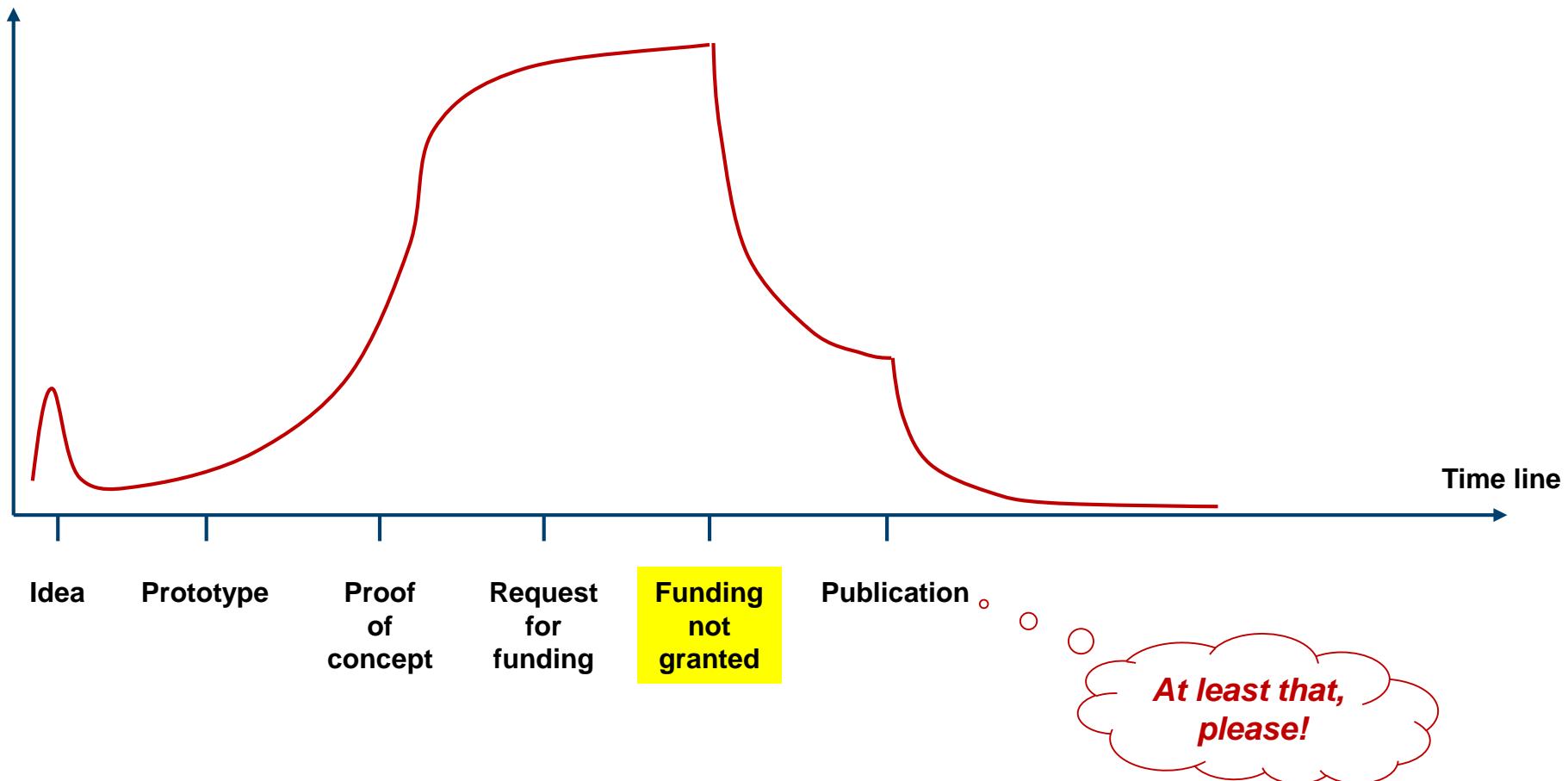


- 1) chamber
- 2) cover
- 3) Upper aortic root holder
- 4) Lower aortic root holder
- 5) Aortic root mounting tools

The background to the whole affair



Vismara et al., *Ann Biomed Eng* 2010

Enthusiasm

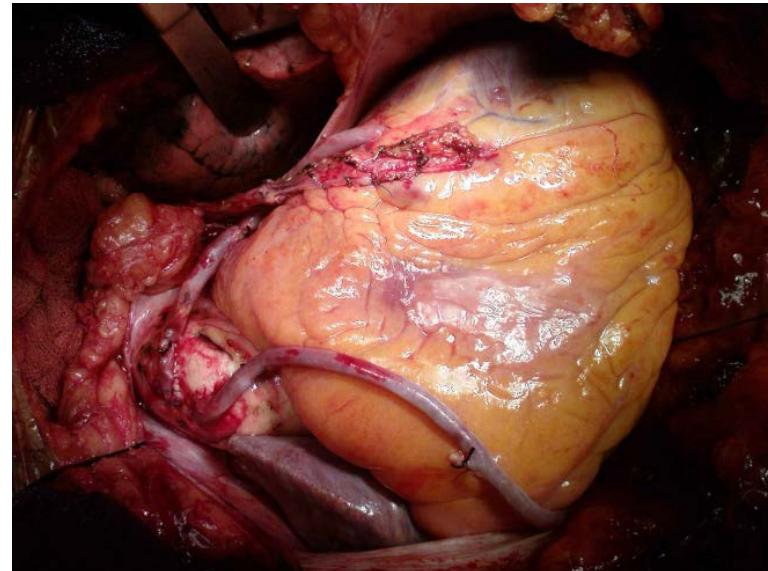
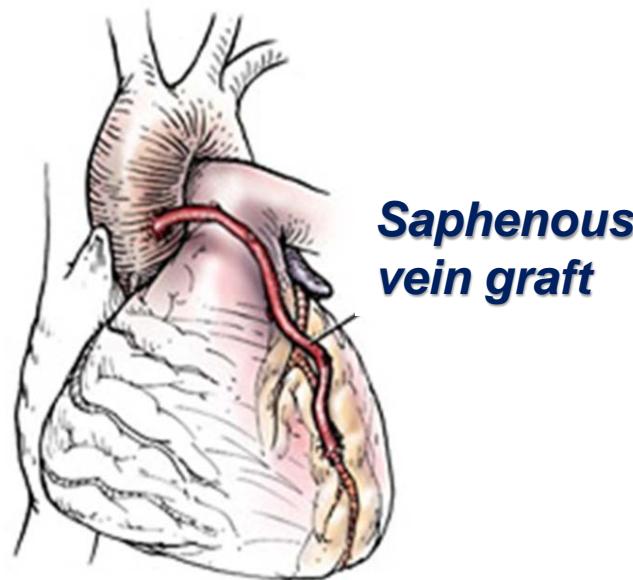
The Vein Graft Disease (VGD)

- Saphenous vein (SV) highly used in multiple Coronary Artery Bypass Grafting (CABG)
- Long-term patency of SV decreases over time after CABG due to **pathological remodeling** of the vessel wall

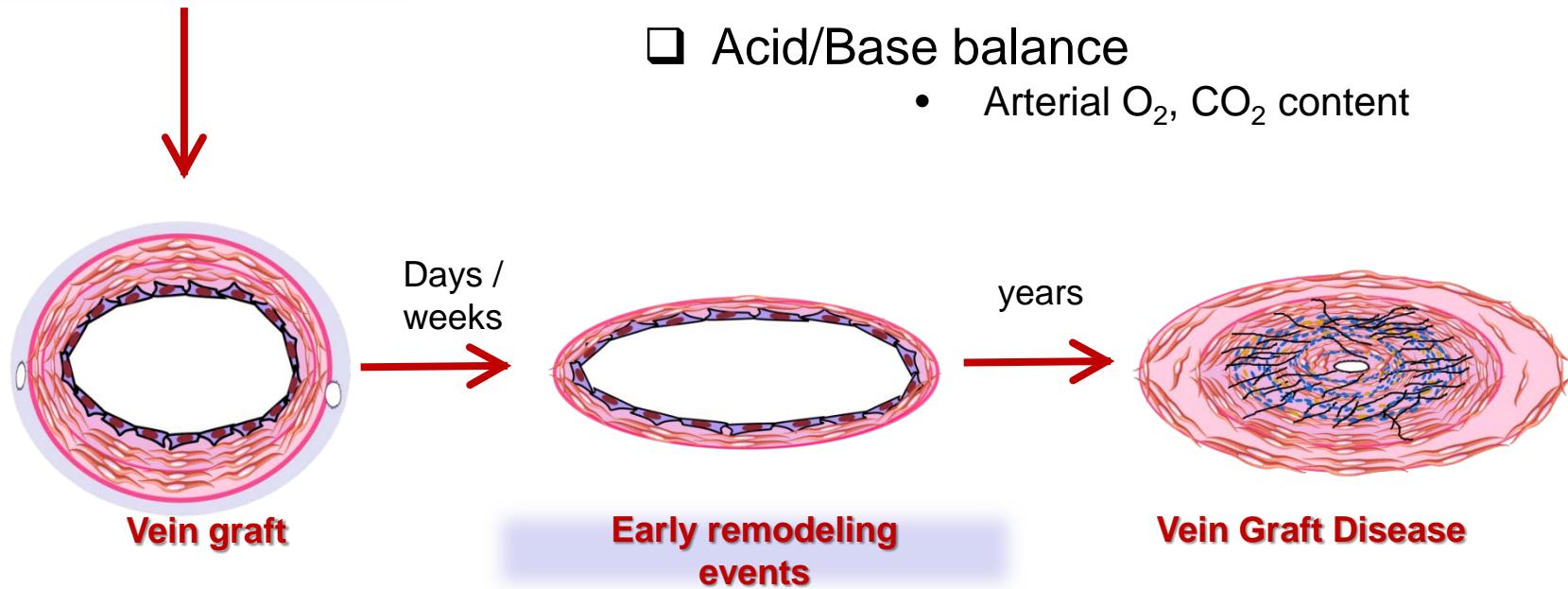


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*Dip. to malattie
cardiovascolari*

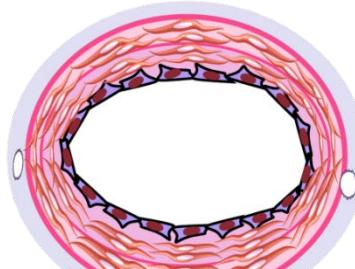


**Patient
(self-transplant)**



Piola, et al., *Recent Pat Cardiovasc Drug Discov*, 2012

**Patient
(OR-discarded
sample)**



Vein sample

Arterialization of the vein graft:

Mechanical:

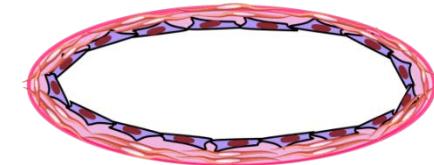
- 80-120 mmHg, pulsatile
- Shear stress (1-7 Pa)

Acid/Base balance

- Arterial O₂, CO₂ content



**Ex-vivo vessel culture
(days / weeks)**

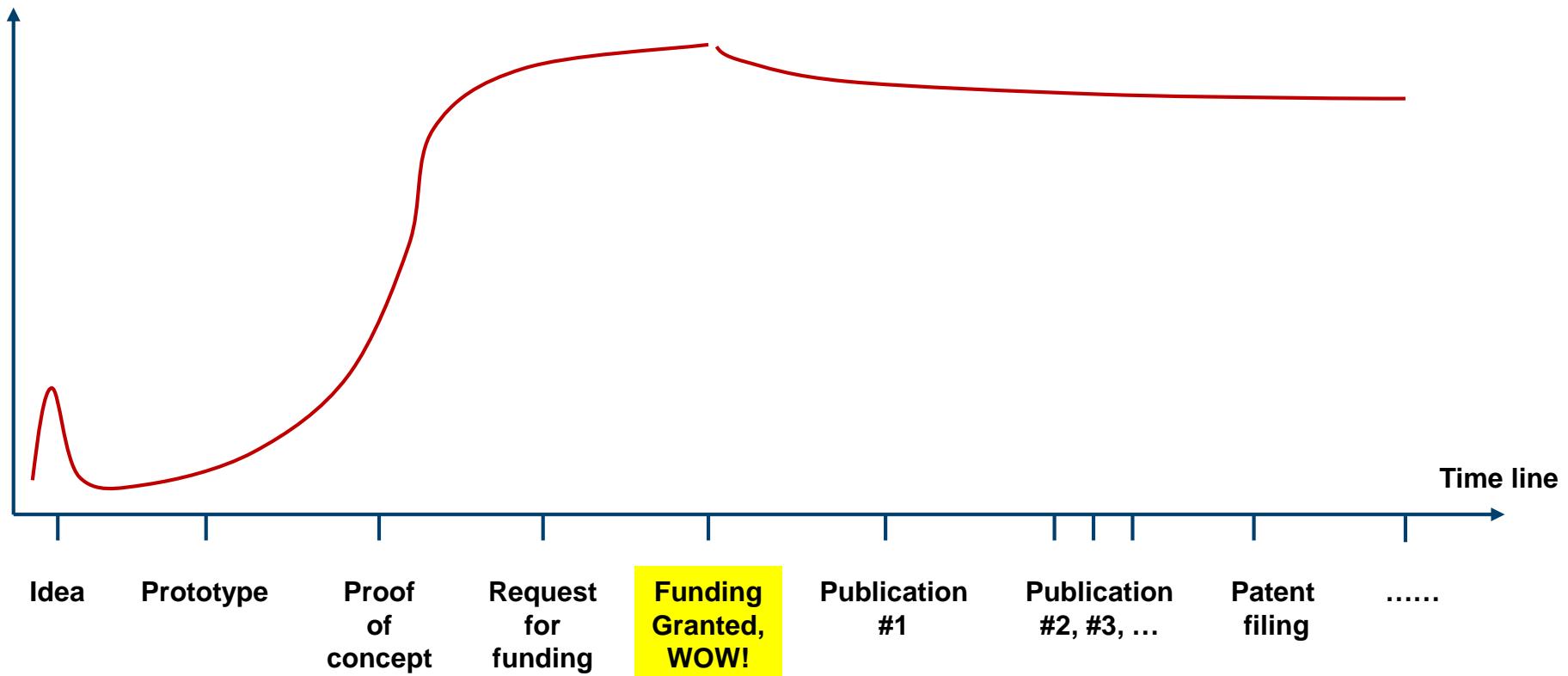


**Early remodeling
events**

Years 2011 - today: *The affair history thereafter*

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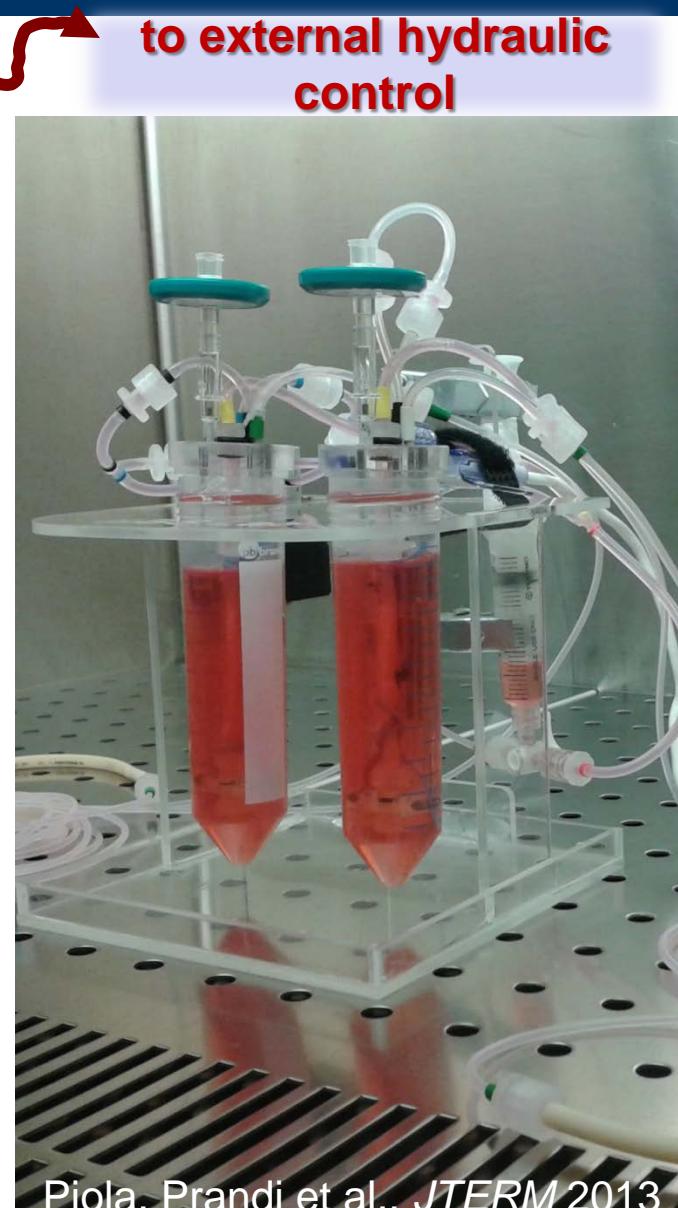
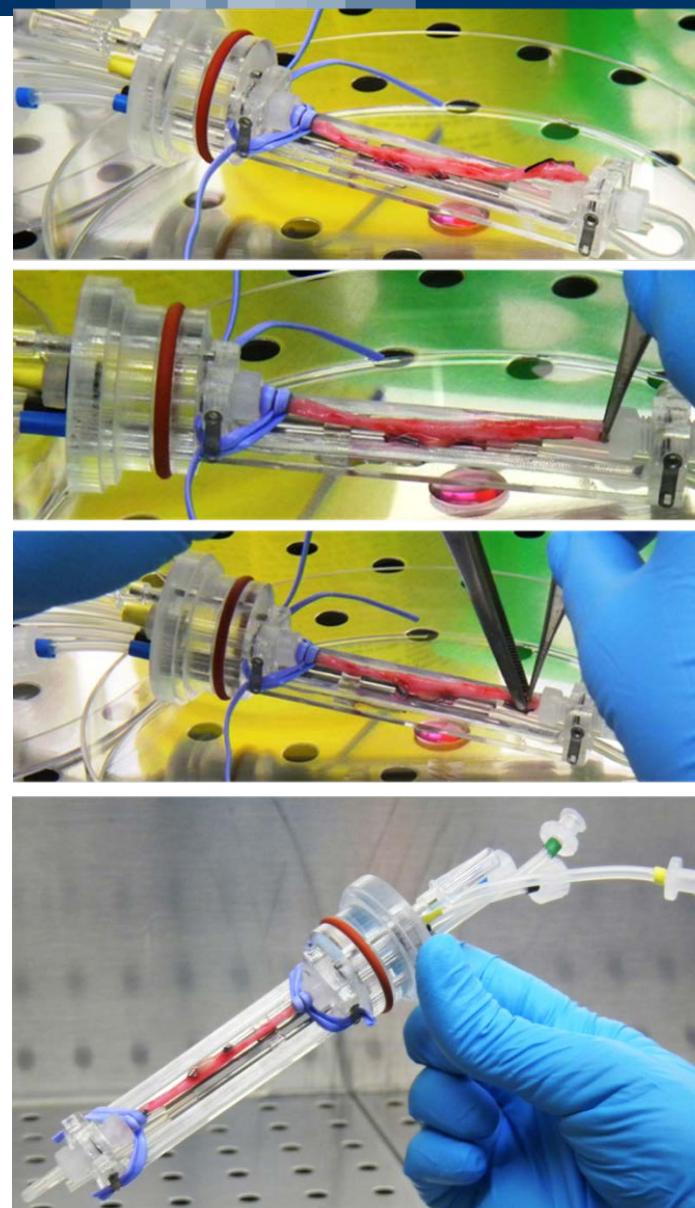
Enthusiasm





Pulsatile ex-vivo culture system(s)

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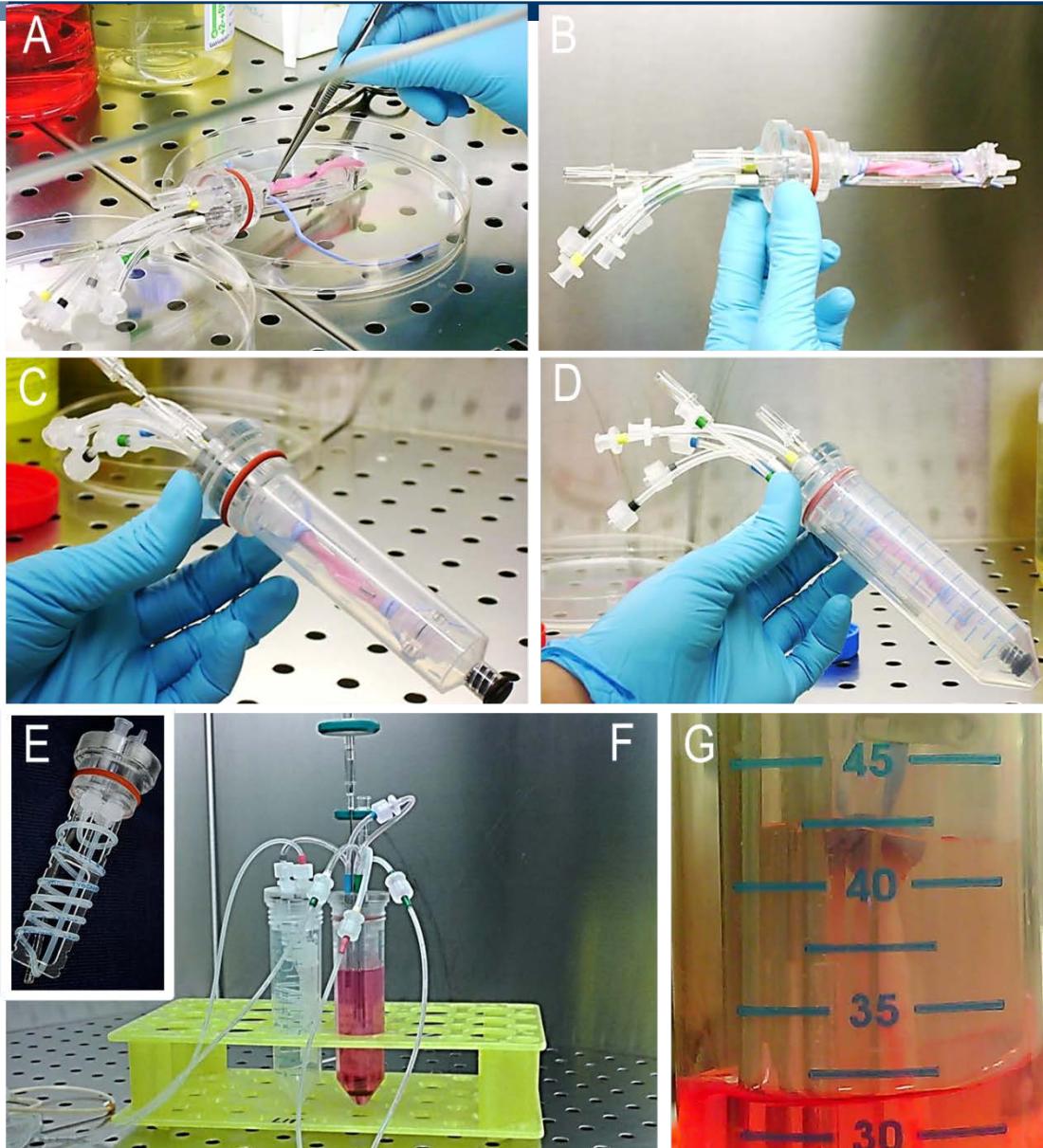


Piola, Prandi et al., JTERM 2013



Compartmental ex-vivo culture system

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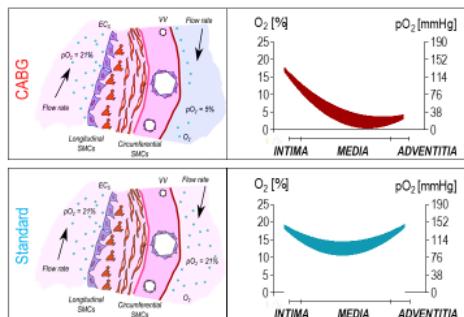


Piola et al., Ann
Biomed Eng 2016

Compartmental ex-vivo culture system



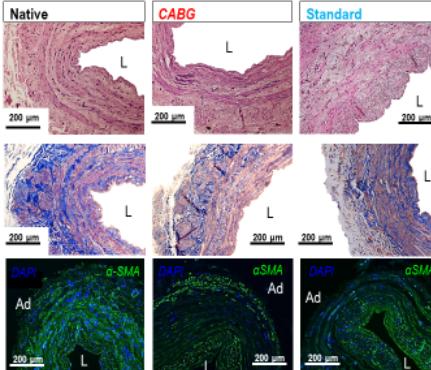
OXYGEN PROFILES IN THE SVs WALL



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MORPHOLOGICAL APPEARANCE



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Main results

Integrity of the hSVs after 7 days culture

No signs of tissue swelling or necrotic areas

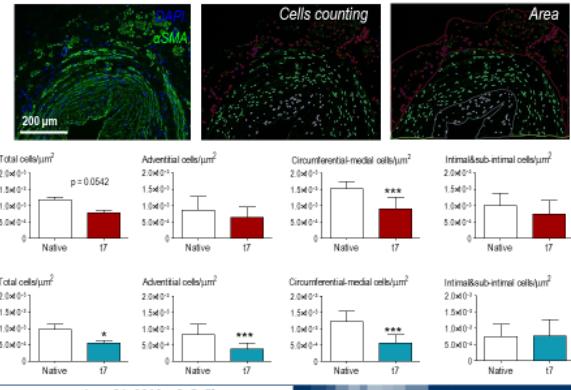
CABG condition

- loose of circ. SMCs
- lower α -SMA content

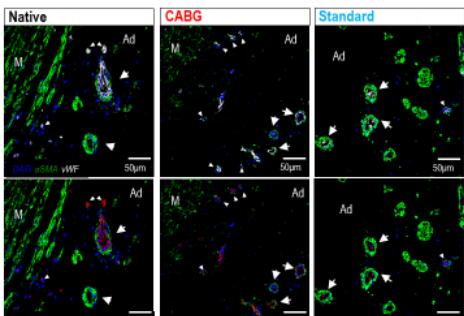
Standard condition

- loose of circ. SMCs

CELL DENSITY QUANTIFICATION



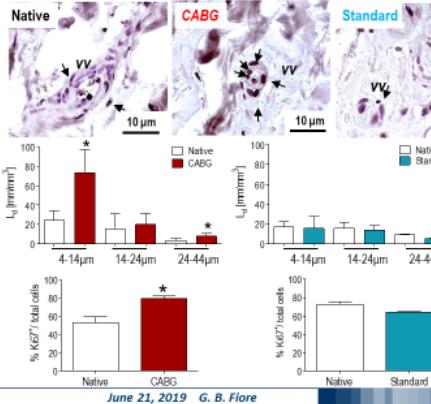
VASA VASORUM GROWTH



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VASA VASORUM GROWTH



June 21, 2019 G. B. Fiore

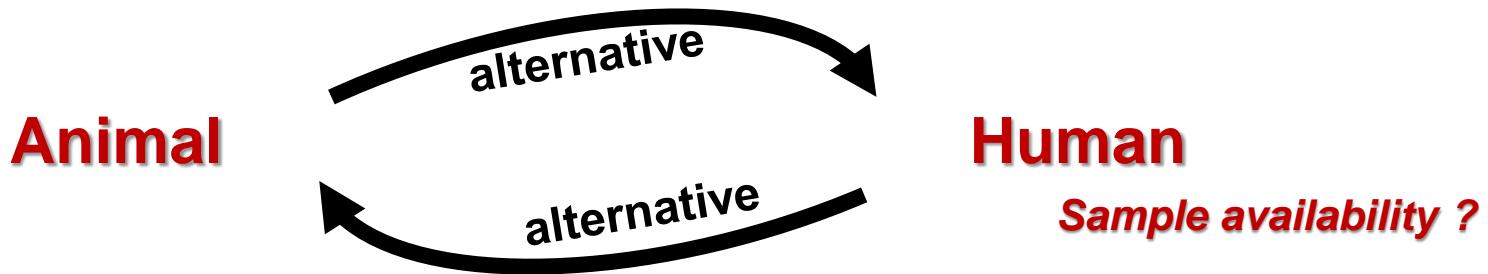
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Read the story at:

<https://www.doi.org/10.1007/s10439-015-1434-0>

- A **bioengineering approach** was used to develop *ex vivo* models for studying the cellular and molecular pathways activated by exposure of the human SV to biomechanical and biochemical arterial-like conditions.
- Our *ex vivo* vessel culture systems are **advanced, safe, strictly controlled and reliable bioengineering tools** that enable studying VGD issues directly with human samples.
- We laid the basis for **a potential clinical translation of graft preconditioning and pharmacologic treatments** for reducing the clinical impact of vein graft disease in patients undergoing CABG implantation.

Lessons learned...



- In vivo
- Large vessel transposition
- Paradigmatic
- Rabbits do not give consent

imental result x + https://www.google.com/search?rlz=1C1GGRV_enIT751IT751&ei=l_AIXYWICcHNwQKN75yYDg&q=translati

translation of experimental results to human

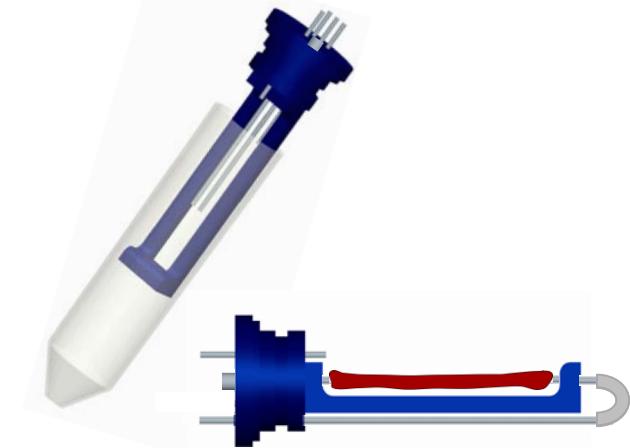
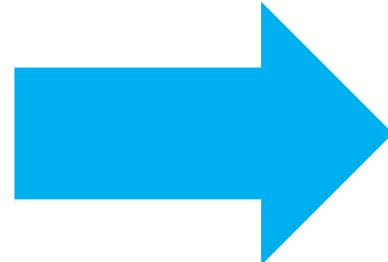
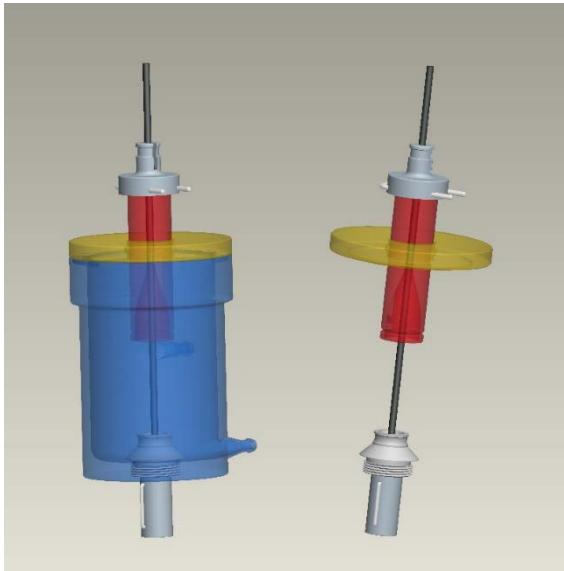
A guide to translation of research results from model organisms to ...
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4962550/> ▾ Traduci questa pagina
di RC Hardison - 2016 - Citato da 2 - Articoli correlati
Passa a **Translation of research results from mouse to human** - The human ortholog of the gene investigated in ... thus validation experiments in human cell systems ... ease or difficulty in translation of results to human.
Is it not obvious that tissue ... - After some dispute ... Embrace the diversity in ...

Lost in translation: animal models and clinical trials in cancer treatment
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3902221/> ▾ Traduci questa pagina
di IVMY Mak - 2014 - Citato da 460 - Articoli correlati
In vitro (test tube or cell culture) and in vivo (animal experiments) studies examine ... The ultimate goal of cancer researchers is to translate scientific findings into ... In the first human clinical trials of TGN1412, the drug caused catastrophic ...

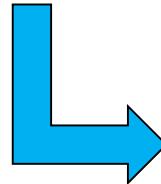
Of mice and men: why animal trial results don't always translate to ...
theconversation.com/of-mice-and-men-why-animal-trial-results-don-t-always-translate-to-human-trials-75000 ▾ Traduci questa pagina
29 ago 2017 - But we can't assume what works in animals will in humans. ... radiation therapy – owes its existence, at some level, to animal experiments.

- Ex vivo
- SV; simulated CABG
- Potentially patient-specific
- Informed consent

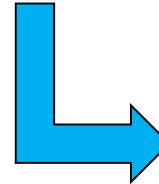
Working with samples of human origin: a kind of ‘forma mentis’



Intrinsic value of human samples



**Quality experiments
imply quality design**



**A sort of
Refinement
concept?**



Thank-you's

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