Engineers and Biologists Solve Long-Standing Heart Development Mystery

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An engineer comparing the human adult heart and the embryo heart might never guess that the former developed from the latter. While the adult heart is a fist-shaped organ with chambers and valves, the embryo heart looks more like tube attached to smaller tubes. Physicians and researchers have assumed for years, in fact, that the embryonic heart pumps through peristaltic movements, much as material flows through the digestive system.

But new results in this week's issue of *Science* from an international team of biologists and engineers show that the embryonic vertebrate heart tube is indeed a dynamic suction pump. In other words, blood flows by a dynamic suction action (similar to the action of the mature left ventricle) that arises from wave motions in the tube. The findings could lead to new treatments of certain heart diseases that arise from congenital defects.

According to Mory Gharib, the Liepmann Professor of Aeronautics and Bioengineering at the California Institute of Technology, the new results show once and for all that "the embryonic heart doesn't work the way we were taught.

"The morphologies of embryonic and adult hearts look like two different engineers designed them separately," says Gharib, who has worked for years on the mechanical and dynamical nature of the heart. "This study allows you to think about the continuity of the pumping mechanism."

Scott Fraser, the Rosen Professor at Caltech and director of the MRI Center, adds that the study shows the promise of advanced biological imaging techniques for the future of medicine. "The reason this mechanism of pumping has not been noticed in the heart tube is because of the limitations of imaging," he says. "But now we have a device that is 100 times faster than the old microscopes, allowing us to see things that previously would have been a blur. Now we can see the motion of blood and the motions of vascular walls at very high resolutions."

The lead author of the paper is Gharib's graduate student Arian Forouhar. He and the other researchers used confocal microscopes in the Beckman Institute's biological imaging center on campus to do time-lapse photography of embryonic zebrafish. According to Fraser, embryonic zebrafish were chosen because they are essentially transparent, thus allowing for easy viewing, and since they develop completely in only a few days.

The time-lapse photography showed that peristalsis, an action similar to squeezing a tube of toothpaste, was not the pumping mechanism, but rather that valveless pumping known as "hydroelastic impedance pumping" takes place. In this model fewer active cells are required to sustain circulation.

Contraction of a small collection of myocytes, usually situated near the entrance of the heart tube, initiates a series of forward-traveling elastic waves that eventually reflect back after impinging on the end of the heart tube. At a specific range of contraction frequencies, these waves can constructively interact with the preceding reflected waves to generate an efficient dynamic-suction region at the outflow tract of the heart tube.

"Now there is a new paradigm that allows us to reconsider how embryonic cardiac mechanics may lead to anomalies in the adult heart, since impairment of diastolic suction is common in congestive heart-failure patients," says Gharib.

"The heart is one of the only things that makes itself while it's working," Fraser adds. "We often think of the heart as a thing the size of a fist, but it likely began forming its structures when it was a tiny tube with the diameter of a human hair."

"One of the most intriguing features of this model is that only a few contractile cells are necessary to provide mechanical stimuli that may guide later stages of heart development," says Forouhar. According to Gharib, this simplicity in construction will allow us to think of potential biomimicked mechanical counterparts for use in applications where delicate transport of blood, drugs, or other biological fluids are desired.

In addition to Forouhar, Gharib, and Fraser, the authors are Michael Liebling, a postdoctoral scholar in the Beckman Institute's biological imaging center; Anna Hickerson (BS '00) and Abbas Nasiraei Moghaddam, graduate students in bioengineering at Caltech; Huai-Jen Tsai of National Taiwan University's Institute of Molecular and Cellular Biology; Jay Hove of the University of Cincinnati's Genome Research Institute; and Mary Dickinson of the Baylor College of Medicine.

The article is titled "The Embryonic Vertebrate Heart Tube is a Dynamic Suction Pump," and appears in the May 5 issue of *Science*.

Source: Caltech