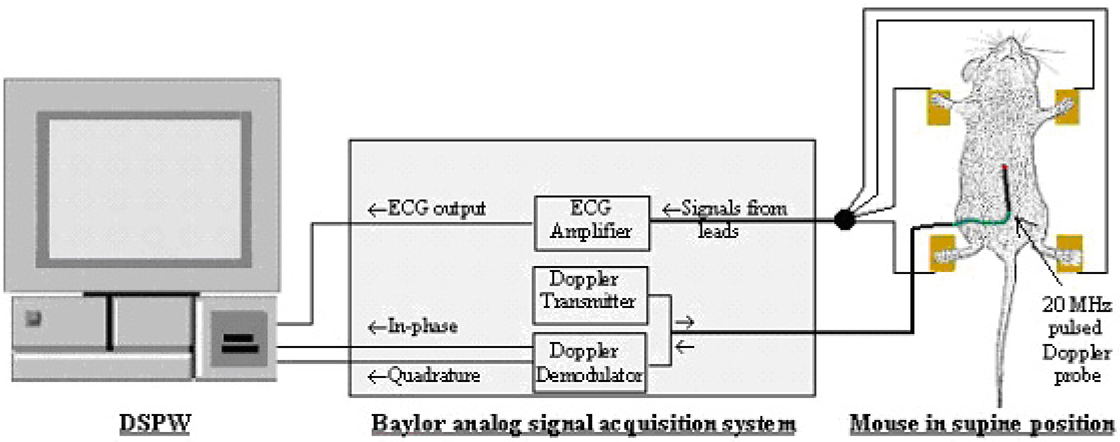
美国健康医疗仪器国际公司
American Health & Medical Supply International Corp.
35 Weaver Street, *Scarsdale*, New York 10583. U.S.A.

无创伤性小鼠多普勒超声血流动力学研究系统

是由美国 **Indus Instruments** 仪器公司最新推出的，具有世界一流最先进技术和专利的无创伤性小鼠心脏功能及血流动力学动态连续研究系统。

EXPERIMENTAL SETUP TO ACQUIRE DOPPLER BLOOD FLOW VELOCITY DATA FROM MICE

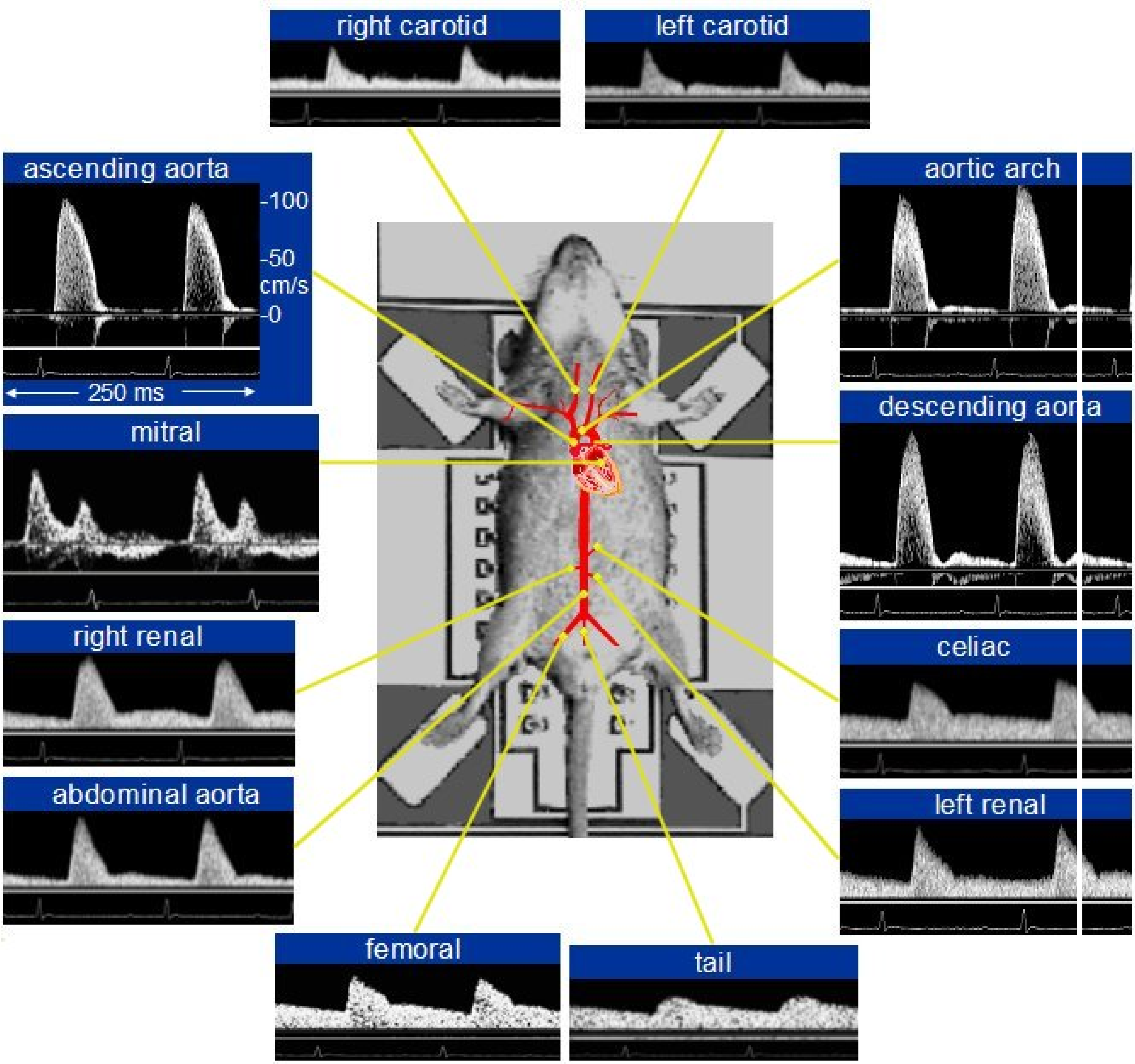


The overall experimental setup to acquire Doppler blood flow velocity data from mice is shown above. The mouse is anesthetized with Ketamine/Xylazine/Acepromazine cocktail, Nembutal cocktail, or other anesthetics depending on the desired type of study.

The mouse is placed in supine position with its four limbs taped to four electrode plates mounted on a board. These electrodes are connected via a cable to the ECG module in a signal processing system that will provide the mouse ECG signal output.

A 10 MHz pulsed Doppler probe is used with its tip placed just below the sternum and positioned to obtain a blood flow velocity signal from the aortic outlet or mitral inlet. In addition, blood flow velocities from peripheral arteries of mice can be obtained using a 20 MHz pulsed Doppler probe. These probes are plugged into analog pulsed Doppler signal generators (10 or 20 MHz) such as the “Baylor Multichannel High Frequency Pulsed Doppler Analog Mainframe”. Other equivalent systems such as those from Crystal Biotech / Data Sciences Inc. can also be used. These systems will generate in-phase and quadrature Doppler demodulated audio signals.

In the figure above, the Doppler signals are acquired, processed, and displayed as a real-time spectrogram along with the ECG signal using the DSPW. The software also allows the user to perform offline analysis of the data and to generate reports.



Mouse Cardiovascular Research Package - This includes a THM100 (for ECG monitoring), a three channel analog mainframe with a 20MHz Pulse Doppler Module, and a 20MHz tubing mounted ultrasound transducer. This popular package is customizable to your needs with 10MHz Doppler modules/transducers, blood pressure modules, and a large selection of probes, etc.

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DOPPLER SIGNAL PROCESSING WORKSTATION (DSPW)

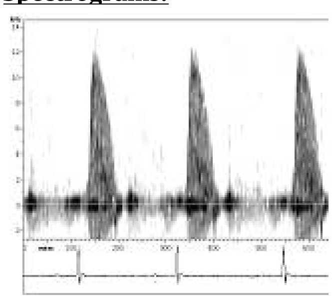
The Indus Instruments Doppler Signal Processing Workstation (DSPW) is a real-time spectrum analyzer plus a data analysis and report generation tool, designed specifically for researchers interested in measuring cardiovascular function in mice and other small animals such as rats, hamsters, and rabbits.

DSPW can accept signals from any analog ultrasonic Doppler system capable of generating in-phase and quadrature demodulated audio signals. Shown above is a completely configured unit. The high sampling rates (up to 125 KHz) and good temporal resolution (up to 0.1 msec) of the DSPW are especially suitable for working with high heart rates, fast blood velocities and accelerations present in mice.
View some sample doppler spectograms from mice.

DSPW processes the Doppler signals using a Fast Fourier Transform algorithm and displays a real-time grayscale spectrogram. The signals can be recorded to disk and later analyzed for report generation purposes.

Extensive software support allows rapid data analysis and report generation resulting in increased productivity. Some of the parameters the DSPW has available for measurement are listed below.

Sample Murine Spectrograms:



Some of the Parameters the DSPW can measure:

General Parameters
- Heart Rate
- Pulse Wave Velocity

Systolic Indices
- Peak/Mean Aortic Velocity
- Aortic Acceleration
- Rise Time
- Ejection Time
- Stroke Distance

Systolic-Diastolic Relationships
- Isovolumic relaxation time
- Isovolumic contraction time

Diastolic Indices
- Peak Early (E) Velocity
- Peak Atrial (A) Velocity
- Durations of E and A
- E/A Ratio

Peripheral Flow Velocity Indicies
- Peak/Minimum/Mean Velocity
- Pulsatility & Resistivity Index

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DSPW July 28, 2002

Aortic Outflow Velocity of a Mouse

File Name	: mo_20s.udf	Doppler Angle	: 0 degree
Analysis by	: A.K. Reddy	Crystal Freq	: 10 Mhz
Acquisition date	: Unknown	Range Depth	: 9 mm
Analysis date	: November 23, 1998 - 22:32:09	Subject Model / ID	: Mouse / Control
Data Type	: Doppler	Gender / Age / Weight	: Male / 34.0 weeks / 30.0 g
Signal Type	: Aortic Outflow	Type (Strain)	:

Measurements:

Heart Rate	244.10 bpm	Ejection Time	77.83 msec
R-R Interval	245.83 msec	Rise Time	19.67 ms
Pre-ejection Time	15.42 msec	Mean Velocity	21.96 cm/s
Peak Velocity	104.70 cm/s	Mean Acceleration	5503.65 cm/s²
Stroke Distance	5.40 cm	Peak Acceleration	12094.56 cm/s²

Image 1

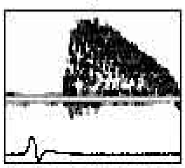
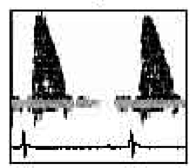


Image 2



Comments:

This is aortic outflow signal of a mouse obtained with a 10 MHz pulsed Doppler flow probe. Several parameters are measured from this signal, which provide information on left ventricular infarction, aortic stenosis, and other left ventricle diseases. All or some of the parameters shown above are used in evaluating the systolic function in a mouse.

DSPW July 28, 2002

Mitral Inflow Velocity of a Mouse

File Name	: mo_16s.udf	Doppler Angle	: 0 degree
Analysis by	: A.K. Reddy	Crystal Freq	: 10 Mhz
Acquisition date	: Unknown	Range Depth	: 9 mm
Analysis date	: July 28, 2002 - 16:40:00	Subject Model / ID	: Mouse /
Data Type	: Doppler	Gender / Age / Weight	: Male / 34.0 weeks / 30.0 g
Signal Type	: Mitral Inflow	Type (Strain)	:

Measurements

Heart Rate	240.31 bpm	E-Peak to ½E-Peak Time	17.77 msec
R-R Interval	250.17 msec	A-Peak Velocity	37.49 cm/s
E-Peak Velocity	71.07 cm/s	A-Stroke Distance	1.09 cm
E-Stroke Distance	2.75 cm	A-Time Duration	42.25 msec
E-Time Duration	95.33 msec	E-A Peak Velocity Ratio	1.95
E-Acceleration Time	18.17 msec	E-A Area Ratio	2.46
E-Deceleration Time	77.17 msec	Isovolumic Contraction Time	15.00 msec
E-Linear Deceleration Time	35.53 msec	Isovolumic Relaxation Time	25.67 msec
E-Linear Deceleration Rate	2004.31 cm/s²		

Image 1

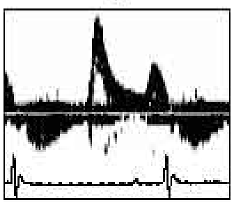
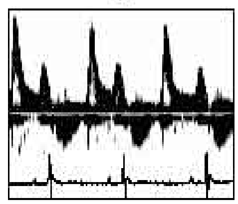


Image 2



Comments

This is mitral inflow signal obtained with a 10 MHz probe consists of 2 peaks within a single beat. The large 1st peak is called early (E) flow and the small 2nd peak is called atrial (A) flow. This signal provides information on diastolic function. For heart rates below 400 beats/min the 2 peaks are nicely separated. As the heart rate goes up these peaks come closer and eventually fuse into a single peak. E/A ratio is an important parameter in evaluating diastolic function. To make sure that E & are separated drugs are often administered to slow down the heart rates in mice.

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THM100: Temperature & ECG Monitoring in Mice

Temperature Control & Heart Rate Monitoring in Mice

KEEP MICE WARM DURING STUDIES!

PROBLEM

When mice are anesthetized either for non-invasive studies or for surgery, their temperature regulating mechanisms do not work properly. This can lead to a rapid drop in body temperature in a few minutes and can have fatal results. The conventional solution to this problem is a cumbersome pad with circulating hot water or an overhead heat lamp that can cause electrical interference with ECG monitoring equipment.

SOLUTION

The Indus Instruments THM100 is a compact tabletop solution that allows you to electronically control a heating element while simultaneously monitoring temperature and ECG activity.

TEMPERATURE CONTROL & MONITORING

- Complete solution for temperature control and heart rate monitoring
- Compact table top design without circulating water
- Electronic control of heater to maintain temperature
- Monitor either rectal temperature or skin temperature

ECG MONITORING

- Built in ECG electrode contact pads
- Electrically isolated ECG amplifier
- Monitor ECG activity and obtain heart rate
- Audio alert when ECG activity is present/absent
- Amplified & filtered analog ECG signal available for chart recorder
- Digital ECG trigger signal available

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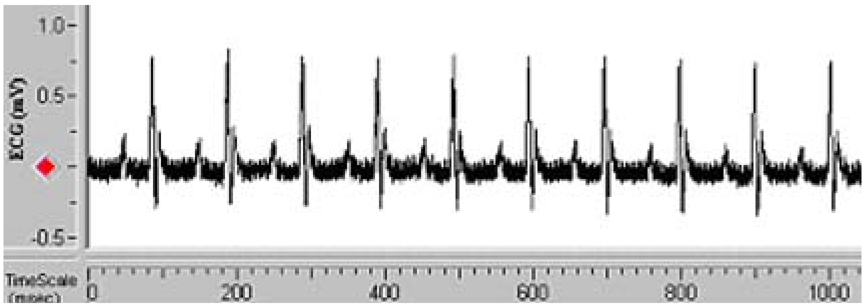
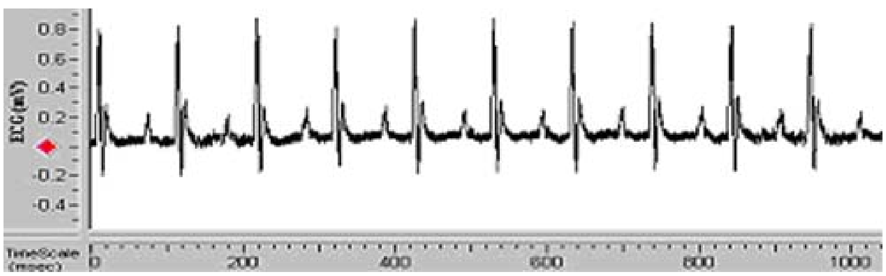
Sample Mouse ECGs Acquired Using the THM100

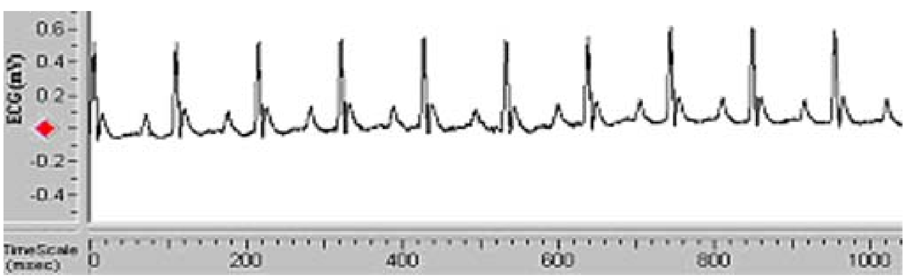
ECG without Lowpass Filter



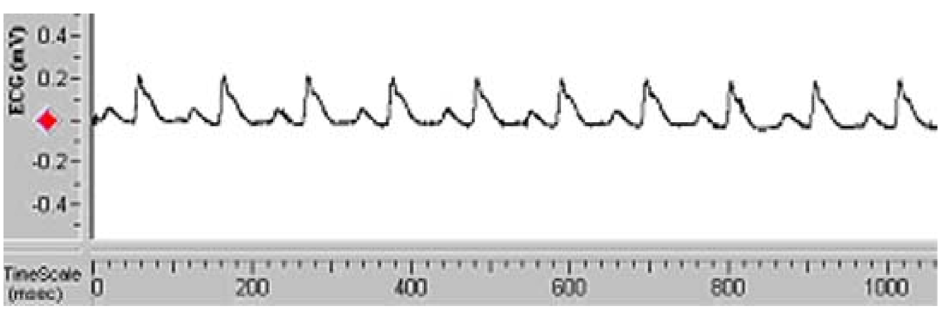
ECG with 1 kHz Lowpass Filter



ECG with 100 Hz Lowpass Filter



ECG with 30 Hz Lowpass Filter



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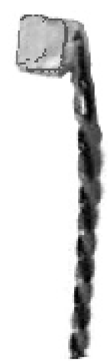
MULTI-CHANNEL MAINFRAMES

The 6 Channel Ultrasonic Flow/Dimension Mainframe is the standard and most widely used version and can accept any of the modules listed on the next page. It has a built in speaker for listening to a selected Doppler channel and can be connected to a high frequency oscilloscope for monitoring the ultrasonic signals from Length Gauge or Doppler Displacement modules. Recorder outputs from each channel are in the +/ 10 volt range and are suitable for connection to a strip chart recorder, FM tape recorder, computer A D input, or a physiologic monitor scope. With few limitations, all six channels can be operated simultaneously without interference. For more ambitious laboratories a 12 Channel Mainframe is available, and for more limited applications or where a more compact size is needed, a 3 Channel Mainframe is available.

3-Channel mainframe with modules **6-Channel mainframe with modules**

High Frequency Pulsed Doppler Transducers

10 or 20 MHz Epoxy Flow Cuffs



Rigid epoxy cuffs are generally the preferred type for use in acute or chronically instrumented animals on vessels from 2 to 8 mm dia. Standard sizes, are 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 6.0, 7.0, and 8.0 mm inside diameter. They are available with either of two methods for attaching the probe to the vessel: holes drilled near the slot for suture ties, or umbilical tape glued around the outside of the probe. Umbilical tape is usually used for chronically implanted probes which will not be reused, and sutures are best for acute or reusable probes because they are easier to replace and clean. Standard lead length is 30".

10 or 20 MHz Silastic Flow Cuffs

For smaller size vessels (0.5 to 2.0 mm) or where a more pliable probe is required transducers made from flexible silastic are available. Silastic probes have imbedded sutures for ties and form a full circle around the vessel when closed.

10 or 20 MHz Curved Flow Patches

For larger vessels or where a non-encircling probe is desired the ultrasonic crystal may be imbedded in a curved fabric/silastic patch for suturing to the vessel wall. This type of probe is often used on the aorta or pulmonary artery. The diameter of the curve must be specified, and it is usually better to be slightly oversized. This type of probe can be trimmed by the surgeon to fit the available exposure.

5 MHz Segment Length Crystals

The crystals consist of 2 mm discs of 5 MHz material with convex diverging epoxy lenses molded to each face to spread the sound beam. A 3 cm long piece of 20 gauge Teflon sleeving is placed around the leads to aid in inserting the crystal into the myocardium.

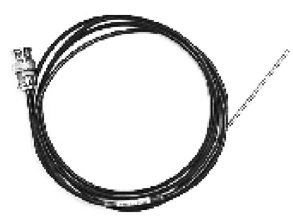
10 or 20 MHz Epicardial Patches

These probes are used to measure ventricular wall thickening with the displacement module. Two standard types are available: a 2 mm disc or square of 10 MHz material attached to a wire loop in the shape of a shamrock or clover leaf for use on large ventricles (dogs), or a similar 1 mm square of 20 MHz crystal for use on thin ventricles (rats). Each can be sutured to the epicardium.

10 or 20 MHz Catheter Stub Probes

These probes are used to sense flow in an exposed vessel by holding the probe against the side of the vessel. They are commonly used intraoperatively during reconstructive procedures to verify flow in anastomosed arteries and veins. They are available in 5, 6, or 7 French sizes, 4" long with 6' leads and can be used on vessels as small as 0.5 mm dia. They are lighter than needle mounted probes and less likely to be damaged if dropped.

Tubing or Needle Mounted Probes



For applications where a rigid, end-mounted transducer is required, we can mount crystals to the end of a piece of tubing or needle. The smallest size is a 16 gauge needle (recess for 1 mm dia 20 MHz crystal), and the largest is 1/4" brass tubing (recess for 5 mm dia 10 MHz crystal). We can also mold epoxy lenses to the crystal face to focus the sound beam. This type of focussed probe has been applied in mice to measure cardiac and peripheral blood velocity noninvasively.

10 MHz Catheters Doppler catheters for research use in animals can be made as small as 3 French (1 mm dia) on a custom basis. For clinical applications, standard and custom catheters operating at 10 or 20 MHz are available from Millar Instruments.

Publications:

1. Hartley CJ, Taffet GE, Reddy AK, Entman ML, and Michael LH. "Noninvasive Cardiovascular Phenotyping in Mice", Institute for Laboratory Animal Research, 43(3):147-158, 2002.

2. Hartley CJ, Reddy AK, Madala S, Martin-McNulty B, Vergona R, Sullivan ME, Halks-Miller M, Taffet GE, Michael LH, Entman ML, and Wang Y. "Hemodynamic Changes in Apolipoprotein E-Knockout Mice", American Journal of Physiology Heart Circulatory Physiology, 279: H2326-H2334, 2000.

3. Hartley CJ, Lacy JL, Dai D, Nayak N, Taffet GE, Entman ML, Michael LH. "Functional Cardiac Imaging in Mice Using Ta-178", Nature Medicine, 5:237-239, 1999.

4. Michael LH, Ballantyne CM, Zachariah JP, Gould KE, Pocius JS, Taffet GE, Hartley CJ, Pham TT, Daniel SL, Funk E, Entman ML. "Myocardial Infarction and Remodeling in Mice: Effect of Reperfusion." American Journal of Physiology, 277: H660-H668, 1999.

Other Related Publications:

1. Hartley CJ, Taffet GE, Michael LH, Pham TT, Entman ML. "Noninvasive Determination of Pulse-wave Velocity in Mice", American Journal of Physiology. 273:H42-47, 1997.

2. Taffet GE, Pham TT, Hartley CJ, "The Age-associated Alterations in Late Diastolic Function in Mice are Improved by Caloric Restriction." Journal of Gerontology A Biol Sci Med Sci 52: B285-B290, 1997.

3. Taffet GE, Hartley CJ, Wen X-Y, Pham TT, Michael LH, Entman ML. "Non-invasive Indices of Cardiac Systolic and Diastolic Function in the Hyperthyroid and Senescent Mouse", American Journal of Physiology, 270:H2204-H2209, 1996.

Abstracts/Presentations:

1. Madala S, CJ Hartley, and AK Reddy, "Digital Signal Processing in Diagnostic Ultrasound Systems: An Overview", Houston Society for Engineering in Medicine and Biology, 19th Annual Conference, Houston, Texas, February 2001.

2. Reddy AK, GE Taffet, CJ Hartley, S Madala, TT Pham, LH Michael, and ML Entman, "Measurement of Aortic Input Impedance in Mice", Houston Society for Engineering in Medicine and Biology, 19th Annual Conference, Houston, Texas, February 2001.

3. Hartley CJ, AK Reddy, S Madala, TT Pham, LN Ochoa, J Pocius, LH Michael, ML Entman, and GE Taffet, "High Resolution Ultrasonic Blood Flow Sensing in Mice", Houston Society for Engineering in Biology and Medicine, 19th Annual Conference, Houston, Texas, February 2001.

4. Hartley CJ, LN Ochoa, AK Reddy, LH Michael, JS Pocius, TT Pham, CW Scott, ML Entman, J W Clark Jr., and GE Taffet, "Vascular Adaptations to Transverse Aortic Banding in Mice", IEEE-EMBS conference, Istanbul, Turkey, October 2001.
5. Hartley CJ., AK Reddy, S Madala, B Martin-McNulty, R Vergona, ME Sullivan, M Halks-Miller, LH Michael, GE Taffet, ML Entman, and Y Wang, "Altered Hemodynamics of Atherosclerotic Mice", Houston Society for Engineering in Medicine and Biology, 18th Annual Conference, Houston, Texas, February 2000.

6. Ochoa LN, TT Pham, J Pocius, CW Scott, DP Doan, AK Reddy, CJ Hartley, LH Michael, and GE Taffet, “Doppler Evaluation of Aortic Constrictions in Mice”, Houston Society for Engineering in Medicine and Biology, 18th Annual Conference, Houston, Texas, February 2000.

7. Reddy AK, GE Taffet, CJ Hartley, S Madala, TT Pham, R Kwun, T Treviño, J Pocius, LH Michael, and ML Entman, “Noninvasive Systolic and Diastolic Blood Pressure Measurement in Mice Using Tail-Cuff Method”, Houston Society for Engineering in Medicine and Biology, 18th Annual Conference, Houston, Texas, February 2000.

8. Hartley CJ, AK Reddy, S Madala, B Martin-McNulty, R Vergona, ME Sullivan, M Halks-Miller, GE Taffet, LH Michael, ML Entman, and Y Wang, “Hemodynamics of Atherosclerotic Mice”, Chicago-2000 World Congress on Medical Physics and Biomedical Engineering, Chicago, July 23-28, 2000.

9. Michael LH, AK Reddy, GE Taffet, TT Pham, J Pocius, ML Entman, and CJ Hartley, “Cardiovascular Physiologic Genomics in Mice”, Houston Society for Engineering in Medicine and Biology, 17th Annual Conference, Houston, Texas, February 1999.

10. Madala S, AK Reddy, and CJ Hartley, “Design of Ultrasonic Doppler Instrumentation for Mice”, Houston Society for Engineering in Medicine and Biology, 17th Annual Conference, Houston, Texas, February 1999.

11. Hartley CJ, JL Lacy, D Dai, N Nayak, AK Reddy, GE Taffet, ML Entman, and LH Michael, “Functional Cardiac Imaging in Mice Using Ta-178”, HIRES 1999, Amsterdam, The Netherlands, September 1999.

12. C. J. Hartley, S. Madala, J. L. Lacy, A. K. Reddy, G. E. Taffet, K. Kurrelmeyer, J. Pocius, T.T. Pham, N. Nayak, M. L. Entman, and L. H. Michael, "Noninvasive Methods to Measure Cardiovascular Function in Mice", National Institutes of Health Bioengineering Symposium, Bethesda, Maryland, USA, February 27-28, 1998.

13. A.K. Reddy, C. J. Hartley, G. E. Taffet, S. Madala, T. T. Pham, and M. L. Entman, "Noninvasive Measurement of Aortic Blood Flow Parameters in Mice", Houston Society for Engineering in Biology and Medicine, 16th Annual Conference, Houston, Texas, USA, April 2-3, 1998.

14. A.K. Reddy, C. J. Hartley, G. E. Taffet, S. Madala, T. T. Pham, and M. L. Entman, "Measurement of Pulse-Wave Velocity in Mice", Houston Society for Engineering in Biology and Medicine, 16th Annual Conference, Houston, Texas, USA, April 2-3, 1998.

15. C.J. Hartley, J. L. Lacy, J. Pocius, S. Daniel, E. Funk, G. E. Taffet, N. Nayak, M. L. Entman, and L. H. Michael, "Characterization of a Murine Model of Heart Failure by Nuclear Angiography", Experimental Biology (FASEB), San Fransisco, California, USA, April 18-22, 1998.

16. C.J. Hartley, J. L. Lacy, G. E. Taffet, S. Madala, A. K. Reddy, M. L. Entman, and L. H. Michael, “Noninvasive Characterization of Heart Failure in a Murine Model of Coronary Occlusion”, XIII Congress of the CSDS; Gent, Belgium, August 27-30, 1998.

17. C.J. Hartley, J. L. Lacy, M. L. Entman, J. Pocius, G. E. Taffet, H. C. Thompson, D. Dai, C. S. Martin, N. Nayak, and L. H. Michael, "Quantitative Left and Right Ventricular Function in Mice with 178Ta Nuclear Angiography", American Heart Association 70th Scientific Sessions, Circulation 96-Supplement I, Orlando, Florida, U.S.A., November 9-12, 1997.

18. C.J. Hartley, G. E. Taffet L. H. Michael, T. T. Pham, L. A. Schildmeyer, G. Karsenty, R.J. Schwartz, and M. L. Entman, "Doppler Assessment of Aortic Pulse-Wave Velocity Velocity in Genetically Altered Mice", American Heart Association 70th Scientific Sessions, Circulation 96-Supplement I, Orlando, Florida, U.S.A., November 9-12, 1997.