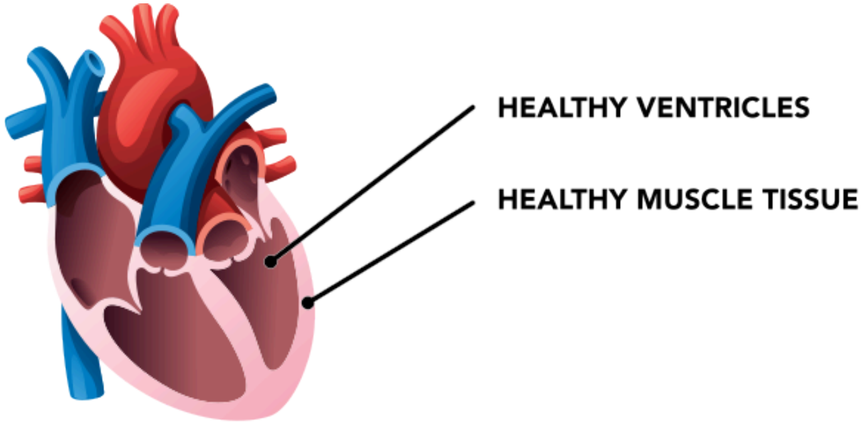
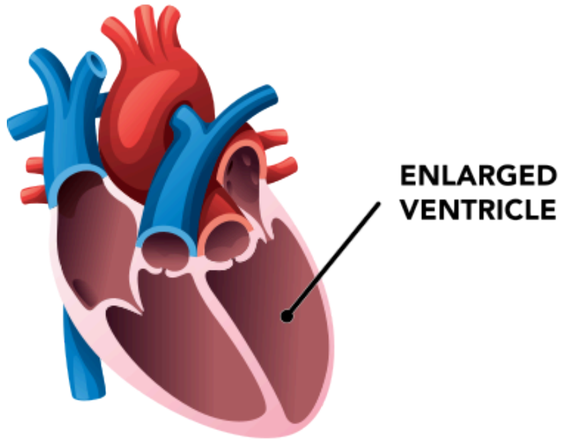
Cardiomyopathy scaffold

Virginia Leombruni

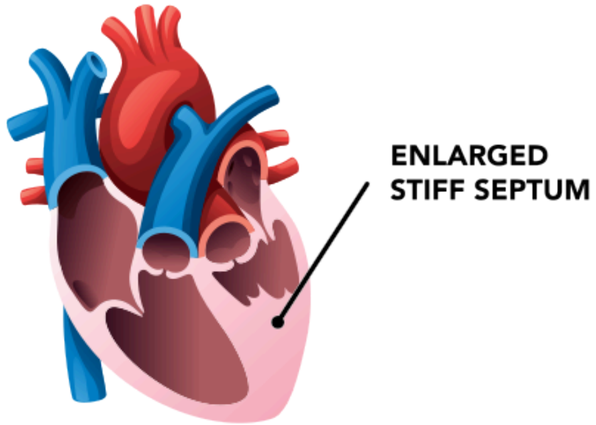
Cardiomyopathy

HEALTHY HEART

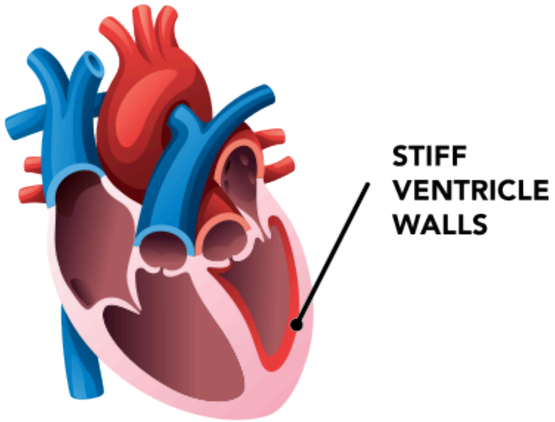




DILATED



HYPERTROPHIC



RESTRICTIVE

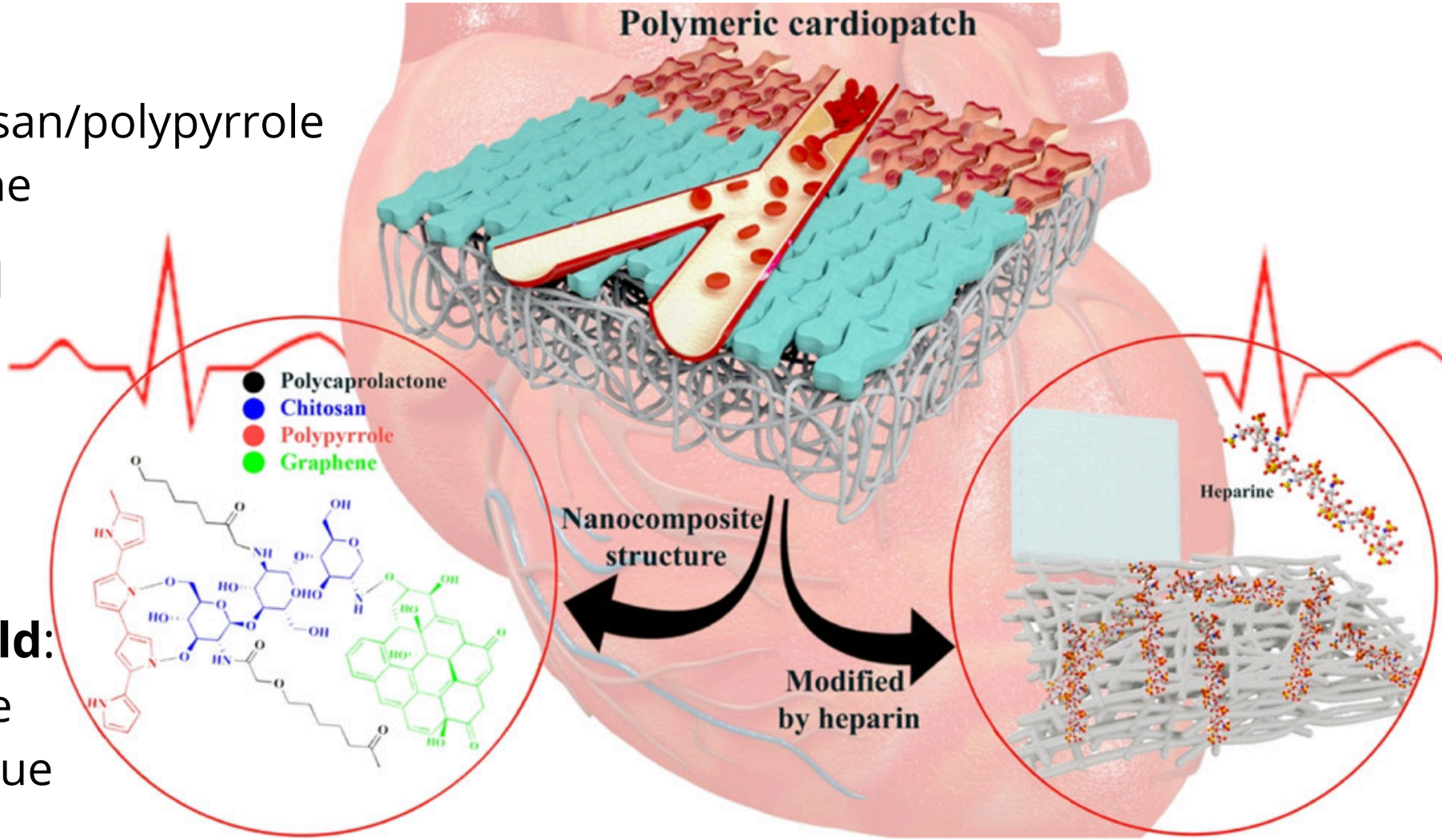
Ciarambino et al. *Cardiomyopathies: An Overview,* 2021

Scaffold properties

Materials:
polycaprolactone/chitosan/polypyrrole combined with graphene

Biocompatibility and Biodegradability:
both chitosan and polycaprolactone

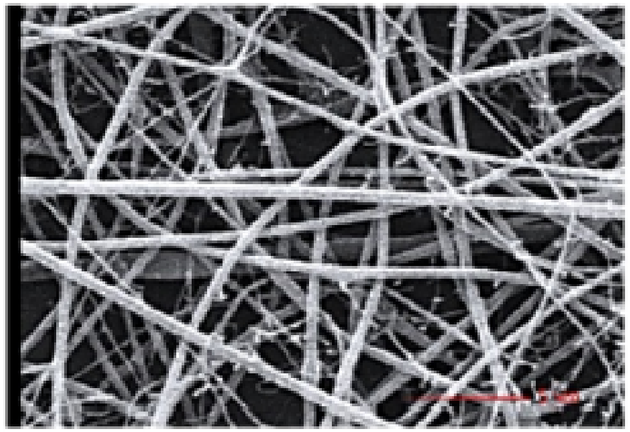
Technique for producing the scaffold:
blend of PCPG using the electrospinning technique



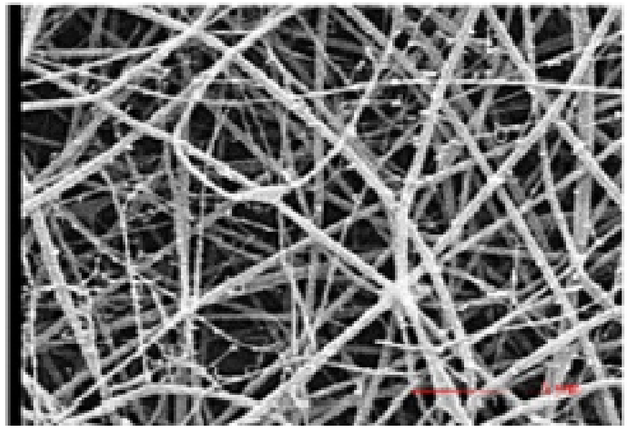
Talebi, A., Labbaf, S., Karimzadeh, F., Masaeli, E., & Nasr Esfahani, M-H (2020).
Electroconductive Graphene-Containing Polymeric Patch: A Promising Platform for Future Cardiac Repair.

Properties

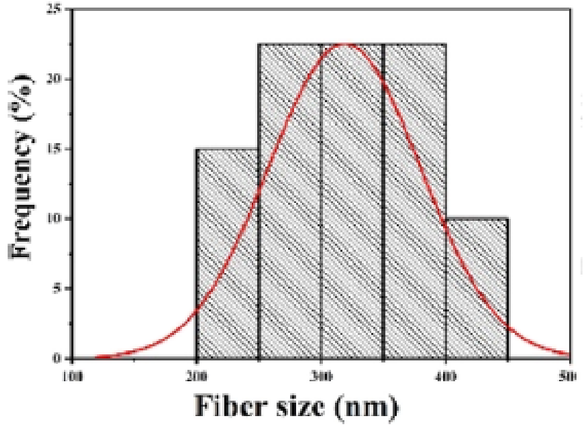
Physical Properties

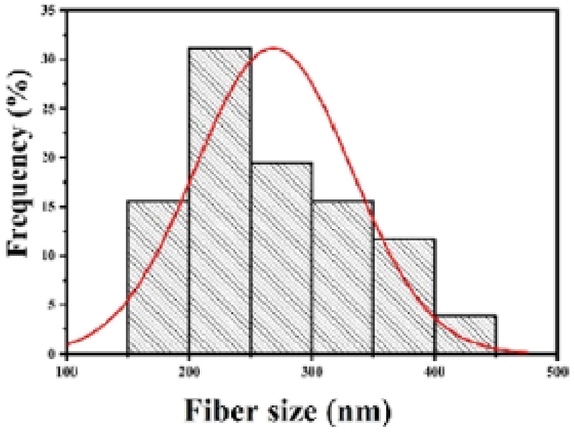


PCPG0



PCPG2.5

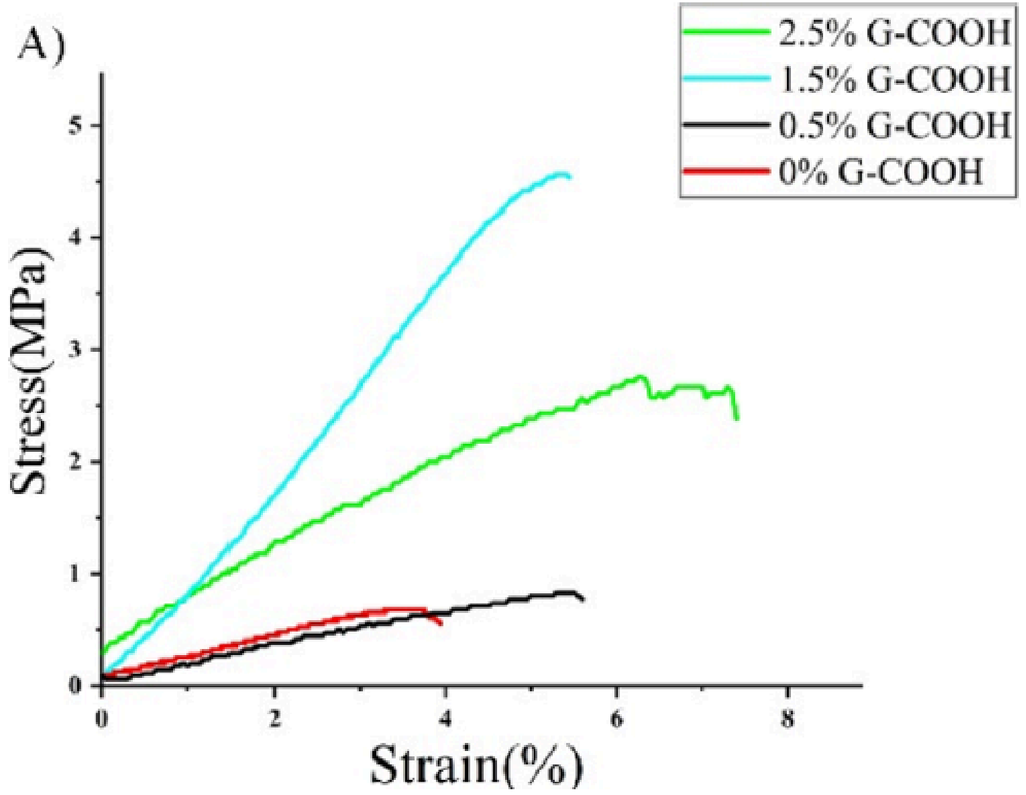




↑ graphene: ↓ fiber dimension

↑ hydrophilicity

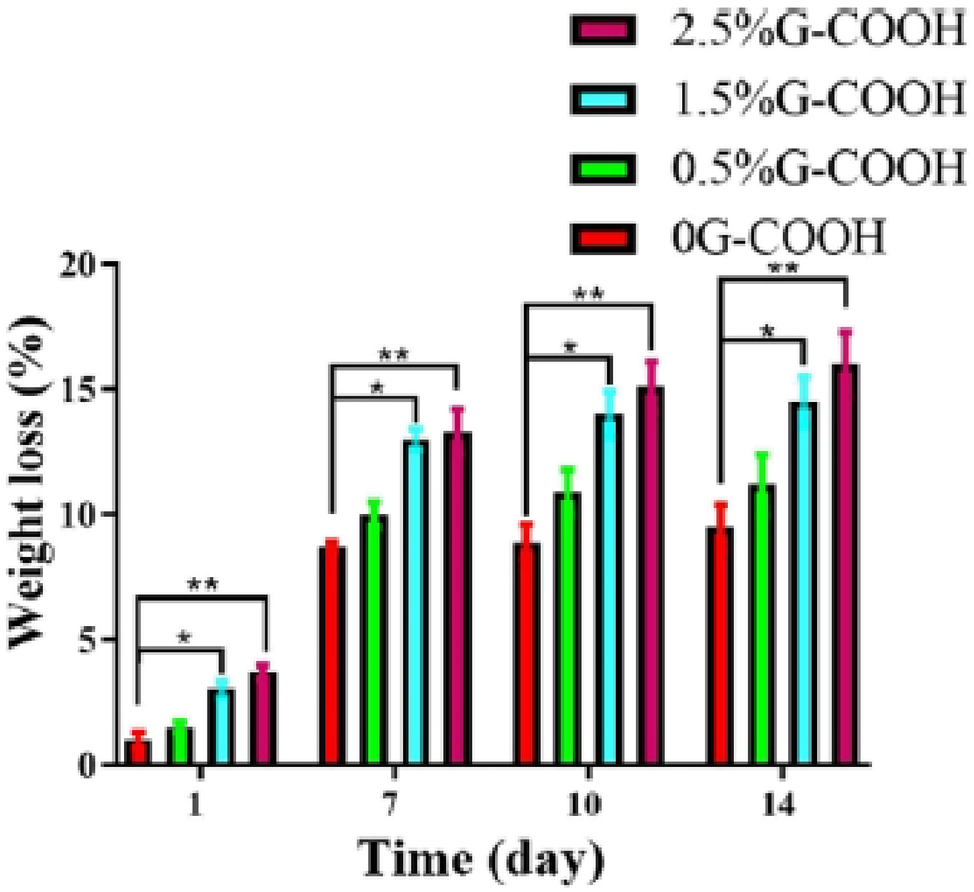
Mechanical properties



↑ elasticity: ↑ graphene

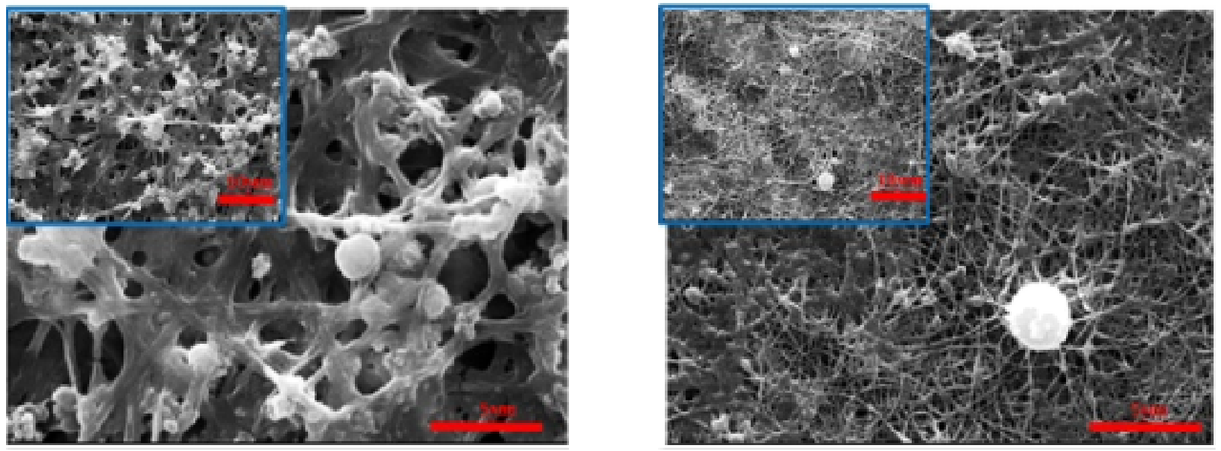
dry conditions

Degradation



graphene: degradation

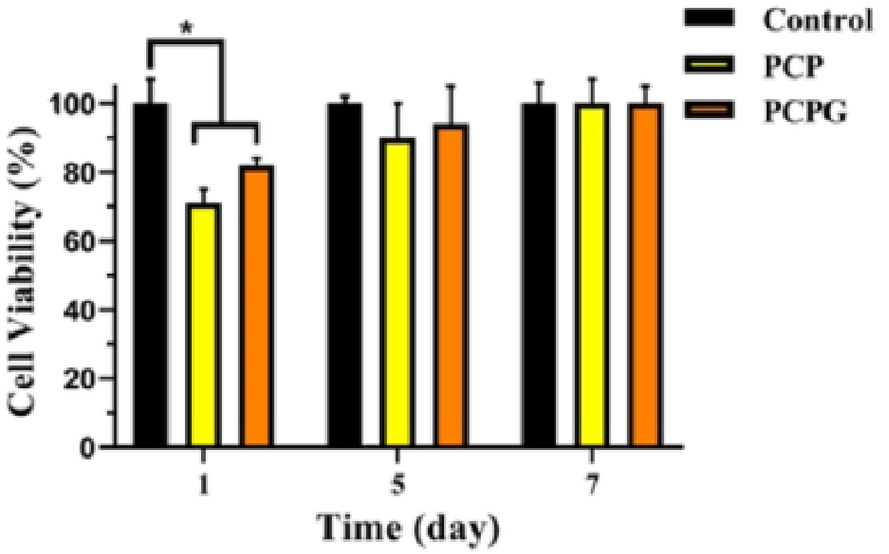
Hemocompatibility



PCP PCPG

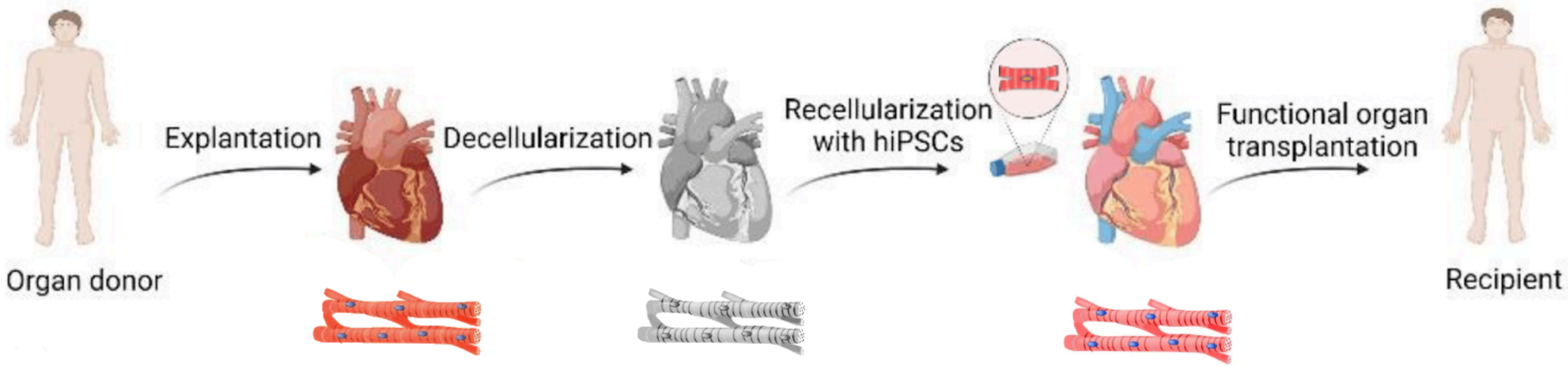
- low risk to blood clotting and thrombosis
- minimal platelet aggregation

Cell studies

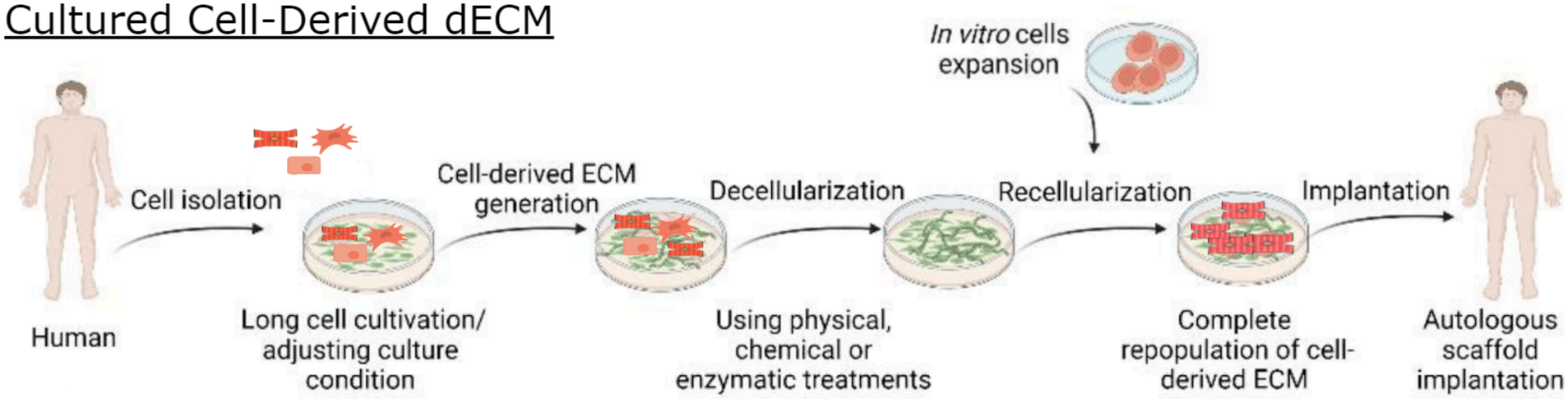


Decellularization extracellular matrix (dECM) procedure

Native Tissue-Derived dECM

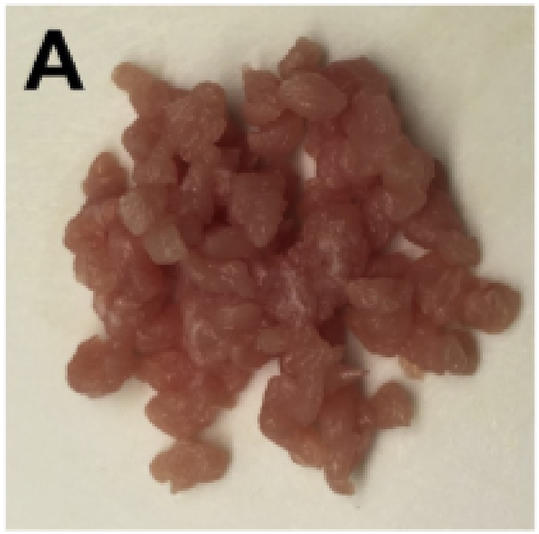


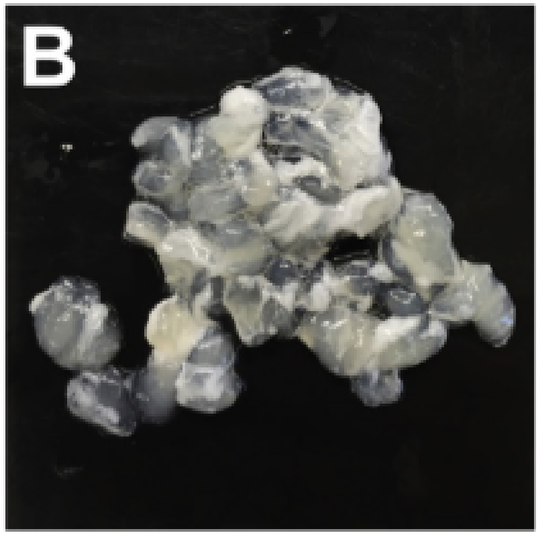
Cultured Cell-Derived dECM

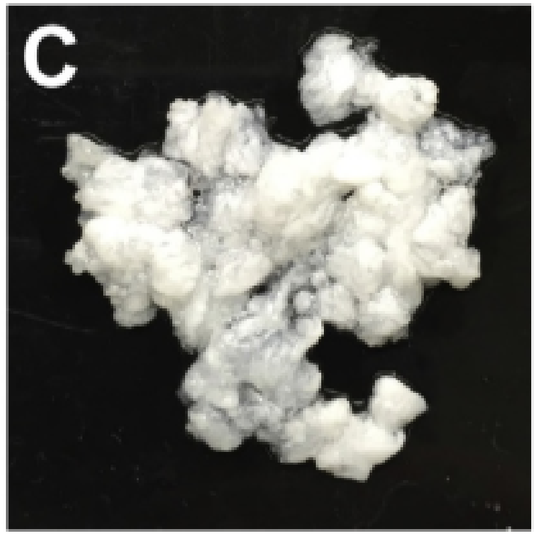


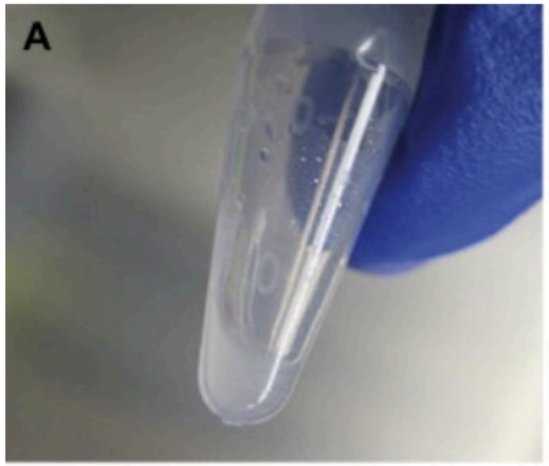
Barbulescu, G. et al (2022). Decellularized extracellular matrix scaffolds for cardiovascular tissue engineering: current techniques and challenges.

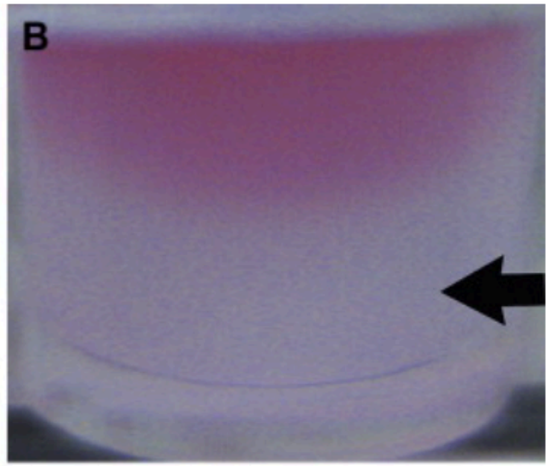
Ventrigel properties

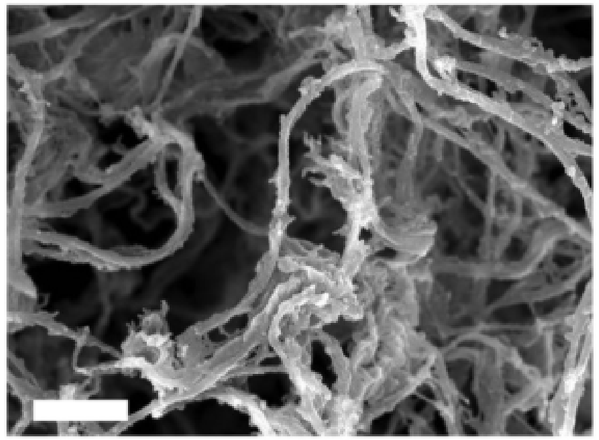










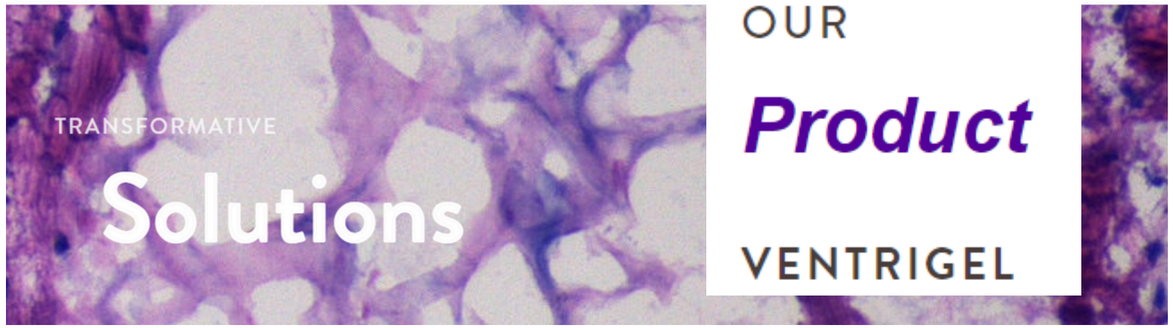


Ungerleider, J. L et al (2015). Fabrication and characterization of injectable hydrogels derived from decellularized skeletal and cardiac muscle.
Singelyn, J. M. B. et al (2009). Naturally derived myocardial matrix as an injectable scaffold for cardiac tissue engineering.

Ventrigel - Clinical trial

ventrix

VENTRIX BIO SCIENCE PRODUCT CONTACT



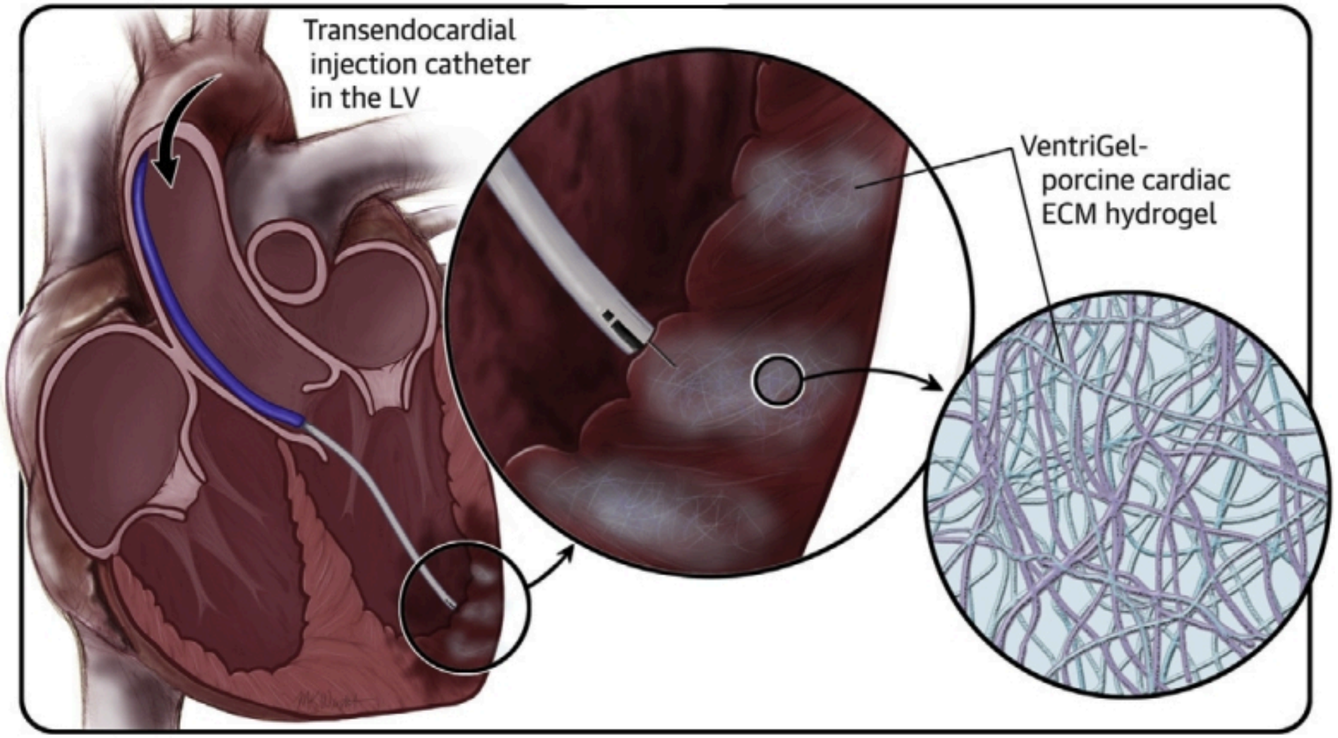
OUR

Product

VENTRIGEL

KEY FEATURES

- Improves cardiac function in both subacute and chronic MI preclinical models
- Mimics the native extracellular matrix (ECM) scaffolding in the heart
- Offers a new healthy microenvironment within the myocardium to facilitate cardiac repair
- Implantable via a variety of methods including minimally-invasive cardiac catheter technology



✓ Safety
✓ Feasibility

↑6 min walk
↓NYHA class
↓LV remodeling in the late group

Link to the procedure: https://today.ucsd.edu/story/ventrigel_phase1, link to the company: https://ventrixbio.com/product

Traverse, J. H. et al (2019). First-in-man study of a cardiac extracellular matrix hydrogel in early and late myocardial infarction patients

Evaluation on advantages and limitations

Native Tissue-Derived dECM

Advantages:

- Similarity to original tissue in composition and mechanical properties

Disadvantages:

- Donors needed
- Higher immune response
- Pathogen transmission

Cultured Cell-Derived dECM

Advantages:

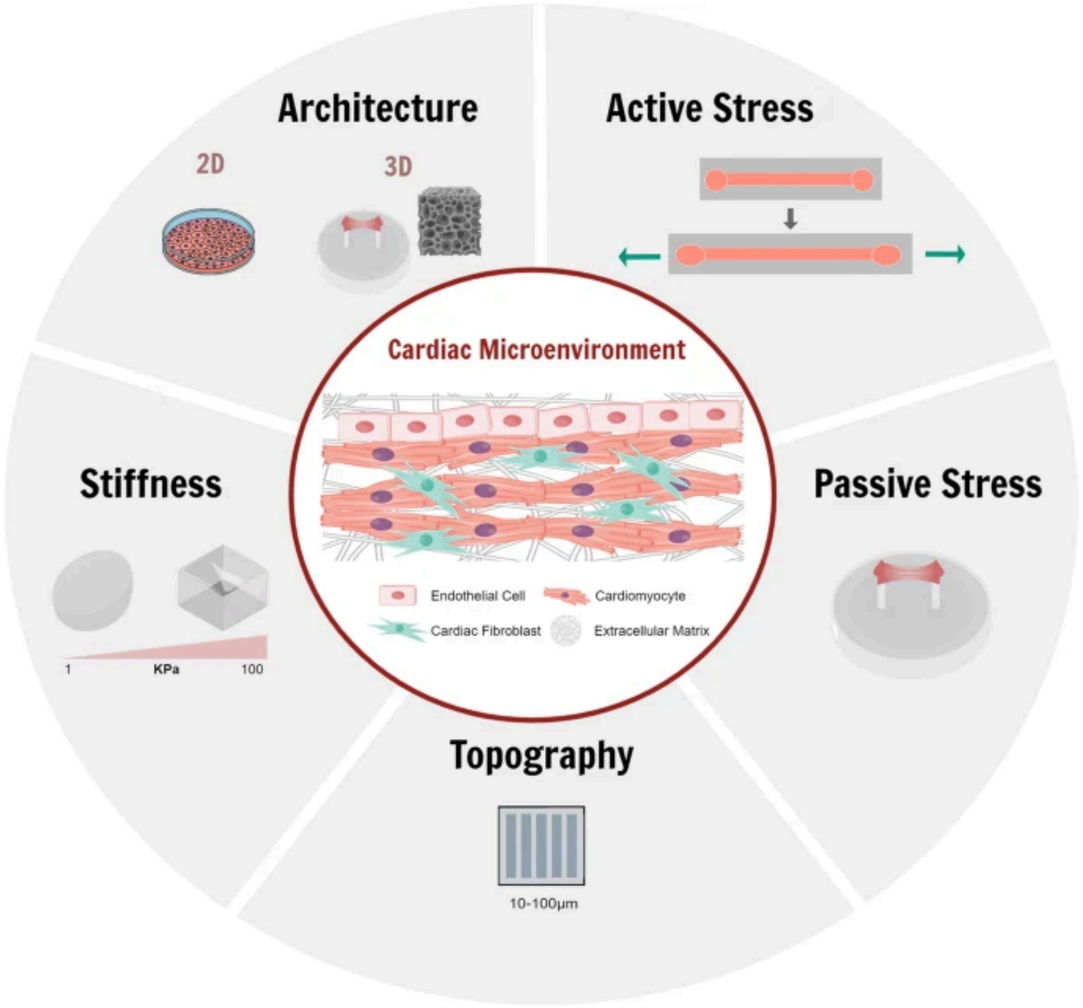
- Large scale in vitro study
- Lower immune rejection
- Easier to obtain

Disadvantages:

- Poorer mechanical properties
- Challenging to prepare at a large-scale

Barbulescu, G. et al (2022). Decellularized extracellular matrix scaffolds for cardiovascular tissue engineering: current techniques and challenges.

Requirement: mechanical properties



<u>12.5% uniaxial static stretch:</u>

-> Upregulated MYH7, CASQ2 and SERCA2

-> the alignment of collagen I, collagen III and vimentin fibrils increased

<u>5% cyclic strain:</u>

-> promote cardiac differentiation, expression of MYH6, MYH7, Cx43, and TropI

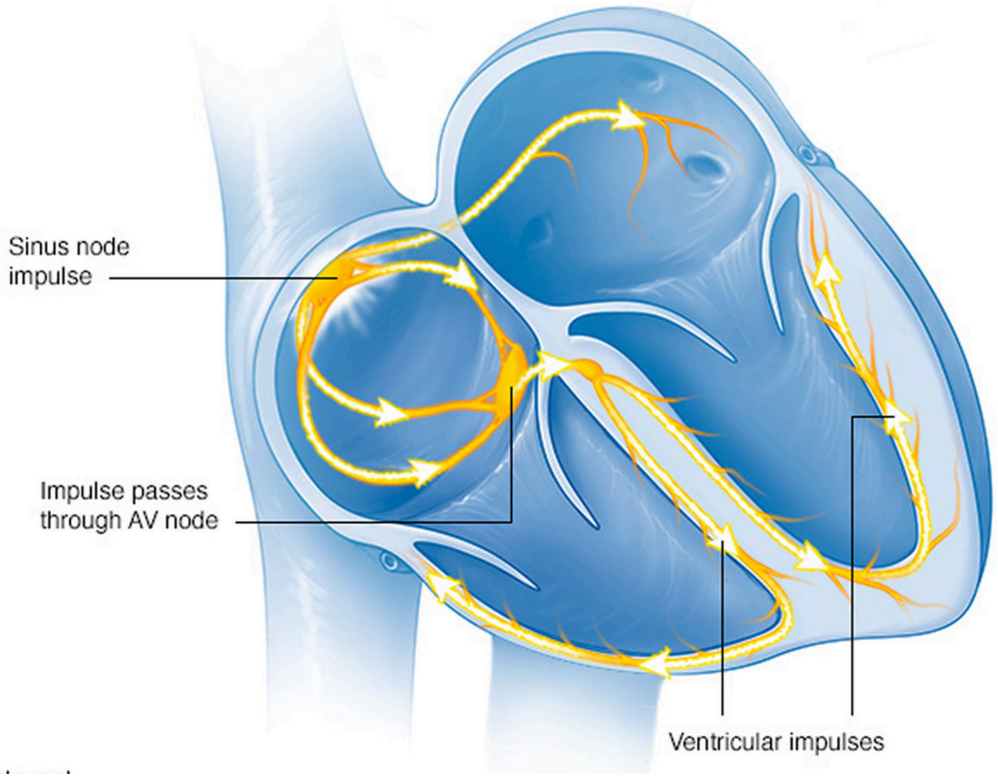
<u>Cyclic compression:</u>

-> More aligned cellular morphology

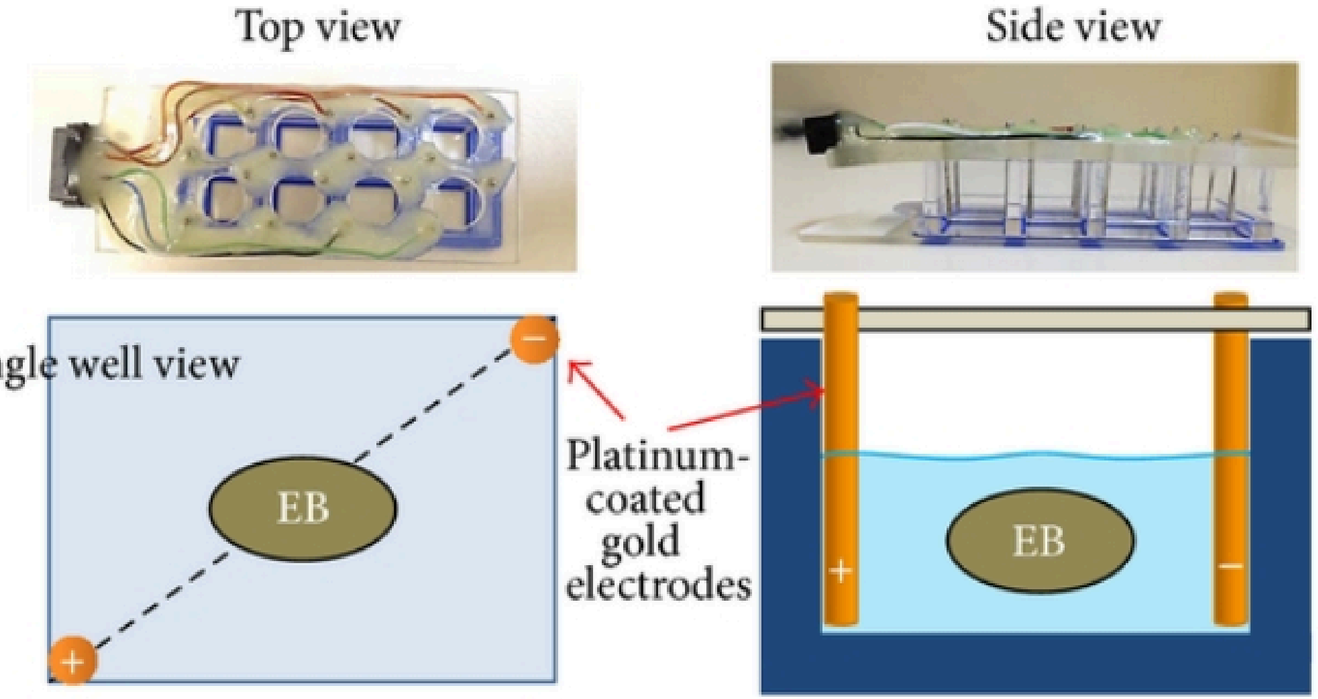
-> Better preserved key cardiomyocyte markers (α-actinin and n-cadherin)

Carlos-Oliveira, M. et al (2021). Current strategies of mechanical stimulation for maturation of cardiac microtissues.

Requirement: electrical stimuli



Each current pulse was 1 ms/phase and was stimulated at 1 Hz



-> Expressions of GATA4, NKX2.5, MEF2C, and TBX5

-> Expression of cardiac contractile muscle proteins ACTC1, TNNT2, MYH7, and MYL7

Hernández, D. et al (2016). Electrical stimulation promotes cardiac differentiation of human induced pluripotent stem cells..

Ventrigel - porcine cardiac dECM
Temperature responsive
Decrease diameter of ventricle

Additional requirement for injectable hydrogel - lesson from the clinical trials

Algisyl-LVR - Calcium-Alginate hydrogel
2 components: Na+-Alginate and Ca2 +-Alginate mix before use
Increase wall thickness

IK-5001 -1% sodium alginate plus 0.3% calcium gluconate
Ability to reversibly cross-links
Degradable, excreted via kidney

Traverse, J. H. et al (2019). First-in-man study of a cardiac extracellular matrix hydrogel in early and late myocardial infarction patients
Anker, S. D., et al (2015). A prospective comparison of alginate-hydrogel with standard medical therapy to determine impact on functional capacity and clinical outcomes in patients with advanced heart failure (AUGMENT-HF trial).
Mann, D. L., et al (2016). One-year follow-up results from AUGMENT-HF: a multicentre randomized controlled clinical trial of the efficacy of left ventricular augmentation with Algisyl in the treatment of heart failure.
Frey, N., et al (2014). Intracoronary delivery of injectable bioabsorbable scaffold (IK-5001) to treat left ventricular remodeling after ST-elevation myocardial infarction: a first-in-man study.

For our scaffold: Chitosan based hydrogel

Requirement:

- Injectable liquid
- Having parameter to activate to gel state such as: ions, pH, and temperature
- Promote regeneration of the tissue
- Biocompatibility
- Degradable
- Support mechanical and electrical properties of the tissue
- Should not trigger chronic inflammation
- Promote formation of blood vessels

Scaffold idea:

- Biocompatibility and mechanical support: chitosan, collagen, gelatin
- Parameter activate to gel state (ex: combine with alginate activate through Calcium ion)
- Electrical properties: metal nano particles
- Formation of blood vessels: VEGF

Xu, Q., et al (2024). Hydrogel-based cardiac repair and regeneration function in the treatment of myocardial infarction.