

Echocardiological Assessment of Diastolic Dysfunction using the Vevo®

Objective

- Review the biology of diastolic dysfunction
- Illustrate how the Vevo can be used to
 - monitor pathological progression of disease
 - capture key measurements and calculations necessary to understanding the disease process

Overview of the Biology of Diastolic Dysfunction

Diastole is the filling of the heart during the relaxation phase of the cardiac cycle. There are active and passive processes involved in this phase which are further complicated by complex pressure changes that involve the left atrium and other cardio/pulmonary structures and vessels. When referring to diastolic function, one is most often referring to the filling of the left ventricle and this will be assumed throughout the remainder of this document.

Diastolic dysfunction is then a disruption of the normal filling pattern of the ventricle, often as a result of increased stiffness in the myocardium preventing optimal relaxation of the ventricle walls. Effectively a normal ventricle would behave as a thin walled balloon upon filling, while in diastolic dysfunction the balloon would have thickened walls requiring more pressure to fill the chamber.

The etiology of diastolic dysfunction is varied but most reflect changes in pressure or overload with increases strain; some examples of clinical diseases in which diastolic dysfunction is apparent are myocardial infarction, intracardiac shunting, valvular disease, hypertension, congenital heart disease, diabetes or infectious diseases leading to constrictive pericarditis.

There are varying stages of disease. In the first grade, systolic function or cardiac output is not affected because of cardiac reserve or compensation; however as the disease progresses patients develop clinical heart failure. It is therefore important to study diastolic dysfunction as it relates to the variety of cardiac pathologies involved. Further, characterizing the various molecular pathways induced by diastolic

dysfunction could produce effective therapeutics and interventions.

Why the Vevo Can Help

Echocardiography is a non-invasive, real time technique in which cardiac function as well as hemodynamics can be assessed. In the case of diastolic function one must characterize blood flow through the mitral valve as well as Tissue Doppler at the mitral annulus; additionally, cardiac function should be assessed to gauge the extent of disease and progression towards heart failure.

The Vevo High Frequency Ultrasound Systems have been developed specifically for use in small animal imaging and are ideally suited for mouse or rat echocardiography, as well as for studying the developing chick embryo. With center operating frequencies ranging from 15MHz to 50MHz one imaging system can be used to assess cardiac function from embryo to adult in many commonly used small animal models.

Utility of the Vevo in Pulmonary Hypertension Research

There are various chemically induced or transgenic models of diseases in which diastolic function is of interest; one such model is induced by dosing mice with isoproterenol, in this model remodeling of the myocardium occurs resulting in diastolic dysfunction with maintained cardiac output¹. In this article Schumacher et al create a model of diastolic dysfunction in mice and investigate the various parameters measured by echocardiography. They performed investigations using Pulsed Wave Doppler on the mitral valve, Tissue Doppler and the mitral annulus, as well as analysis on the left ventricular systolic function and LV mass.

Preliminary work done with Vevo® 660 elegantly demonstrates the imaging planes and measurements possible in mouse echocardiography². While the article mentioned above from Schumacher defines the key parameters necessary to monitor the extent of dysfunction in this disease model.

Below are the key measurements which can be performed using the Vevo High-Frequency

Ultrasound System to investigate models of diastolic dysfunction:

Mitral Valve

Diastolic dysfunction is a disturbance in the filling of the left ventricle, therefore one of the most important images to acquire in monitoring this disease is Pulsed Wave Doppler on the mitral valve. This image is typically acquired from a modified apical four chamber view. There are numerous measurements made on this blood flow spectrum including the E and A peak velocities, a velocity time interval (VTI), as well as the deceleration rate and time for the E peak. These measurements can be used to perform various calculations which give an indication of diastolic function.

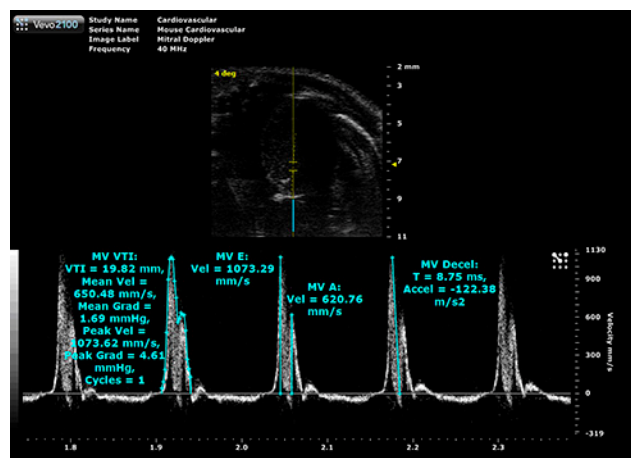


Figure 1 – Pulsed Wave Doppler is used to assess flow through the mitral valve. Here the peak velocities of the early (E) and atrial (A) peaks are measured, along with the velocity time interval (VTI) and deceleration time and rate of the E peak.

The myocardial performance index (MPI) is an index of diastolic as well as systolic function and is also measured using Pulsed Wave Doppler at the mitral valve. This calculation involves the isovolumic relaxation and contraction times (IVRT and IVCT), as well as the aortic ejection time (AET).

$$\text{MPI} = (\text{IVRT} + \text{IVCT})/\text{AET}$$

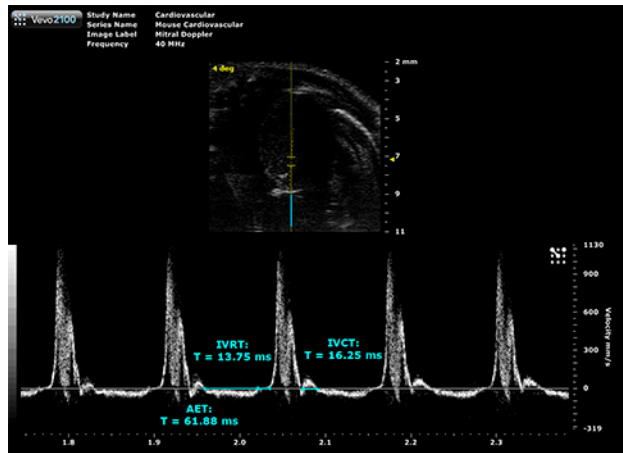


Figure 2 – Pulsed Wave Doppler is used to assess flow through the mitral valve, here the isovolumic relaxation and contraction times (IVRT and IVCT) and the aortic ejection time (AET) are measured for inclusion in the myocardial performance index (MPI) calculation.

Mitral Valve Annulus

Tissue Doppler imaging, as with Pulsed Wave Doppler is used to assess diastolic dysfunction at the mitral valve. The sample volume is typically placed at the annulus of this valve to quantify the movement of the tissue in this area. Again this image is acquired from a modified apical four chamber view. The key measurements made from this spectrum are the peak velocities for the E and A peaks. These are referred to as E' and A' to distinguish them from the peaks measured in Pulsed Wave Doppler. These values are combined with various measurements made in Pulsed Wave Doppler which give an indication of diastolic function.

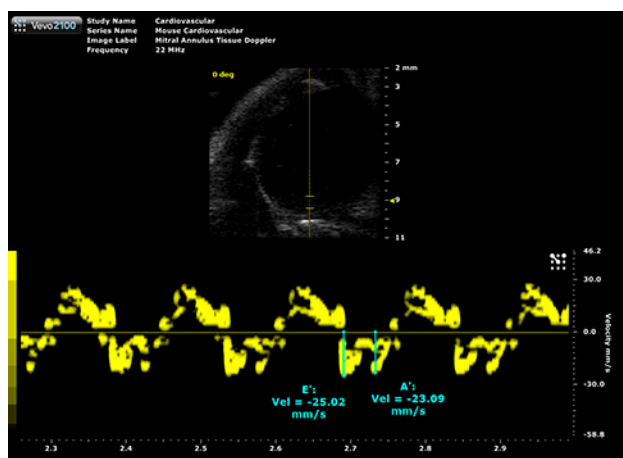


Figure 3 – Tissue Doppler is used to assess tissue motion at the mitral valve annulus. Here the peak velocities of the early (E) and atrial (A) peaks are measured.

Application Note: Echocardiological Assessment of Diastolic Dysfunction using the Vevo

Left Ventricle

As diastolic dysfunction progresses along with disease pathology, most often cardiac function is also affected and should therefore be measured. There are various measurements and calculations, which can be used to assess cardiac function in the left ventricle, both from B-mode and M-mode images, also from either the parasternal long or short axis views. Here examples from a modified Simpson's type measurement are used to assess cardiac function as well as LV mass. Measures of cardiac function include stroke volume, ejection fraction, fractional shortening, fractional area change, cardiac output; additionally the LV mass and average wall thicknesses are also calculated.

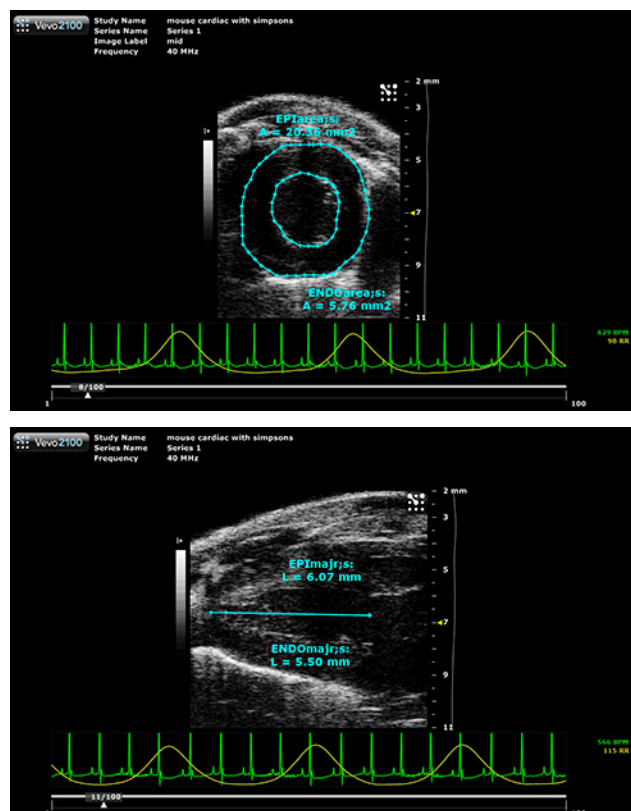


Figure 4 – B-Mode imaging can be used to assess cardiac function. Epicardial and endocardial areas are traced in both systole and diastole from a short axis view (A), while the endocardial and epicardial lengths are measured again in both systole and diastole from a long axis view (B).



Figure 5 – Measurement and Calculation Report, showing all the measurements and subsequent calculations described throughout this application note.



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Conclusion

The Vevo High-Frequency Ultrasound Systems are well suited for a complete echocardiography exam in which the key measurements and calculations can be completed to fully assess diastolic function in various disease models in which dysfunction is present. Due to the non-invasive nature of ultrasound imaging repeated exams would be possible on the same mouse over the course of a longitudinal study to either study the progression or regression of disease, adding to the strength of the acquired data and reducing the number of animals required to complete a powerful study.

References

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2. Zhou, Y.Q., S. Foster, B.J. Nieman, L. Davidson, et al. 2004.
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