Optical coherence tomography captures embryonic heart dynamics

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An advanced imaging technique has both the spatial and temporal resolution to investigate the developing heart in important animal models such as chicks and mice.

In studying the mechanisms that drive early heart formation, researchers rely primarily on static methods such as histology and immunohistochemistry. During cardiac looping, the minuscule heart transforms from a tubular form to a four-chambered heart, a complex process which relies upon mechanical stresses from the functioning heart for feedback. Optical coherence tomography (OCT) imaging—a sophisticated, noninvasive technique that can capture detailed images of biological tissue by measuring optical scattering—offers the ability to visualize and quantify heart dynamics in three dimensions in real time. Understanding how the normal heart functions during development will enable us to better understand abnormal processes and could lead to preventative treatments for congenital heart defects.

OCT is based on low-coherence interferometry and capable of micrometer-scale resolution 1–2 mm deep into embryonic tissue. The approach has been used to investigate the static embryonic heart, including phenotyping mutant mouse embryos. In principle, OCT could be used as a high-throughput screening tool, but to investigate cardiac dynamics it is necessary to image the beating heart in real time. Early papers describing dynamic cardiac OCT imaging reported only 1- and 2D imaging of the beating heart. Our group and other researchers are now developing technology and refining techniques to fully characterize embryonic cardiac dynamics during looping by capturing the living, beating heart in 3D.

To achieve high spatial and temporal resolution we have employed cardiac gating, which involves synchronizing image data acquisition to the heart cycle, and ultrahigh-speed OCT. Using these methods, it is possible to build up 4D (3D plus time) image sets over many heart cycles. We first demonstrated gated imaging of paced, excised hearts, and subsequently intact embryos in vivo.

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mode locked (FDML) laser, which has allowed us to visualize embryonic systolic dynamics for the first time.\textsuperscript{7}

Our initial 4D imaging was carried out using avian and mouse hearts that were excised and maintained in vitro.\textsuperscript{6} The hearts were electrically paced, and the pacing signal was also used to gate the image acquisition. Image rendering and processing techniques were employed to visualize the hearts in 4D and measure physiological factors such as cardiac volume, ejection fraction, and wall thickness. However, although this work demonstrated the feasibility of cardiac-gated OCT imaging, the excised embryonic heart is limited as a model of natural heart function.

To image the beating heart within the intact, living embryo, we used laser Doppler velocimetry of embryonic blood flow to gate the image acquisition.\textsuperscript{8} While electrocardiography is commonly used as the gating signal for cardiac-gated imaging of adult human and animal hearts, the electrical signal from the embryonic heart is extremely small during early development. Using these methods, we obtained 4D image sets of live embryos with 8 volumes per heartbeat. Figure 1 shows 2D cross-section OCT images and 3D sum-voxel images of the heart in dilation and in contraction. A sum-voxel movie of the beating heart is also available online.\textsuperscript{12}

To further characterize the functioning heart, we implemented an OCT system using a buffered FDML laser for ultrahigh-speed imaging of the embryonic heart at more than 100,000 axial scans per second.\textsuperscript{7} This high scan rate enabled us to capture systolic dynamics, which occurs over 50ms in cross-section at 200 frames per second. We were also able to record 10 volumes per second for real-time 4D imaging without gating. Figure 2 shows the embryonic heart in cross-section at several stages of development. Figure 3 shows the 3D volume of the heart at different phases in the cardiac cycle. Videos of Figures 2 and 3 are available online.\textsuperscript{13, 14}

We are continuing this work by improving the technology to acquire image data and to culture developing embryos. The combination of cardiac gating and ultrahigh-speed imaging is allowing us to record systolic dynamics in 4D with up to 90 volumes per heart cycle. We are also developing techniques

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to culture avian and mouse embryos in a healthy state with natural cardiac function and development that are compatible with imaging, allowing us to capture the growing embryo under normal physiological conditions.

This research is supported by the National Institutes of Health 1RO1HL083048.

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References

12. http://spie.org/documents/newsroom/videos/1458/Fig1.wmv Sum voxel projection video of a beating stage 14 embryonic heart. Credit: Michael Jenkins, Case Western Reserve University.
13. http://spie.org/documents/newsroom/videos/1458/Fig2.wmv Ultrasound cross-sectional OCT images from six different stages of development. Credit: Michael Jenkins, Case Western Reserve University.

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