

A semi-implantable multichannel telemetry system for continuous electrical, mechanical and hemodynamical recordings in animal cardiac research

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Abstract

We have developed an eight-channel telemetry system for studying experimental models of chronic cardiovascular disease. The system is an extension of a previous device that has been miniaturized, reduced in power consumption and provided with increased functionality. We added sensors for ventricular dimension, and coronary artery blood flow and arterial blood pressure that are suitable for use with the system. The telemetry system consists of a front end, a backpack and a host PC. The front end is a watertight stainless steel case with all sensor electronics sealed inside; it acquires dimension, flow, pressure and five cardiac electrograms from selected locations on the heart. The backpack includes a control unit, Bluetooth radio, and batteries. The control unit digitizes eight channels of data from the front end and forwards them to the host PC via Bluetooth link. The host PC has a receiving Bluetooth radio and Labview programs to store and display data. The whole system was successfully tested on the bench and in an animal model. This telemetry system will greatly enhance the ability to study events leading to spontaneous sudden cardiac arrest.

Keywords: telemetry, sudden cardiac death, electrophysiology

Introduction

Many of the most common and troubling cardiovascular diseases in modern society are chronic. In many cases, the use of acute animal models to study the mechanisms of the

disorders and their therapy is inadequate. Thus, we have developed a semi-implantable, multichannel telemetry system that is appropriate for following instrumented animals over weeks and months with batteries changed periodically. The initial focus of the system was the study of the events leading to sudden cardiac arrest (SCA) in clinically relevant animal models.

SCA is the leading cause of death in the industrialized world (Myerburg and Castellanos 1997). The primary cause of SCA is ventricular fibrillation (VF), but in as many as 31% cases of SCA, the first rhythm seen by the rescue personnel is asystole and in 28% cases of SCA is pulseless electrical activity (Cobb *et al* 2002). Because of the chronic nature of ischemic heart disease and congestive heart failure, both associated with SCA, and the complexity of carrying out investigations in the patient population, a desirable approach is the development and study of animal models of SCA that closely mimic the clinical phenomenon.

In previous work, we developed an eight-channel radio telemetry device that allowed acquisition and storage of eight unipolar cardiac electrograms from large, ambulatory animals (Rollins *et al* 2000, Yarger *et al* 2000). Using this system, we studied seven dogs with an experimental occlusion of the left anterior descending coronary artery and a wire implanted in the left circumflex coronary artery to induce thrombotic events. Five of the seven dogs died 19–64 h after surgery with the final event of recorded VF. However, two of the dogs died with a final event of profound bradycardia (Killingsworth *et al* 2000). Because the telemetry system was unable to capture mechanical and hemodynamic variables, such as arterial blood pressure and left ventricular wall motion as well as coronary blood flow, it was impossible to define the time course of the mechanistic events leading to SCA. It is possible that bradycardia was the initial arrhythmia, followed by functional failure or perhaps ischemic changes led to mechanical dysfunction, followed by a reflexive slowing of the heart rate.

In addition to the lack of channels recording mechanical and flow variables, the telemetry system had other limitations. Because the goal of the original development had been speed of implementation, off the shelf parts were used that were readily available, so that neither size nor power consumption was optimized for implantation. Commercial systems have been available for many years, but their capabilities were inadequate to effectively study SCA (Shiotani *et al* 2005, Smith and Salb 1975). As a result, we have developed a new system that will allow convenient, accurate and physiologically meaningful investigations in chronic animal models of SCA. The new system integrates dimension, flow and pressure measurements with five unipolar electrograms for a more complete characterization of SCA. Critical design goals were (1) low power consumption for long battery lifetime, (2) ability to use multiple sensors simultaneously without their interfering with each other and (3) sufficient information to characterize phenomena associated with SCA.

System design

The system consists of the implantable front end, backpack and a host PC, as shown in the block diagram in figure 1. The front end consists of electronics and sensors for the sonomicrometer, flowmeter, pressure meter and five cardiac electrogram channels. The desired physiological data are transduced in the experimental animal and collected and amplified in the front end. The backpack contains the control unit, Bluetooth radio, and batteries which power the system, including the front end. The control unit in the backpack digitizes the data with eight channels of onboard A/D converters. The data are conditioned and forwarded to the Bluetooth radio for transmission. The host PC has a receiving radio and the received data are saved to the hard drive and displayed on the screen. This telemetry system was designed in modules so that partial upgrades could be easily accomplished without affecting other parts. Miniaturization

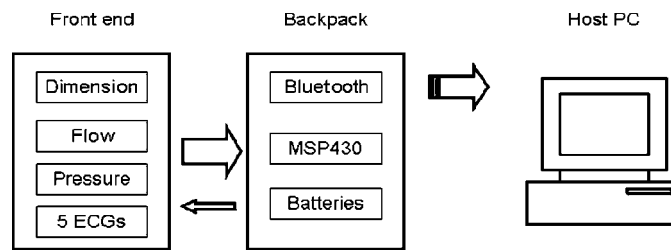


Figure 1. A block diagram of the telemetry system. This telemetry had a front end, a backpack and a host PC. The front end included electronics and sensors. The data collected were forwarded to the backpack through a cable. The front end also received power from the backpack via the same cable. The backpack had a control unit, a Bluetooth radio and batteries. The control unit in the backpack digitized the data and sent them to the host PC through the Bluetooth radio. The host PC archived the data and displayed them on the screen.

was achieved by (1) optimal design to keep the circuits at minimum size, (2) using suitable parts with the smallest form factors, (3) reduced printed circuit board (PCB) area with six layers PCB in the front end and double layer PCB in the backpack and (4) a custom-made package with minimum volume. The power consumption reduction was achieved by (1) using ultra low power parts for circuits, (2) replacing the general purpose 386 computer with an ultra low power microcontroller MSP430F149 and (3) replacing the power consuming wireless LAN card with a lower power Bluetooth interface.

Front end

The front end consists of all of the implantable sensors and electronics. Two 2 mm circular piezoelectric crystals (Sonometrics, Inc., London, ON, Canada) were used with a sonomicrometer for dimension measurements. A 10 MHz Doppler flow probe from Iowa Doppler Products, Inc (Iowa City, IA) was used with the continuous wave flowmeter. The detailed design and test of the sonomicrometer and flowmeter have been published previously (Kong *et al* 2005). The pressure channel contains a two-stage amplifier using INA114 instrumentation amplifier (Texas Instruments, Inc., Dallas, TX) with a gain of 600. The pressure sensor used for validation was a Millar Mikro-Tip pressure transducer catheter, SPR-524 (Millar Instruments, Inc., Houston, TX). Other pressure sensor could be used. Cardiac electrical channels were imported from the original system. The electrodes are custom-made unipolar screw-in electrodes adopted from Medtronic electrodes (Medtronic, Minneapolis, MN). The gain for the cardiac electrograms is 50. All of the sensor electronics are built on a 4.7 cm × 5.9 cm six-layer PCB. The components are soldered with reflow solder. The PCB is housed in a custom-made stainless steel case measuring 8.9 × 5.5 × 2.3 cm. A plastic lid with two O-rings, when pushed into the stainless steel case, makes the package watertight. All transducers except the pressure probe are connected to the front end case with commercial IS-1 lead connectors (Oscor, Inc., Palm Harbor, FL) for easy replacement and waterproofing. All IS-1 female connectors are fixed inside the lid with implantable grade silicone adhesive (Rhodia Silicones, Inc., Ventura, CA). The front end, with sensors and electronics, is designed for implantation inside the animal. A wire through the skin connects the front end and the backpack. Power is supplied to the front end through this cable and collected data are forwarded from the front end to the backpack.

Backpack

The backpack contains the control unit, Bluetooth module and batteries. The MSP430F149 microprocessor (Texas Instruments, Inc., Dallas, TX) was chosen as the control unit for its ultra low power and small form factor. It has a 16-bit CPU and two on-board universal asynchronous receiver/transmitters. The main timing for the MSPF149 is provided with an external 3.58 MHz clock. This clock rate provides a good balance between performance and low power consumption. The MSP430F149 was programmed in assembly language. The microprocessor was programmed to stay in low power mode for most of the time. An interrupt wakes up the microcontroller at a rate of 1 kHz, at which point the analogue signals from the front end are sampled and digitized with eight channels of A/D converters. The universal asynchronous receiver/transmitter is configured to a baud rate of 115 kbps. One start bit, eight data bits and one stop bit are used. The data are conditioned and sent to a serial send buffer for transmission to the host PC via the Bluetooth link. The microcontroller then reverts into low power mode and this process continues in a loop. The front end and backpack are powered with two AA batteries. Two MAX1674 dc–dc converters (Maxim, Sunnyvale, CA) regulate the 3 volts from the batteries to two power voltages, 3.3 V and 5 V. The microcontroller MSP430-F149 and Bluetooth module are powered with 3.3 V and the front end is powered with 5 V. There is also a 67.5 V battery in the back pack for sonomicrometer excitation (Kong *et al* 2005). The control unit and the dc–dc converter are built on a 6.4 × 4.8 cm PCB. The PCB, the Bluetooth radio and the batteries are hosted in a plastic box measuring 9.1 × 6.5 × 2.8 cm.

Host PC

The host PC has another Bluetooth serial adapter to receive the radio signal. The Bluetooth adapter in the backpack and the Bluetooth adapter on the PC are configured to talk only to each other, and the data transmission is password protected. Data throughput was verified at 115 kbps when the telemetry system and the host PC were placed 10 m apart with one wall between them.

On the PC end, we have developed two applications in Labview (National Instrument, Inc., Austin, TX). One application receives the data and saves it on a disk every 10 s. It uses the current time to generate a unique file name. The application is preset to record for 10 s, close the file and create another data file. The data can be joined together when analyzed later. The data display is accomplished by another application program. This program reads the latest written data file and displays it on the screen.

Validation

Each channel was extensively tested on the bench and in animals. The battery life was tested by powering up the telemetry system with two AA batteries until the batteries were depleted. The front end package was tested by submerging it and all leads and transducers in tap water at room temperature. The front end was powered on and stayed underwater for three days. The current draw of the front end and backpack was measured with an ammeter. The power consumption was calculated by multiplying respective currents and voltages. Since this system will be used in animal models and since a bench test may not simulate the animal environment perfectly, we tested eight channels of the front end in five pig models and tested the whole telemetry system in three pig models. The animal preparation followed the methods described by Killingsworth *et al* (2000). Basically, the animal was placed in dorsal recumbency on the surgical table. The

chest was opened via a median sternotomy. Five custom-made screw-in epicardial electrodes were placed over the coronary arterial beds to monitor electrograms. The left leg served as the ground for electrograms. The pressure sensor was placed in the lumen of the ascending aorta. Two sonomicrometer crystals were placed on the base and apex of the LV to measure one dimension of the heart. A segment of the left anterior descending coronary artery LAD was isolated and a 1.5 mm Doppler flow probe was wrapped around the vessel. The places chosen for the sensors were only for testing purposes and the sensors can be moved to other places if desired. The animal was allowed to recover for 30 min from the screw-in electrode injuries. The flow and pressure channels were verified against commercial instruments by making simultaneous measurements at adjacent locations. For the flow measurement, the flow transducer from a pulsed Doppler flowmeter (the University of Iowa, Iowa City, IA) was placed next to a telemetry flow cuff on the LAD. The audio signal from the pulsed Doppler flowmeter and the flow signal from the telemetry system were recorded at a sampling rate of 100 kHz with an NI DAQcard-6024 E (National Instrument, Austin, TX) on a laptop computer. The audio signal was then analyzed and frequency changes were converted to flow. Pressure measurement was verified with the pressure channel of a Hewlett Packard monitor 78534 C (Hewlett Packard, Palo Alto, CA). The pressure sensor of the Hewlett Packard monitor was placed in the aorta near the pressure sensor of the telemetry system. Pressure from the Hewlett Packard monitor was recorded by replacing an electrogram channel with signals from the pressure channel of the Hewlett Packard monitor. The simultaneously measured flow and pressure signals were compared with cross correlation test. Then VF was induced by applying a dc current to the epicardium. The VF was allowed to continue for about 20 s and then a defibrillation shock was applied. Acute ischemia was simulated by tying a 4.0 suture to the LAD just above the flow cuff for 30 min. Data were recorded for 4–6 h continuously throughout the studies. The implant was examined and there was no damage to the front end package and transducers.

Results

A new telemetry system with expanded capabilities has been designed, built and tested successfully. We can acquire dimension, flow and pressure measurements, as well as five cardiac electrograms, with this system. The size and power consumption of the new system were greatly reduced compared to our original telemetry system. The combined front end and backpack volume was reduced from 2.60 L to 0.29 L. The weight was reduced from 2.10 kg to 0.40 kg. The average power consumption was reduced from 2.50 W to 0.23 W even with the additions of sonomicrometry, flow and pressure measurements (Rollins *et al* 2000). The batteries were reduced from eight AA batteries and twelve C batteries to two AA batteries yet the battery life was extended from 12 h to more than 28 h. The submerge test for the watertight front end package lasted three days and no leak was found. Verification recordings of flow and pressure are shown in figures 2 and 3, respectively. The cross-correlation coefficient R is 0.93 at a lag of 24 ms for simultaneous flow measurements and is 0.99 at a lag of 10 ms for pressure measurements. In figure 2, the small difference in flow signal shapes may be caused by different probe locations, since the probes for the telemetry system flowmeter and the Iowa flowmeter are placed next to each other, but not on the same spot. In figure 3, the pressure notch was present in telemetry measurement but absent in Hewlett Packard monitor measurement. The pressure notch is caused by the close of the semi-lunar valves when the LV changes from systole to diastole and should be present normally. The absence of the pressure notch in Hewlett Packard monitor measurement is likely due to heavy filtering of signals. Figure 4 shows simultaneous recordings of all eight channels in a pig model. Figure 5 shows

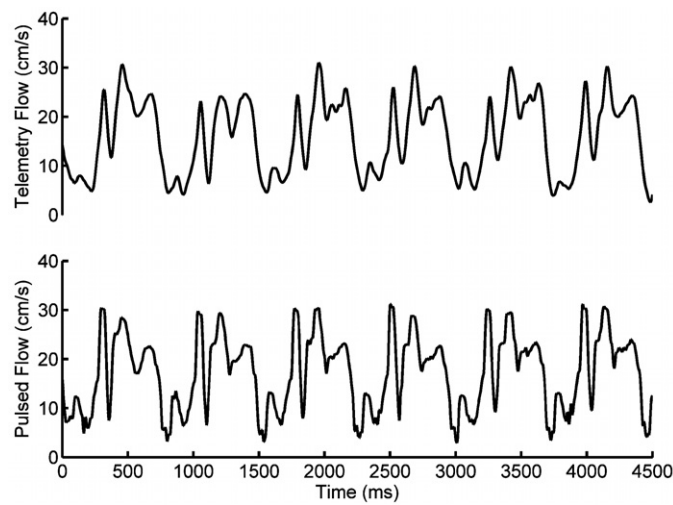


Figure 2. Verification recordings of flow. Flow measurements from the telemetry system and pulsed Doppler flowmeter are shown. They were recorded simultaneously from the LAD. The top trace was from the telemetry system and the bottom trace was from the pulsed Doppler flowmeter.

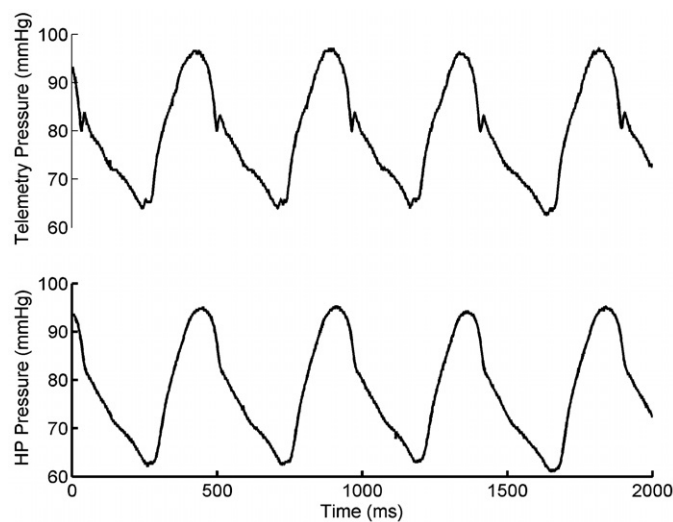


Figure 3. Verification recordings of pressure. Pressures recorded simultaneously in the aorta are shown. The top trace was from the telemetry system and the bottom trace was from the pressure channel of a Hewlett Packard monitor.

the induction and termination of VF with a shock from a Lifepak 12 defibrillator (Medtronic, Minneapolis, MN).

Discussion

We have designed, implemented and tested an eight-channel biotelemetry system optimized for the study of chronic cardiovascular disease. Earlier systems have lacked sufficient capability

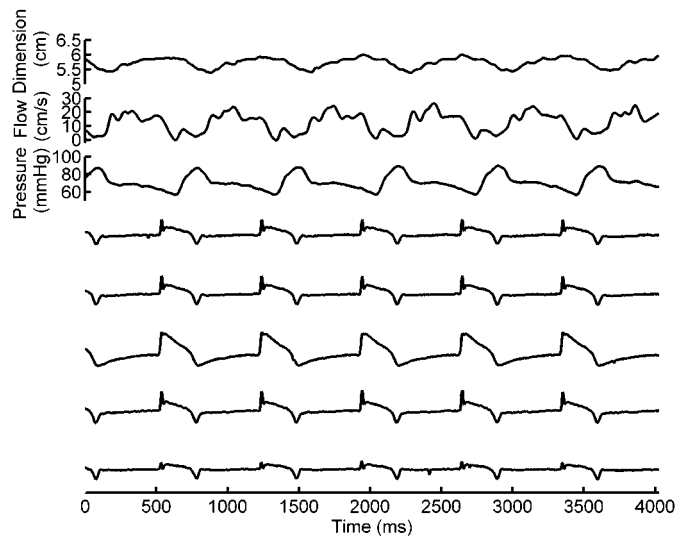


Figure 4. An example of eight simultaneous recordings. Simultaneous recordings for dimension, flow, pressure and five cardiac electrograms (in that order) are shown from top to bottom.

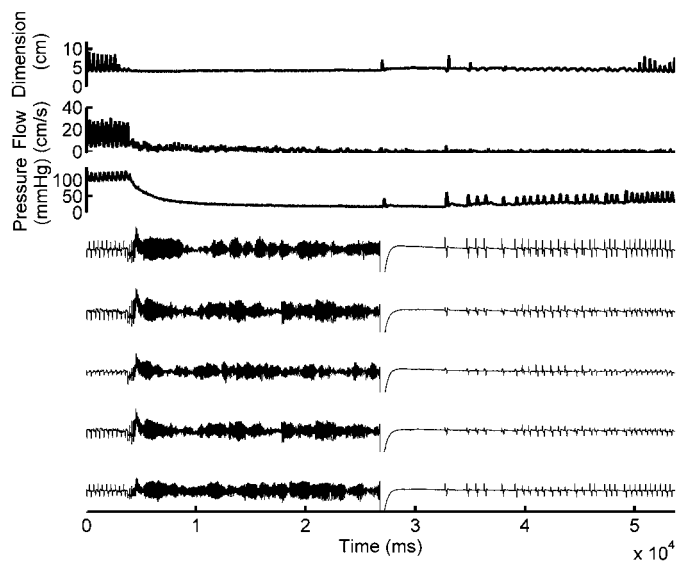


Figure 5. Recordings of induced VF and defibrillation. A VF was induced by applying a dc current to the epicardium of the LV. The VF was sustained for about 20 s and was terminated by a defibrillation shock.

to characterize adequately physiological changes leading to cardiac events. The system was designed for initial use in understanding the phenomena that lead to sudden cardiac arrest in clinically relevant animal models. The system is an adaptation and extension of a previous device used for long-term studies that showed that simultaneous acquisition

of electrophysiological and mechanical variables would be necessary for understanding the temporal changes in the minutes to hours before SCA.

The system would also be useful in other chronic cardiac diseases. In particular, it would be possible to study chronic animal models of heart failure. Patients with heart failure are at elevated risk for SCA (Bardy *et al* 2005) and the interaction between electrophysiological and mechanical perturbations as heart failure progresses could reveal the complex interplay between the two and provide insights into the phenomena causing the increased arrhythmic mortality as well as determine if it is possible to predict the occurrence of SCA.

In many cases, chronic conditions such as ischemic heart disease and heart failure are difficult to study since human research is ethically and technically constrained and the development and use of animal models is expensive and time-consuming. Biotelemetry offers an opportunity to define progression of pathology in a direct and clinically relevant way. It might be possible to learn to predict the onset of catastrophic events with enough specificity, sensitivity and timeliness to intervene or, at least, to alert patients or caregivers.

There are several approaches to improving the system described here. First, the microcontroller could be incorporated into the front end. Multiple signals could be multiplexed at this level, leaving only the battery box external and reducing the diameter of the cable. This would impose fewer burdens on the animal and allow convenient expansion to more channels. Second, power consumption could be reduced substantially by exploiting the modular design of the system. The low power Bluetooth radio consumes most of the total power in the current system. The Bluetooth link could be replaced with an Ultra Wide Band or other technology for wider bandwidth and lower power when they become available. Third, the sonomicrometer could be expanded to two or three channels so that heart volume can be estimated from dimension measurements (Appleyard and Glantz 1990, Visner *et al* 1983). Finally, the number of cardiac electrograms acquired could be increased to provide a more precise definition of the spread activation fronts. With these advances, there is an opportunity to use this telemetry system to understand the mechanisms of several chronic cardiac conditions and their therapies.

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