ETH zürich

Materials and Mechanics in Medicine: Paper 2

3D bioprinting of collagen to rebuild components of the human heart (Lee *et al., 2019)*

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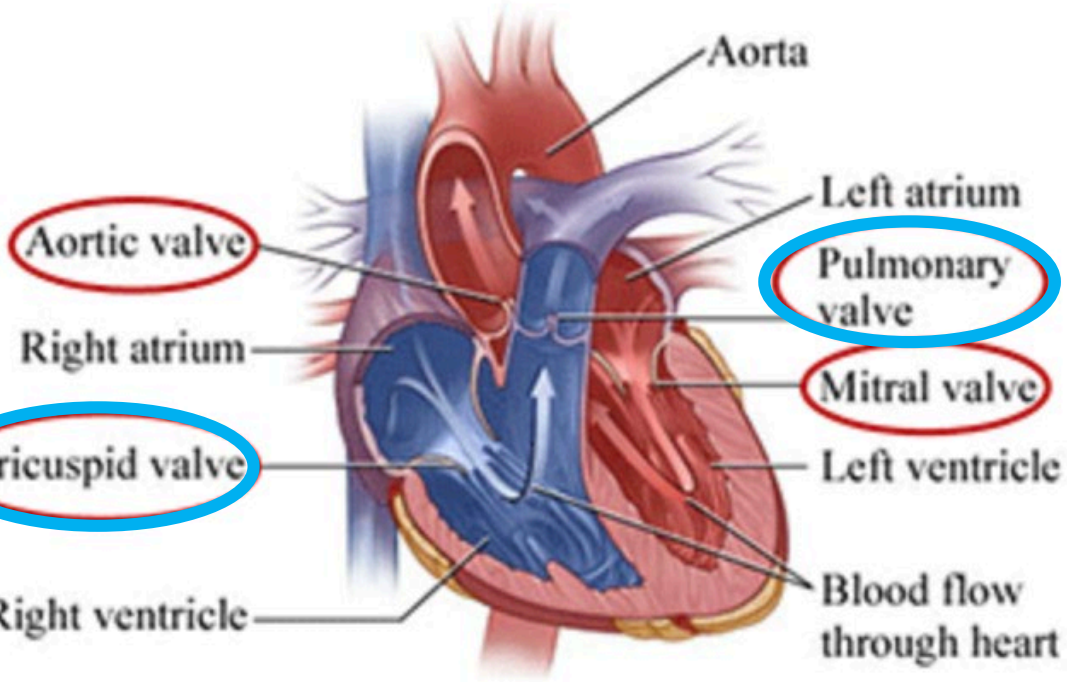
Introduction

- **“3D bioprinting of collagen to rebuild components of the human heart”**
- This paper deals with:
  - Bioprinting as a form for creating scaffolds
  - Importance of collagen as a vital component
  - Novel way to produce parts of the human heart

Background – the human heart

3 Segel



3 Segel

3 Segel

2 Segel

”Taschenklappe” = Semilunarklappe
“Segelklappen” = Atrioventrikularklappe

Research Aim & Results

- Collagen as main ECM component
- Not simple to print complex organs & tissues w/ collagen
- **New**: 3D bioprinting of collagen with *FRESH (2.0)*
- Small to large → capillaries to full organ
- **Unique** gelation method gives high resolution filaments!
- Specifically, *FRESH (2.0)* printed hearts reproduce anatomical structures with high fidelity.
- Cardiac ventricles even mimic native behavior!

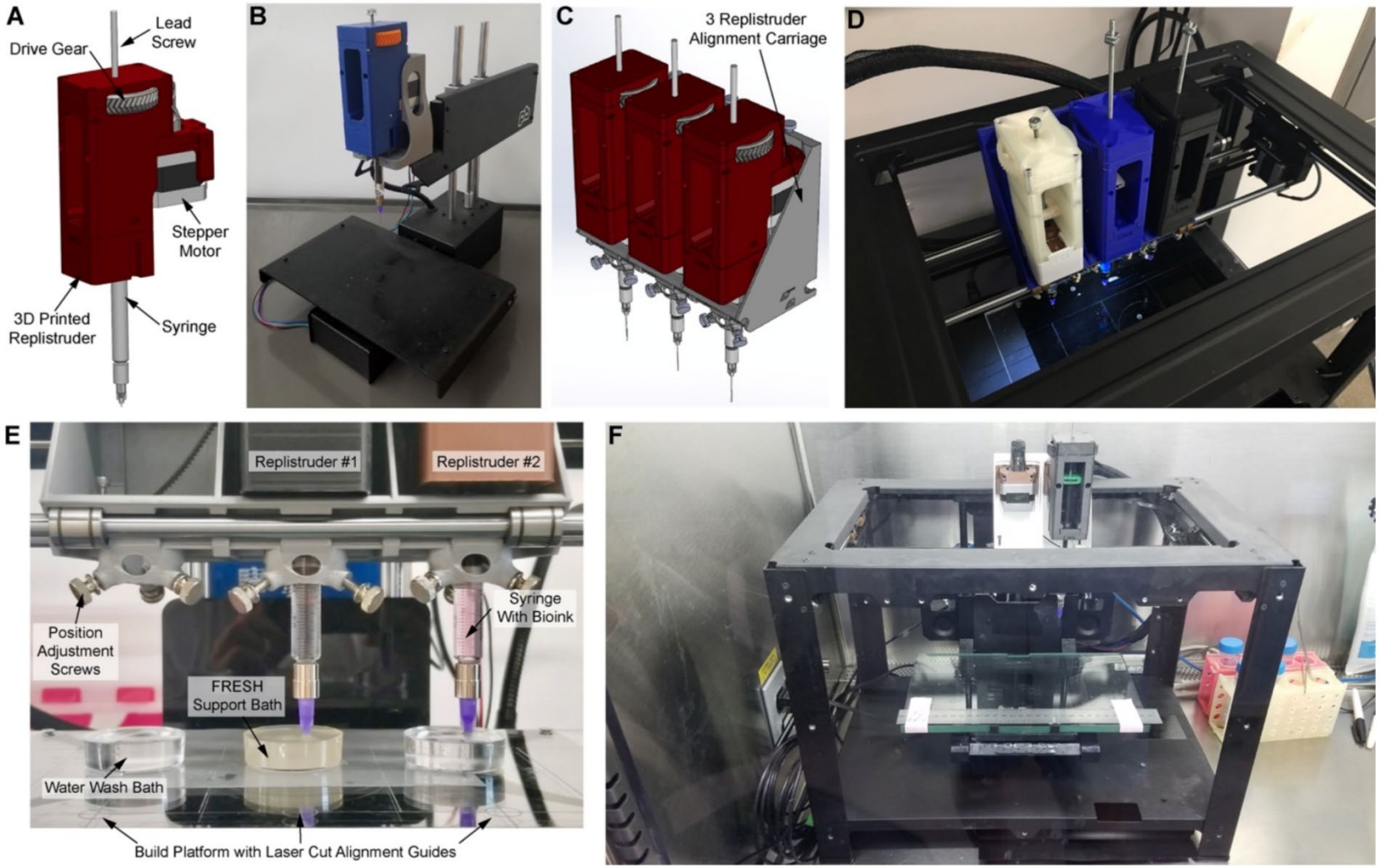
Research Aim & Results

- Ability to directly 3D-bioprint collagen with precise control of composition and microstructure
- Engineer tissue components of the human heart
- Collagen as bio-ink because of its critical role in the ECM!
  - Structural integrity & organization of cells and compartments
  - Depot for cell adhesion and signaling molecules

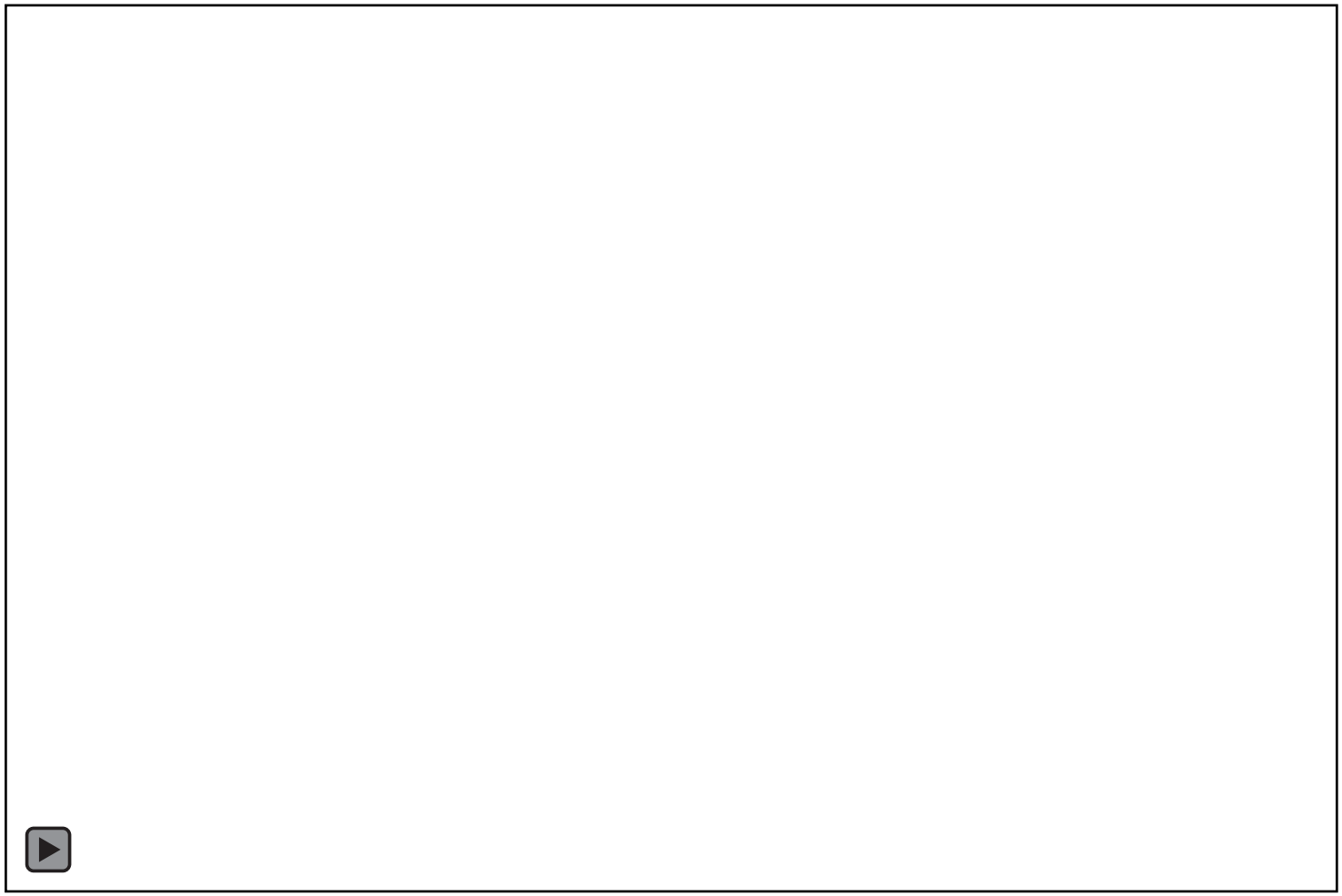
Main Methods and Materials

- Novel approach to drive collagen self-assembly, can…
  - …use chemically unmodified collagen as bio-ink
  - …enhance mechanical properties (high concentration collagen)
  - …create complex structural and functional tissues

Main Methods and Materials



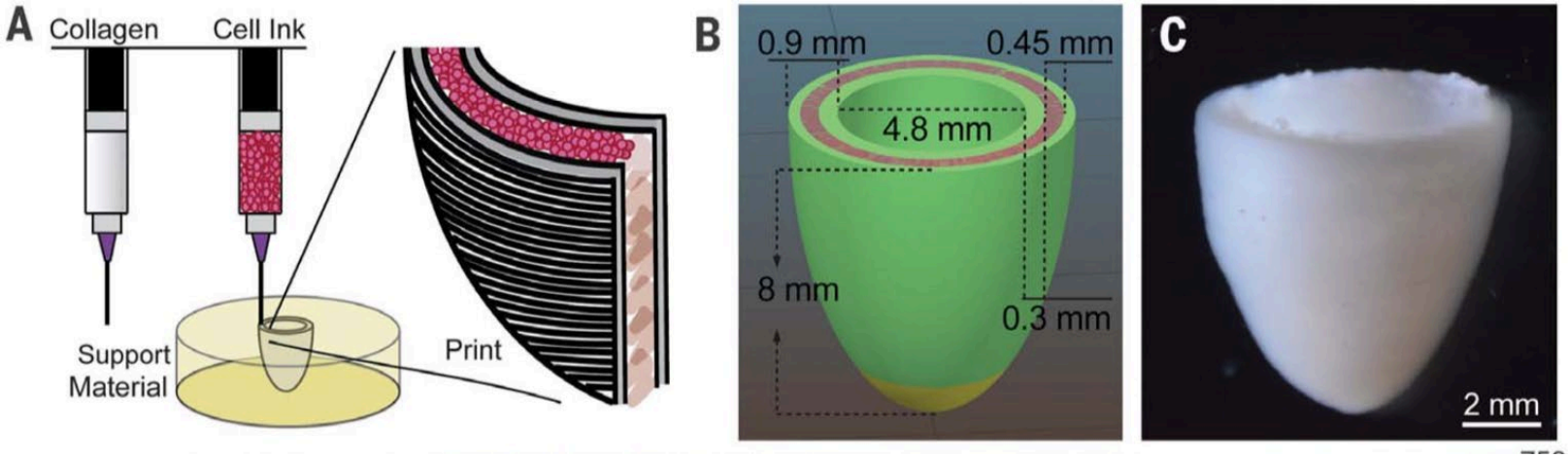
Methods and Materials

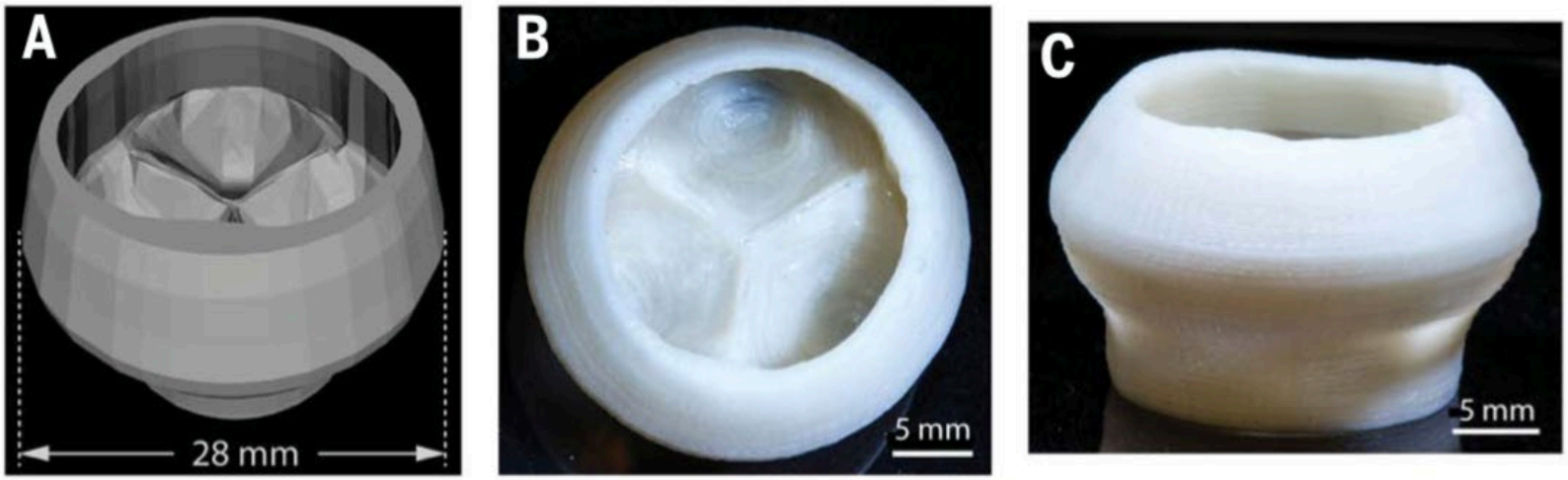


Methods and Materials

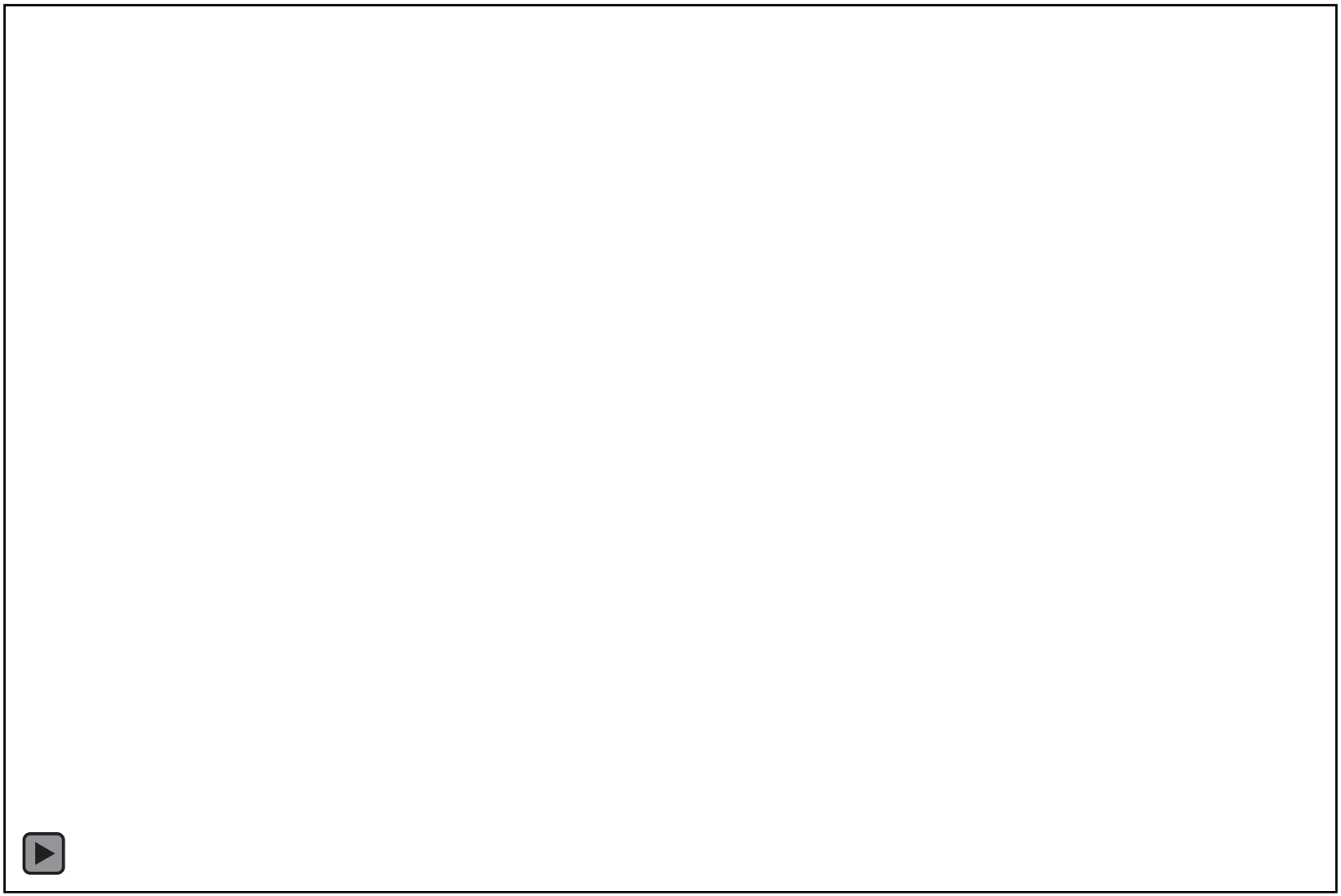
- First focused on FRESH-printing a simplified model of a small coronary artery–scale linear tube from collagen
  - Mouse myoblast cells cast around the tube to evaluate the ability to support a volumetric tissue
- Next, FRESH-printed a model of the left ventricle, with dual-material printing strategy
- Finally, print tri-leaflet heart valve 28 mm in diameter

Methods and Materials





Methods and Materials



Results

Results

- FRESH 3D-bioprinted hearts reproduce patient-specific anatomical structures
- Cardiac ventricles printed with human cardiomyocytes showed:

→ **synchronized contractions**

baseline spontaneous beat rate of 0.5 Hz, could be paced at 1 and 2 Hz

→ **directional action potential propagation**

→ **wall thickening (at peak systole)**

printed ventricle expanded inward and outward during a contraction with decrease in cross-sectional area of interior chamber during peak systole with a max of 5% at 1Hz

→ **Electrophysiological behavior**

multiple propagating waves and pinned rotors

Results

- FRESH v2.0 printing of collagen can build advanced tissue scaffolds for a wide range of organ systems

- Now we have the ability to build constructs that start to recapitulate the structural, mechanical and biological properties of native tissues

Limitations

Bioprinting of a full organ is not possible yet:

→ Generating billions of cells required to 3D-bioprint large tissues

→ Achieving manufacturing scale

→ Creating regulatory processes for clinical translation