Development of an instrument to indirectly monitor arterial pCO_2 during cardiopulmonary bypass

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Arterial blood carbon dioxide tension (P_aCO_2) during cardiopulmonary bypass (CBP) is important to the conduct of perfusion with alpha-stat or pH-stat strategy. Temperature changes during CBP complicate any attempts to monitor carbon dioxide tension in the exhaust outlet of an oxygenator ($P_{ex}CO_2$) because CO_2 becomes more soluble with decreasing temperatures. Normally, this would have been the obvious and easy choice of method to indirectly measure the patient's P_aCO_2.

Several tests have been performed with ordinary capnographs modified to measure pCO_2 at the oxygenator exhaust gas port. These tests have shown varying degrees of precision (*Br J Anaesth* 1999; 82(6): 843–46; *J Extra-Corpor Technol* 2003; 35(3): 218–23; *Br J Anaesth* 2000; 84: 536; *J Extra-Corpor Technol* 1994; 26: 64–67). Some of the best results have been achieved by Potger *et al*. (*J Extra-Corpor Technol* 2003; 35(3): 218–23), who found a strong correlation between the arterial temperature-corrected $P_{ex}CO_2$ when using a standard capnograph monitoring the P_aCO_2 measured from a blood gas analyser (P_bCO_2).

Our group has developed a new instrument, especially designed for oxygenator gas exhaust monitoring. The new instrument has automatic temperature correction, enabling it to show both original and corrected pCO_2 values, simultaneously. Ordinary capnograph functions, such as zeroing, flow control and calibration routines, are included. The solution consists of a pCO_2 sensor module, a temperature sensor, a water trap and a dedicated PC mounted on a heart-lung machine. Since the heart-lung machine was already equipped with a computer for data logging and a temperature sensor, only a box containing the pCO_2 sensor module and the water trap had to be added.

The PC uses a specially written program designed to collect data, make the necessary calculations and display the results on the computer screen. A temperature correction was developed based on a linear regression analysis for a data-set of 15 patients, assuming that the deviation between the measured $P_{ex}CO_2$ from the oxygenator exhaust outlet and the P_bCO_2 from the blood gas analyser was linearly dependent on arterial temperature alone.

Eighty-six blood gas samples were compared to the corrected $P_{ex}CO_2$ values. The final product displayed good qualities of stability and was accurate when temperature fluctuated from 32 to 38°C, even during rewarming, which has been reported to be a problem for other $P_{ex}CO_2$ investigations (*J Extra-Corpor Technol* 2003; 35(3): 218–23). *Perfusion* (2006) **21,** 13–19.

Introduction

Alpha-stat and pH-stat are used as strategies to manage pH while the patient is cooled during cardiopulmonary bypass (CBP). For the alpha-stat strategy, pH is varied with an approximately constant arterial blood carbon dioxide tension (P_aCO_2) value while pH-stat requires a constant pH level with varying P_aCO_2 levels. For both strategies, P_aCO_2 monitoring is of interest. There are two different ways to monitor the arterial CO_2; either with the use of a regular blood gas analyser or with highly specialized invasive monitoring equipment. Both methods give reliable results, but tend to have some drawbacks in practical use. The major objection to both methods is the overall expense attendant with the two methods. Blood gases are relatively expensive and have to be measured repeatedly during the surgical procedure. Invasive inline monitoring equipment is usually able to monitor P_aCO_2 continuously with other blood parameters, but disposables raise expenses considerably. The ideal solution is a low-cost instrument that is able to give reliable, continuous CO_2 measurements without expensive disposables.

There have been numerous attempts to fulfil the ideal solution with modified capnographs connected to the exhaust port of the oxygenator. Conclusions have varied from a total rejection of the

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principle,[1] to significantly good results, a cautious recommendation of the method and a request for further investigations.[2–4] Our aim has been to develop a new P_aCO_2-measuring instrument customized for the exhaust port of the oxygenator. Furthermore, we sought to prove that this principle is feasible for clinical use.

Method

The development of the instrument was divided into three steps. The first step was creating a solution with a stable, non-pulsatile, controllable pCO_2-measuring instrument. Most capnographs on the market are designed for measuring the pCO_2 in each breath of a respiratory cycle, and are, thus, unsuitable for measuring a laminar flow from the exhaust port of an oxygenator. This instrument was equipped with a user-friendly interface connected to the oxygenator exhaust outlet. The next step was a clinical trial with a comparison between the measured $P_{ex}CO_2$ and P_aCO_2 from blood gases in order to develop an algorithm for temperature compensation. Standard blood gas P_aCO_2 was considered as the gold standard. The final step was a clinical trial to verify the precision of the instrument with the temperature algorithm developed in step two.

The first step was to find an accurate, cheap and controllable pCO_2 sensor. Extensive searches were made, and two good candidates from Square One Technology (later Dolphin Medical Sensors, Hawthorn, CA, USA) and CardioPulmonary Technologies Inc. (Sussex, WI, USA) were found. Both could offer a small, low-power and fully digitalized infra-red (IR) side-stream gas analyser for a reasonable price. Square One's 2125 non-dispersive IR (NDIR) detector CO_2/N_2O sensor was chosen, mainly because of the suitable command set, high accuracy and good technical support.

The main principle of a NDIR pCO_2 analyser is to take advantage of the high spectral absorption in the CO_2 gas for the IR range at 4.26 μm. Various gases indicate substantially increased absorption characteristics at specific wavelengths in the IR spectrum, and higher gas concentrations exhibit proportionally and greater absorption. Infra-red power pulses travel through two parallel cells, one of which includes a test cell with a sample of the gas mixture to be analysed, and one reference cell with a reference sample. An alternative solution with only one cell is possible if both sample gas and reference gas are inserted into the chamber alternately, similar to Square One's 2125 patented sensor.

The digital IR side-stream gas analyser is connected to the exhaust outlet from the oxygenator through a plastic tube mounted at the bottom of the oxygenator (Figure 1).

The Square One 2125 CO_2/N_2O gas analyser communicates with the PC through an RS-232 serial interface (Distributor for Motorola 68331). All communication with the sensor is executed through this interface, controlled by a Motorola 68331 microprocessor. A great variety of functions and outputs can be assessed through the interface, from calibration to flow control. After the necessary initializing of the serial port, all commands can be addressed to the unit by sending an ASCII code, typically a two-character code for each function. Response

Figure 1 Overview of the capnograph set-up.

from the sensor follows a strict pattern where the position of a character decides the significance of the output. All communication and set-up routines are fully automated, the only manual action needed from the perfusionist is to insert the sample line into the oxygenator and switch on the capnograph.

Correct pCO_2 values can be presented as soon as the temperature is accessible. No pulsatile CO_2 levels are expected and no apnea alarms or any non-laminar effects will occur. When results are acquired on the PC, calculations and rendering are performed and the actual $P_{ex}CO_2$ value is presented on the computer screen as a virtual instrument (Figure 2). All communication with the gas analyser is executed through the virtual instrument interface on the computer screen, which allows the user to control the gas analyser, similar to a real device. Several functions can be performed, such as zeroing, calibration and unit and gas flow selections, in order to optimize the capnograph appearance and the functionality of the device.

The second step was a small clinical trial including 10 patients, where arterial temperature along with other relevant parameters were collected in order to prepare a base for developing a correction algorithm. These parameters were entered into a statistical computing program (SAS version 11, SPSS Inc., Chicago, IL, USA) and correlation studies were performed. Statistical analysis showed that arterial temperature was strongly correlated to the $P_{ex}CO_2$ discrepancy and this parameter was chosen as a variable for the correction algorithm.

Step three was then initiated to evaluate the algorithm we found in step two. Samples were taken regularly at 32, 35 and 38°C, analysed on an ABL 725-blood gas analyser (Radiometer, Copenhagen, Denmark) and compared to values read from the specialized capnograph.

Results

We used the Dideco Avant 903(d-903) hollow-fibre oxygenator (Dideco, Mirandola, Italy) as oxygenator of choice, mainly because this was the commonly used oxygenator for adult patients in our hospital. After initial testing without patients, but with two oxygenators connected in series, as oxygenator/deoxygenator, we accomplished a test of 20 patients to reach the first milestone, which was to develop a stable, controllable and user-friendly capnograph and to build a data set for developing the correction factor. The disappointing results can be seen in Figure 3. There were apparently no stable correlations between the measured $P_{ex}CO_2$ as a function of temperature and the blood gas P_aCO_2.

Investigations were made and two possible sources of error were revealed. There was no water trap in the gas circuit at the capnograph inlet, only a simple humidity filter. This filter tended to increase the internal flow resistance as it absorbed the humidity in the gas tube. No passage at all was experienced in an extreme case during a long-lasting perfusion. This filter, which was one of the original accessories shipped with the CO_2 sensor, was replaced with a new water trap from Micro Medical Ltd, Rochester, Kent, UK.

The second source of error was the placement of the sample tube in the oxygenator gas outlet. We made a plastic tube with the sample tube mounted in the middle, and mounted the plastic tube on the oxygenator gas outlet, as shown in Figure 4.

We suspected room air was being pulled into the sampling line together with the exhaust gas from the oxygenator, and decided to remove the plastic tube and insert the sample line directly into the oxygenator's exhaust chamber, as shown in Figure 5.

It is extremely important not to obstruct the exhaust gas flow from the oxygenator. If obstruction occurs, pressure may rise inside the hollow-fibre membrane oxygenator causing penetration of gas bubbles into the arterial line. As can be seen from Figure 5, the sample line is far too slim to obstruct the gas flow and there are also several independent gas outlets at the bottom of the oxygenator in addition to the exhaust port. Obviously, there is no risk of pressure gradients over the membrane.

Another topic is sterilizing considerations. The sample line is originally not sterilized, but is

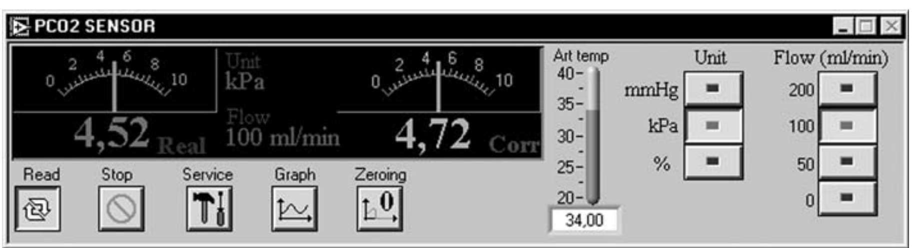

Figure 2 The virtual instrument as shown on the computer screen. All buttons can be pushed as for a regular device.

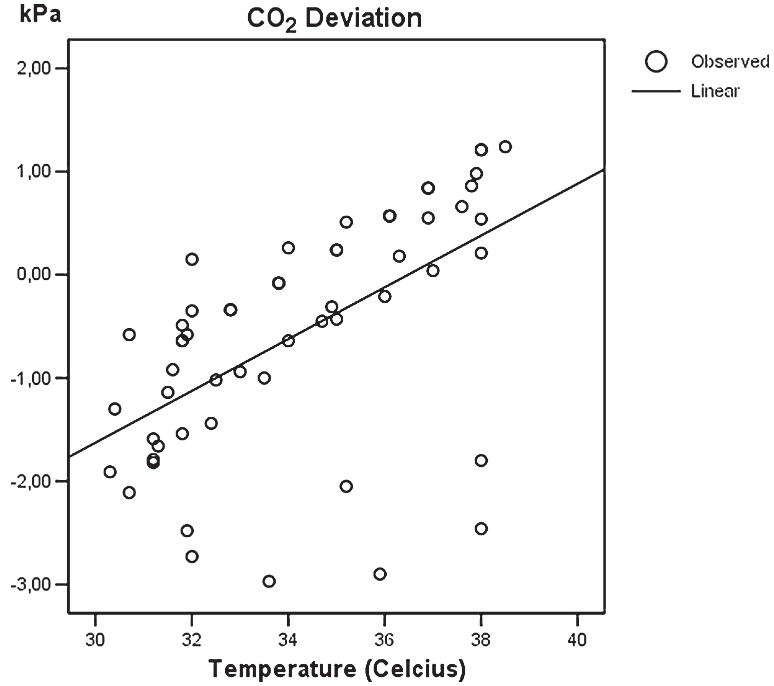

Figure 3 Regression plot for the deviation as a function of arterial temperature. The sample line is located outside the oxygenator exhaust chamber, as shown in Figure 5. The linear expression is given by $Y = -9.152 + 0.251{*}\text{Temp}_{\text{arterial}}$ and $R^2 = 0.323$.

inserted into a sterilized device, which means that the sample line needs a sterilization routine before it can be assembled into the exhaust port. There are several ways to sterilize a sample line, but the long flexible tube and the moisture filter complicate the sterilization process. The most suitable process for our purpose is gas plasma sterilization. Plasma sterilization is a fast and low-temperature process, well suited for long tubes when used in combination with a booster. The booster is mounted in the end of the sample line and ensures enough flow of H_2O_2 through the entire flexible tube. We used a Sterrad 100S Gas Plasma sterilizer (ASP c/o Ethien GmbH, Hamburg, Germany) for sterilizing the water trap.

When these two modifications were put into action, results improved dramatically, as can be seen in Figure 6. It was now time for step two, calculation of a temperature correction factor to compensate for unwanted temperature effects on the $P_{ex}CO_2$ measurements. Based on linear regression, a correction factor was found:

$$\text{pCO}_{2\ \text{adjusted}} = \text{pCO}_{2\ \text{measured}} + (0.240 \times \text{Temp}_{\text{arterial}}) - 8.23$$

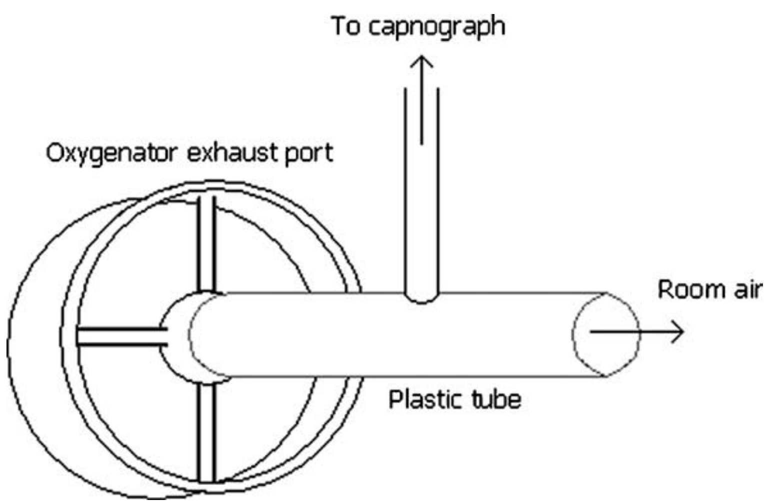

Figure 4 Detail of the gas outlet of the oxygenator with an improper placement of the sample tube, which leads to erroneous measuring results.

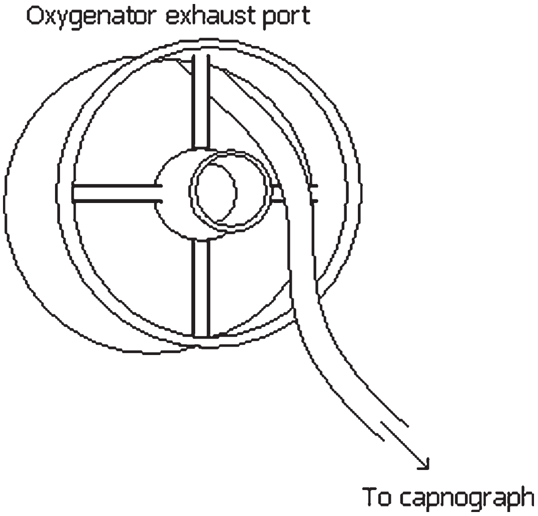

Figure 5 Detail of the gas outlet of the oxygenator with the correct placement of the sample tube.

The corrected values and other results are shown in Table 1.

There is a good correlation between the corrected values and the measured blood gas pCO_2 values. Standard deviation is 4.1%. For the follow-up group, results were even better, with a standard deviation of 3.6%. These results lead to the conclusion that the invented instrument is a stable and accurate supplement to or substitute for other complex and expensive measuring methods for P_aCO_2 measurements during CBP.

The device is a typical low maintenance instrument. Three factors should be controlled regularly: pressure verification, flow verification and calibration of CO_2 sensor. Pressure and flow are controlled with sensors not likely to fluctuate much, but calibration of the CO_2-sensor must be performed regularly. The manufacturer recommends a calibration interval of 1 year for the CO_2 sensor, and even more infrequently for pressure and flow. Calibration and verification is performed by pushing the 'Service'-button (Figure 2) and choosing the desired function. When calibration is selected, the calibration gas should be allowed to flow through the device for 1 min. After 1 min, the user will be prompted for the percent CO_2 in the calibration gas and the calibration procedure is completed. No maintenance is necessary for the water trap as it is used as a disposable and is changed for every patient.

Another topic of interest is the ergonomics. Heart-lung machines are already quite overcrowded with different types of hardware, and additional equipment is undesirable. Since the computer for data logging is already in place, the only new hardware needed to be introduced is a plastic box measuring $9 \times 16 \times 12$ cm (height × width × depth) and a water trap. In our setup, the device was placed under a shelf near the oxygenator, as shown in Figure 1. This configuration has several advantages, the device is close to the oxygenator, protected from liquids and

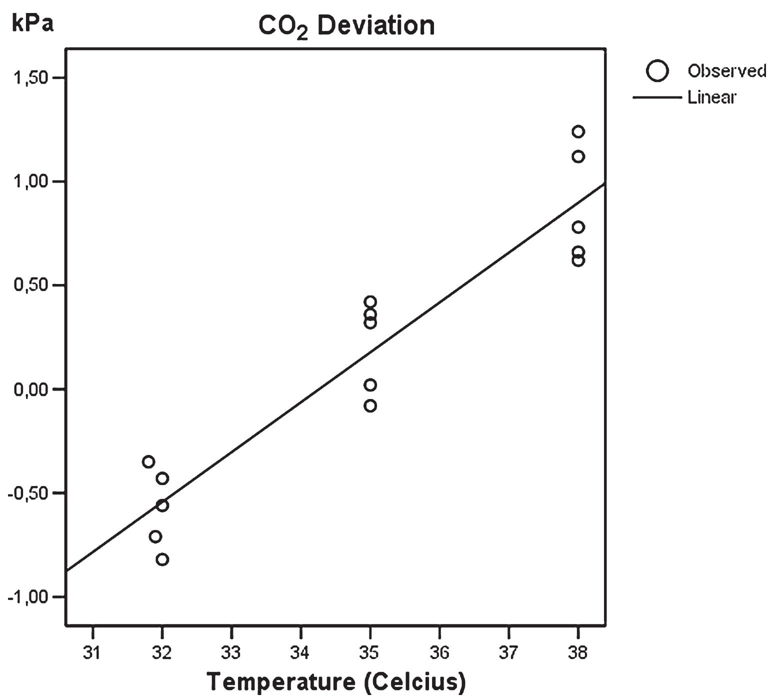

Figure 6 Regression plot for the deviation as a function of arterial temperature. The sample line is located inside the oxygenator exhaust chamber. The linear expression is given by $Y = -8.23 + 0.24{*}\mathrm{Temp}_{\mathrm{arterial}}$ and $R^2 = 0.885$.

Table 1 Summary of pCO_2 tests

Linear regression for sample line	*No. of patients*	*Mean absolute error (kPa)*	*Standard deviation (kPa)*	*Standard deviation (%)*	*Maximum absolute error (kPa)*
Outside the exhaust chamber	20	0.67	0.92	7.3	2.84
Inside the exhaust chamber	10	0.20	0.22	4.1	0.27
Inside the exhaust chamber follow up	5	0.14	0.19	3.6	0.47
Inside the exhaust chamber follow up without temperature correction	5	0.34	0.34	6.4	0.91

dirt, and not interfering with the other equipment on the heart-lung machine. It is important to stress that the device is a prototype and that a stand-alone device is being developed.

Discussion

Whether or not the result from this study is transferable to other types of oxygenators has yet to be proven. We have focused on one single oxygenator, Dideco Avant 903(d-903), and other oxygenators may differ regarding pCO_2 equilibrium and other factors that might affect the measurement. Ideally, there should be a follow-up study with different categories of patients and oxygenators to verify that the developed capnograph is suitable for all combinations of equipment and patients. It is reasonable to believe that there should be no difference between different patient categories. Naturally, there will be different blood characteristics between patients, but we have not found good correlation between other measurable blood parameters and the divergence between measured $P_{ex}CO_2$ and P_bCO_2 from the blood gas analyser.

More likely is a dependence of oxygenator type. Oxygenators of the same type show the same characteristics and will have the same regression line. This indicates that the regression line is calculated for one oxygenator type based on a set of five to 10 patients. The pre-calculated regression line is used in the device for all future procedures using the actual oxygenator type. Carbon dioxide exchange in the membrane might vary from oxygenator to oxygenator, especially when considering oxygenators with fundamentally different constructions. Still, discrepancy between $P_{ex}CO_2$ measurements for different types of oxygenators is expected to be approximately linear. There is no reason to believe that other oxygenators should introduce any considerable new non-linear elements that are not present in our study. If so, a type-specific linear factor should be sufficient to maintain accuracy and reliability for the capnograph.

Another topic of interest is the dependence of a good water trap. The pCO_2 sensor that was chosen is based on IR absorption in gases, and a problem is the condensation on the windows used for separating the gas passageway from the IR light source and the IR detector. Even a good water trap cannot be expected to remove all moisture from the sample gas, and condensation must be expected for long-lasting interventions. During re-warming, this risk is especially considerable, and may explain the increased variance we observed during re-warming from 32 to 38°C. Thus, less suitable water traps may give increased discrepancy and instability in $P_{ex}CO_2$ measurements, and this effect should be taken into consideration when a capnograph setup is evaluated. The device works fine, even during long bypass procedures (more than 2 h) with large temperature variations, but a slightly increased error between the measured $P_{ex}CO_2$ and the P_aCO_2 from the blood gas analyser can be observed.

We have not scrutinized the possible connection between room temperature and condensation inside the device. There are several reasons why this was not a topic for this study, but the main reason was that the results were accurate enough for clinical purposes even when room temperature was lowered to 16°C. However, it is possible there is a relationship between room temperature and $P_{ex}CO_2$ divagation, but, from our findings, this contribution to the total error is believed to be marginal.

The position of the sample line is crucial for obtaining a correct pCO_2 value. However, the major difference seems to be if the sample line is placed inside or outside the exhaust chamber. In our study, the sample line was positioned approximately 5–10 mm inside the exhaust chamber, but the exact position would differ slightly from time to time. However, no reposition has been necessary so far, indicating a positioning success rate of up to 100%. A minor difference in the $P_{ex}CO_2$ measurements as a result of varying positions is not impossible, but is believed to be negligible, according to the data from the test patients.

Accuracy is crucial for establishing a reliable capnograph. Potger *et al.*[2] had an overall precision of 95% for samples 4.7 mmHg above or below, while Weightman and Sheminant had a precision of ±5.0 mmHg.[3] The average precision for our patients with temperature correction was 0.21 kPa, or approximately 1.58 mmHg. However, there are some differences between the studies. Firstly, we sampled at 32, 35 and 38°C, while Potger *et al*. also monitored patients at deep hypothermia down to 25°C. The basis for the temperature correction algorithm is linear regression, which means that we assume a linear relationship between the divagation and the temperature. Other studies have indicated that this assumption might be valid for minor temperature variations, but not for larger temperature variations.[4] This difference in the temperature span might be an important contributor to the decreased accuracy for other studies.

Another difference between the studies is the number of patients included in the study. While we had a total of 86 blood gas samples in our study, Potger *et al*. had a total of 157 blood samples.[2] The overall accuracy is, of course, dependent on the number of samples; the risk of spreading samples increases when the total number increases. On the other hand, Weightman *et al*.[3] and McCloskey *et al*.[4] had fewer patients, 19 and 26, and less accuracy in their studies compared to our results.

Conclusion

Monitoring of $P_{ex}CO_2$ levels from an oxygenator gas outlet with a dedicated instrument with online temperature correction is a cheap, simple and reliable alternative to other methods, such as blood gas analysis and various invasive arterial line measuring devices. The cost of production of the unit is relatively low, and the only disposable is the simple plastic line with a water trap – approximately €20 in our hospital. This water trap is cheaper than the expensive disposables belonging to invasive measuring methods, like the Terumo CDI-500 (Terumo, Mirandola, Italy). Still, more studies are needed to identify any possible differences between various types of oxygenators, temperatures and patient categories. Our data set indicates that temperature is the major contributor to the observed $P_{ex}CO_2$ discrepancy, but we are still receptive to the suspicion that there might be other type-specific contributions to the $P_{ex}CO_2$ discrepancy. The accuracy of the specialized instrument is higher than any other study regarding oxygenator exhaust capnography that we know, and this has convinced us that this type of instrument has a future in CBP operations.

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