A novel, fully implantable, multichannel biotelemetry system for measurement of blood flow, pressure, ECG, and temperature

M. Axelsson,1 Q. Dang,2 K. Pitsillides,3 S. Munns,4 J. Hicks,4 and G. S. Kassab2,5,6

1Department of Zoology, Göteborg University, Göteborg, Sweden; 2Department of Biomedical Engineering, Indiana University Purdue University Indianapolis, Indianapolis, Indiana; 3EndoSomatic Technologies LLC, Sacramento, California; 4Department of Ecology and Evolutionary Biology, University of California Irvine, Irvine, California; and Departments of 5Surgery and 6Cellular and Integrative Physiology, Indiana University Purdue University Indianapolis, Indianapolis, Indiana

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Axelsson M, Dang Q, Pitsillides K, Munns S, Hicks J, Kassab GS. A novel, fully implantable, multichannel biotelemetry system for measurement of blood flow, pressure, ECG, and temperature. J Appl Physiol 102: 1220–1228, 2007. First published November 22, 2006; doi:10.1152/japplphysiol.00887.2006.—Biotelemetry provides high-quality data in awake, free-ranging animals without the effects of anesthesia and surgery. Although many biological parameters can be measured using biotelemetry, simultaneous telemetric measurements of pressure and flow have not been available. The objective of this study was to evaluate simultaneous measurements of blood flow, pressure, ECG, and temperature in a fully implantable system. This novel system allows the measurement of up to four channels of blood flow, up to three channels of pressure, and a single channel each of ECG and temperature. The system includes a bidirectional radiofrequency link that allows the implant to send data and accept commands to perform various tasks. The system is controlled by a base station decoder/controller that decodes the data stream sent by the implant into analog signals. The system also converts the data into a digital data stream that can be sent via ethernet to a remote computer for storage and/or analysis. The system was chronically implanted in swine and alligators for up to 5 wk. Both bench and in vivo animal tests were performed to evaluate system performance. Results show that this biotelemetry system is capable of long-term accurate monitoring of simultaneous blood flow and pressure. The system allows, within the room, recordings, since the implant transmission range is between 6 and 10 m, and, with a relay, backpack transmission distance of up to 500 m can be achieved. This system will have significant utility in chronic models of cardiovascular physiology and pathology.

The use of telemetric techniques makes it possible to record and study physiological variables during long-term experiments with a minimum of disturbance to the animal. The absence of physical restraint and the ability to free range reduces stress and leads to more easily interpretable data. Fully implantable telemetric techniques also greatly reduce the risk of infection associated with leads and catheters protruding from the skin. In addition, telemetric techniques make it possible to study animals in their natural habitat (ecophysiology) and during social interactions to correlate normal behaviors with physiological variables. It is clear that many interpretations of previous physiological data are hampered by stress induced from confinement or human interaction. This unwanted stress is greatly reduced by using a fully implantable telemetric system.

The objectives of this study were to evaluate a novel multichannel telemetric system capable of simultaneous measurements of four Doppler-based blood flows, three blood pressures, ECG, and temperature over extended periods of time (months). One important aspect is the longer transmission range of the implant and base station with a capacity for bidirectional communication “within the room” compared with most commercially available systems. The system was tested in vitro and in vivo in chronic swine and alligator models. The limitations and potential applications of this system are considered.

MATERIALS AND METHODS

The implantable biotelemetry system consists of four channels of Doppler-based flow, three channels of blood pressure, a temperature, and an ECG channel. The Doppler flowmeter, which has the highest power demand, is based on a design that has reduced power consumption through the use of micropower analog and radio-frequency (RF) integrated circuits. Power consumption is further reduced by incorporating advanced power management techniques, such as analog and digital subsampling and very fast power-up and shutdown of unused circuits. The first successful transmission of biological information from a living animal was performed in 1869 by Marey (18). This was followed by Einthoven’s experiment in 1903 in which he used a telephone line to transmit ECG data over a 1.5-km distance (9). If we adopt a modern definition of biotelemetry as “measurements from an unrestrained animal or patient using radiolinks” (8), Winters may be the inventor of telemetry in 1921 (26), followed by Fuller and Gordon in 1948 (14). A breakthrough in the design of telemetric and electronic equipment came in 1952 with the introduction of transistor technology (8). Two of the central variables in cardiovascular research are blood flow and blood pressure. Unfortunately, none of the fully implantable telemetric systems commercially available today provide blood flow capability. Furthermore, there are no simultaneous telemetric measurements of pressure and flow. Hence, it is currently not possible to monitor total or regional blood flow in large or small vessels, such as aorta, coronary, or pulmonary arteries. Measurements of cardiac output would, for example, provide more accurate estimates of metabolic rate compared with estimates based on heart rate (6, 8). The development of such an implant requires a flowmeter design that is specific for biotelemetry applications and not merely a miniaturization of a desktop version.

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Address for reprint requests and other correspondence: G. S. Kassab, Dept. of Biomedical Engineering, SL-174, Indiana Univ. Purdue Univ. Indianapolis, 723 West Michigan St., Indianapolis, IN 46202 (e-mail: gkassab@iupui.edu).
circuits between Doppler measurements. Synchronization control between the various circuit elements and management of the power-saving protocols are achieved by a microcontroller. This results in a multichannel implant that can operate continuously, with all nine channels enabled, for ~30 days when powered from two AA-size lithium battery pack. Table 1 provides a summary of technical specifications of the system. The system is presently suitable for animals with body weight >2.5–3 kg (where weight of implant is <5% of body weight). The system can be purchased from EndoSomatic Technologies (http://vivaldi.zool.gu.se/telemetry/).

**Implant description.** A simplified block diagram of the system is shown in Fig. 1. The implant microcontroller (Fig. 1A) generates all power control and timing signals to the Doppler flowmeter module and blood pressure amplifier subsystems. It serves as data acquisition and processor for the signals generated by the Doppler, blood pressure, ECG, and temperature subsystems. The microcontroller also encodes and formats the data for transmission through the RF link and processes any received commands the user issues through the base station decoder/controller.

The Doppler flowmeter module operates at 20 MHz and consists of four time-multiplexed channels. Each channel has independent adjustment controls for range-gate positioning, signal direction (inverted or noninverted), calibration, and channel on/off. The design of this section results in a low-power Doppler flowmeter that is suitable for long-term implantation. The system uses commercially available soft silicone perivascular flow probes of various lumen diameters with 0.5-mm diameter PZT-5A piezoelectric transducer (Iowa Doppler Products, Iowa City, IA).

Blood pressure is measured using custom-developed blood pressure catheters (1 mm in diameter, 3F, Millar Instruments, Houston, TX) based on Mikro-Tip sensors. The signals from these catheters are amplified and digitized by the microcontroller. An offset adjustment is provided for each amplifier to allow for maximum dynamic range at various altitudes. The offset adjustment is performed by remote commands issued by the user from the base station decoder/controller. These Millar pressure catheters provide a higher bandwidth (10 kHz) and quality signal than fluid or gel-filled pressure catheters and reduce blood clotting.

The ECG subsystem uses a two-lead configuration; the electrodes are stainless steel for long-term stability. A temperature sensor embedded within the implant case is used to measure body temperature.

Communication with the remote base station decoder/controller unit is performed with a bidirectional RF link. Data are sent out, and commands are received from the base station decoder/controller unit. Maximum range is ~6–10 m, depending on enclosure and antenna orientation. The communications link protocol for this implantable system is optimized for low power and data management (as opposed to a general link protocol such as Bluetooth), which is more appropriate for handheld and other portable devices due to the much higher power consumption.

The implant is powered by lithium batteries (one to three), and the expected battery life using two AA-size batteries is at ~1 mo when all nine channels are active continuously. Enabling fewer channels, especially Doppler flow channels, results in extended implant battery life. An automated timed-acquisition mode is also implemented, and in this mode the implant is operated, for example, for 2 min and shuts down for 15 min (for ~85 measurements per day). This extends battery life to over 6 mo. Alternatively, since the battery is attached to the implant using an implantable connector, and it is ideally located near the skin, it can be replaced without taking out the implant itself. The connector between the battery and the implant is a commercially available, miniature circular connector from Omnetics (Omnetics.com). Hermeticity is achieved using a custom-designed compression sleeve with four O-rings. This design was implemented in many of our experiments, and no leakage was detected. Similar type connectors are used to connect the Doppler and blood pressure transducers and ECG electrodes to the implant.

**Table 1. A summary of the specifications for the E-4311 system**

<table>
<thead>
<tr>
<th>Dimensions and battery life</th>
<th>Doppler flowmeter</th>
<th>Blood pressure</th>
<th>ECG</th>
<th>Temperature</th>
<th>Radio frequency link section</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implant dimensions</td>
<td>6 × 5.5 × 1.8 cm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Battery pack dimensions</td>
<td>5.5 × 4.5 × 1.6 cm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total weight</td>
<td>130 g in air</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>~30 days continuous (with all channels enabled and 2 AA-cell pack)</td>
<td>~30 mW</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure range</td>
<td>Greater than ±20 kHz</td>
<td>Greater than ±100 cm/s</td>
<td>±0.5 mm</td>
<td>DC ~25 Hz</td>
<td>914–916 MHz for United States 868 MHz for European Union</td>
</tr>
<tr>
<td>Bandwidth</td>
<td>DC ~50 Hz</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of channels</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ultrasound frequency</td>
<td>20 MHz</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulse repetition frequency</td>
<td>64 kHz maximum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimum range gate adjustment</td>
<td>1 mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum range gate adjustment</td>
<td>12 mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood velocity range</td>
<td>Greater than ±100 cm/s</td>
<td>Greater than ±100 cm/s</td>
<td>±0.5 mm</td>
<td>DC ~50 Hz</td>
<td>914–916 MHz for United States 868 MHz for European Union</td>
</tr>
<tr>
<td>Bandwidth</td>
<td>DC ~50 Hz</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of channels</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pressure sensors diameter</td>
<td>1 mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pressure catheter length</td>
<td>50 cm</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Minimum blood pressure</td>
<td>−50 mmHg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum blood pressure</td>
<td>300 mmHg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Offset adjustment</td>
<td>±50 mmHg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bandwidth</td>
<td>DC ~50 Hz</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of channels</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Input impedance</td>
<td>&gt;10 MΩ</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bandwidth</td>
<td>2–50 Hz</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of channels</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Temperature range</td>
<td>15–30°C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resolution</td>
<td>0.3°C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frequency</td>
<td>914–916 MHz for United States 868 MHz for European Union</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Power out</td>
<td>0 dBm</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Base station decoder/controller description. As shown in the simplified block diagram in Fig. 1B, the majority of the functions in the base station decoder/controller unit are handled by the internal microcontroller. There are four basic functions that are performed in the base station decoder/controller unit: 1) reception and decoding of data from the implant; 2) transmission of user-selected commands and configuration parameters to the implant; 3) conversion of decoded implant data to analog signals (using the digital-to-analog section) and RS232-type serial data stream; and 4) provision of a trigger output signal for synchronization with an external “computer-based” data-acquisition system.

The front panel liquid crystal display uses an integrated touch screen for access to the functions and commands used to control the implant. It is also used as a display monitor for the incoming analog data for verification and adjustment. The controls and waveforms for each of the nine channels and the configuration and control settings are shown as a single screen per channel. This approach shows only the relevant adjustment controls for each channel in each screen, which reduces clutter.

A remotely positioned RF transceiver link is attached to the base station decoder/controller unit by a 6-m cable. This allows the base station decoder/controller unit to be placed in a remote location, away from the animal housing. This minimizes the effects of human presence on the animal.

**Doppler bench test.** Bench tests on the Doppler flowmeter and the ultrasonic receiver/Doppler decoder were performed to assess linear-
ity, dynamic range, and sensitivity. The linearity was tested using a high-stability RF source (HP 8647A, 50 Ω terminated) connected to the input of the implant’s ultrasonic receiver at 20 MHz. The frequency was varied in the range of −20 to 20 kHz on either side of 20 MHz in steps of 5 kHz. The receiver’s dynamic range was tested by applying an RF signal at three different levels (10 μV, 1 mV, and 100 mV).

Doppler in vivo test. In one acute cat study, the implant Doppler flow measurements were validated against a Triton Instruments model 100 Doppler flowmeter. An adult cat was anesthetized by intramuscular injection of ketamine (30 mg/kg) followed by intravenous injection of α-chloralose (50 mg/kg) as needed. The animal was intubated and ventilated using a Harvard pump. A midline sternotomy was performed to expose the heart and aorta. A segment of the thoracic aorta was exposed for flow measurements, and a 4-mm perivascular Doppler transducer was mounted around the aorta. Since the two systems cannot be synchronized and operated simultaneously, they shared the same Doppler transducer sequentially.

Instrumented animals. The system was chronically implanted in both alligators and swine for up to 5 wk. Two American alligators, *Alligator mississippiensis*, were obtained from the Rockefeller Wildlife Refuge, Louisiana, and transported to the University of California, Irvine. The animals used in the experiments were young, of either sex, with a mean body weight of 5.27 ± 0.26 kg. During the experiments, the alligators were kept in a constant temperature room set at 30°C in a tank with shallow water (20–30 cm) where they could submerge at will. Five swine with a body weight of 42 ± 6 kg were also used in this study. The implant was positioned in the abdomen in the alligator, and under the skin in the abdominal region in the pig studies. The implant has silicon tubing suture loops that are used to attach it to nearby muscle for security. All animal experiments were performed in accordance with national and local ethical guidelines, including the Institute of Laboratory Animal Research (ILAR) guide, Public Health Service (PHS) policy, Animal Welfare Act, and approved University of California, Irvine-Institutional Animal Care and Use Committee (IACUC) protocols. The animal protocol was approved by the university IACUC.

Alligator surgical procedure. Anesthesia was induced using a custom-designed mask containing gauze dampened with isoflurane (Isoflo, Abbott Laboratories, North Chicago, IL). Alligators were then intubated and artificially ventilated (SAR-830, CWE, Ardmore, PA) with room air that had been passed through a vaporizer (Dräger, Lubeck, Germany). The vaporizer was initially set at 5% and was then reduced to 3–4% for the duration of surgery.

The animals were incised ventrally using aseptic techniques. To access the heart and major outflow vessels for placement of the flow probes, pressure catheters, and ECG wires, it was necessary to part the sternum 3–4 cm. The heart and outflow tract were then cleared of surrounding tissue to expose the major arteries as they extend from the anterior portion of the outflow tract. Doppler flow probes (ES-2.5 or ES-4.5, Iowa Doppler Products) were placed around the right aorta (RAo), left aorta (LAo), and left pulmonary artery (PA) immediately anterior to the outflow tract. Millar 3F pressure catheters were non-occlusively implanted facing downstream into the RAo, LAo, and...
common PA section of the outflow tract. The two ECG wires were attached inside the open chest, on each exposed side of the sternum. After implantation of flow probes, pressure catheters, and ECG wires, the implant and battery pack were placed in the abdomen as far caudally as possible. The sternum was then closed using interrupted sutures, and the ventral incisions in the body wall and skin were similarly closed. Intramuscular injections of the antibiotic enrofloxacin (Baytril, Bayer, Shawnee Mission, KS) and the anesthetic flumaxine meglumine (Flunixinime, Fort Dodge, Madison, NJ) were given at the conclusion of surgery. Enrofloxacin injections were repeated every second day after surgery.

Ventilation with room air was continued until the alligator regained consciousness and reinitiated spontaneous breathing. After full recovery from anesthesia, the animals were placed in a temperature-controlled recovery room. The temperature was maintained at 30°C. After a few days when the surgical wound was healed, the animals were allowed to have access to water.

Swine surgical procedure. Surgical anesthesia was induced with ketamine hydrochloride (25 mg/kg im) and atropine sulfate (0.05 mg/kg im). Animals were maintained on surgical anesthesia with isoflurane (1–2%) and oxygen. A left lateral fourth intercostal space thoracotomy was performed using sterile techniques. Lidocaine (80 mg iv) was administered as a bolus before cardiac instrumentation. The root of the ascending aorta was dissected free from the PA in preparation for the placement of an inflatable cuff around the PA, and the tube of the occluder was exteriorized through the back of the animal near the spine. The proximal coronary arteries (left anterior descending and left circumflex) were dissected free from surrounding tissue. A Doppler flow transducer in the shape of a circular band (4-mm diameter, 2-mm peak height) was tied through sutures around the coronary artery to measure flow velocity. The angle of the ultrasonic crystal (0.5 mm in diameter) in the transducer was fixed relative to the blood vessel wall. The pressure transducers consisted of 3F Millar pressure catheters, specially designed for the telemetry system. The Millar pressure catheters were inserted into the left or right ventricles (RV) through tiny punctures made on the proximal portions of the ascending aorta or PA, respectively. Systemic pressure was measured through a Millar pressure catheter similarly placed in the aortic arch. The implant and the battery enclosures were then implanted in the subcutaneous skin layer.

The Millar catheters have their sensing element positioned on the side of the catheter tip to avoid overestimation of blood pressure due to the effects of the pressure wave kinetic energy. We verified that rotation of the catheter in the pig aorta did not significantly change the recorded blood pressure values. The Millar catheters were calibrated before implantation, as per manufacturer specifications. The calibration used the supplied pressure dome and, in conjunction with a two-point calibration, used a solid-state-based manometer as reference. Before calibration, the implant and the transducers were immersed in a temperature-controlled bath for ~2 h to stabilize. This also allows the hygroscopic membrane on the catheter sensor to exchange fluids and moisture with the sensor surface to stabilize. These steps ensure that the catheters do not require recalibrations during the implant, as this is not feasible, and the offset was found to be within ±3–5 mmHg after 30 days of implantation. The Millar catheters are sturdy and given enough attention during implant and explant, they can last for at least 10–15 implantations.

After the animal was instrumented for telemetry, the thoracotomy was closed, and the animal was allowed to recover. After the animal recovered for 1 wk, the PA was banded using the externalized inflatable cuff. While the animal was free ranging, the cuff was inflated with glycerin, while the RV pressure was telemetrically measured and adjusted until the RV systolic pressure was raised to the desired level. The inflatable constrictor was fixed to maintain the degree of stenosis.

RESULTS

Doppler bench test. Figure 2 shows the data obtained from the output of the base station decoder/controller in the test for linearity, dynamic range, and sensitivity of the Doppler flowmeter section of the implant. The linearity shown in Fig. 2 is reflected by a correlation coefficient of 0.999 for the entire range of ±20 kHz (0.1% deviation from full scale). Assuming a piezoelectric transducer angle of 45°, this range corresponds to blood velocities >1 m/s. The maximum sampling rate of the Doppler flowmeter is 64 kHz, which can resolve Doppler shifts up to 25 kHz or blood velocities >1.25 m/s. The sensitivity tested covers an 85-dB range and does not result in any saturation of the ultrasound receiver, especially at the highest RF input levels.

Doppler in vivo test. The implant telemetry Doppler was compared with a standard Triton system. Figure 3, A and B, shows ~2 s of implant Doppler and a Triton Doppler flowmeter recording, respectively. A direct comparison between the two systems is made in Fig. 3C. The relationship between the two measurements is not significantly different from an identity line. The data indicate a 2.2% average deviation (from full scale) between the two flowmeters.

Instrumented animals. Selected data from the two alligators are presented in Fig. 4. Phasic signals for three blood flows (RAo, LAo, and left PA) are shown in Fig. 4, together with corresponding blood pressure tracings. The fourth Doppler channel was not used in these experiments. The data were sampled at 100 Hz from the base station decoder/controller analog output using Acknowledge software version 3.7.2 (Biopac, Goleta, CA).

A smaller battery pack was used in the in vivo studies to reduce the total size of the implant. This battery pack consists of a single lithium AA battery instead of the standard two AA battery pack. The system was taken out of the alligator after 3 wk, and Fig. 4 shows representative traces of the phasic signals for the recorded variables from days 1, 7, 14, and 21.
In Fig. 5, the phasic LAo blood flow and heart rate from the second alligator are shown with the animal quietly resting in the constant temperature room. The flow pattern in the LAo reveals a shunt, which is attained during resting conditions. In Fig. 5, left, the door to the room housing the alligator was opened (indicated by the arrow). Although the animal was housed in an opaque enclosure and could not see the door open, it reacted to the sound with a decrease in LAo blood flow and a small increase in heart rate. In Fig. 5, right, the door and the lid to the enclosure were opened (arrow). This resulted in a massive and long-lasting increase in heart rate and a pronounced decrease in LAo blood flow.

Figure 6 shows representative hemodynamic tracings in an awake, untethered swine. The recordings in Fig. 6 correspond to aortic velocity, left anterior descending coronary artery velocity, carotid velocity, and RV and aortic blood pressure, in order. The telemetry system was used to monitor banding of the PA and, consequently, pulmonary hypertension in the awake, free-ranging animal. Figure 7 shows blood pressure data before and after PA banding. The expected increase in PA pressure is apparent.

**DISCUSSION**

**Flow telemetry.** Over the past 30 yr, there has been a number of attempts to develop an implantable flowmeter. Initially, the desktop flowmeter architecture of choice was the electromagnetic flowmeter, which was considered the “gold standard.” A design that used an electromagnetic flowmeter for use in an implantable biotelemetry system incorporated a number of techniques for dealing with the high-power consumption rates of this system (13). The system used rechargeable batteries and limited power-on periods to extend system operation. This system consisted of a single channel of blood flow, two channels of blood pressure, and a channel each of ECG and temperature. Continuous operation of all channels with fully charged batteries was limited to ~2.5 h. The user could turn off the flowmeter section to increase operation life to 16 h, but 10 h of recharging the implant batteries were subsequently needed. Despite these limitations, the authors reported useful data from resting and exercising animals.

An alternative flowmeter technique used to measure blood velocity is based on the ultrasonic Doppler shift technique. Both continuous wave- and pulsed-Doppler-based implants have been developed (1, 2, 7). Although they were miniaturized using custom-developed integrated circuits, power consumption was still high. For a single-channel Doppler flow system, the battery life was estimated at ~100 h of continuous use. Again, limited power-on periods using an RF-activated switch were used to extend implant life. The design of this system necessitated the animals wearing a jacket to carry the receiving and processing equipment, as well as batteries.

An interesting blood flow implant development was based on an interferometric ultrasonic technique (22). The complete system consisted of a blood flow and a blood pressure channel. In this system, the battery life was limited to ~100 h of continuous use. Using an RF-activated command switch, a preprogrammed 8-min power-up period was initiated. The authors reported that two such activations per day (for a total of 16 min) extended the battery life to ~1 yr. The flow probe with this design was rather large, and animal movements could cause severe motion artifacts. A number of other flowmeter designs also appear in the literature, but most describe externally mounted systems that require frequent battery replacements and are too bulky for implantation (12, 24, 27, 28).

Currently, a commercially available telemetry system by Transonic Systems includes a two-channel transit-time blood flow telemetry unit (PhysioGearTM; http://www.transonic.com). One of the disadvantages of this system is that it is an externally mounted system. The issues with exit wound management and infections are of concern and require constant attention by the investigators. These concerns often negate the gains obtained from a wireless measurement. Furthermore, the telemetry system offered by Transonic does not measure simultaneous pressure, and, most importantly, it cannot be implanted due to its large size and very high-power consumption.

It is evident from the literature that battery life and, in some cases, the flow probe design is a limiting factor. The technique most often used to extend battery life is to simply reduce the time of operation. Although this allows for flow measurements,
infrequent data sampling provides only a limited insight into the complete long-term status of the phasic blood flow and the correlation to phasic blood pressure.

For the development of a telemetric blood flow system, pulsed-Doppler-based techniques have a number of advantages over other flow techniques, such as lower power consumption, baseline stability, smaller and lighter flow probes, and ease of calibration. Although the Doppler system measures velocity of blood, several studies have shown that this correlates well with changes in volumetric blood flow (19, 28). In addition, Doppler flow probes can be made in a variety of probe styles appropriate for a particular application. Specifically, they are commercially available as soft silicone perivascular cuffs, intravascular catheters, and epivascular probes. Finally, it has been argued that the vessel cross-sectional area may be a normalizing factor for the size of organ, and hence velocity is proposed as the preferred measurement (20). Here, we present a system with several simultaneous Doppler-based flow probes and pressure transducers with exceptional battery life.

**Alligator studies.** The quality of the phasic blood flow signals in the alligator (Figs. 4 and 5) are similar to data collected in other crocodilian species using bench top Doppler-based, electromagnetic, or transit-time systems (4, 5, 21, 23), demonstrating that this new system can produce high-quality phasic blood flow signals. The pressure signals are also similar to previously recorded pressure signals in laboratory-based studies. The use of catheter-tipped blood pressure transducers ensures high-frequency response of the measured signals and reduces the incidence of clotting associated with gel or fluid-filled transducers. The frequency response of the pressure system has not been tested, but the limiting factor in this case is not the sensor itself, but the implant sampling rate (average of 120 Hz per channel).

The telemetric measurements revealed that both alligators showed periods of pulmonary-to-systemic shunting pattern.

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**Fig. 4.** Phasic traces of blood flow (three top traces) and blood pressure (three bottom traces) in alligator 2, a 5.52-kg animal, 1, 7, 14, and 21 days after implantation. The signals were sampled at 100 Hz from the analog output of the base station decoder/controller unit. QPulm, pulmonary blood flow; QRAo, right aorta blood flow; QLAo, left aorta blood flow; PRAo, right aorta blood pressure; PL Ao, left aorta blood pressure; PPulm, pulmonary blood pressure.

**Fig. 5.** Phasic QLAo and heart rate (fH) in alligator 1, 24 h after surgery. The animal shows an increase in fH and a decrease in QLAo when disturbed (indicated by the arrows). Left: the animal reacts to the sound of the door opening (no visual contact); right: the lid to the enclosure, where the animal was housed, was opened.
mixed with nonshunting. In Fig. 4, the LAo trace at day 1 shows a shunting pattern, whereas days 7, 14, and 21 show nonshunting pattern. The issue of shunting in crocodiles has been the subject of numerous studies (3, 10, 11, 15–17).

In both alligators (Fig. 5), resting heart rate (24 h after surgery) was lower than reported from most other laboratory-based studies in crocodilians, indicating a low level of stress. Both animals also showed pulmonary-to-systemic shunting
breakage of a transducer cable. This can be avoided by proper placement of implant and transducers. Placement of the transducer cables in high-bending and high-stress areas should be avoided, since the chances of breakage are higher. If there is no cable or transducer breakage, the implant-limiting factor is the battery life. Since this can be extended by either changing the battery every 30 days, or utilizing the timed-acquisition mode, then the implant should be capable of staying in the body for a very long period of time (as long as 6–12 mo). Obviously, this needs to be verified by long-term studies in the future.

Summary and conclusions. In summary, this novel telemetry system is capable of acquiring high-quality data over extended periods of time. This is the first fully implantable system that can measure the combination of blood flow and blood pressure simultaneously in free-ranging animals. The transmission range is greater than most other systems (6–10 m or “within a room”). The battery life (two AA lithium cells) is in the range of 30 days when all nine channels are operating, and this can be extended further by using the built-in automated timed-acquisition data recording mode. The use of implantable connectors enables the user to replace the battery pack and transducers without any refurbishment delays. Due to the size of the implant and battery, the present system is limited to animals with body weight >2.5–3 kg, but a smaller version of the system is under development. This comprehensive telemetry system has enormous utility for understanding cardiovascular physiology and the hemodynamic progressions of cardiovascular disease.

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DISCLOSURES

K. Pitsillides owns EndoSomatic Technologies, LLC, which developed the biotelemetry system described in this manuscript.

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