HYDRODYNAMIC ASSESSMENT OF SMALL INTESTINAL SUBMUCOSA TUBULAR VALVES

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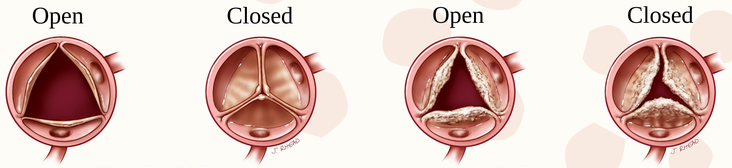
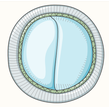
Cardiovascular Matrix Remodeling Laboratory

INTRODUCTION

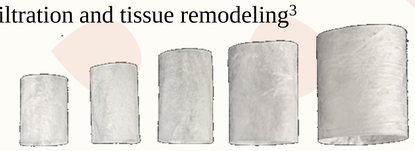


- Cardiovascular diseases is the #1 killer worldwide
- More than 25,000 people in the USA die from heart valve diseases every year[1]
- Heart valve diseases cost USA $23.4 billion annually[2]
- Limited treatment options:

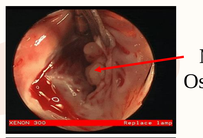
Mechanical Valves	Bioprosthetic Valves
	
Lifelong anticoagulants	Not durable
• Limited sizing • No somatic growth • May require multiple operations	

- Heart Valves with Regenerative Capacities:
  - Provide somatic growth
  - Self-repair
  - Infection resistance and permanent approach
- Porcine Small Intestinal Submucosa (PSIS):
  - FDA approved
  - Used for other cardiovascular applications
  - Evidence of host native cell infiltration and tissue remodeling[3]

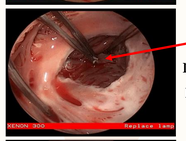
CorMatrix® CARDIOVASCULAR REGENERATIVE



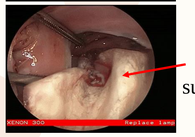
- Cylindrical, stentless, seamless with acellular extracellular matrix (ECM)
- Currently applied in the tricuspid position in clinical settings



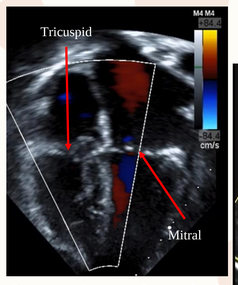
Metastatic Osteosarcoma



Original valve removed, papillary muscles identified

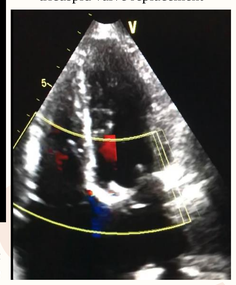


PSIS valve sutured in place



Post-op peak ventricular systole of an 11 year-old patient with mestatic osteosarcoma on the tricuspid valve

Peak ventricular systole of an 12 year-old patient 1 year after tricuspid valve replacement



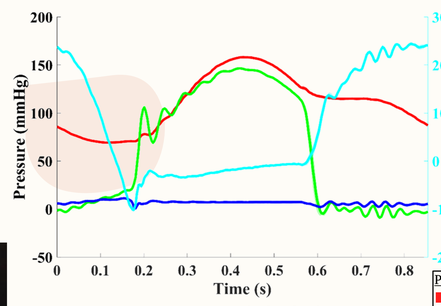
Little or no regurgitation

- **PROBLEM:** While clinical echocardiographic outcomes of CorMatrix PSIS cylindrical valve in the tricuspid position are favorable and known, functional assessments in the mitral position is not known
- **OBJECTIVE:** Conduct hydrodynamic testing CorMatrix PSIS cylindrical valve in the mitral position and compare their performance with a bi-leaflet mechanical valve

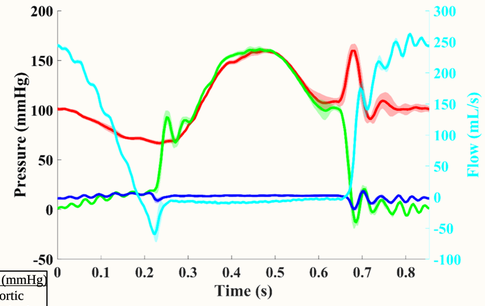
Cylindrical PSIS valves facilitate **robust** hydrodynamic valve function

RESULTS & CONCLUSION

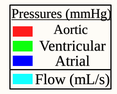
Valve Type (Mitral Position)	Q_{RMS} (ml/s)	EOA (cm^2)	ΔP (mmHg)	Regurge %
CorMatrix Tubular PSIS Valve (R = 5)	128.65 ± 1.60	1.00 ± 0.02	6.17 ± 1.35	9.23 ± 0.61
Bi-leaflet Mechanical Valve (N = 2)	128.58 ± 4.33	0.96 ± 0.04	6.84 ± 3.05	2.31 ± 0.87



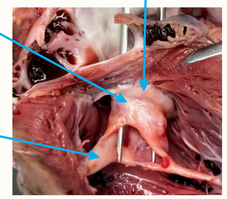
CorMatrix PSIS Cylindrical Valve



Bi-Leaflet Mechanical Valve



- Cylindrical PSIS valves appear to facilitate robust hydrodynamic valve function
  - Tricuspid – based on clinical data
  - Mitral (potentially) – based on preliminary hydrodynamic data
- Material may serve as scaffold for *de novo* valvular tissue growth[4]

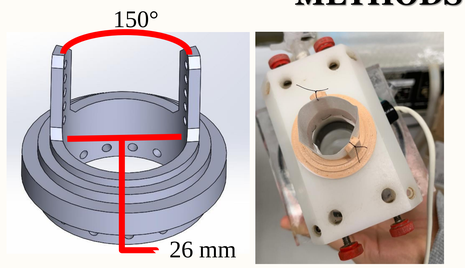


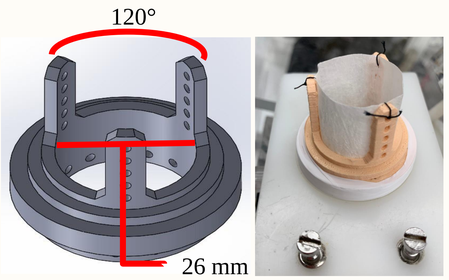
11-Month Explant[4]

PITFALLS & FUTURE WORK

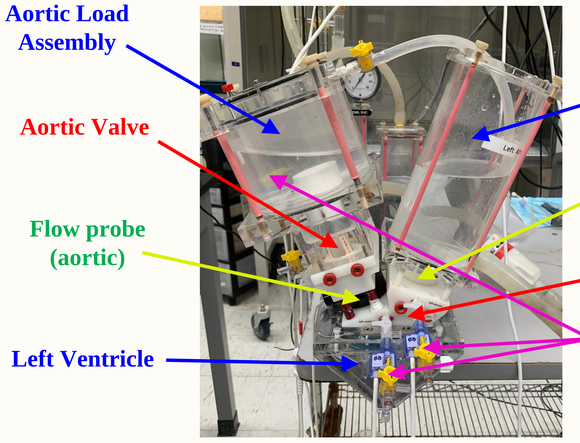
- Increase mitral position sample size
  - Anchorage points for suturing and sealing the annulus
- Testing in tricuspid and aortic positions
- Seeding PSIS with cells and conditioning them in bioreactors to assess the effects of both mechanical and biochemical stimuli on valve performance

METHODS





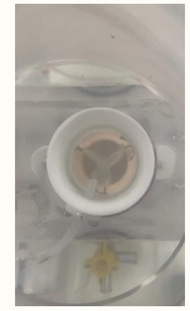
- Test Conditions
  - 70 beats/min
  - CO: 5 L/min
  - MAP: 100 mmHg
  - 35%-systolic
  - 65%-diastolic



Mitral (ventricular)

Mitral (top view)

Aortic (top view)



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[1]The Silver Book: Valve Disease. (2018)
[2]Moore M, *et al. Clinicoecon Outcomes Res*. (2016) 8:613–27
[3]Gerdisch, M. W, et. al., (2014). *J Thorac Cardiov Surg*, 148(4), 1370-1378.
[4]Gonzalez, B. A., et al. (2020). *Tissue Engineering Part A*.