

Hydrodynamic Assessment of a Small Intestinal Submucosa Tubular Mitral Valve

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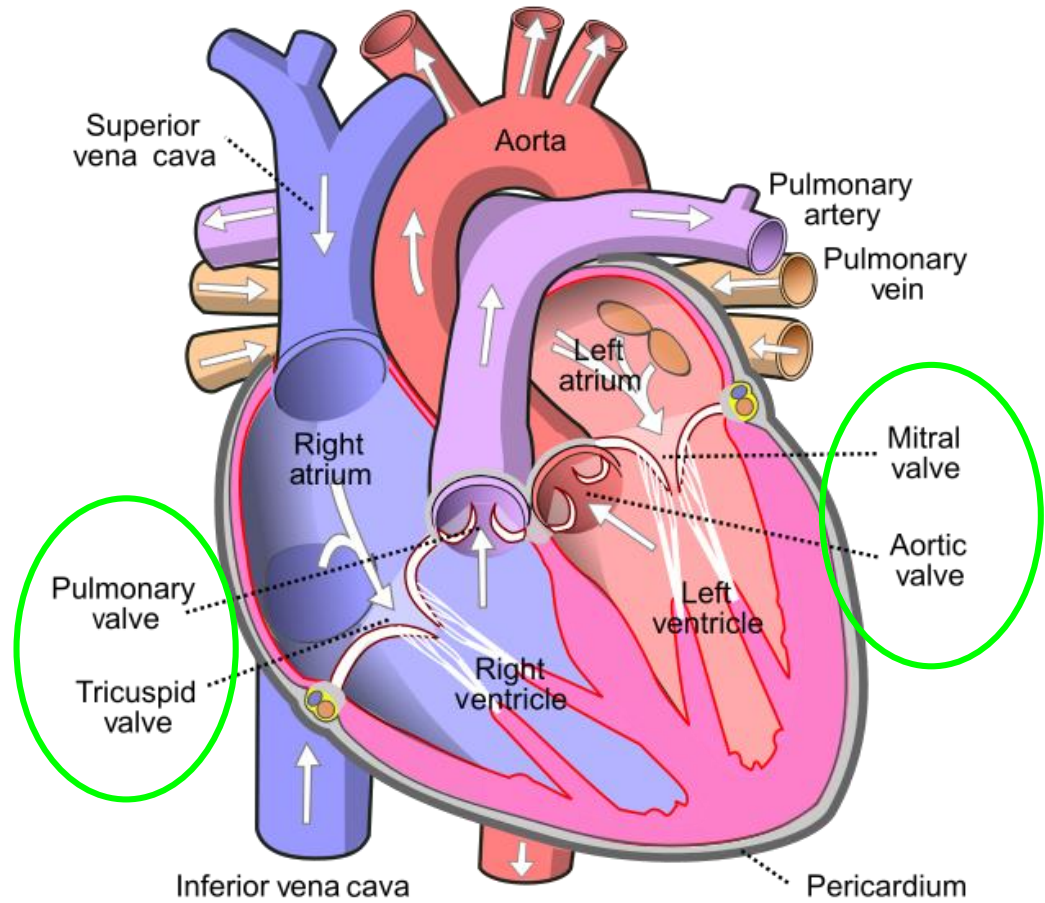
CorMatrix[®]
CARDIOVASCULAR
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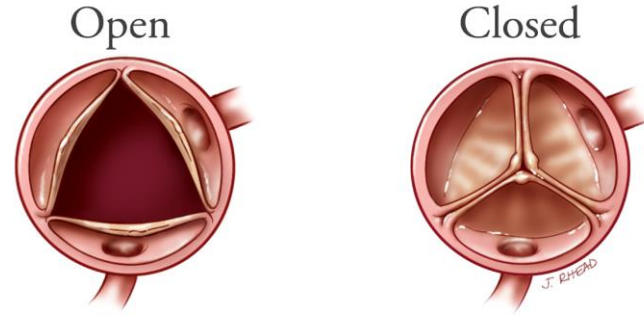
Heart Valve Function

- Maintain proper **direction** of blood flow into and out of each heart chamber
- **4 valves**: consist of flaps that open and close during each heartbeat

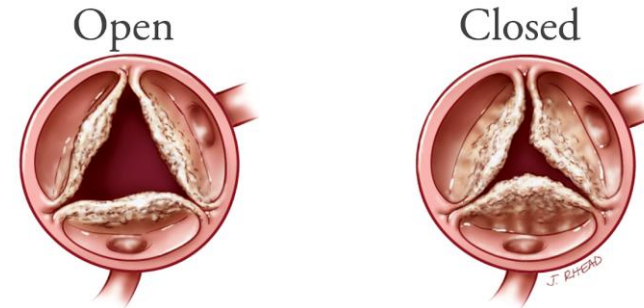


Heart Valve Diseases

- **Cardiovascular diseases** is the **#1 killer worldwide** (World Health Organization)
- More than **25,000 people** in the USA die from heart valve diseases every year¹
- Heart valve diseases cost USA **\$23.4 billion** annually²



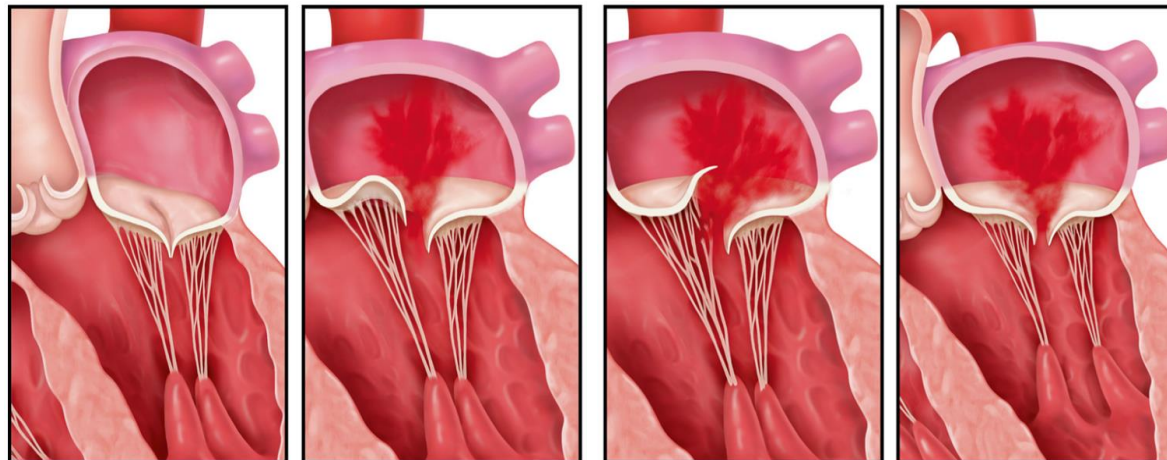
Healthy Valve



Valve Stenosis

Causes of Heart Valve Diseases

- Congenital valve defects
- Calcification
- Tumor
- Valve degeneration



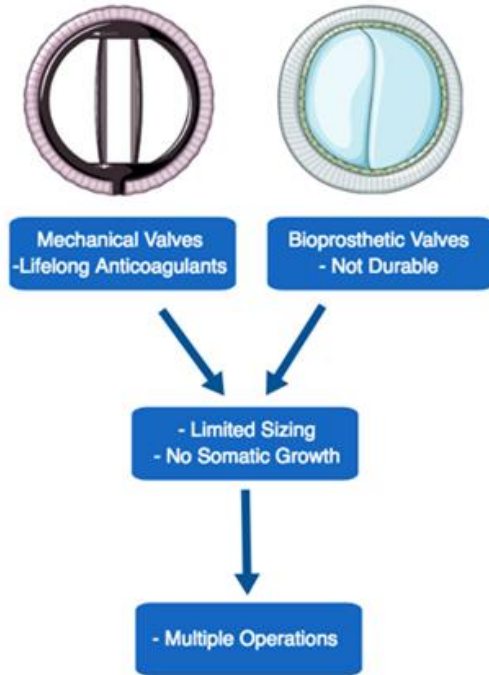
Normal

Prolapse

Flail

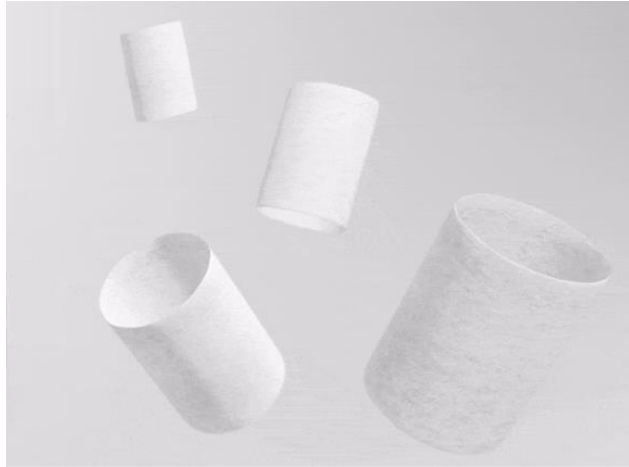
Functional
Degeneration

Treatment Options: Tissue Engineered Scaffolds

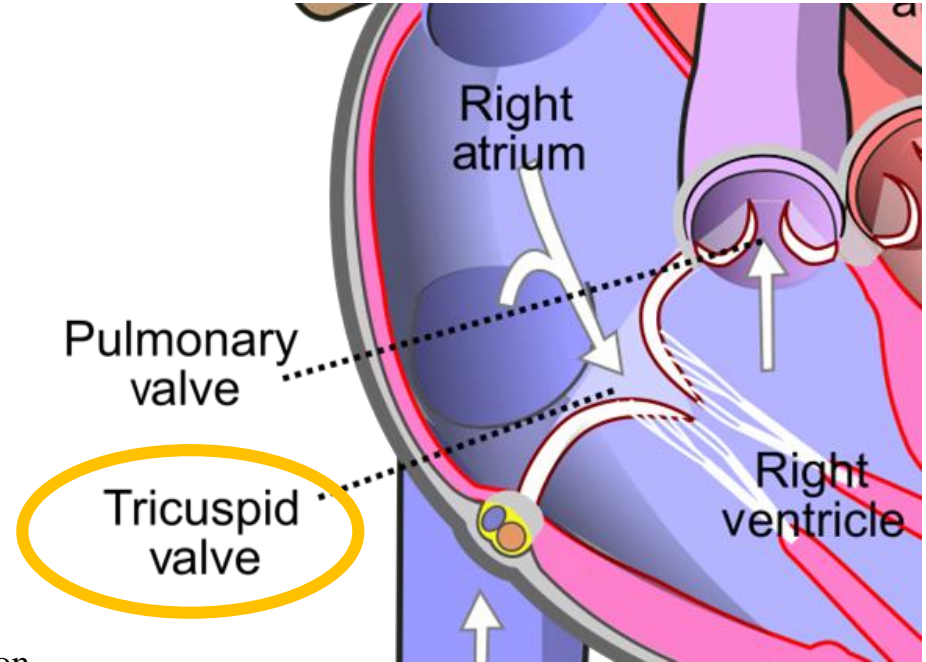


- Heart Valves with Regenerative Capacities:
 - Provide somatic growth
 - Self-repair
 - Infection resistance and permanent approach
- Porcine Small Intestinal Submucosa (PSIS):
 - FDA approved
 - Used for other cardiovascular applications
 - Evidence of host native cell infiltration and tissue remodeling¹

Cor™ TRICUSPID ECM®

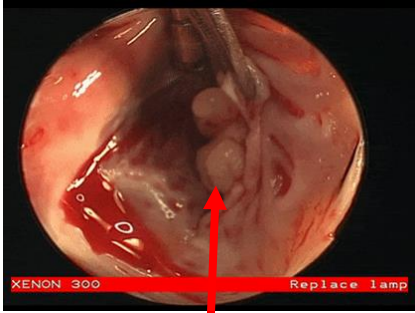


- Tubular valve made of PSIS material
- Acellular extracellular matrix (ECM)
- Stentless, seamless
- Currently being applied in the tricuspid position



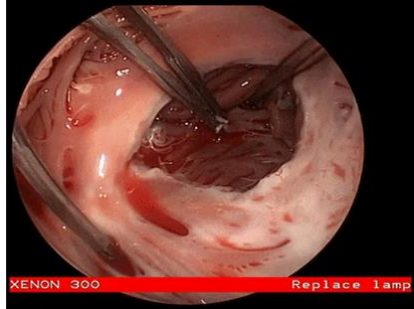
Cor™ Tricuspid ECM in the Tricuspid Position

Patient 1 Outcome

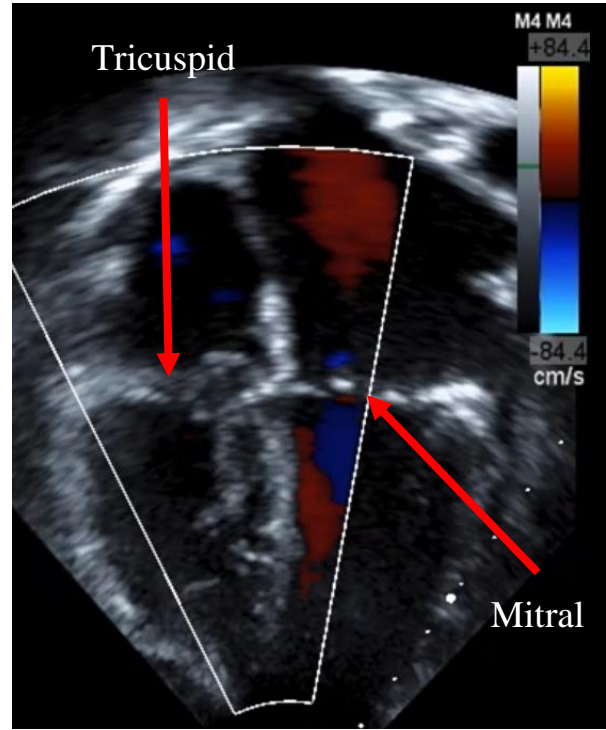
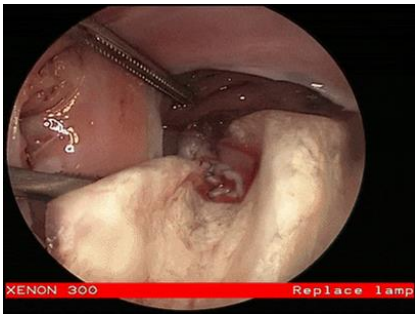


Metastatic
Osteosarcoma

11 year old boy

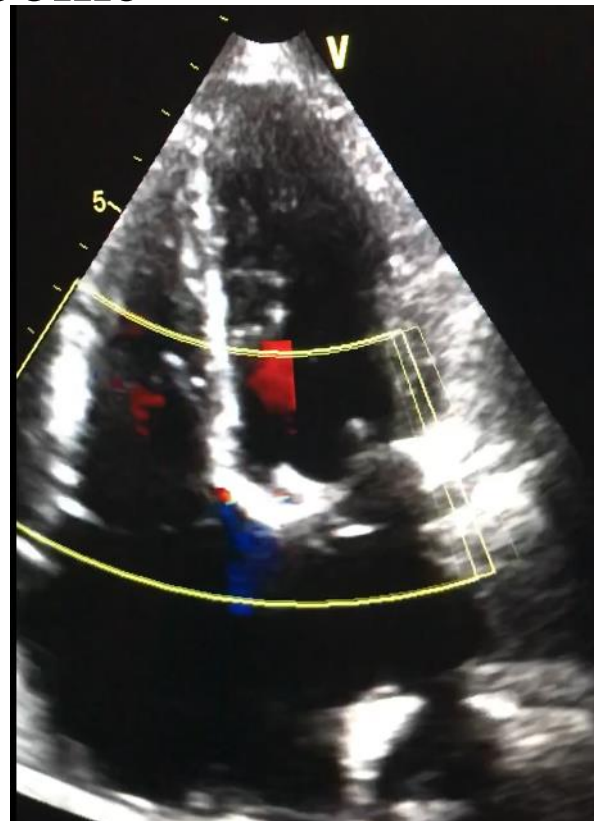


Currently 12 years
old and disease free

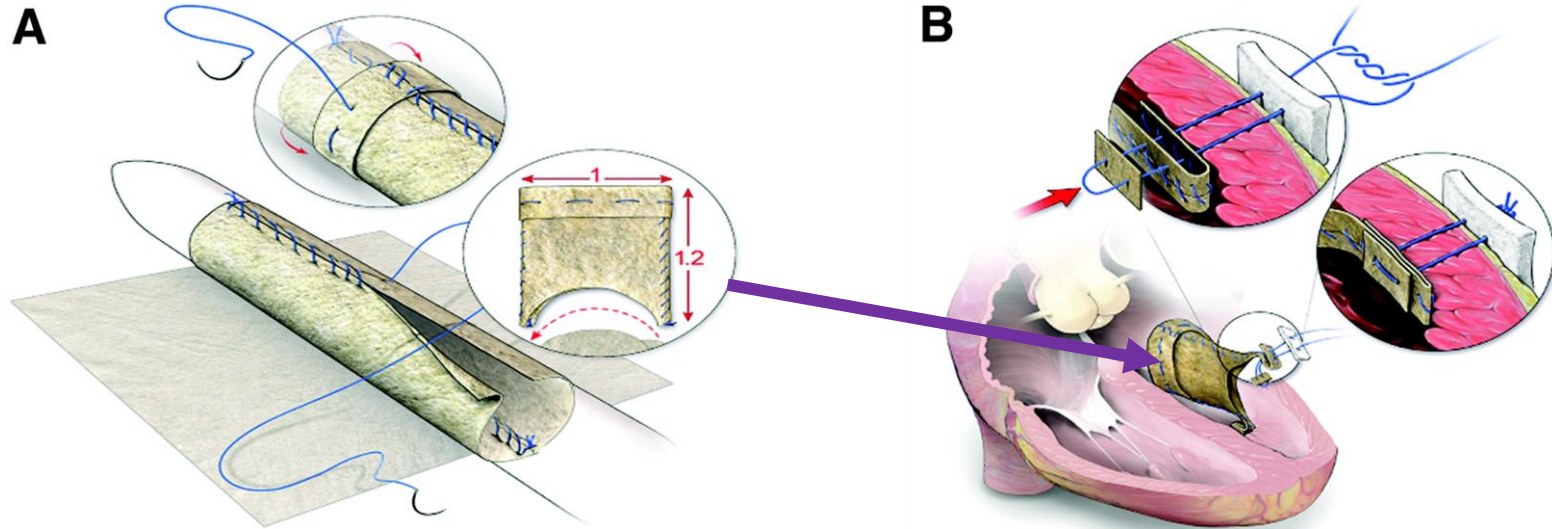


Cor™ Tricuspid ECM in the Tricuspid Position Patient 2 Outcome

12-year-old Pediatric Patient
1 year post-op
(Peak Ventricular Systole)
Little to no regurgitation



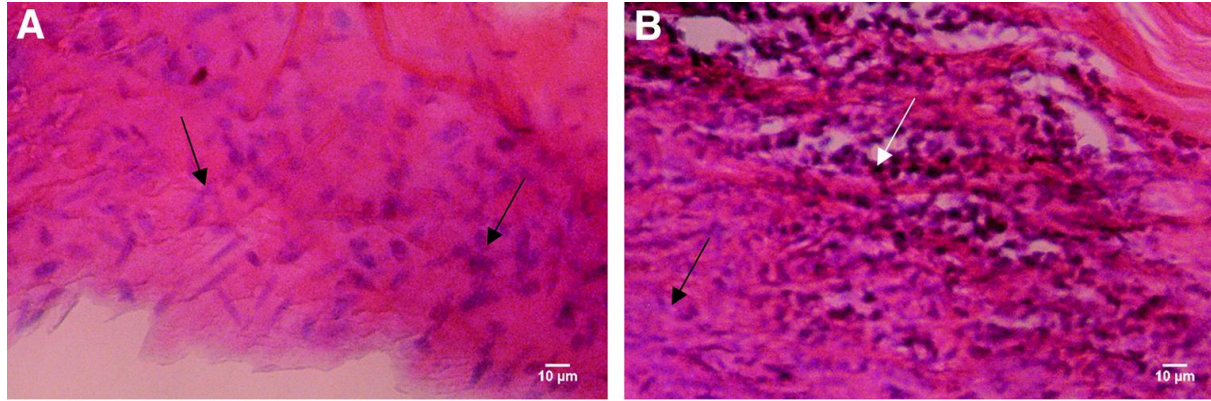
PSIS in Mitral Position - Baboon Model Implantation



(A) Assembly of a hand-made tubular PSIS mitral valve

(B) Attachment of mitral valve to the papillary muscles with pledget strips

In vivo Baboon PSIS Explant - Mitral Valve Remodeling



90 days post-implantation

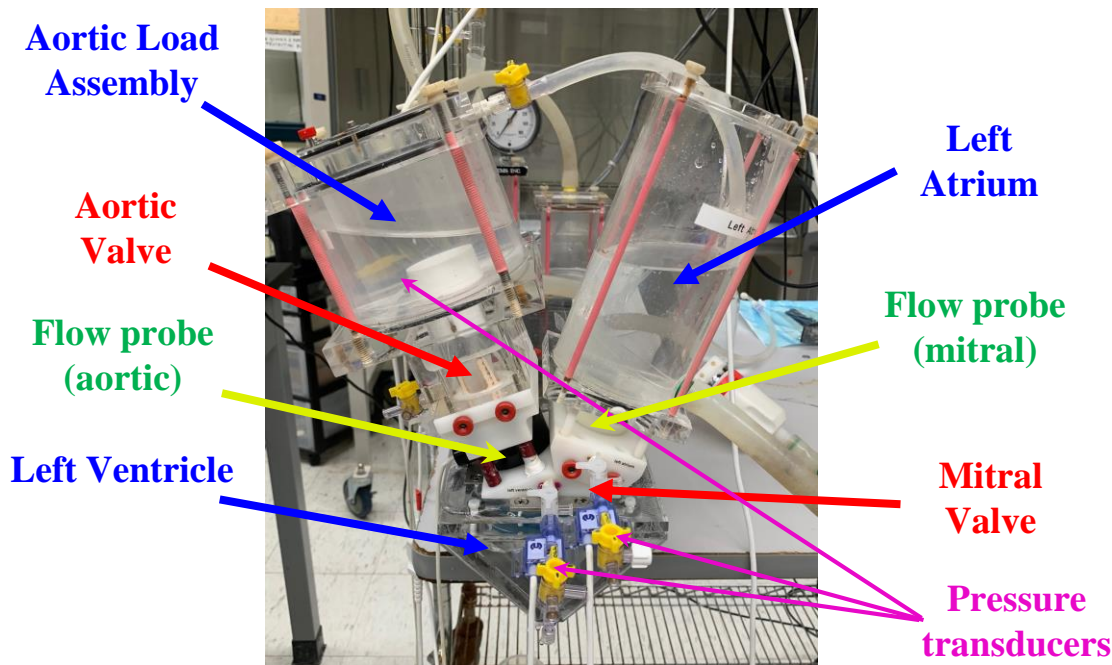
A) Raw un-implanted decellularized PSIS

B) Explanted valve showing new native Baboon cells alongside remaining porcine cells

Objective and Problem Statement

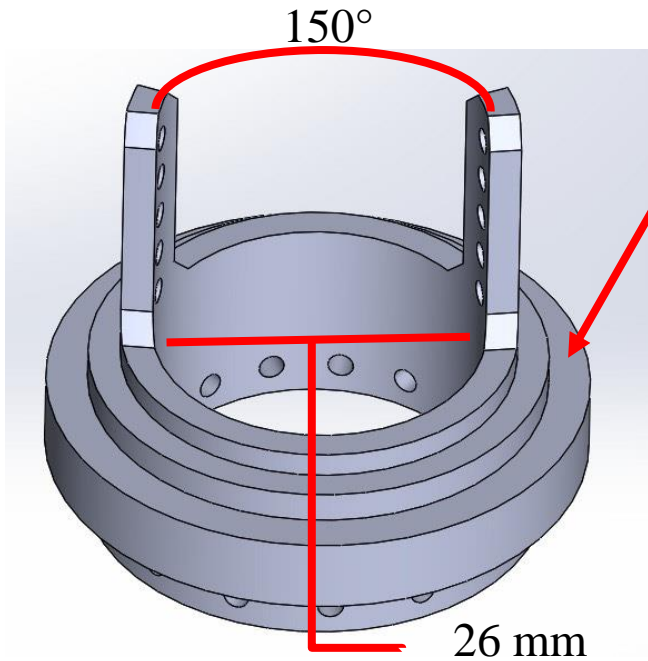
- **PROBLEM:** While clinical echocardiographic outcomes of Cor™ TRICUSPID ECM tubular valve in the tricuspid position are favorable and known, functional assessments in the mitral position is not known
- **OBJECTIVE:** Conduct hydrodynamic testing of Cor™ TRICUSPID ECM valves in the mitral position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

Vivitro Pulse Duplicator - Hydrodynamic Testing



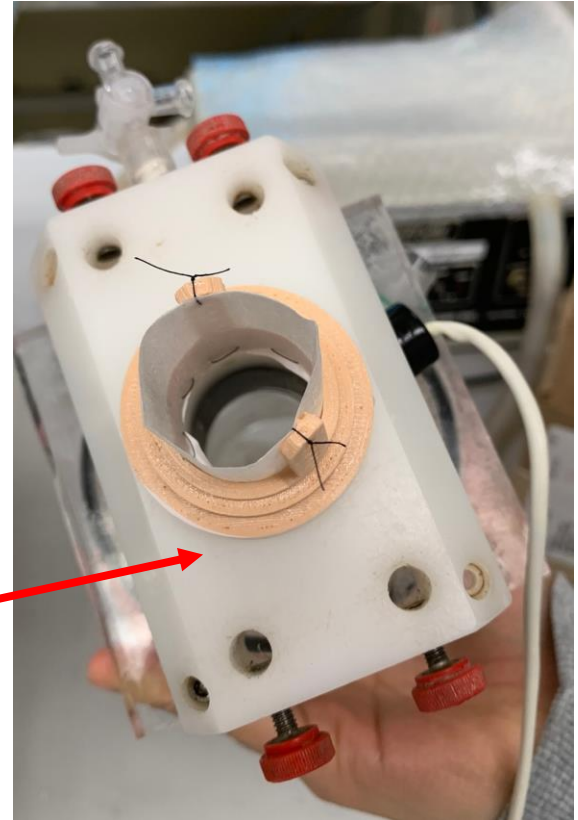
- Pressure transducers
 - Aortic
 - Ventricular
 - Atrial
- Flow Probe
 - Mitral or aortic
- Nominal Test Conditions
 - 70 beats/min
 - Cardiac Output: 5 L/min
 - Mean Arterial Pressure: 100 mmHg
 - 35%-systolic 65%-diastolic

Custom Built Mitral Valve Holder



Material:
Thermoplastic
Polyurethane (TPU)

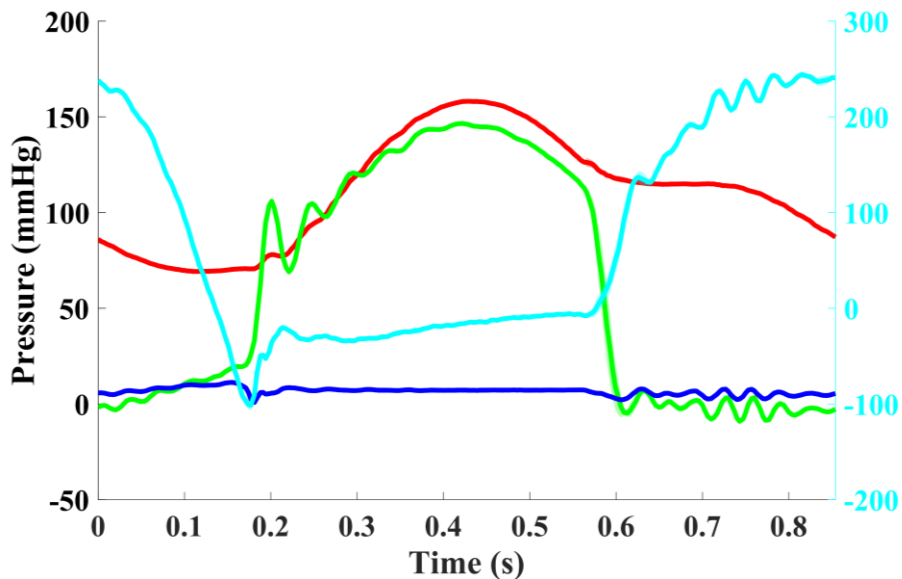
Mitral valve
holder in Vivitro
assembly



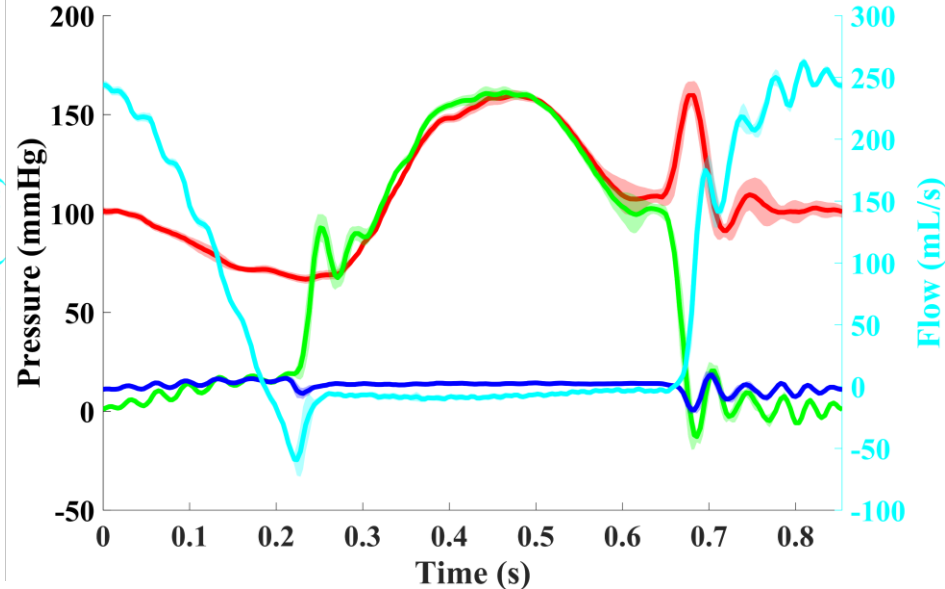
Videos of Mitral Valve in Vivitro



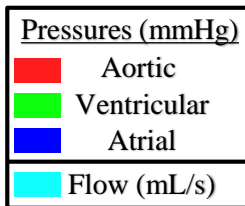
Vivitro System - Hydrodynamic Results



Cor™ TRICUSPID ECM



Bi-Leaflet Mechanical Valve



Mitral Position - Hydrodynamics

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

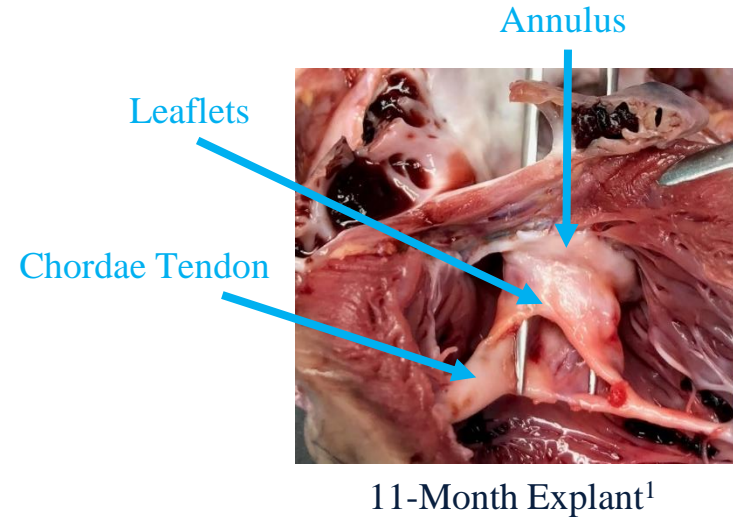
Values reported as Mean \pm SEM

Pitfalls and Limitations

- Valve holder has no pledget strip anchorage
- Annulus is not completely sealed
- Only one anchorage point around the annulus → over-estimation of regurgitation

Discussions / Conclusions

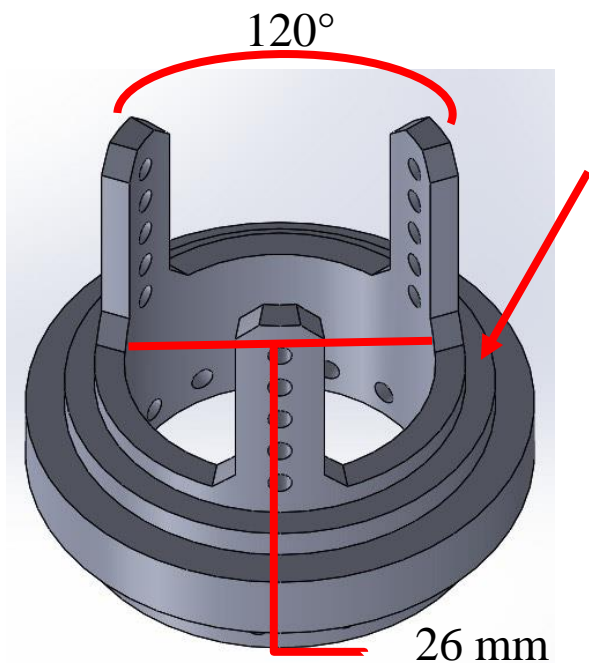
- Tubular PSIS valves appear to facilitate **robust hydrodynamic valve function**
 - Tricuspid – based on clinical data
 - Mitral (potentially) – based on preliminary hydrodynamic data
- Material may serve as scaffold for *de novo* valvular tissue growth¹



Future Works

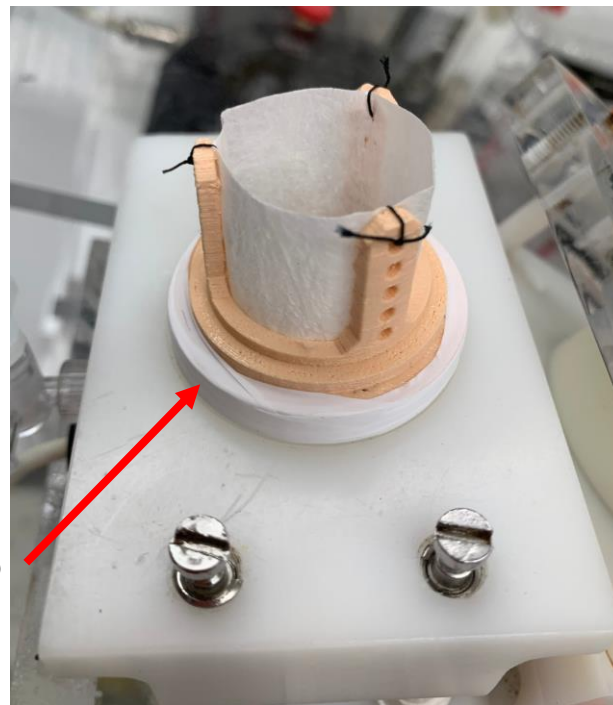
- Increase mitral position sample size
 - Anchorage points for suturing
 - Sealing the annulus
- Testing in tricuspid and aortic positions

Future Works - Aortic Valve Application



Material:
Thermoplastic
Polyurethane
(TPU)

Aortic valve
holder in Vivitro
assembly

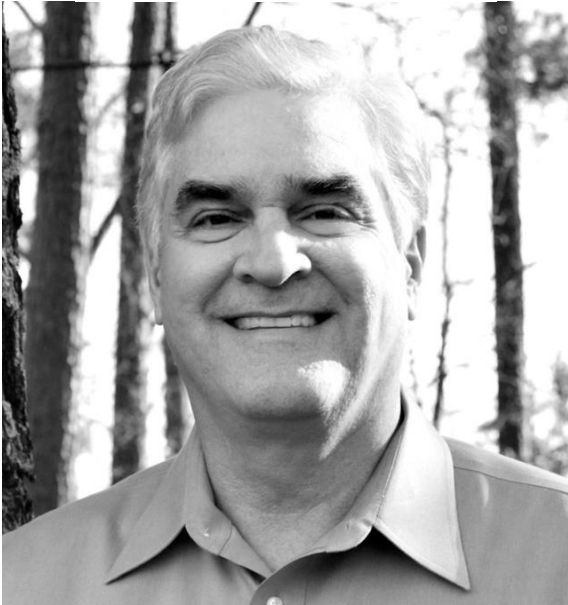


Future Works - Aortic Valve Application



Acknowledgments

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Asad Mirza
Dr. Robert Matheny
Ramaswamy Lab
ICTEHV/HVS 2020



THANK YOU!
Questions?

Equations

Q_{RMS} : Root mean square forward flow during positive differential pressure period

Effective Orifice Area = $(Q_{RMS} / (51.6 * \sqrt{\Delta P / \rho}))$

ΔP : pressure gradient during forward flow = mitral pressure - ventricular pressure

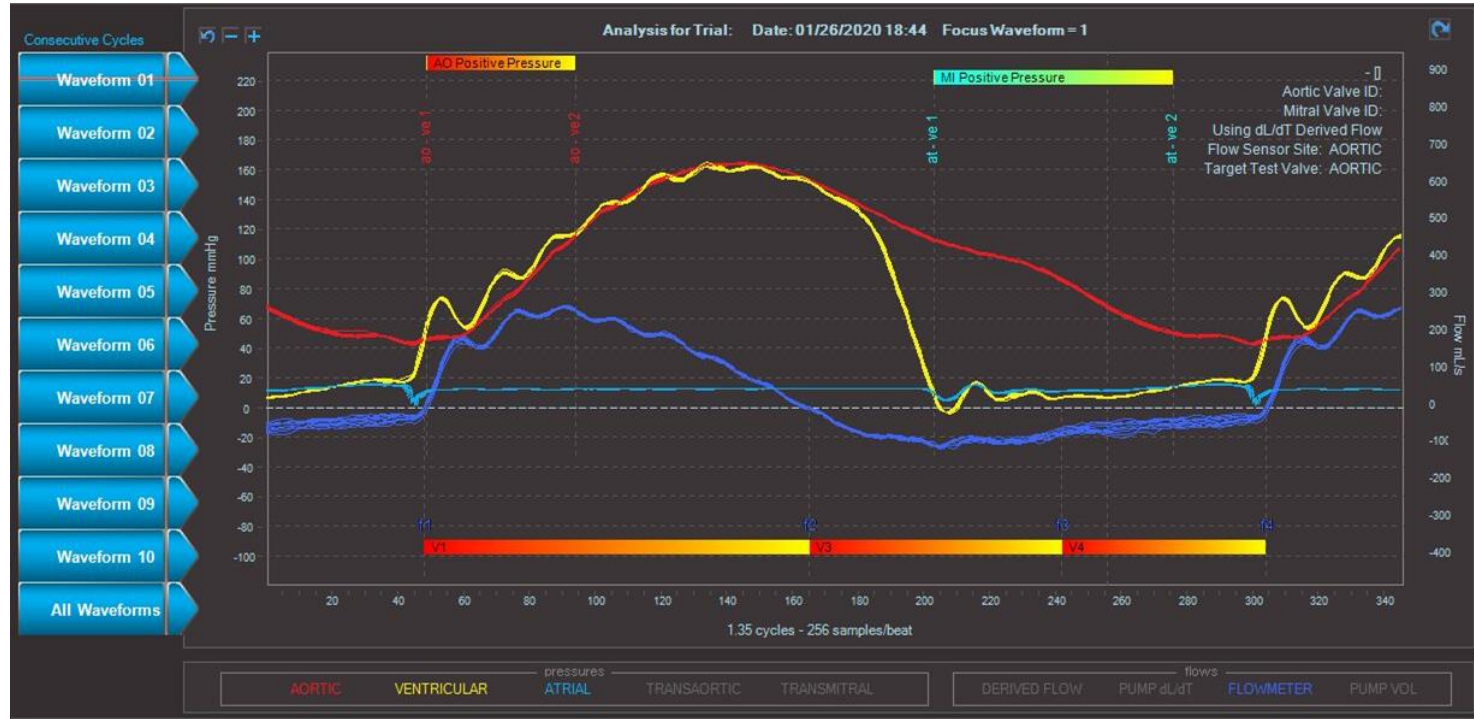
RF: Regurgitation factor [leakage volume / (stroke volume + leakage volume)]

Source: <https://vivitrolabs.com/wp-content/uploads/2014/03/Pulse-Duplicator-Manual.pdf>

Tricuspid Test Conditions

- 70 beats/minute
- SV: 55 mL/s
- Mean Pulmonary Pressure: 15 mmHg
- 35%-systolic 65%-diastolic

Aortic Valve Preliminary Hydrodynamics Data

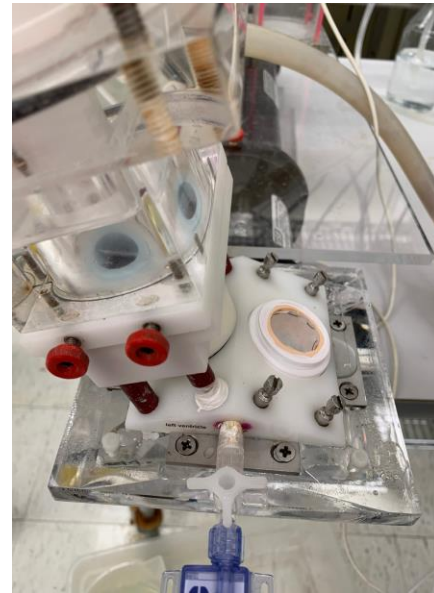
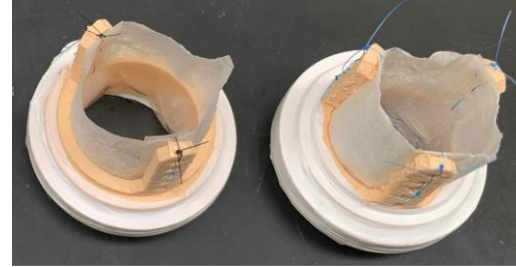


Aortic Tubular PSIS Valve - Hydrodynamics

Tubular PSIS Valve (N = 1)

Q_{RMS} (ml/s)	EOA (cm ²)	ΔP (mmHg)	Regurge %
182 ± 5.65	0.73 ± 0.46	10.47 ± 2.02	9.57 ± 1.12

Vivitro Setup

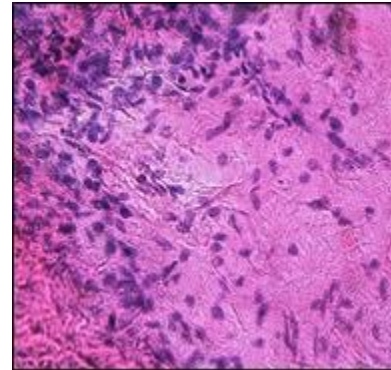


Bringing the factors together

Recapitulating the embryologic environment

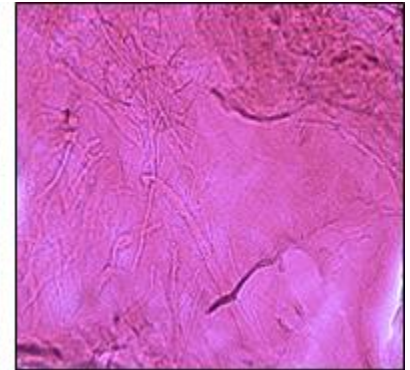
- Altered microenvironment
- Normalized acellular proliferative matrix
 - Architecture, functional proteins, exosomes
- Attraction of progenitor cells
 - Marrow and local origin
- Decreased inflammatory response
 - Immunomodulatory, no scar tissue formation
- Stimulate angiogenesis

First Generation ECM



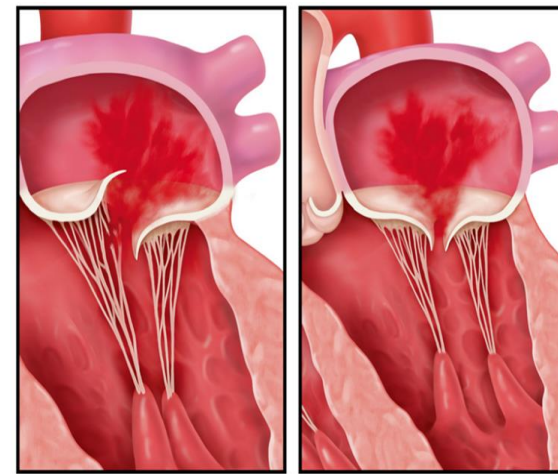
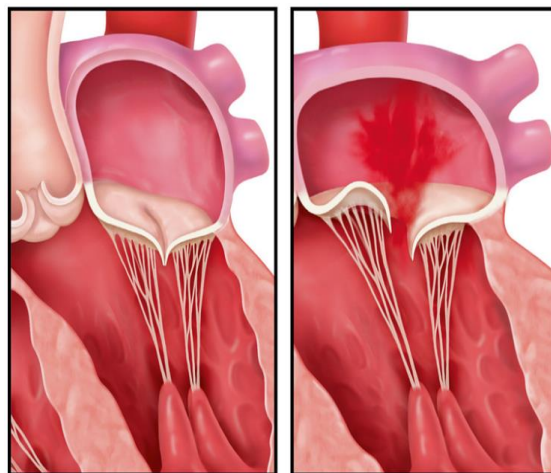
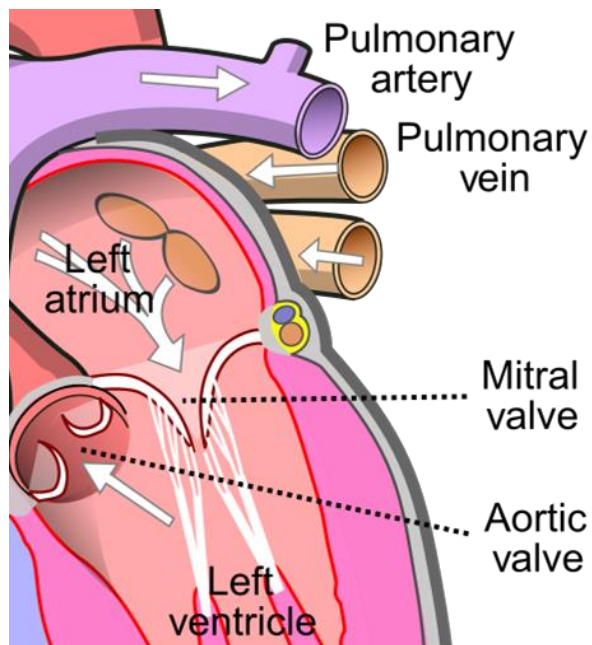
H&E from marketed first generation product. Numerous nuclei and cell membrane fragments remaining.

Second Generation ECM



Completely clear of nuclei and antigen fragments.

Valve Flow and Disease



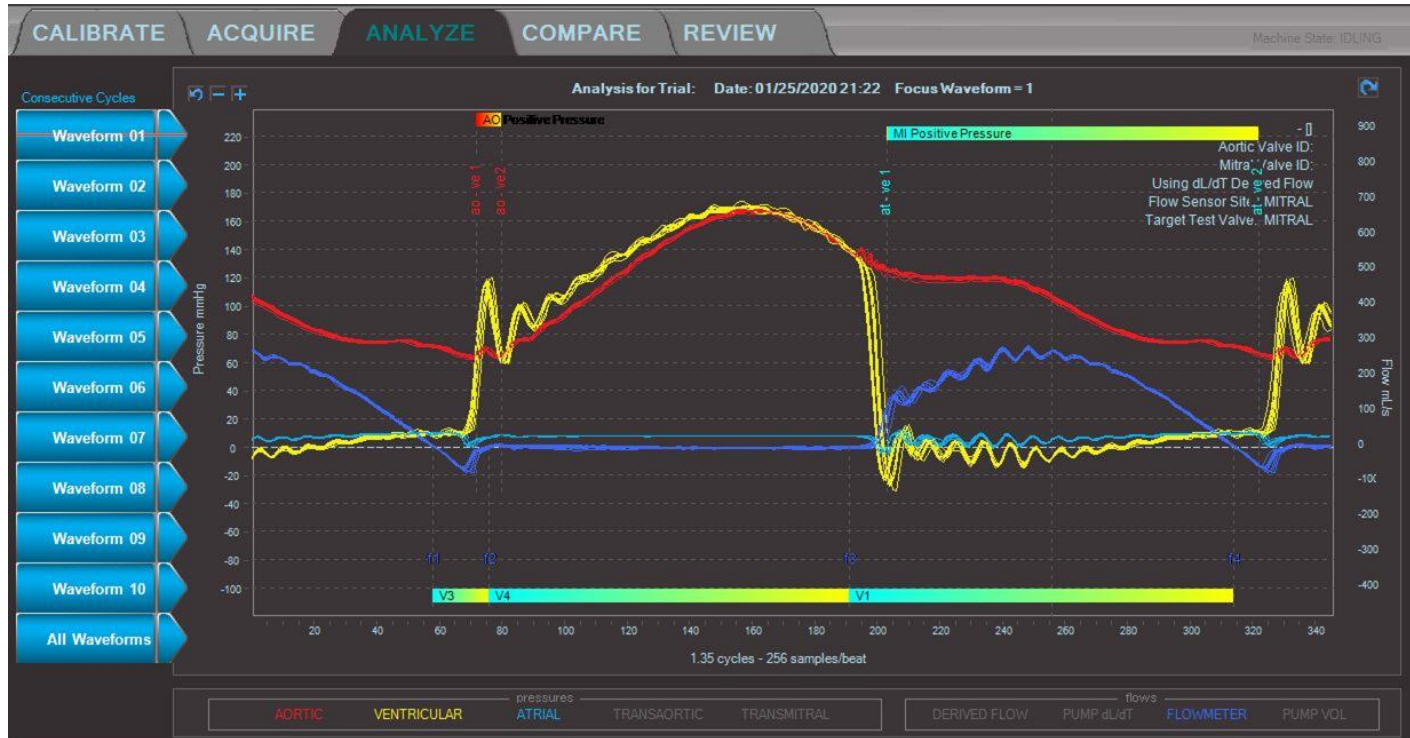
Photograph by Wapcaplet and Yaddah, distributed under a [CC-BY 3.0 license](https://creativecommons.org/licenses/by/3.0/).

¹Moore M, Chen J, Mallow PJ, Rizzo JA. *Clinicoecon Outcomes Res.* (2016) 8:613–27.

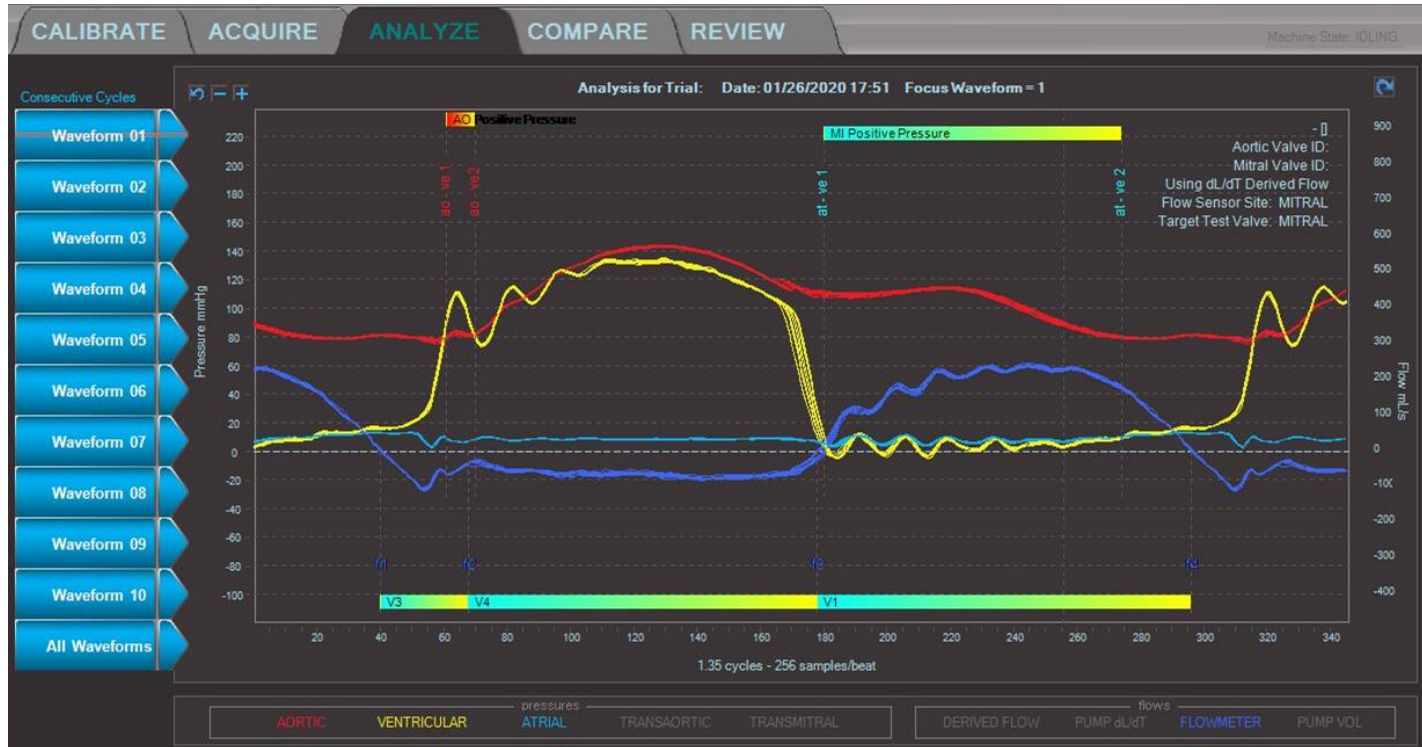
²Gössl, M., Farivar, R.S., Bae, R. *et al.* Current Status of Catheter-Based Treatment of Mitral Valve Regurgitation. *Curr Cardiol Rep* 19, 38 (2017).

REMOVED SLIDES

Vivitro System - Mechanical Mitral Valve Hydrodynamics



Vivitro System - PSIS Mitral Valve Hydrodynamics



Videos of Mitral Valve in Vivitro



Video of Aortic Valve in Vivitro

