# Altered Inflow Hemodynamics Affect Heart Development in a Side-Specific Manner in the Embryonic Heart

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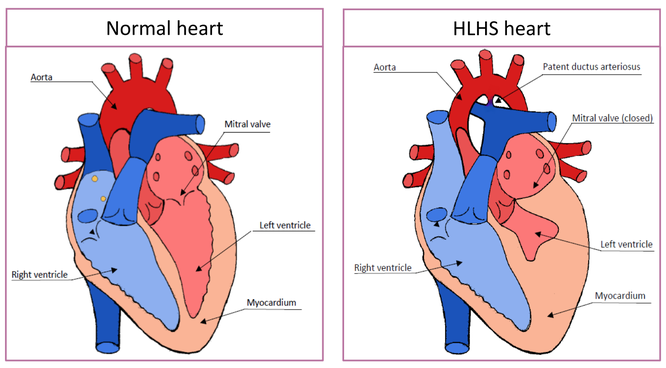
## Background

- Hemodynamics, forces from the flowing blood in the heart, is a major epigenetic factor for heart development. Disturbed hemodynamics were shown to induce cardiac malformations in the embryonic heart.
- Clinically relevant congenital heart defects (CHDs) can be introduced surgically in the lab by disturbing the hemodynamics, like Hypoplastic left heart syndrome (HLHS).
- HLHS is characterized by underdeveloped left ventricle is underdeveloped, it is rare but serious and lethal, it accounts for 25% of congenital heart defects (CHDs).
- Left atrial ligation (LAL) on chick embryo is an experimental technique to produce a HLHS-like phenotype. Right Atrial ligation is expected to cause hypoplastic right heart syndrome.



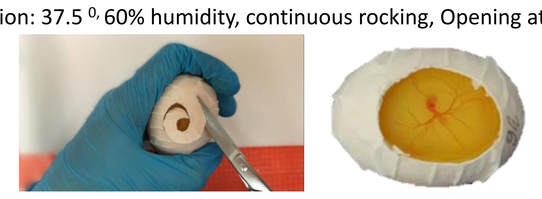

## Objectives

- To surgically induced disturbed hemodynamics using LAL and RAL.
- To evaluate the cardiac development and function after the surgeries.
- To assess hemodynamic parameters (blood flow velocity, wall shear stress (WSS) and vorticity) after the surgeries.

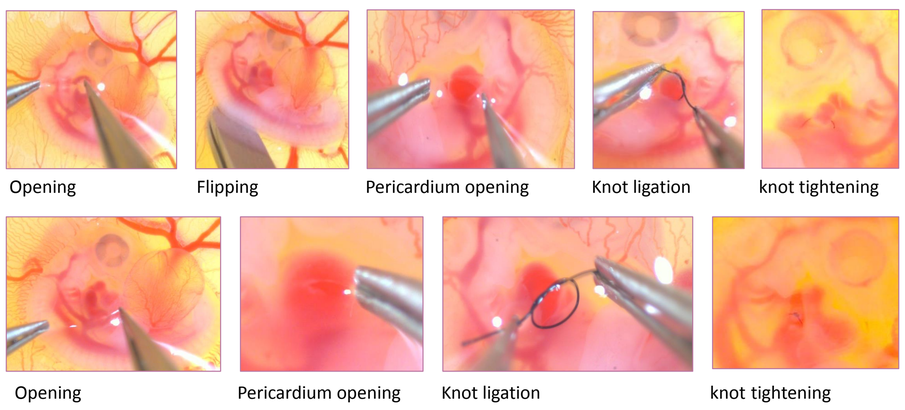
## Methodologies

### Chick embryo culture

Incubation: 37.5 $^{0}$, 60% humidity, continuous rocking, Opening at HH 21

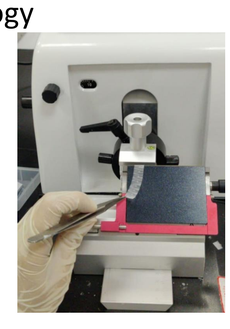


### Surgeries



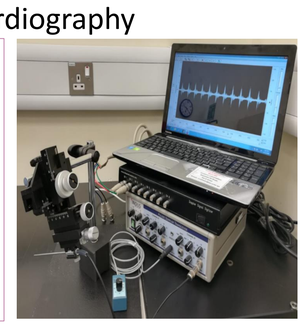

### Histology

- Fixation: 24 and 72 hours post-LAL hearts in (PFA)
- Paraffin wax embedding
- Sectioning
- H & E staining



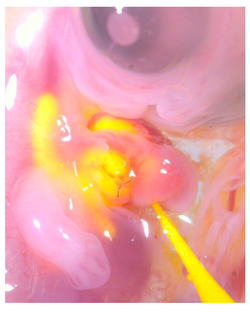
### Echocardiography

Cardiac assessment using doppler 24 and 72 hours post-LAL and RAL



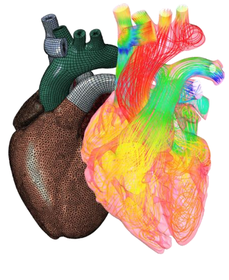
### Microfil for Micro-CT imaging

At HH24 and HH30 stages



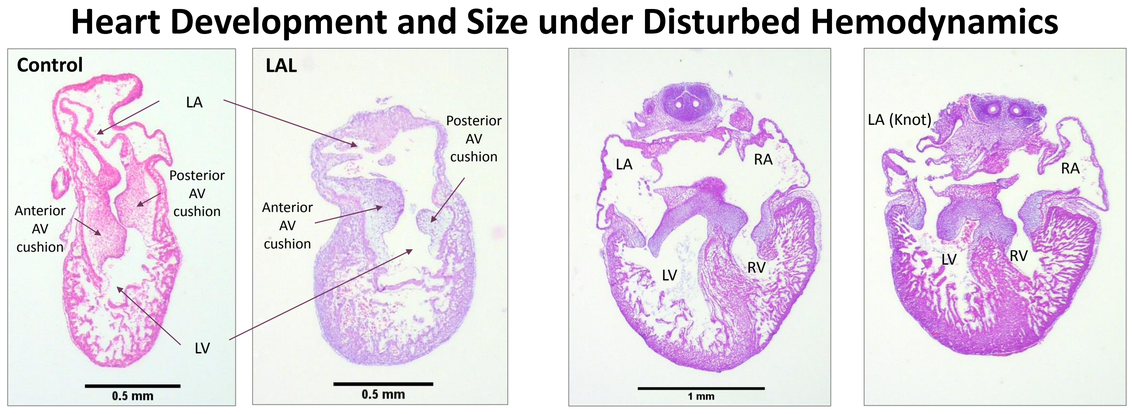
### Computational fluid dynamics (CFD):

Blood flow velocity
Wall shear stress (WSS)
Vorticity



## Results and Discussion

### Heart Development and Size under Disturbed Hemodynamics

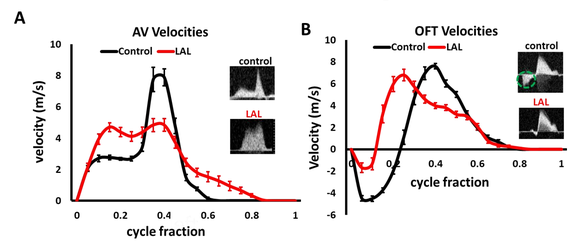



H&E stained control and LAL hearts at embryonic day5 (24h-post LAL)

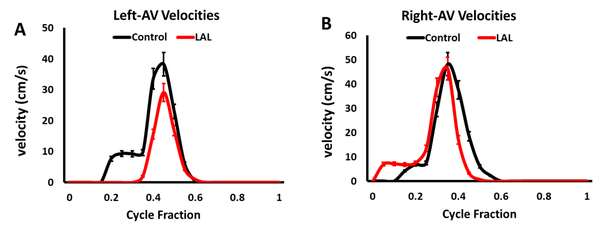
H&E stained control and LAL hearts at embryonic day 7 (72h-post LAL)

### Heart Echocardiography under Disturbed Hemodynamics

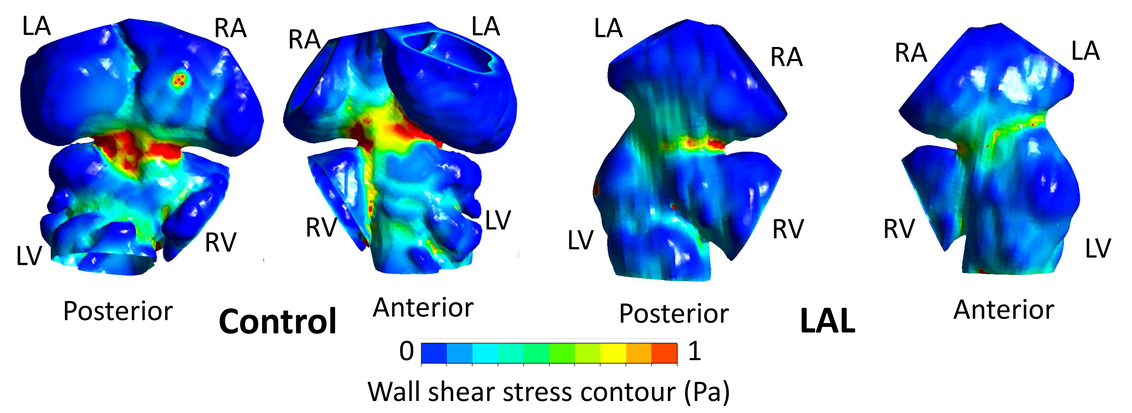
Velocity profiles of chick embryos at HH23 (A) AV canal and (B) OFT canal. Normal AV canal shows distinct velocity peaks, while LAL shows spread peaks. OFT control velocity profile involves an initial regurgitating flow whereas LAL OFT velocity profile does not show this behavior.




Velocity profiles of chick embryos at HH27. AV velocity profiles for left (A) and right (B) AV canals. LAL results in clear decrease in velocity levels in left AV canal and no change in velocity levels in right AV canal.

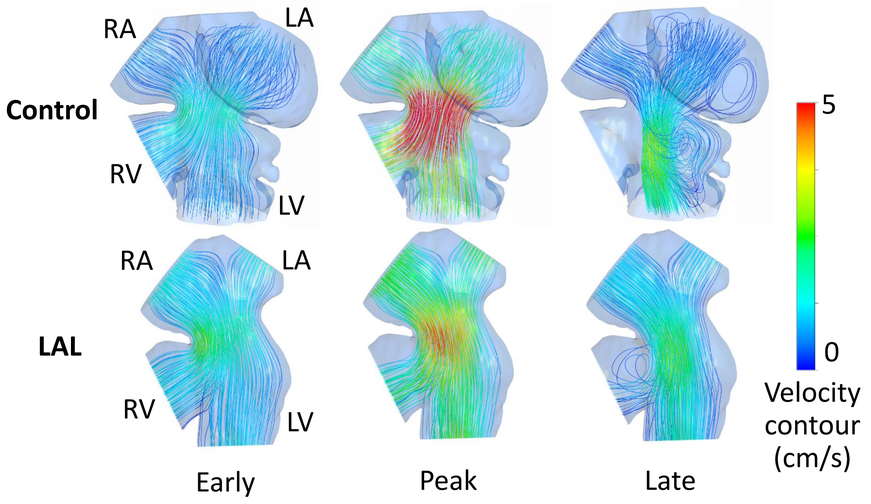



### Wall Shear Stress under Disturbed Hemodynamics




Wall shear stress (WSS) plots for LAL and control cases at peak systolic flow rate. LAL resulted in significantly **lower** WSS at AV cushions and lower peak WSS at left and right AV cushions.

### Velocity Streamlines under Disturbed Hemodynamics




Velocity streamlines for LAL and control geometries at early, peak and late systolic phase. There are significant changes in the hemodynamics between LAL and control cases.

## Conclusions

The present study contributes to the field of cardiogenesis and highlights the critical importance of hemodynamics in proper ventricular development.

The results reveals the hemodynamics, biological and structural alterations in the embryonic heart after LAL procedure. We identified correlations of disturbed hemodynamics with morphological growth, blood velocity through the valves, WSS and velocity streamlines in different parts of the embryonic heart. We also highlighted that CFD analysis can be used to predict the initiation and growth of congenital heart defects.

## Acknowledgments

This project is supported by Qatar National Research Fund (QNRF), National Priority Research Program NPRP 10-0123-170222. We acknowledge the College of Health Sciences (CHS), Department of Biological and Environmental Sciences (DBES), and Laboratory Animal Research Centre (LARC), QU