

Functional Effects of Therapeutic Ultrasound for Calcific Degenerative Mitral Stenosis

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Background

The only disease-modifying therapies for degenerative mitral stenosis (DMS) are surgery and transcatheter therapies in various stages of development. There is an unmet need for less-invasive strategies.

Objectives

We aimed to determine whether pulsed cavitation ultrasound (PCU) can yield functional improvements in an in vitro model of DMS

Methods

Valve functional testing was performed by mounting excised cadaveric human mitral valves (Figure 1) onto a validated left heart in vitro simulator under steady flow conditions (flow rates ranging from 2.5 to 25 L/min). (Figure 2)

Mitral geometric orifice area (GOA) and transmitral pressure gradient were measured before and after PCU.

Baseline valve kinematics were assessed to identify therapeutic targets.

PCU was performed in degassed, deionized water.

PCU settings were PRF: 60 Hz, duty cycle: 8×10^{-4} , # half-cycles (calculated): 29.3, Pulse duration (calculated): 13.3 microseconds, estimated peak pressure of 34.6 MPa.

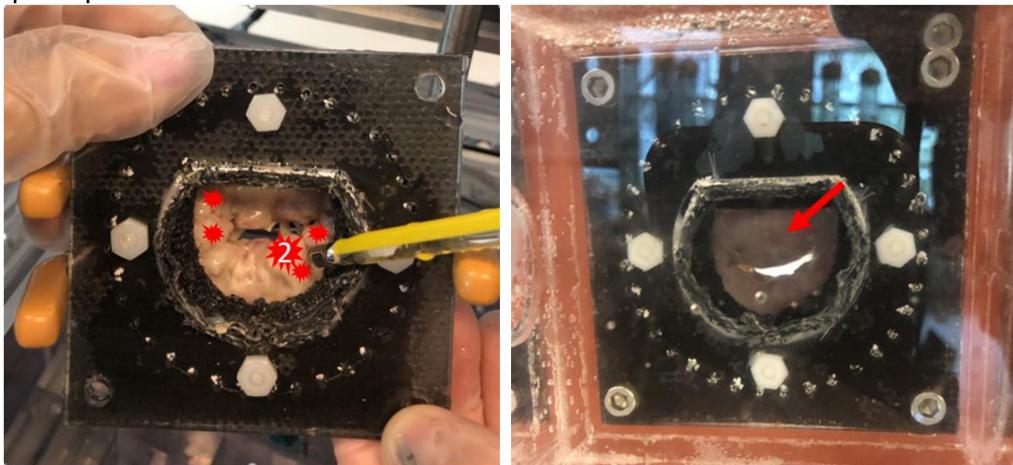


Figure 1. Two mounted excised cadaveric human mitral valves. Valve 1 and valve 2, respectively.

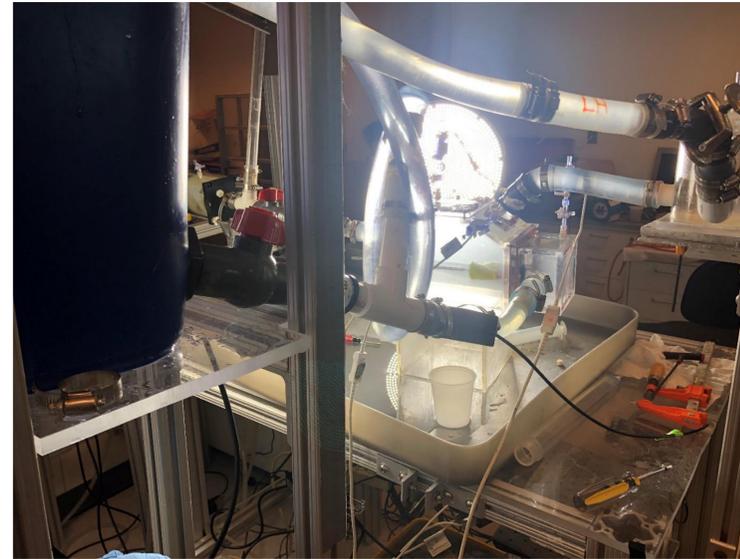
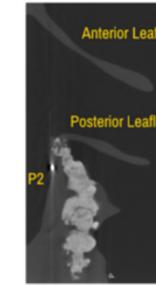
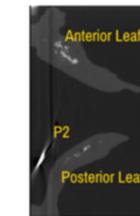


Figure 2. In vitro simulator, steady flow loop.

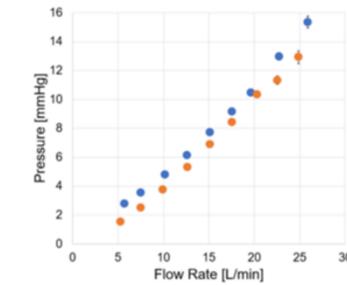
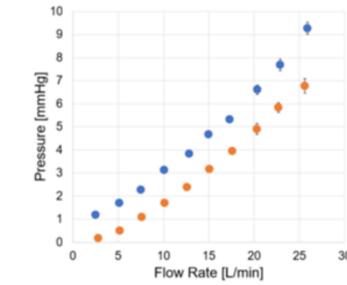
Valve 1



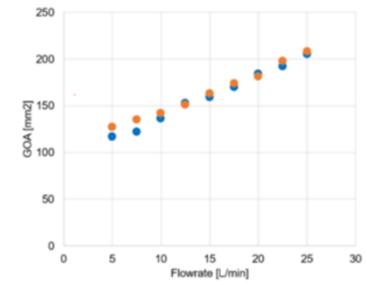
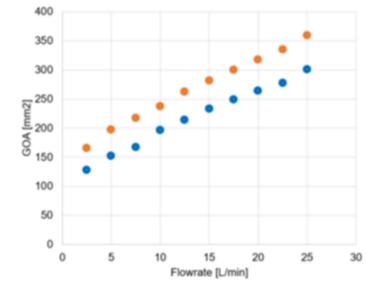
Valve 2



Micro CT



Transmitral Gradient



Geometric Orifice Area

● baseline

● post-treatment

RESULTS

Micro CT qualitatively demonstrated more dense calcification of Valve 1. Across all flow rates, there was a mean reduction in the transmitral gradient of 1.6 mmHg (42.5%) for Valve 1 and 1.1 mmHg (17.5%) for Valve 2 and a mean increase in GOA of 48.9 mm² (23.8%) for Valve 1 and 4.1 mm² (3.3%) for Valve 2 (Figure 3)

Figure 3. Results of transmitral gradient and GOA for Valve 1 and Valve 2 pre and post therapy.

CONCLUSIONS

Therapeutic ultrasound may allow for improvement in mitral function in DMS. There appear to be more pronounced changes in the more densely calcified valves, suggesting a potential calcium-dependent effect.