

## **A Continuous Cardiac Output Computer Based on Thermodilution Principles**

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*A totally self-contained instrument for the measurement of cardiac output is described. The microcomputer controlled instrument is based upon the principles of thermodilution and is capable of making cardiac output determinations on a minute by minute basis. A bolus of heat is delivered to the blood via a resistive heating element wound on the surface of a conventional thermodilution catheter, and the resulting transient pulmonary artery blood temperature increase is monitored with the thermistor located near the tip of the catheter. The performance of the instrument was tested in a mock circulatory loop and in dogs for periods of up to 13 hours. The accuracy and reproducibility of flow determinations made with the system compare favorably with those made with a conventional cardiac output monitor. This study demonstrates the feasibility of a stand-alone cardiac output computer that can provide virtually continuous measurements of blood flow without the intervention of a technician.*

**Keywords**—*Thermodilution, Indicator dilution, Continuous cardiac output computer, Cardiac output, Canine cardiac output, Blood temperature noise.*

### **INTRODUCTION**

The impetus to create a new instrument for the measurement of cardiac output stems from an appreciation of the utility of the measurement and the labor intensive nature and poor accuracy and reproducibility of the conventionally used techniques. Cardiac output, the volume of blood pumped by the heart per minute, is the fundamental index of heart performance. All other indices of the state of the heart (heart sounds, EKG, peripheral blood flow, blood gas measurements, etc.) can often correlate with cardiac output, but they are not causal in accomplishing the heart's primary

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task of pumping blood. In the intensive care setting, this vitally important parameter is measured in most patients using conventional thermodilution methods. Because of the labor intensive nature of the conventional method, a self-contained continuous cardiac output monitor should enhance patient care.

The conventional technique used to measure cardiac output is based upon the thermodilution principle (3,5). A narrow multilumen catheter is inserted into a vein and positioned such that its tip traverses through the right heart into the pulmonary artery. A bolus of either room temperature or ice cold saline is injected directly into the vena cava or right atrium via a port in the catheter. The temperature of the blood is monitored with a thermistor located near the tip of the catheter in the pulmonary artery. The injected cold saline causes a transient drop in the blood temperature measured with this thermistor. Cardiac output is inversely proportional to the time integral of this reduction in blood temperature:

$$F = \frac{\rho_I c_I V_I T_I}{\rho_B c_B \int_0^{\infty} T_B dt} \quad (1)$$

where  $F$  is cardiac output in L/min,  $V_I$  is the volume of injected saline,  $T_I$  is the temperature of the injectate relative to mean blood temperature,  $T_B$  is the deviation in pulmonary artery blood temperature produced by the injectate, while  $\rho_I$ ,  $\rho_B$ ,  $c_I$ , and  $c_B$  are the densities and heat capacities of the injectate and blood (3).

The conventional thermodilution approach to measuring cardiac output, while routinely employed, suffers from numerous shortcomings. First, if care is not exercised, pathogens or air can be directly introduced into the blood stream. Second, the conventional thermodilution approach is labor intensive, taking from five to ten minutes per measurement. Because of this fact, only a few measurements are routinely made during an eight hour nursing shift. Finally, the existing technique is inaccurate and suffers from low reproducibility due to variabilities in the temperature of the injected saline, the time required to make the actual injection, the volume of the injected saline, and the rise in saline temperature before it actually reaches the bloodstream (2,3,4,10). Reproducibility is also severely degraded by temperature fluctuations in the pulmonary artery (3,9).

The need for accurate and reproducible cardiac output determinations in terms of patient care, and the problems associated with the existing technique for making the measurements, led us to develop the microcomputer based instrument described herein. The new system, the University of Utah Cardiac Output Monitor (UUCOM), is also based upon the thermodilution principle. The UUCOM is self-contained (i.e., no fluid is injected into the patient), and, once the catheter has been placed, it can operate continuously without the attention of an operator. The UUCOM can make cardiac output determinations on a minute by minute basis. Since the "injectate" is a bolus of heat energy which is electronically controlled, variations in the quantity of injected energy have been eliminated improving the accuracy and reproducibility of the measurement.

The instrument has been evaluated in a mock circulatory loop and in anaesthetized dogs. In the mock circulatory loop the UUCOM has been shown to be linear when compared to flow measured by timed filling of a fixed volume. Further, measure-

ments made with the UUCOM are more reproducible than measurements made with a commercial cardiac output computer (American Edwards 9520A). The feasibility of continuous monitoring with the UUCOM was verified in animal experiments where cardiac output was continuously monitored for periods of up to 13 hours. While the UUCOM determinations of cardiac output were variable, in the animal trials the variability compared favorably to the variability of determinations made with the 9520A.

## DESCRIPTION OF THE INSTRUMENT

### *The Instrument*

The UUCOM has a number of design features which reduce or eliminate the problems associated with the conventional methods and contribute to its performance in flow monitoring. The UUCOM employs an energy storage capacitor to store a fixed quantity of electrical energy,  $\frac{1}{2}CV^2$ , which is then converted into heat energy via a heating coil on the surface of a modified Swan-Ganz catheter. The use of a heating coil for energy delivery eliminates the introduction of foreign material into the blood stream. Further, the electronic delivery of heat is controlled precisely by a microcomputer. This greatly reduces the labor requirements of the cardiac output measurement.

However, the delivery of heat via a heating coil constitutes a shock hazard which is not present in the conventional technique. We designed the energy delivery circuitry of the UUCOM in order to minimize this risk. The energy storage capacitor was charged by connecting its terminals across a power supply with a double-pole double-throw isolation relay. When the relay was activated both terminals of the capacitor were disconnected from the power supply and connected across the heating coil. This insured complete isolation of the energy source from ground and therefore protected the animals from potential shock hazard. In addition, the heating coil and its leads were double insulated to reduce shock hazard. The UUCOM was designed to deliver three energy levels, achieved by controlling the charging voltage of the 0.2 farad electrolytic capacitors. These three levels were 132, 187, and 214 joules. These energies correspond to charging the capacitor to 36.3, 43.2, and 46.3 volts, respectively. The heater coil and capacitive charging system provide the UUCOM with its stand-alone capabilities. A microcomputer (AIM 65, Rockwell International) was employed to control the capacitor charging/discharging cycle and compute flow from the curve area estimates. A block diagram of the complete instrument is shown in Fig. 1.

The UUCOM also features a unique curve area integration method. This method allows accurate determinations of curve area even in the presence of monotonic drift in the baseline temperature. Further, our integration method is compatible with the multiorder exponential character of our thermodilution curve, while the conventional technique of Hamilton *et al.* (5) is not.

### *The Catheter*

The catheter used in the instrument was a modified Swan-Ganz catheter as is shown in Fig. 2. The heating coil consisted of 10 feet of 0.01 inch Teflon insulated Chromel wire which was wound onto the surface of a conventional Swan-Ganz catheter. The total length of the heating coil when wound was 17 cm (from about 18 cm from the tip of the catheter to about 35 cm from the tip of the catheter). The heat-

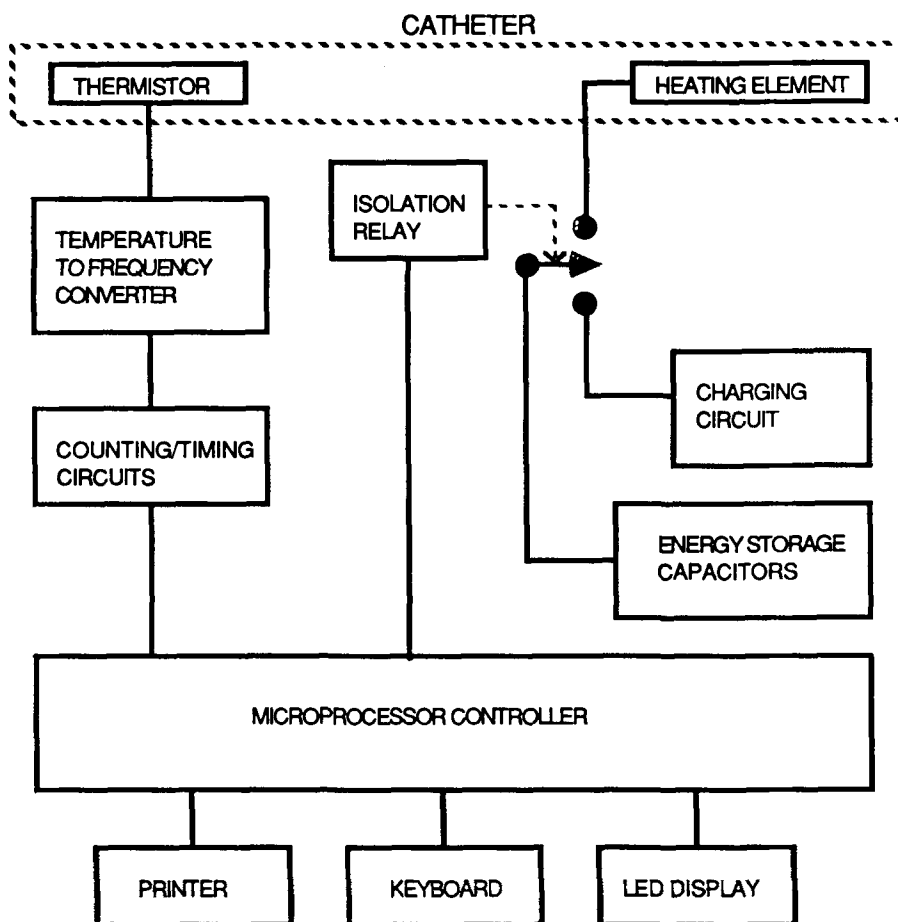


FIGURE 1. Block diagram of the cardiac output computer.

ing coil leads were threaded down the injection port lumen and attached at the center of the coil. The solder joints were insulated with epoxy or lacquer and the entire coil was coated with several layers of Pellethane 1870 in dimethylformamide. The modified catheter was then heated overnight at 60°C to complete the removal of solvent.

Because the lead wires were of a small diameter, 5% of the energy stored in the capacitor was dissipated as heat in the lead wires. Thus, only 95% of the capacitor's stored energy was used in the calculations of cardiac output.

#### *Signal Processing and Control*

The temperature of the pulmonary artery blood was measured with the existing thermistor of the catheter. The resistance of the thermistor was used to modulate a carrier frequency and zero-crossings of the resulting signal were counted by the AIM 65 computer. These counts were not used to compute the thermodilution curve area

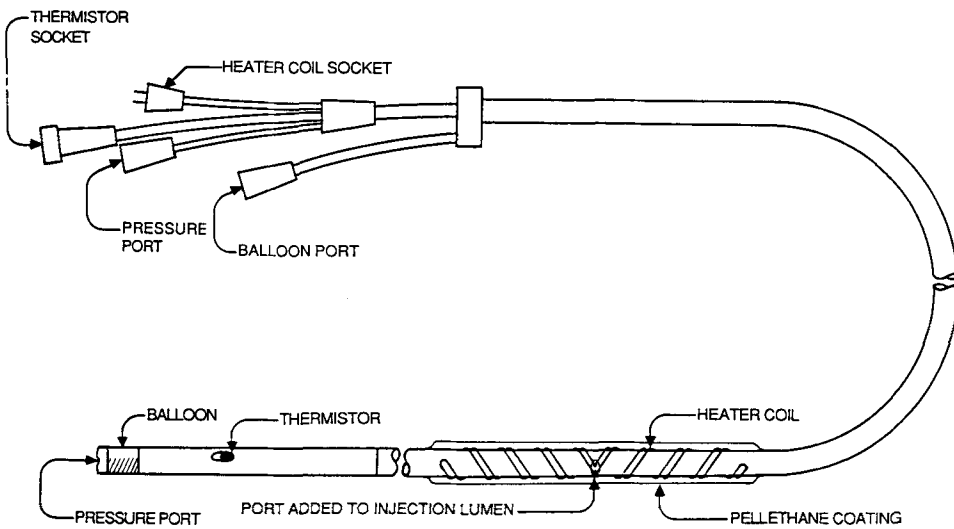


FIGURE 2. Modified Swan-Ganz thermodilution catheter. The main modification consisted of the installation of a resistive heating element on the outside of the catheter.

directly because temperature drifts in the pulmonary artery led to unreliable estimates of the curve area. In order to solve this problem we developed an integration method with band pass characteristics (8). The method is illustrated in Fig. 3. The zero-crossings of the modulated carrier frequency were counted for a period of length  $q$  before and after the thermodilution curve (labeled  $C_A$  and  $C_C$  in Fig. 3), and for a

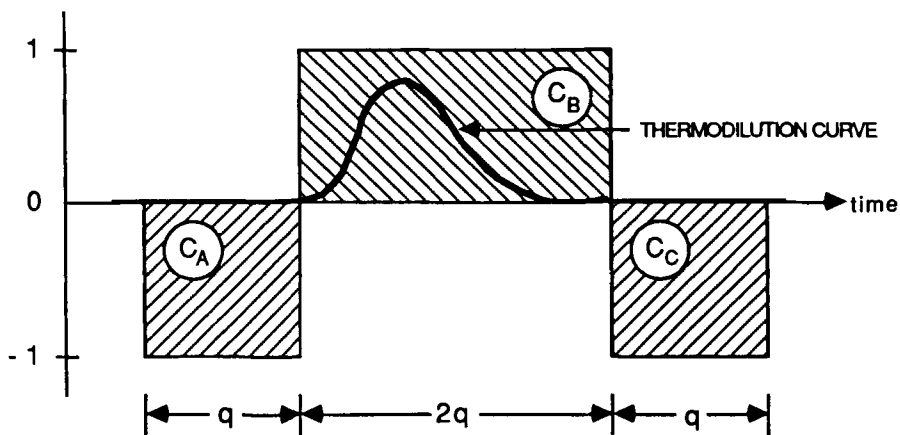


FIGURE 3. The band pass integration scheme employed to estimate the thermodilution curve area. Pulmonary artery temperature was converted into frequency. The zero crossings of the frequency were counted for three time intervals and yielded  $C_A$ ,  $C_B$  and  $C_C$ . Curve area is proportional to  $C_B - (C_A + C_C)$ .

period of  $2q$  over the duration of the thermodilution curve (labeled  $C_B$  in Fig. 3). These counts, which are proportional to area under the temperature curve, were then used to compensate for baseline drift by subtracting  $C_A$  and  $C_C$  from  $C_B$ :

$$C_{\text{curve}} = C_B - (C_A + C_C), \quad (2)$$

where  $C_{\text{curve}}$  is the count proportional to the thermodilution curve area. This integration technique allows the UUCOM to cope with a constant slope baseline drift during the course of the measurement. This integration technique also provides a measure of band-pass filtering to reduce the effects of low frequency temperature fluctuations (8,9). The synchronization of these counting processes, the delivery of energy to the heating coil, and the numerical integration technique were all performed by the AIM 65.

## RESULTS

### *Measurement of Heating Coil Surface Temperature*

The elevated surface temperatures associated with convective heating via a resistive heating element might damage the blood. Further, because of thermal noise in the pulmonary artery, it is desirable to deliver heat energy in as short a time as possible so the thermodilution curve area can be estimated more reliably. Convective heating might produce longer thermodilution curve durations than can be achieved with conventional cold saline injections.

To investigate these issues we measured the surface temperature of the coil by two techniques: thermistors mounted directly on the coil surface and estimation with liquid crystal coatings. A thermistor was mounted on the surface of the heating coil and overlaid with an insulating coating to insure that the thermistor was sensing the coil surface, not flow stream temperature. With this arrangement and a flow rate of 6 L/min we found that a 214 joule heat pulse raised the surface temperature of the coil by 9.8°C. The 9.8°C increase in coil surface temperature would raise the coil *in vivo* to roughly 47°C, which is very close to the 48°C ceiling determined by Thompson (11). The coil temperature increase was also confirmed by applying bands of various cholesteric liquid crystal mixtures (Davis Liquid Crystals, Inc., San Leandro, CA) painted on the surface of the catheter and observing which bands changed color during the heat pulse delivery. We confirmed a coil surface temperature rise of approximately 10°C using this low resolution technique.

The second problem was studied by recording the kinetics of the coil surface temperature as measured with the surface-mounted thermistor described previously. The kinetics of the temperature rise on the surface of the coil in a 6 L/min flow of saline are shown in Fig. 4 and indicate that approximately 90% of the energy is delivered to the flow in 10 seconds. This is sufficiently rapid to allow for flow determinations without significant error due to indicator loss across the vessel walls. The kinetics of the tail of the plot in Fig. 4 are second order exponential and are not appropriate for use with the curve fitting integration method of Hamilton that is used in most conventional thermodilution systems (5).

### *Mock Circulatory Loop*

The linearity of the UUCOM instrument was tested in a mock circulatory loop consisting of a pneumatically driven artificial right ventricle, a compliance chamber,

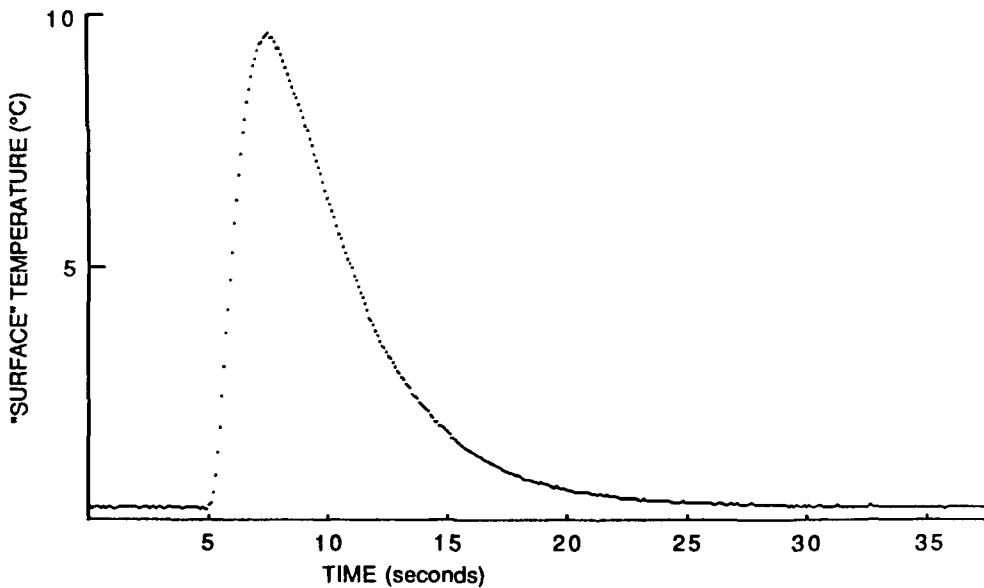


FIGURE 4. The kinetics of the heating coil surface temperature were measured with an insulated thermistor and showed a peak temperature of about 10°C for a 214 joule heat bolus and a flow of 6 L/min.

and normal saline working fluid which was maintained at 37°C. The mock circulatory loop is described in more detail elsewhere (7). Flow rate was varied by modulating percent systole and beats per minute. For each flow rate, flow was determined by timed filling of a measured volume. Figure 5 shows three plots of UUCOM flow determinations versus timed filling measurements. The three plots were made at the three heat energy levels of 132, 187, and 214 joules. The accuracy of the UUCOM measurements can be appreciated by comparison of the data to the unity-slope lines on these plots. The linearity of the device can be seen by the slope, intercept, and correlation coefficient of the linear regression of the data.

The performance of the UUCOM was put into perspective with conventional techniques by comparison to flow determinations made with the Edwards 9520A. Figure 6 shows flow determinations by both the UUCOM and the 9520A versus timed filling measurements. Figure 6A shows the UUCOM determinations made with 214 joule heat pulses over a period of three successive days. Figure 6B shows flow determinations made with the 9520A using 10 cc injections of both iced and room temperature saline during a single day. The reproducibility ( $100\% \cdot \text{STDEV}/\text{AVE}$ ) of the UUCOM measurements was good, typically  $3.2\% \pm 2.2\%$  compared to  $5.8\% \pm 2.7\%$  for the 9520A. This data shows that in the mock circulatory loop the UUCOM performs as well, if not better than, the 9520A.

#### *Animal Trials*

We also evaluated the UUCOM in a series of experiments on six large (27 to 43 kg) mongrel dogs. These experiments were of two classes: reproducibility experiments

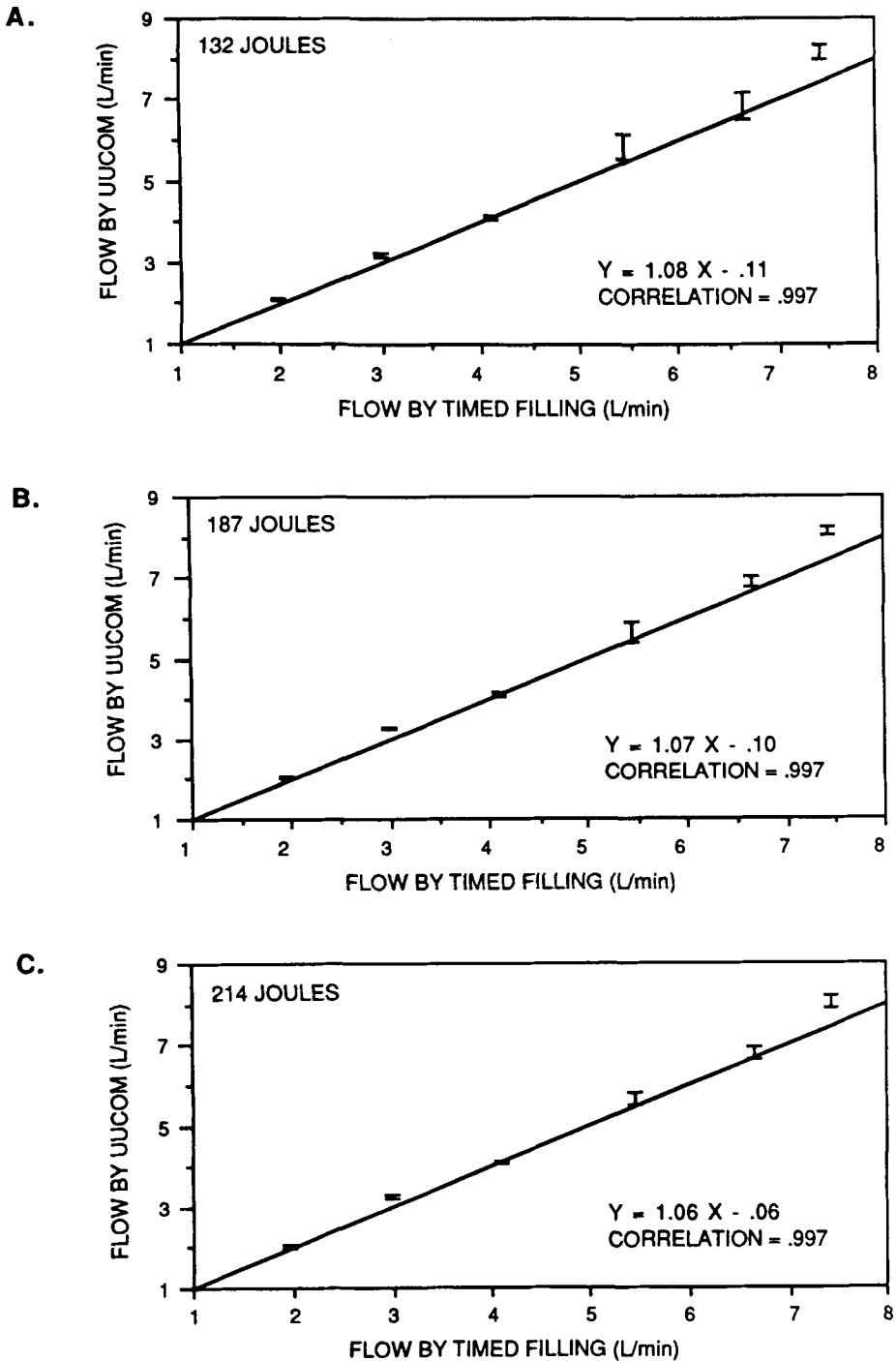


FIGURE 5. The linearity and reproducibility of flow determinations made by the UUCOM at three heater coil energy levels. Flows were measured for six sets of fixed mock circulatory loop settings by the UUCOM and by timed fillings of a volume of working fluid. The equation in each figure shows the linear regression of the data. Also shown are the correlations of the data.



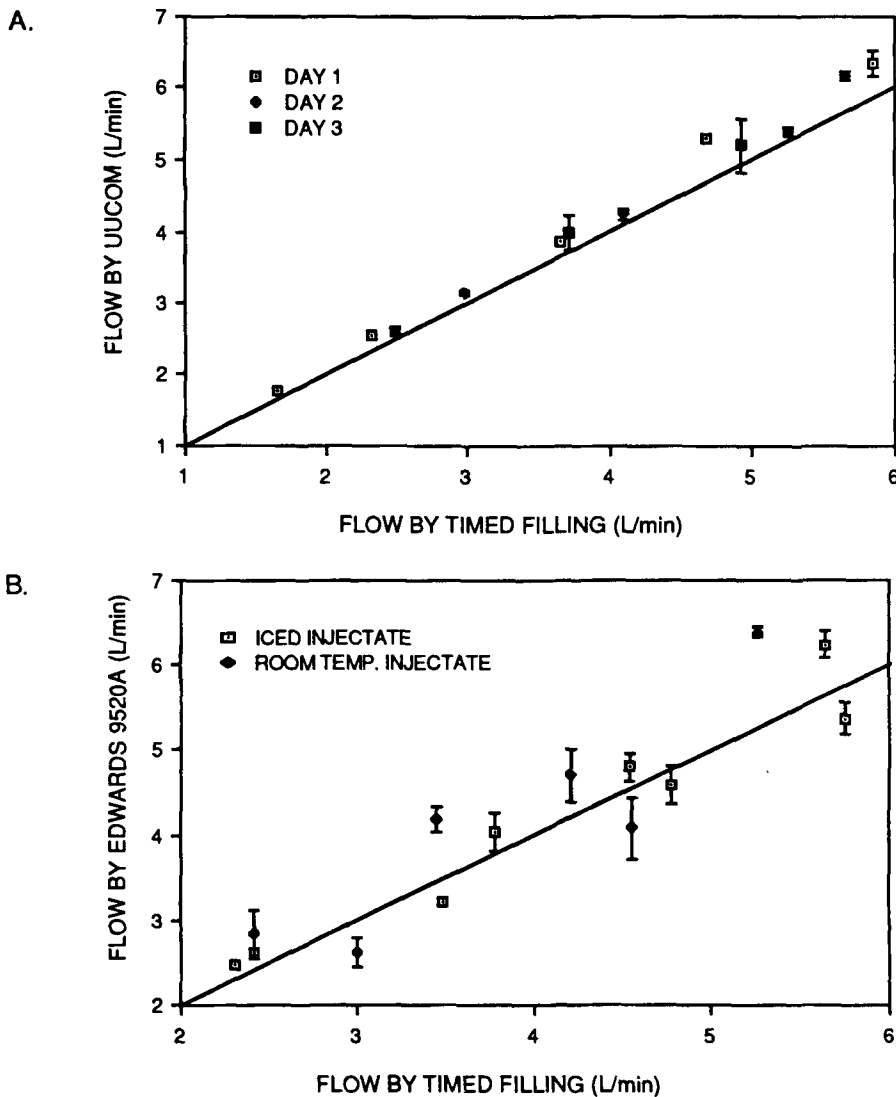


FIGURE 6. Flow determinations made by the UUCOM (6A) and the Edwards 9520A (6B) versus flow determinations by timed fillings of a volume of working fluid. The data in 6A were recorded with 214 joule heat pulses on three successive days, while those in 6B were recorded with 10 cc injections of either iced or room temperature injectate in a single day. The temperature of the mock loop was maintained at 37°C.

where the UUCOM was operated in a stand-alone mode and data was acquired for a period of up to 13 hrs and comparative experiments where a series of UUCOM determinations were compared to a series of 9520A determinations.

The dogs were induced with intravenous injections of Acepromazine and Nembutal and maintained on a Nembutal IV drip into a forelimb of the animal. The animals were intubated and either mechanically ventilated or allowed to breathe spon-

taneously. The catheter for the UUCOM was inserted into a femoral vein and floated into the pulmonary artery. A ligature was used to secure the catheter in the vessel. For conventional thermodilution flow measurements, a second catheter was used for injection of iced saline into the right atrium.

A series of consecutive determinations of cardiac output by the UUCOM over 13 hours in one dog are shown in Fig. 7. Figure 7A is a plot of cardiac output determinations made by the UUCOM. Determinations were made on minute by minute basis with a heater coil energy level of 214 joules. The plot illustrates the variability of the data taken in this particular experiment. The data shown in Fig. 7A are typical of UUCOM performance *in vivo*. The coefficient of variation in this data set was larger than was typically seen in the mock circulatory loop trials. The higher variability could be due to either baseline noise in the pulmonary artery temperature or changes in actual flow. Figure 7 also indicates that the cardiac output measurements

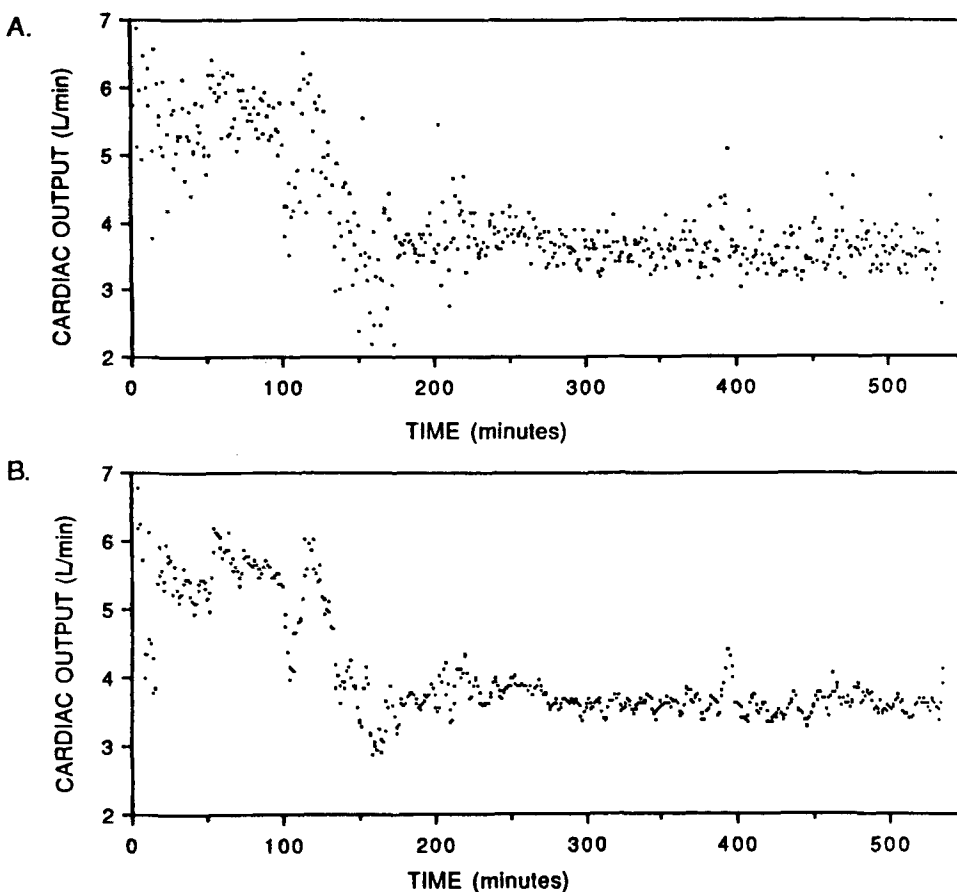


FIGURE 7. *In vivo* determinations of cardiac output in a dog over a nine hour period. Determinations were made on a minute by minute basis with a heater coil energy level of 214 joules. (7A) Successive determinations of cardiac out put. (7B) Same data as in 7A but displayed as a moving average of four successive determinations.

early in the experiment and at the end of the experiment manifested considerably more variability than those taken in the middle. The mechanisms underlying this increased variability are unclear. Figure 7B shows the same data set after moving average smoothing with a width of 4 samples. The moving average smoothing reduces the data scatter to the point that underlying trends can be easily detected. This data clearly demonstrates the feasibility of continuous stand alone monitoring of cardiac output.

In order to assess whether the variability shown in Fig. 7A was a function of the UUCOM or reflected variations in the animal's cardiac output, an experiment was conducted where multiple determinations of cardiac output were made with the UUCOM and compared to multiple determinations with the 9520A. The UUCOM measurements were made using an energy level of 214 joules while the conventional determinations were made with the 9520A using 5 cc of 0-4°C saline, which is equivalent to a 728 joule bolus. The comparison was made at three times during the course of the twelve hour experiment. The first two comparisons were separated by 6 hrs and the dog was mechanically ventilated during the flow determinations. The last determination was made after another 5 hrs and the flow determinations were performed with the dog spontaneously breathing. The results of this experiment are shown in Table 1.

The data of Table 1, average cardiac output (AVECO), standard deviation of the determinations (STDEV), and coefficient of variation ( $CV = 100\% \cdot STDEV / AVECO$ ), indicate that the variability observed with the UUCOM was also seen with the 9520A. The reproducibility of the UUCOM was as good or better than the 9520A. The data also suggest that determinations are more reproducible in mechanically ventilated dogs. This reflects an underlying problem in thermodilution; temperature in the pulmonary artery is not constant. The temperature fluctuations arise from respiratory events which, in spontaneously breathing animals, manifest aperiodic breathing interspersed with large amplitude sighs (1,6,12). The sighs produce large amplitude temperature fluctuations (6) and consequently the lower reproducibility of cardiac output measurements in the spontaneously breathing animals.

The UUCOM has three energy levels which are under the control of the user. This feature was incorporated in the instrument to better assess the impact of pulmonary artery temperature noise on reproducibility by allowing for experimental control of the size of the signal relative to the thermal noise. Table 2 shows average, standard deviation, and coefficient of variation of nine consecutive readings of the UUCOM

TABLE 1. Performance of 9520A versus UUCOM.

No. Determs	Vent.	9520A			UUCOM		
		AVECO (L/min)	STDEV (L/min)	CV (%)	AVECO (L/min)	STDEV (L/min)	CV (%)
10	Mech.	2.65	0.15	6.0	2.88	0.13	4.8
10	Mech.	2.05	0.09	4.2	2.0	0.06	2.9
20	Spont.	2.34	0.19	8.1	2.85	0.21	7.3

at each of the three energy settings. Table 2 shows a trend of improvement in reproducibility with increased delivered energy. The table also indicates that the averaged cardiac output determinations are independent of the delivered energy level.

### *Biocompatibility*

The biocompatibility of convective blood heating was also a concern. In none of the 12 animals studied did we experience any cardiac rhythm problems that were due to current leakage from the heating coil. At the end of each experiment, the animal was heparinized, euthanized, and autopsied. All catheters were left in place to assess thrombus formation on the coil. The femoral vein was exposed from the abdomen and longitudinally transected to reveal the heating coil *in situ*. Large thrombi were found at the insertion site in the femoral vein where a condition of flow stasis was produced by the ligatures securing the catheter. However, the whole length of the catheter in the inferior vena cava showed only minor thrombus formation even on the surface of the heating coil.

To further assess the possible problems with surface heating and thrombus formation we built a catheter which had a second unheated coil mounted proximal to the primary heated coil. After 9 hrs of continuous cardiac output determinations, this animal was sacrificed and the catheter exposed. The unheated coil showed slight thrombus formation while the live coil showed none. This index of biocompatibility suggests that the surface temperatures of the coil do not induce thrombus formation. Similarly, analysis of haptoglobin levels and cell counts during this and other dog experiments showed no significant changes that were not attributable to the introduction of a nonsterile object into the dogs' blood stream.

## DISCUSSION

The approach we have used to continuously monitor cardiac output has been validated in both a mock circulatory loop and animal trials. The reproducibility and linearity of cardiac output determinations made with the UUCOM compare favorably with determinations made with the 9520A. The limited biocompatibility assays that we performed (hematology and direct visualization of the *in situ* catheter) suggest that continuous thermodilution cardiac output monitoring with energy delivery via resistive heating may be no more thrombogenic and hemolytic than conventional thermodilution techniques. Further, the use of an energy storage capacitance, an isolation relay, and double insulation of the heating coil and lead wires reduces the

TABLE 2. Variability of cardiac output measurements versus bolus energy.

Energy (joules)	AVECO (L/min)	STDEV (L/min)	CV (%)
132	2.77	0.32	12
187	2.75	0.24	8.4
214	2.77	0.11	3.9

likelihood of electrical shock hazard while simultaneously assuring the accurate and reproducible delivery of thermal energy.

The use of a system similar to the UUCOM for human cardiac output monitoring should be considered with caution and would require additional study. The coefficient of variation of the determinations should be better than the typical 6% *in vivo* that we have been able to demonstrate with the UUCOM using the 214 joule energy level. At this energy level the coil surface temperature has been shown to increase by approximately 10°C which approaches the limit for blood damage. Therefore, in order to obtain some safety margin the energy level needs to be reduced which will similarly reduce the signal to noise ratio of the measurement.

In order to achieve better reproducibility with a reduced bolus energy level, an effective noise reduction technique is needed. One technique we have considered is subtractive cancellation, whereby a prediction of the temperature noise in the pulmonary artery is subtracted from measured pulmonary artery temperature to reduce the effective baseline noise. We have been working on methods to accomplish this based on knowledge of inferior vena cava and superior vena cava temperatures measured upstream of the heating element. The subtractive cancellation strategy has been shown in mock circulatory loop experiments to have the potential to improve the signal to noise ratio by 35 dB (8). Subtractive cancellation, if applied to the UUCOM *in vivo*, should allow us to achieve the goal of improving reproducibility with reduced energy levels.

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