Biomanufactured Organs-on-demand: Opportunity, Progress, and Implications

Mark SKYLAR-SCOTT, Assistant Professor of Bioengineering, Stanford University

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Organ Transplantation:
A Revolutionary Solution to Organ Failure

From bold pioneers...

CHANGE KIDNEY IN OPERATION ON TWIN BROTHERS

Boston, Dec. 23 (AP)—Two teams of surgeons today—reportedly for the first time in medical history—transplanted a kidney from one identical twin to another.

Ronald Herrick, 23, from whom the kidney was taken, and his brother, Richard, were reported in satisfactory condition after the five and a half hour operation. Permanent success of the surgery cannot be assured for some time.

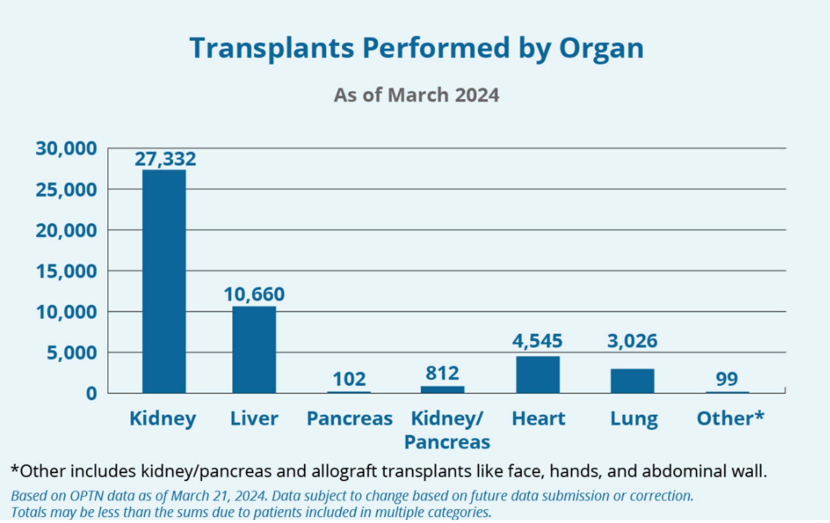
Kidney transplants have been accomplished before, but today's was the first ever performed on identical twins, hospital officials said. Richard, suffering from chronic nephritis, was first treated with an artificial kidney but both kidneys failed to resume normal function. Ronald, a college student, volunteered one of his healthy kidneys in an effort to save his brother's life. Surgeons have hopes that Richard's body will receive his brother's organ without loss of function.

(Left) The National Archives of Plastic Surgery in the Francis A. Countway Library of Medicine
(Right) Chicago Tribune, Dec. 24th, 1954

...To an established life saving medical practice

46,000+

transplants were performed in 2023.



Statistics and graphics from:
https://www.organdonor.gov/learn/organ-donation-statistics.
Accessed: May 31st 2025

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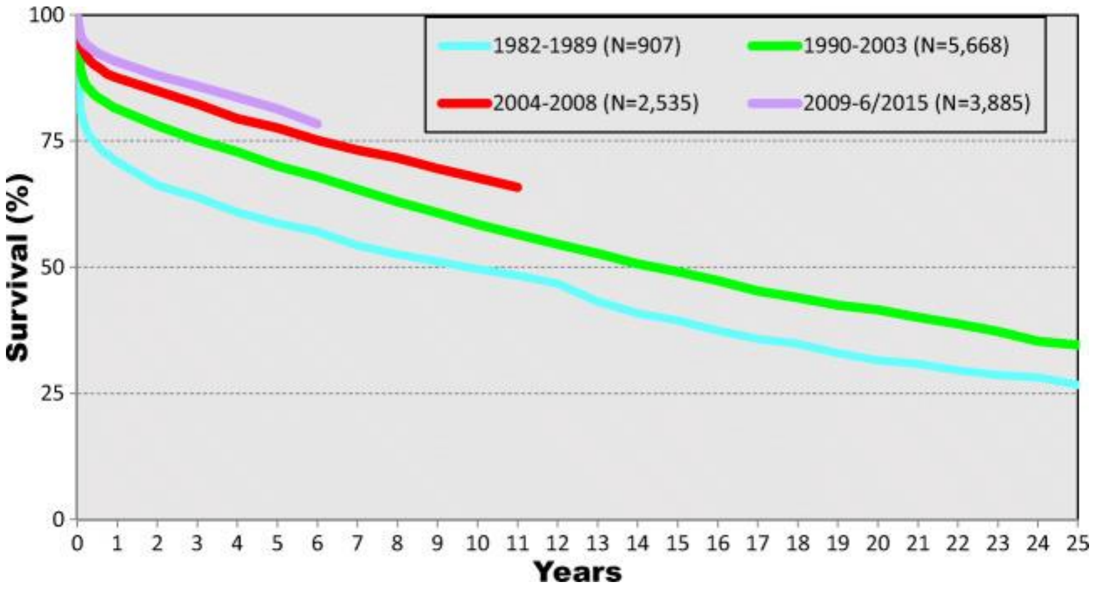
Limitations of Organ Transplantation:
Organ Rejection

Almost every donor organ will ultimately be rejected…



Dipchand et al., *Ind J. Thor. Surg.*, 2019

…which disproportionately impacts pediatric recipients

For a 70 year old,
25 years survival is a cure

For a 1 year old,
25 years survival is a *tragedy*

Limitations of Organ Transplantation: **Donor Shortage**

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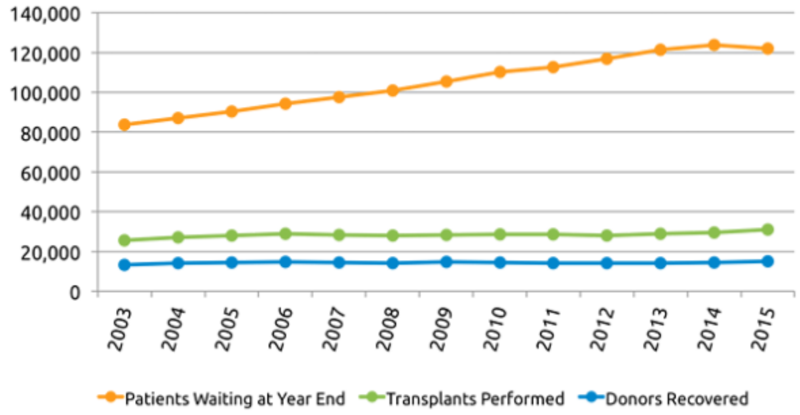
A long and growing waiting list…

103,223

Number of men, women, and children on the national transplant waiting list.



Every 8 minutes another person is added to the transplant waiting list.

…Has grave consequences

17

people die each day waiting for an organ transplant.

Statistics and graphics from: https://www.organdonor.gov/learn/organ-donation-statistics. *Accessed: May 31st 2025*

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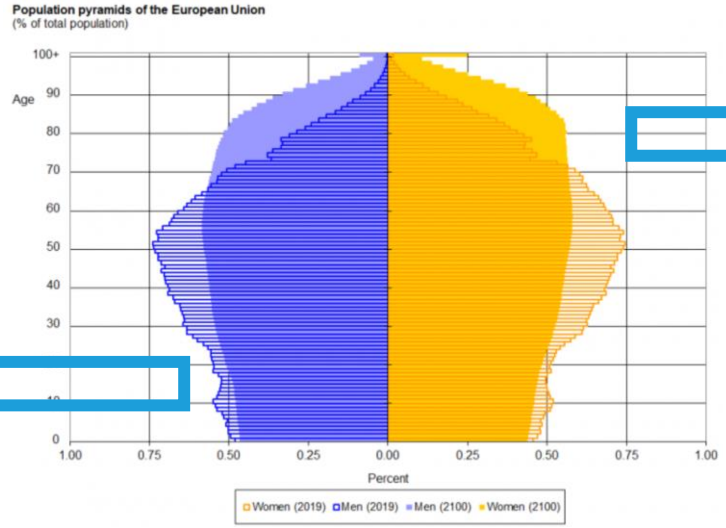
Future Threats to Organ Transplantation

SUPPLY	DEMAND



Increasing elderly population
as potential recipients

Reduced youth population as potential donors

33% of donor organs are derived from motor vehicle accidents

Population pyramid: Eurostat proj_19np

United Network for Organ Sharing (UNOS) Standard Transplant Analysis and Research (STAR)

Emerging Strategies for Alternative Organ Sourcing

Xenotransplantation

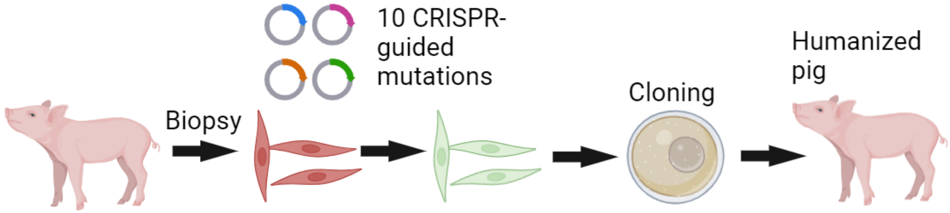
Dr. Bartley Griffith, U. Maryland

BREAKING

In a First, Man Receives A Heart From a Genetically Altered Pig

A 57-year-old man with life-threatening heart disease has received a heart from a genetically modified pig. It is the first successful transplant of a pig's heart into a human being.

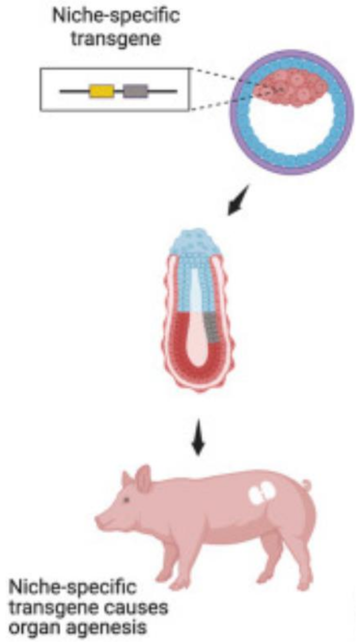
Jan. 10, 2022



- Scalable
- Rapid Progress

- Immunosuppression
- Ethics

Chimeric Organ Production



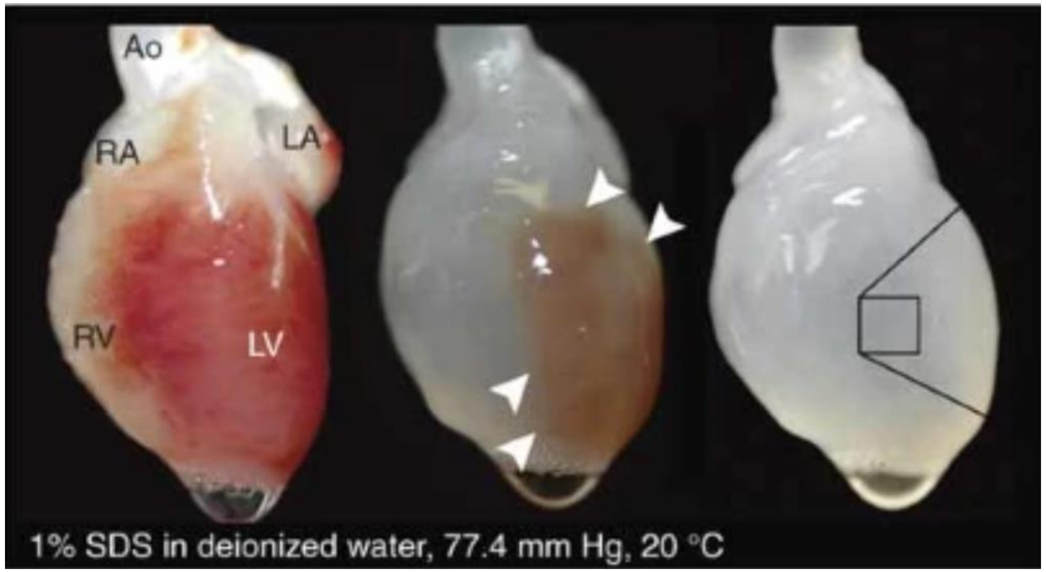
Sarmah et al., *Front. Cell Dev. Biol., 2023*

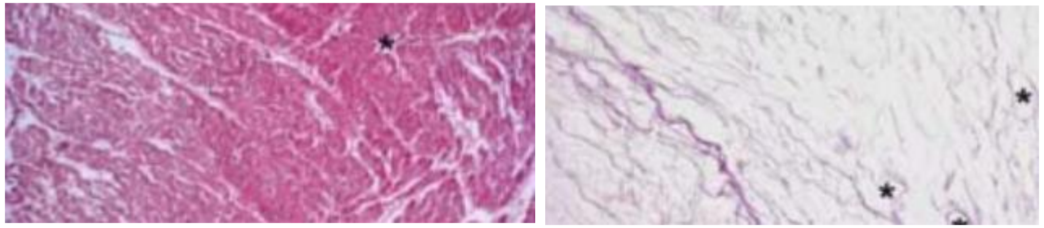
- Human organs

- Immunosuppression
- Ethics

Emerging Strategies for Alternative Organ Sourcing

Decellularization/Recellularization

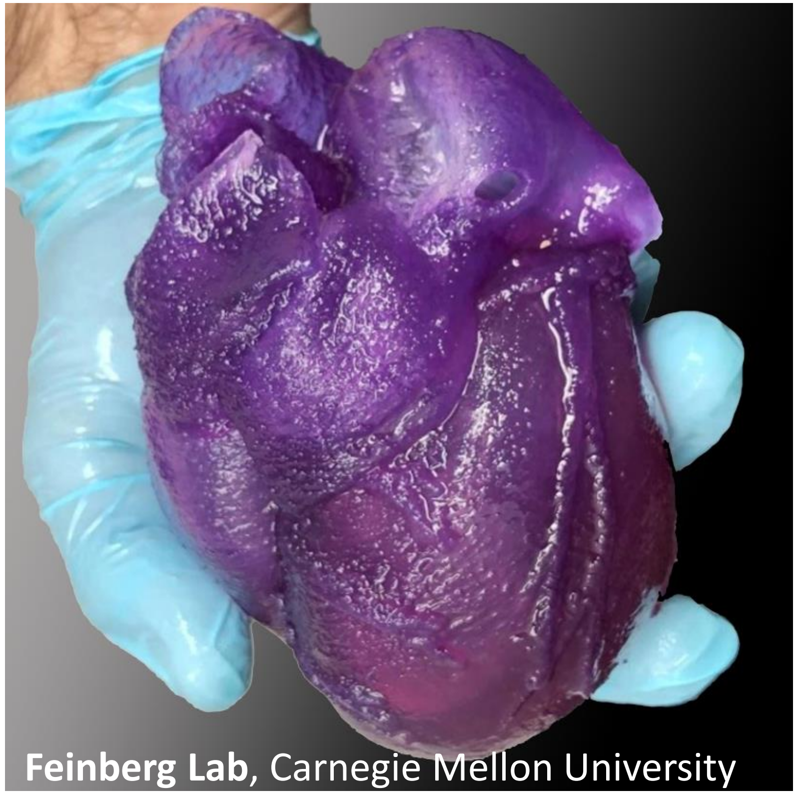




- No immuno-suppression
- Recell is hard
- Cadaver organ needed

Ott et al., *Nat. Med.*, 2008

3D Bioprinting of Organs



- No immunosuppression
- Cell Number, Complexity, Vascularization

Mirdamadi et al., *ACS. Biomater. Sci. Eng.*, 2020

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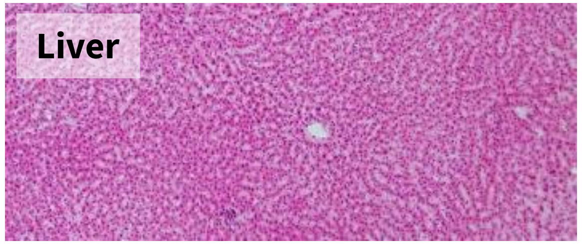
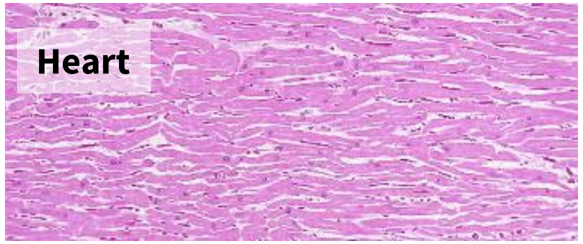
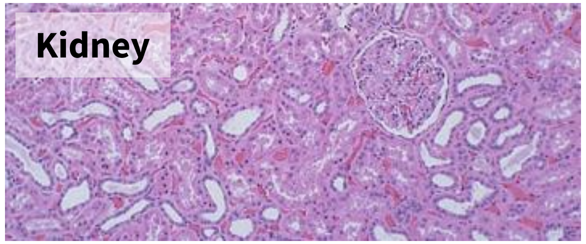
Solid organs are complex

Cell number, density, heterogeneity

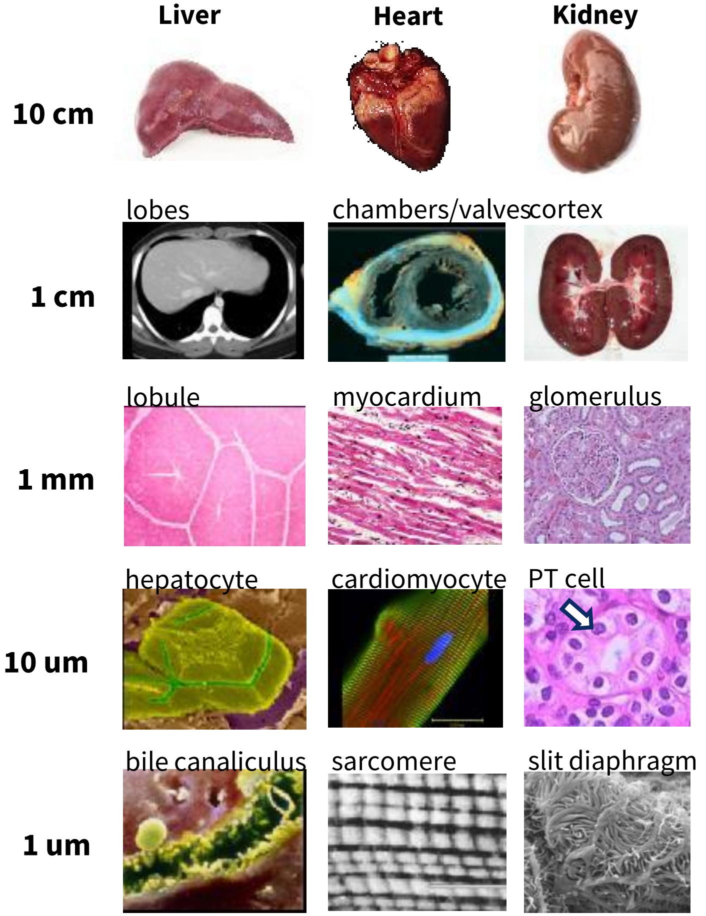
- ~ **100 BILLION** cells per organ
- ~ **100 MILLION** cells / ml
- ~ **10s** of cell types per organ



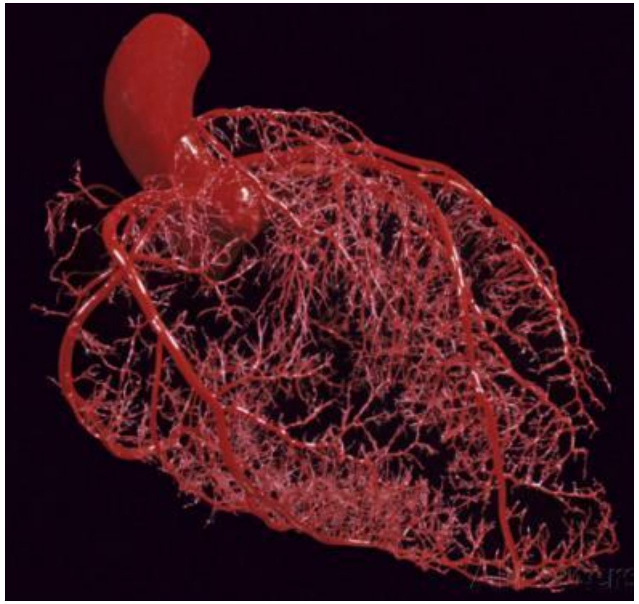


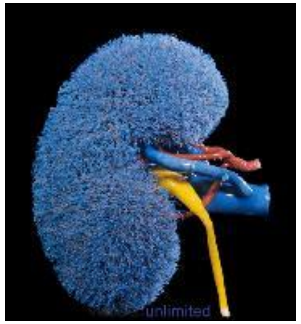


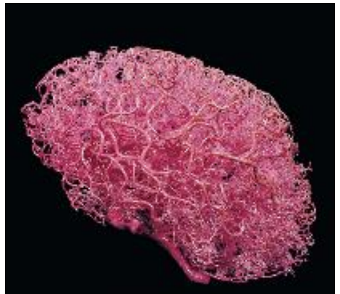
Complexity at multiple length scales



Vascularization and perfusion







Photography by Ralph Hutchings

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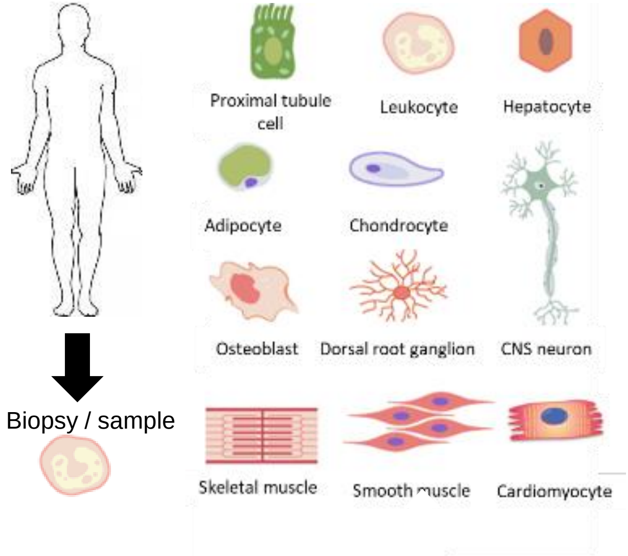
Emerging Solutions for Organ Manufacturing

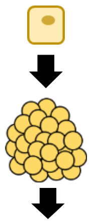
Cell number, density, heterogeneity	Complexity at multiple length scales	Vascularization and perfusion
1) iPSCs & CRISPR *Cell manufacture & manipulation*	**2) Organoids: stem-cell self-assembly** *Complex microscale tissues* *Building-blocks of functional tissues*	**3) Embedded 3D Printing** *Freeform writing of one material into another*

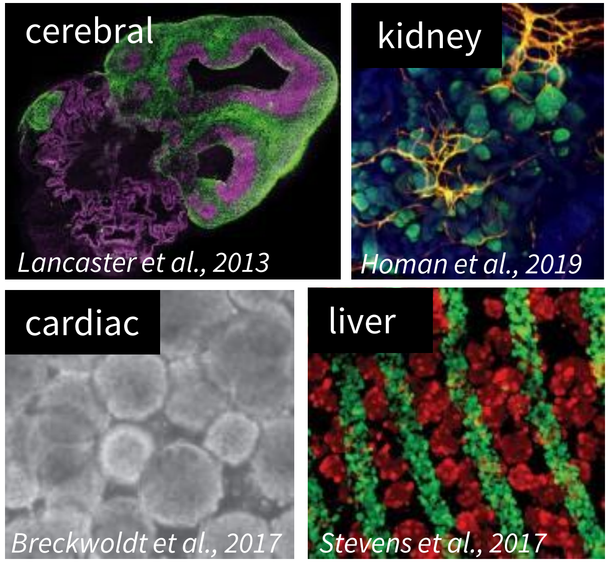
Cell source | iPSCs



iPSC

Embryoid body





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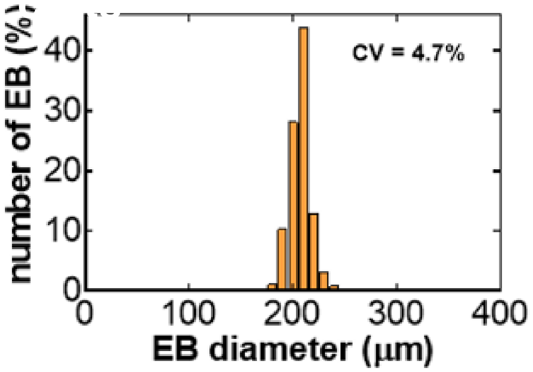
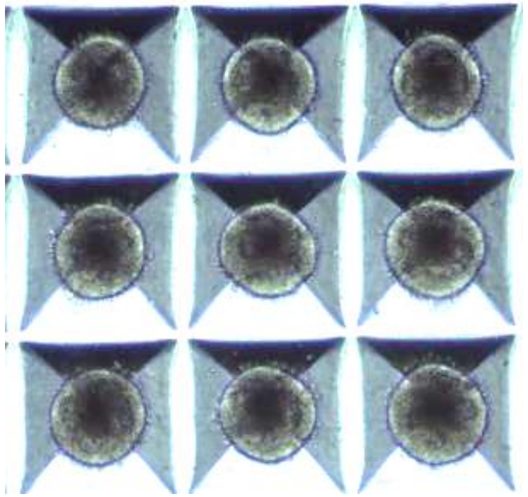
Making Human Stem Cell Mayonaise

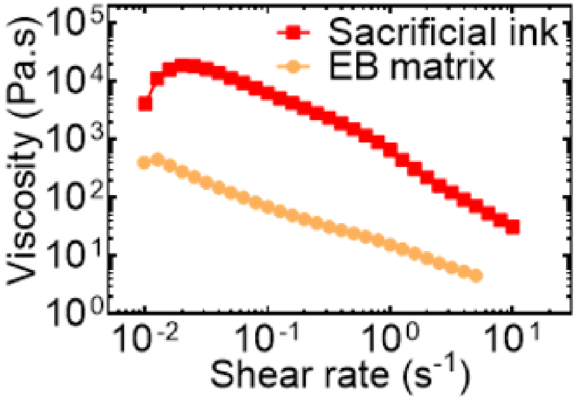
Large-scale culture of



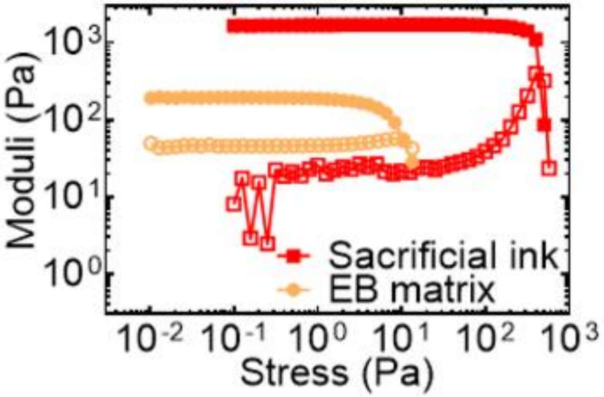


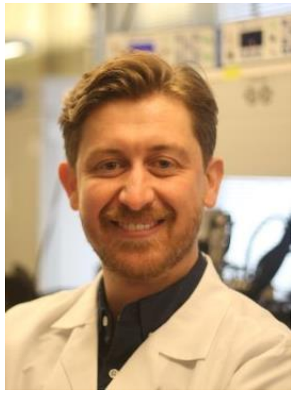
Human stem cells, when compacted, form a mayonaise

Shear Thinning



Viscoelastic





Sebastien Uzel*

Jennifer Lewis

MA Skylar-Scott*, S Uzel* et al., *Sci. Adv., 2019*

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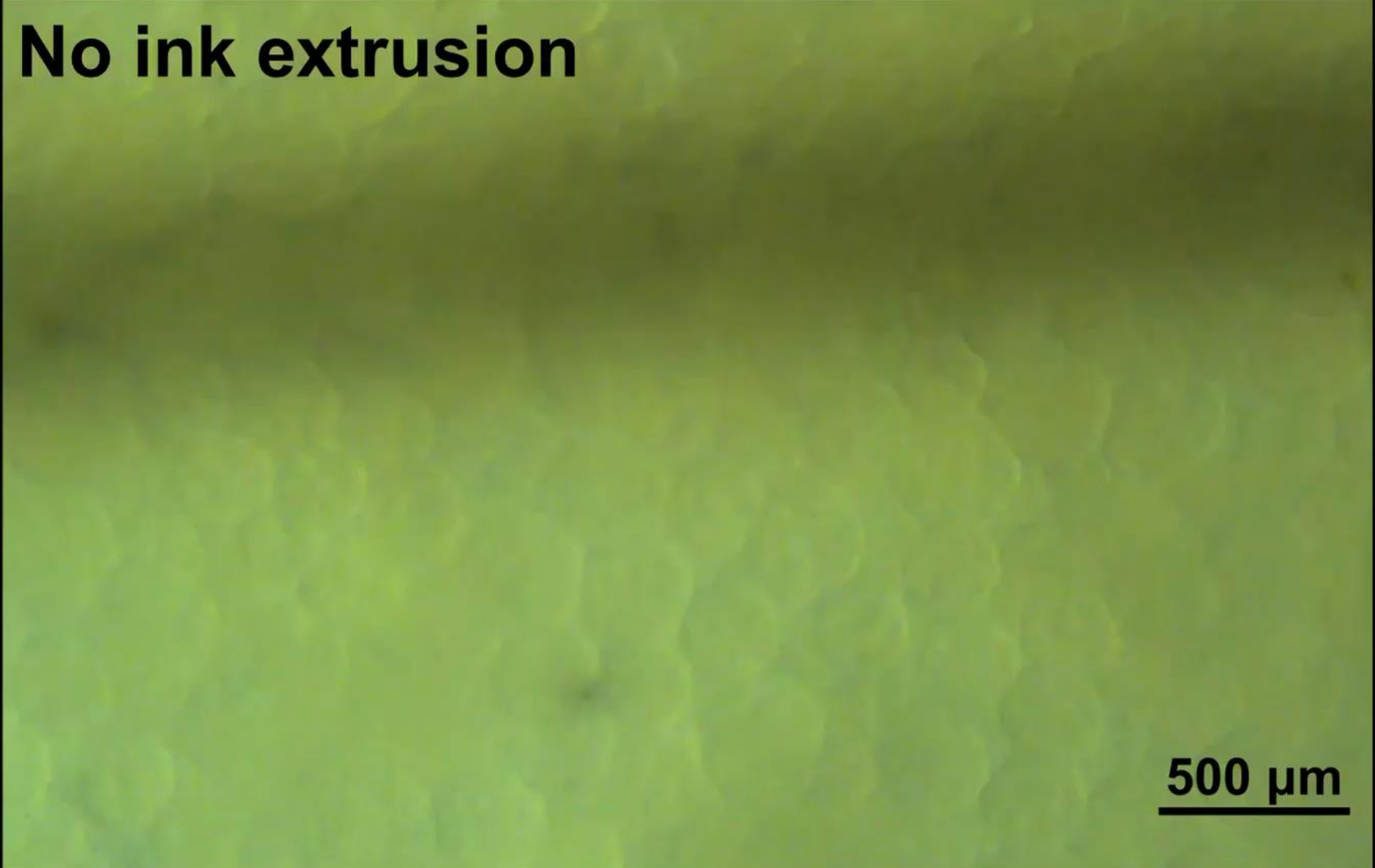
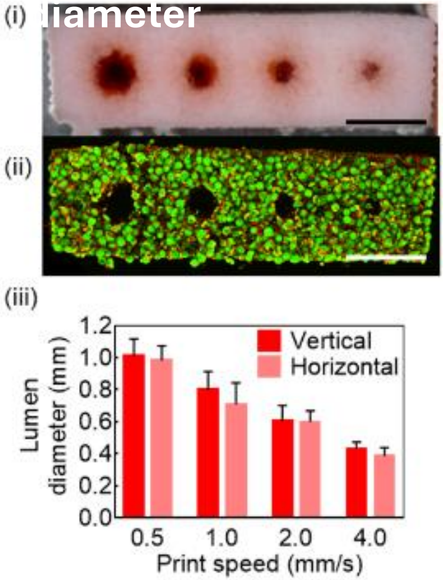

No ink extrusion
500 µm

Printing and perfusion of vascularized tissue matrix via SWIFT

Bioprinting of Branched Perfusable Vessel Networks

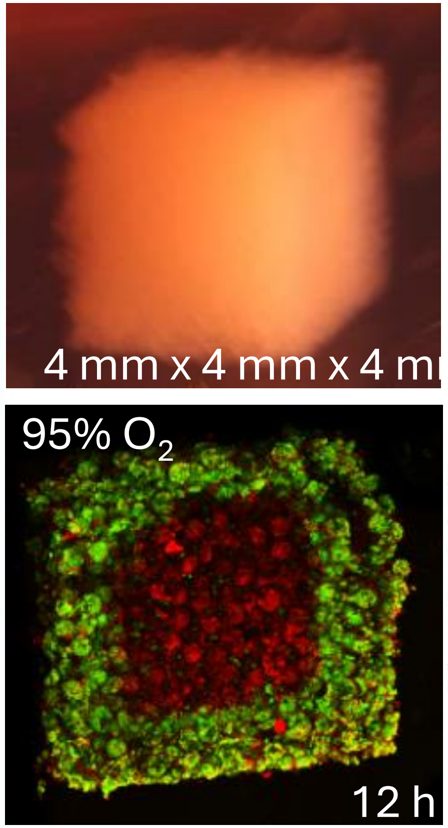
Tailoring vessel diameter



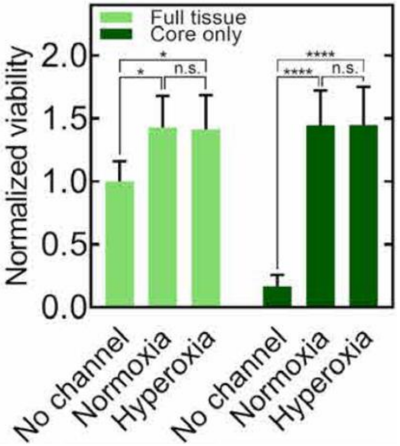
Printing tissue Mold

Bioprinted Vascularized Tissue
Remains Living When Perfused

Avascular tissue

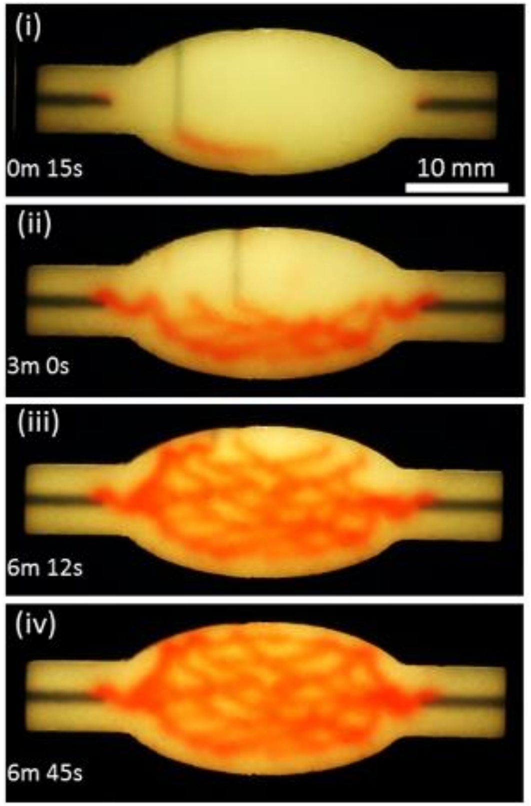


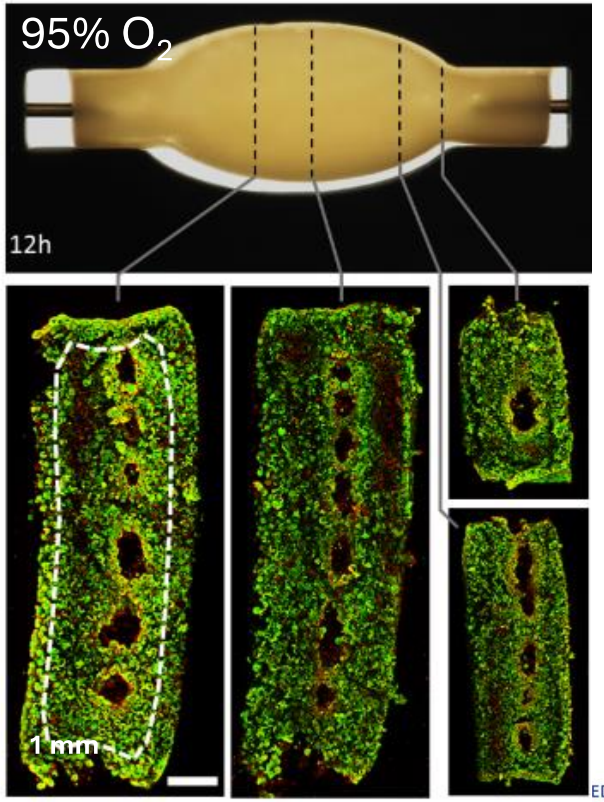
High cell density
200 Million cells/mL
Poor viability
~0.8 mm viable zone



Live/Dead

Vascular tissue





Live/Dead

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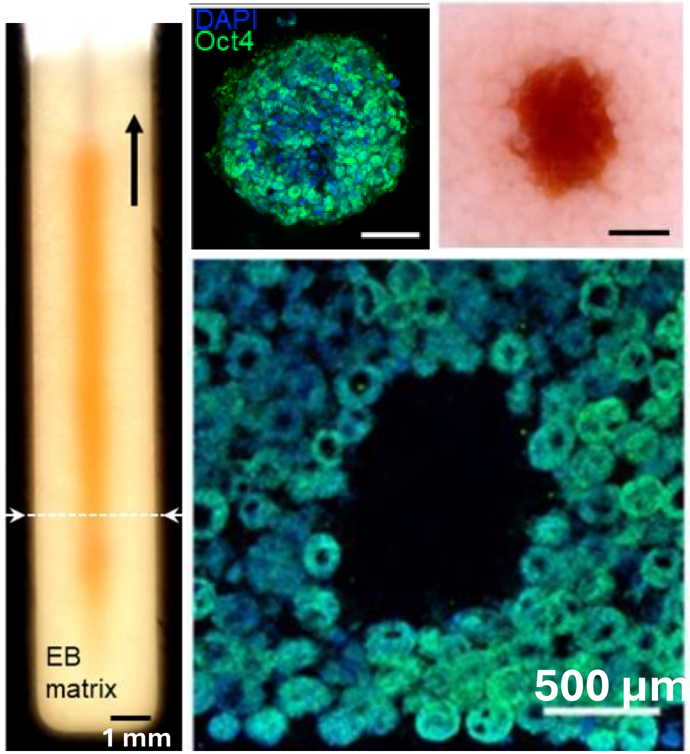
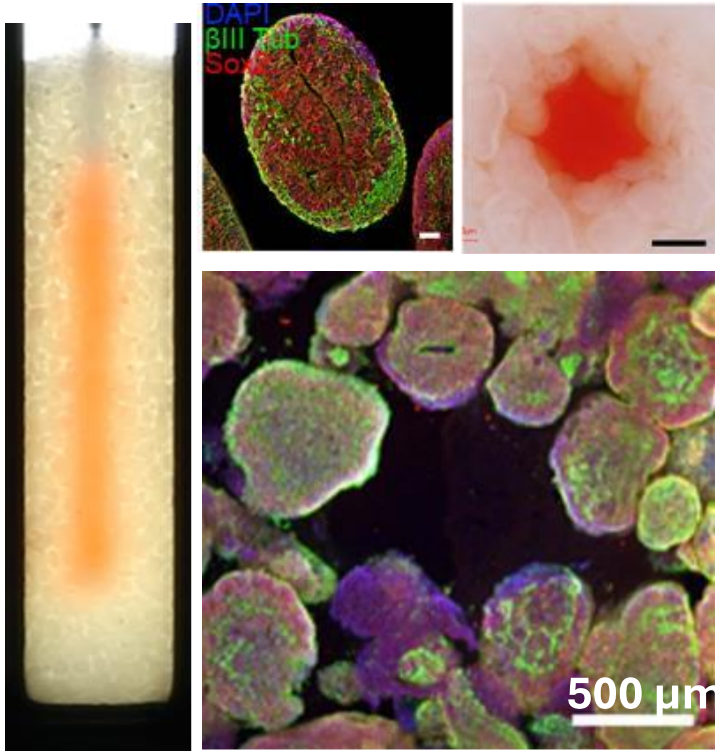
Vascularizing Multiple Tissue Types

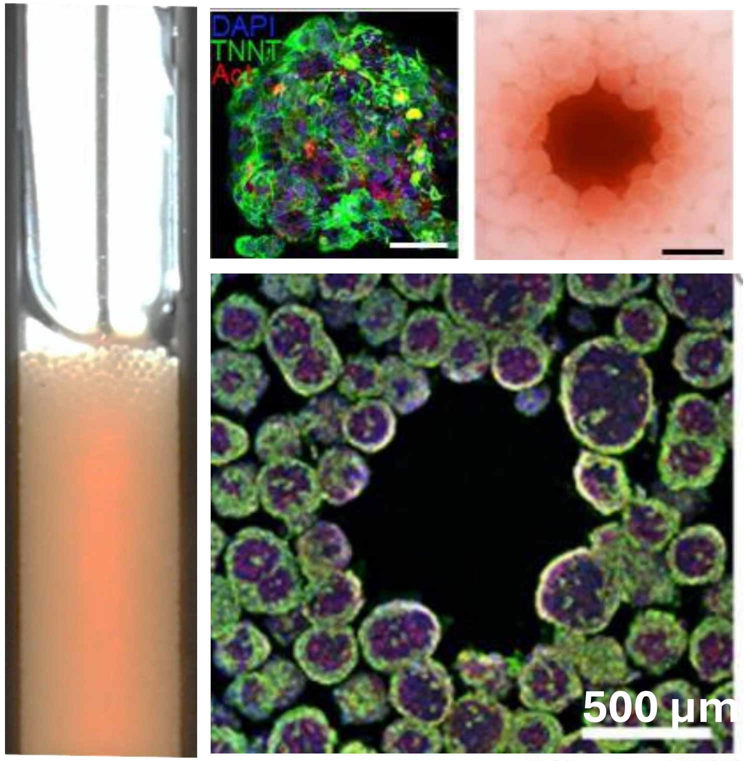
Embryoid bodies



Cerebral organoids

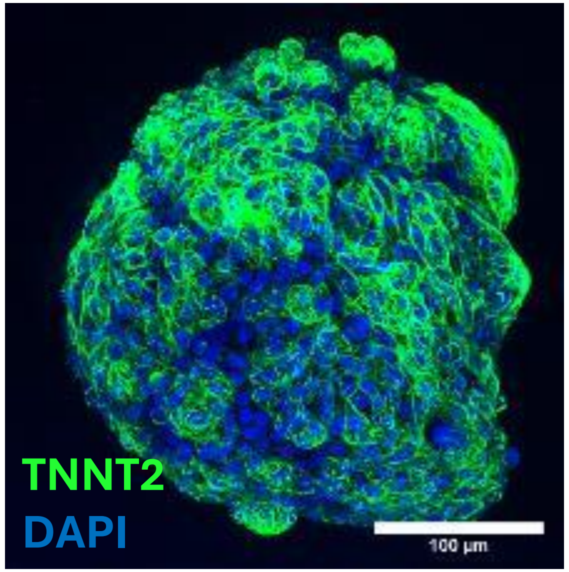


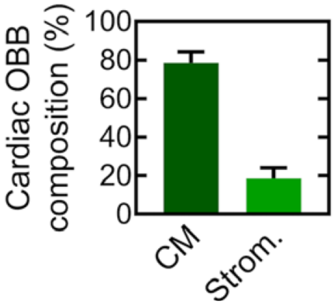
Cardiac spheroids

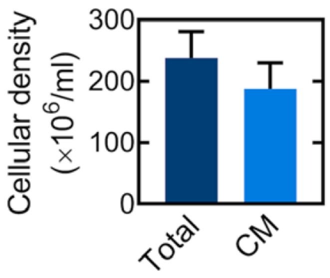


Deriving Billions of Heart Cells in Clusters

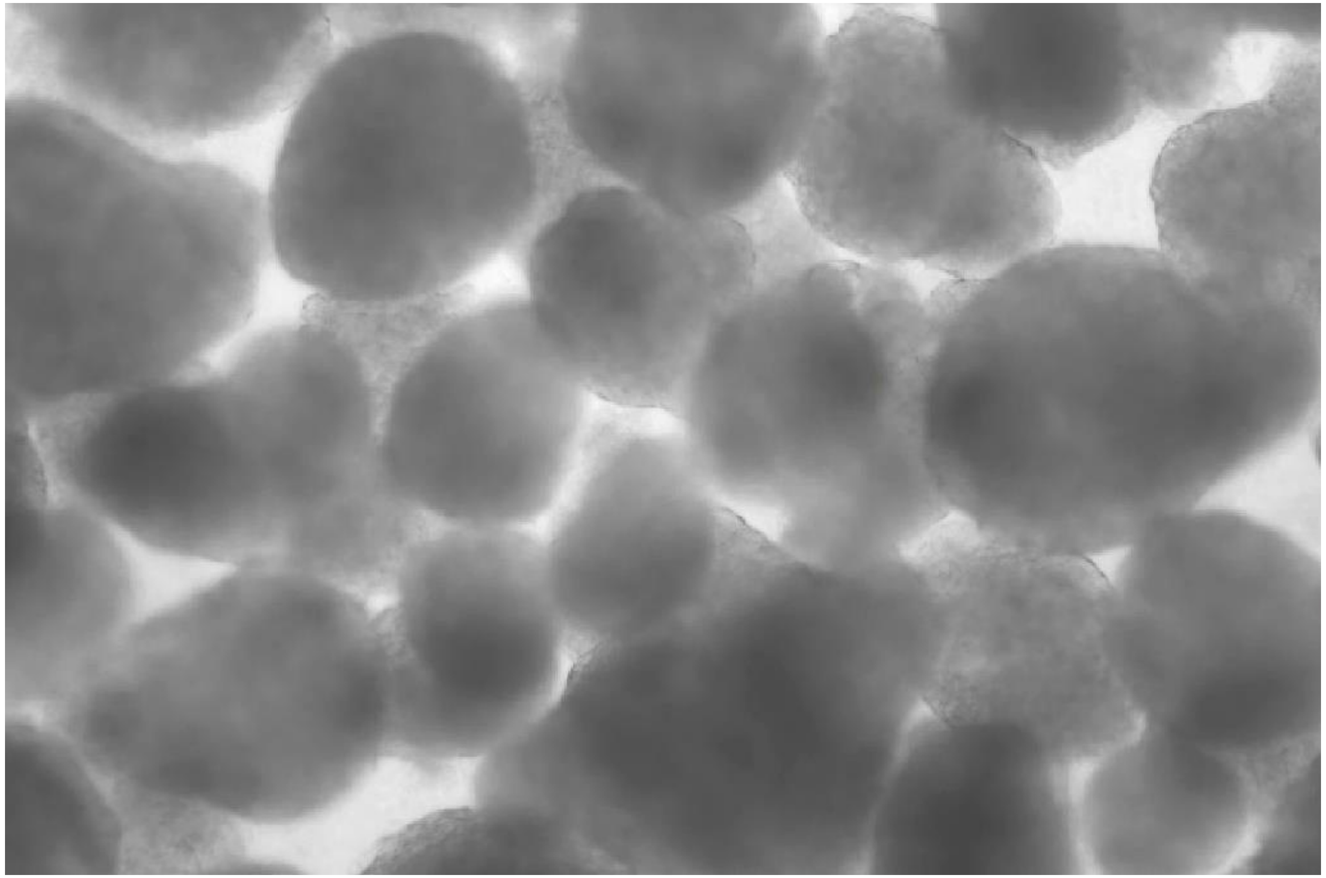
Heart clusters







Heart clusters beating



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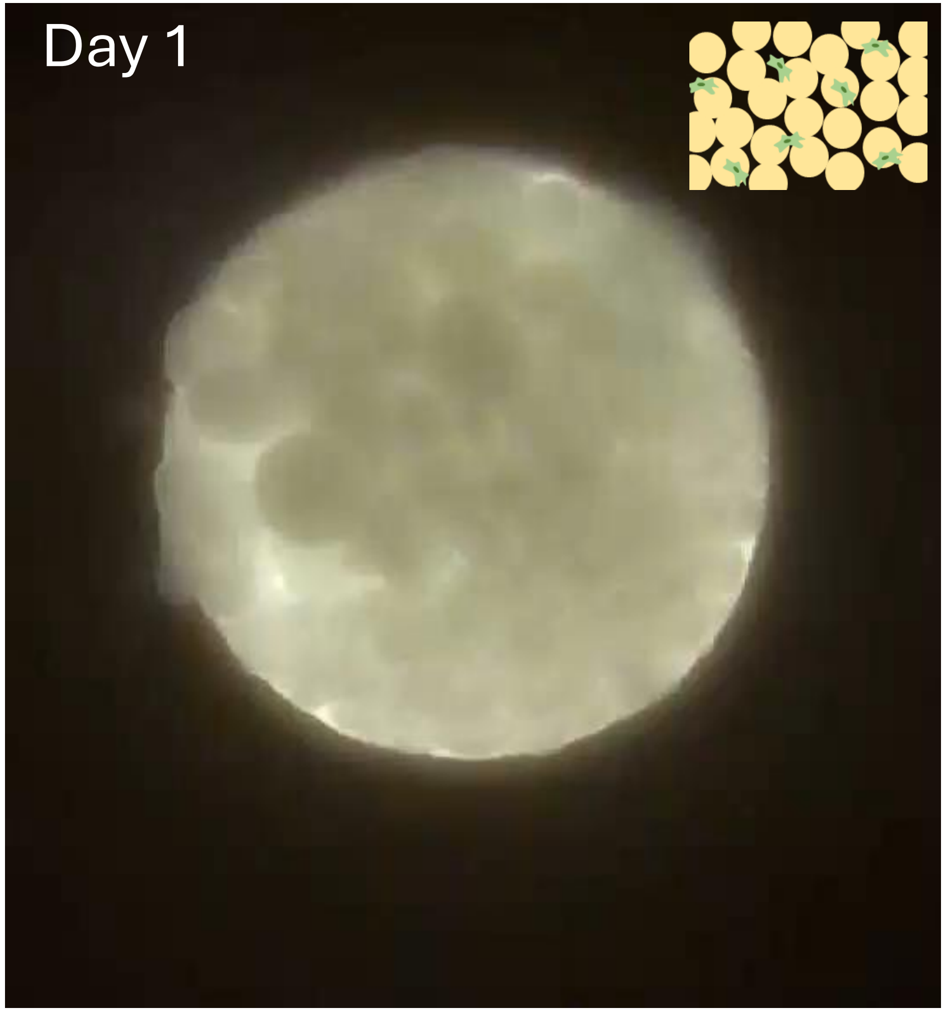
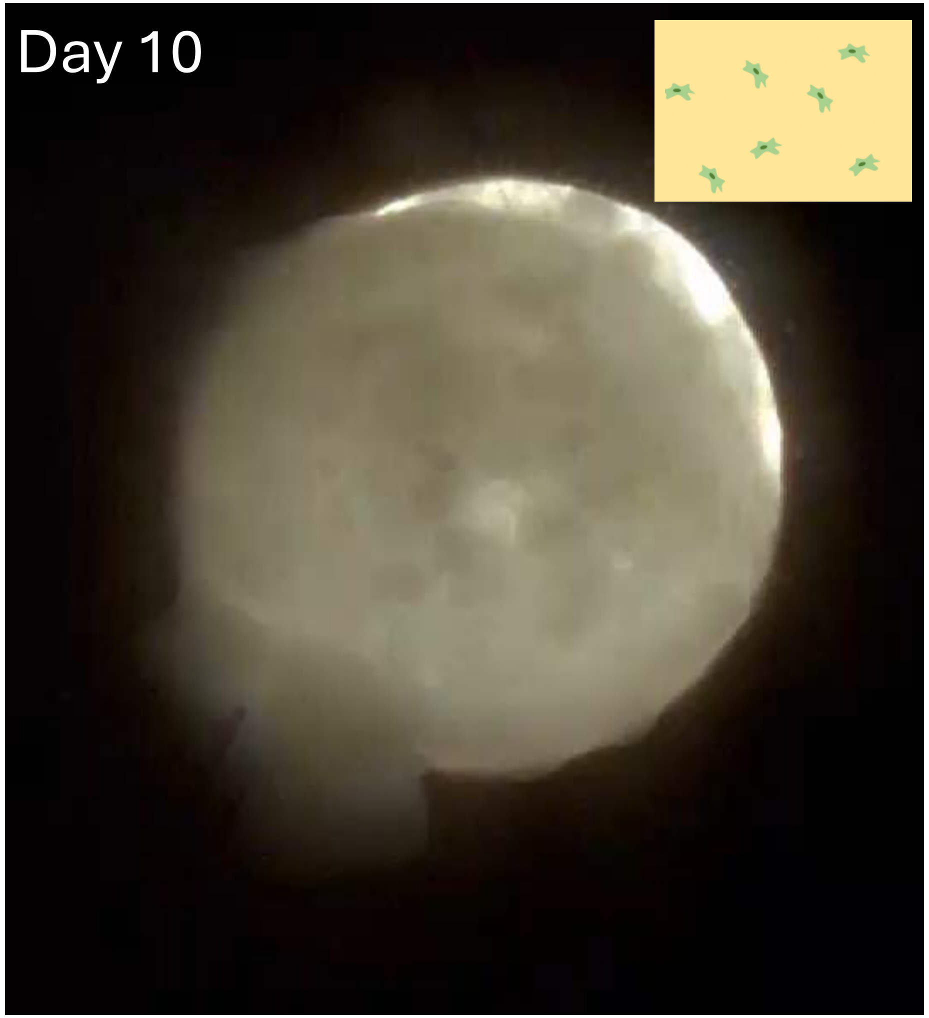
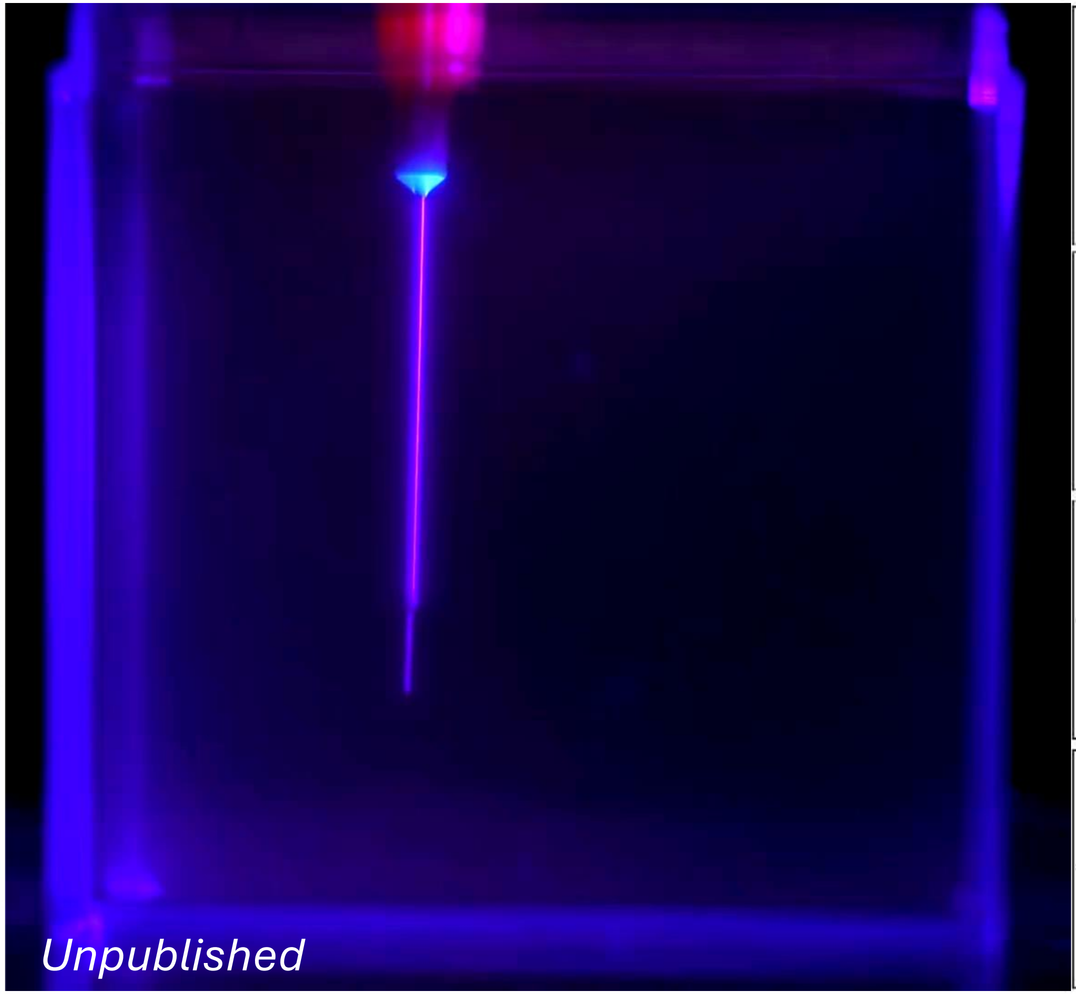
Heart clusters fuse and synchronize over time

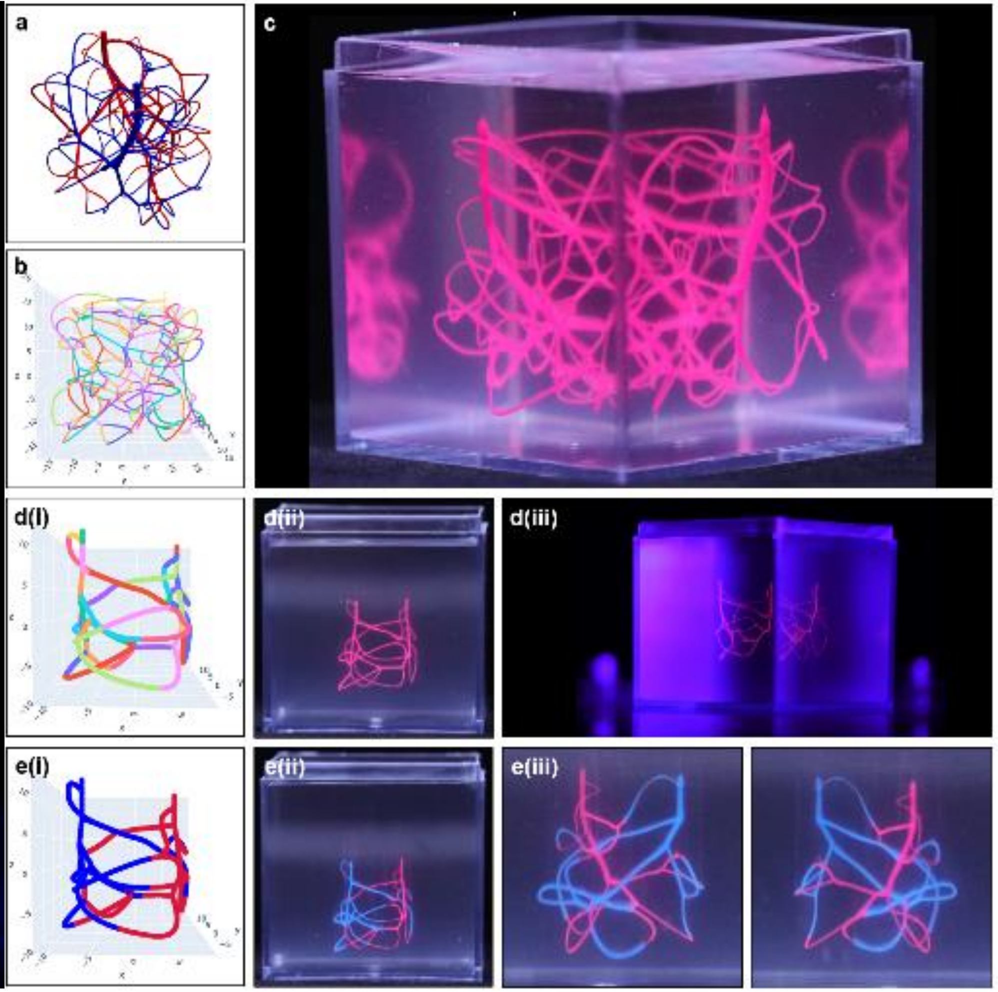




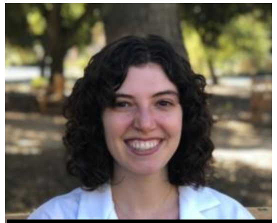
Bioprinting and beating of a vascularized heart tissue

Automated design of vascularized organs






Alison Marsden


Jessica


Zack Sexton

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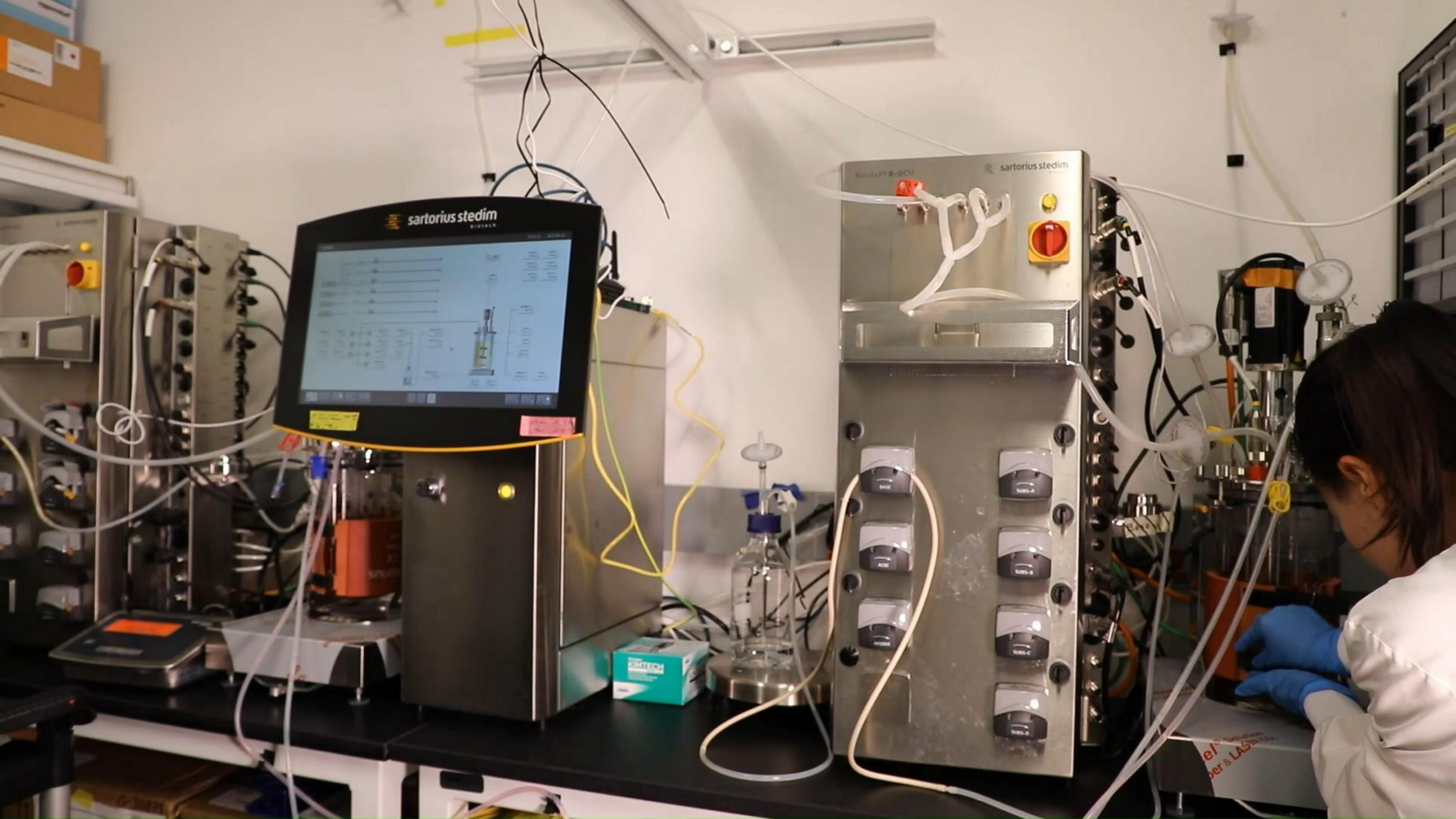
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KIMTECH

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Government Investment into 3D Organ Biofabrication

United States

ARPA H

>>$100M program

Heart, Liver, Kidney

China

HOPE
Human
Organ
Physiopathology
Emulation System

$1B Biofabrication Facility

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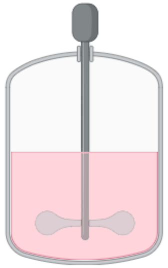
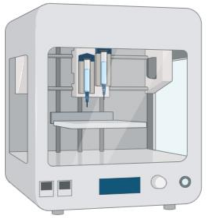
3D Bioprinted Organs on Demand: **Industry & Regulatory Considerations**

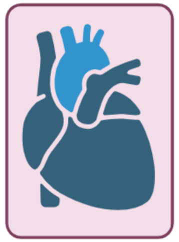
Setting GMP Standards



Cell and organoid bioprocessing

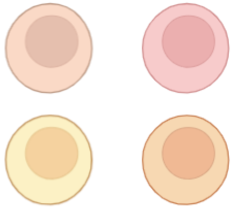


3D Bioprinting materials and procedures

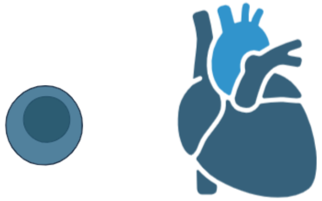


In vitro maturation and measurement

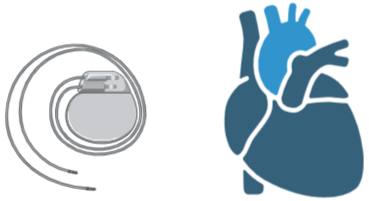
Complex products



Autologous vs allogeneic



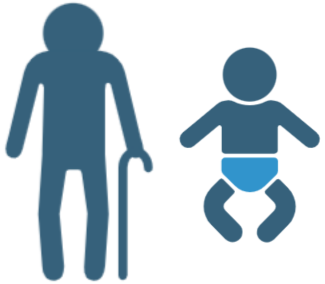
Cells vs organs



Biologic vs device

Ethical Clinical Trials

Risk/reward balancing



Patient selection and consent

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3D Bioprinted Organs on Demand: **Ethical Considerations**

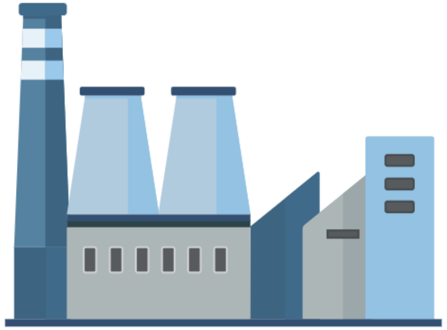
Affordability

- Innovation
- Automation
- Economies of scale

Equitable Access

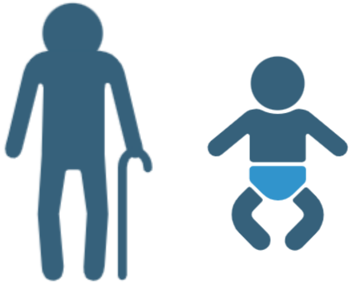
- Economic
- Geographic
- Racial/ethnic diversity

Supply Chain Resilience



- Failsafe supply chain
- Distribution
- Diversification

Triaging Need



- How to handle initial scarcity?

Beliefs

- Stem cell source
- Philosophy of soul

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3D Bioprinted Organs on Demand: Ongoing Engagement with Stakeholders

Healthcare providers

Patients and families

Insurers and health agencies

Patient advocacy groups

Scientists and engineers

Ethicists

Industry and funders

Regulatory bodies

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Thank You!

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