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REVIEW ARTICLES

Continuous intravascular blood gas monitoring: development, current techniques, and clinical use of a commercial device

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This review focuses on the development, current techniques, and clinical use of continuous intravascular blood gas monitoring (CIBM) devices in anaesthesia and intensive care. The operating principles, range of application, performance, limitations, costs, and impact on patient treatment and outcome, are discussed. Studies of early and currently available CIBM devices were analysed. At present, the Paratrend 7+® (PT7+®) for adults and Neotrend™ (NT™) for newborns are the only commercially available CIBM systems. The PT7+® contains three optical sensors to measure P_{O_2}, P_{CO_2} and pH, as well as a thermocouple to measure temperature. The NT™ is a modification of the PT7+® to continuously monitor P_{O_2}, P_{CO_2}, pH and temperature in newborns. Under laboratory conditions, good performance over a wide range of blood gas values was observed with the Paratrend 7® (PT7®). Performance in the clinical setting was not as satisfactory, especially for P_{O_2} values. However, the performance and accuracy of CIBM devices appear to be sufficient for clinical use and they are being used clinically in selected patient groups. Several factors affecting the performance of CIBM are considered.

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Arterial blood gas analyses are essential to monitor gas exchange in critically ill patients and during anaesthesia for major surgery. Usually, arterial blood samples are drawn intermittently and analysed in a central laboratory or by a point-of-care blood gas analyser. Several problems associated with intermittent sampling have been described: indications for sampling are vague; analyses are often performed only after adverse events; sample transportation and analyses may be problematic; a therapeutic response can only be made after a delay; and there is a risk of blood loss and infection.[5 15 26 39 60]

Pulse oximetry, capnometry and transcutaneous blood gas measurement have been used for many years to assess gas exchange continuously and non-invasively. However, these non-invasive methods cannot fully replace arterial P_{O_2} ($P_{a_{O_2}}$), arterial P_{CO_2} ($P_{a_{CO_2}}$), and arterial pH (pHa) analyses in the clinical setting because of their significant limitations.[16 54 83] Oxygen saturation assessed by pulse oximetry ($S_{p_{O_2}}$), or intravascular arterial oxygen saturation ($S_{a_{O_2}}$) sensors cannot detect a high $P_{a_{O_2}}$, and definition of a safe lower saturation limit is difficult.[61 70 72] Moreover, pulse oximetry may display erroneous readings in the presence of dyshaemoglobinaemia, dyes (e.g. methylene blue, indigo carmine, indocyanine green), ambient light, low peripheral perfusion, motion artefacts, and other technical problems.[4 79] Measuring end-tidal CO_2 concentration by capnometry only provides an accurate estimation of $P_{a_{CO_2}}$ in intubated patients with normal pulmonary function, a normal ventilation–perfusion ratio of the lungs, and normal haemodynamics. However, critically ill patients do have varying pulmonary and cardiovascular derangements, leading to unreliable end-tidal CO_2 values. Transcutaneous monitoring of P_{O_2} and P_{CO_2} is known to be accurate in small children, but many factors affect this technology in adults, including patient characteristics (variation in skin thickness, oedema, tissue hypoperfusion, administration of

Table 1 Comparison of optical and electrochemical sensor technology

	Optodes	Electrodes
Miniaturization	Easy	Difficult
Measurement technique	Light	Electrochemical
Interference	Ambient light	Radio frequency emissions
Chemistry of sensor	Change with time, bleaching	Unchanged
Reference electrode	No	Yes
Response time	Limited by membrane	Limited by membrane
Stability over time	High, minimal drifts	Lower, drifts with time
Costs	Expensive	Less expensive

vasoconstrictor agents), or technical problems (trapped air bubbles, improper placement, damaged membranes, inappropriate calibration, and frequent recalibration).[9 55]

During the past decade, marked advances in continuous intravascular blood gas monitoring (CIBM) have been achieved by miniaturization of the sensors measuring P_{O_2}, P_{CO_2} and pH. CIBM appears to be desirable at least in selected patient groups, provided the technique proves to be reliable and cost-effective.

Methods

The literature on CIBM in anaesthesia and intensive care was retrieved using 'Medline' searches (PubMed, National Library of Medicine). The following terms alone and in combination were used: continuous, arterial, intra-arterial, intravascular, blood gas, monitoring, measurement, device, sensor, paratrend, and neotrend. Laboratory and clinical evaluation studies, review articles and studies on risk–benefit, costs and outcome of CIBM were selected. The reference lists of retrieved articles were further studied to complete the search on the topic of this review. Furthermore, manufacturers' instructions were obtained to describe the technology of the currently available commercial CIBM devices.

Statistics

Inconsistencies in the statistical analysis of comparisons between different measurement methods have been addressed by Mantha and colleagues.[41] When assessing new technology, the use of adequate statistical methods and standard nomenclature are essential to draw valid conclusions.

To evaluate a new blood gas measuring device, for example a CIBM device, it should be compared with an established one, such as a laboratory blood gas analyser. Agreement between the two measurement techniques is best described by Bland and Altman analysis.[6–8] The mean difference between values obtained from the new and the established measurement technique is the estimated bias. Measures of dispersion of this difference represent the random error inherent in either or both devices. It is termed precision in some studies. However, precision is a measure of repeatability. In the past, the term precision was often incorrectly defined and was used in the wrong context. It was therefore suggested that this term should be avoided in measurement comparison studies.[41] Instead, upper limit of agreement (ULA) as bias +2 SD and lower limit of agreement (LLA) as bias –2 SD should be used. Bias $\pm$ 2 SD/limits of agreement are only estimates of the values that apply to all the population measured. To know how precise the estimates are, one should also report the confidence intervals (CI). Unfortunately, the correct statistical method has only been applied in a few studies on CIBM.

Development of CIBM

Technology and history

The principles, technology and history of CIBM have been described in detail in previous reviews.[39 57 67 78 80] P_{O_2}, P_{CO_2} and pH can be measured by electrochemical and photochemical/optical sensors (Table 1). If both technologies are combined, it is called a hybrid probe.

Electrochemical sensors

Electrochemical sensors have been used for intravascular P_{O_2} measurement. The principle is a modified Clark electrode.[10] A small polarizing potential is maintained between the platinum cathode and the silver anode. The electrodes are immersed in an electrolyte solution surrounded by an oxygen-permeable membrane. Oxygen diffuses into the chamber, and is reduced at the platinum cathode, producing a current proportional to P_{O_2}.

Photochemical/optical sensors: optodes

Sample chambers containing dyes are illuminated with light of a specific wavelength via optical fibres. The illuminating light will be variably transmitted, reflected, absorbed and re-emitted depending on the concentration of oxygen, carbon dioxide and hydrogen ions. The photochemical changes of the illuminating light will be used to calculate P_{O_2}, P_{CO_2} and pH values.

Early multiparameter CIBM devices

Extensive research was done before commercialization of CIBM technology. Single parameter CIBM devices to measure P_{O_2} electrochemically were developed within a short time of Clark introducing his electrode in 1956.[3 10] Within a decade, Lubbers and Opitz published work on a CIBM probe with optodes to measure P_{O_2} and P_{CO_2}.[36 50] Some years later in 1986, the same group described a multiparameter CIBM probe to assess P_{O_2}, P_{CO_2} and pH optically, and to measure temperature by a thermocouple.[21] These devices preceded the early multiparameter CIBM devices (Table 2).

Table 2 Evaluation studies of early multiparameter CIBM devices. Setting: OR=operating room; ICU=intensive care unit; GS=general surgery; CS=cardiac surgery; CVS=cardiovascular surgery; NS=neurosurgery; OLV=one lung ventilation; ORTHO=orthopaedic surgery. Insertion (site of measurement): RA=radial artery; FA=femoral artery; BA=brachial artery; PA=dorsalis pedis artery; SV=superior vena cava. Application: mean in place duration in h. Recalibration: adjusting the original calibration curve using *in vitro* measured laboratory blood gas determinations

	Setting	Insertion (site)	Subjects (*n*)	Samples (*n*)	Application (h)	Recalibration	P_{O_2}					P_{CO_2}			pH		
							Range (kPa) [mean (min/max)]	Bias	2 SD	Bias	2 SD	Range (kPa) [mean (min/max)]	Bias	2 SD	Range mean (min/max)]	Bias	2 SD
CDI™ 1000 Blood Gas Monitoring System (CDI-3M Healthcare, Tustin, CA, USA)[a]																	
Miller *et al.*, 1987[44]	*In vitro*[b]	–	4	40	–	–	– (2.67/13.33)	–	–	–	–	– (1.33/8.00)	–	–	– (7.05/7.65)	–	–
	Animal, dogs[c]	FA	1	118	4.0	–	– (–/–)	–	–	–	–	– (–/–)	–	–	– (–/–)	–	–
Shapiro *et al.*, 1989[64]	Animal, dogs	FA	6	663	6.0	No	22.15 (3.60/41.73)	–2.27	12.35	–	–	4.53 (2.40/12.27)	0.14	1.01	7.34 (7.05/7.57)	–0.02	0.06
	ICU/OR	RA	12	79	12.6	Yes	12.91 (4.53/32.93)	–0.16	2.49	–	–	5.71 (3.20/8.93)	0.06	0.79	7.43 (7.30/7.62)	0.00	0.04
Mahutte *et al.*, 1990[40]	Volunteers	RA	4	48	–	Yes	– (6.13/84.40)	–0.39	6.77	–5.0	23.6	– (2.93/9.33)	0.10	0.65	– (7.20/7.59)	0.00	0.04
Barker *et al.*, 1991[2]	OR: GS, NS, ORTHO	RA	14	87	4.2	No	– (–/–)	–1.20	6.21	–6.0	20.0	– (–/–)	–0.51	1.25	– (–/–)	–0.03	0.08
Optex Biosentry® System (Optex Biomedical, The Woodlands, TX, USA)																	
Smith *et al.*, 1992[66]	OR: GS, NS	RA	3	13	2.9	Yes	– (–/–)	–1.98	10.46	–	–	– (–/–)	0.41	0.53	– (–/–)	–0.02	0.08
Zimmerman *et al.*, 1993[84]	ICU	RA	5	104	55.4	Yes	– (5.87/34.00)	–0.79	3.52	–	–	– (4.40/9.87)	0.23	1.62	– (7.35/7.52)	–0.02	0.07
PB 3300 System (Puritan Bennett Corp., FoxS Division, Carlsbad, CA, USA)																	
Lumsden *et al.*, 1994[38]	*In vitro*	–	8	–	–	–	– (2.67/33.33)	0.78	0.71	–	–	– (1.33/13.33)	0.26	0.38	– (6.80/7.70)	0.00	0.01
Haller *et al.*, 1994[23]	ICU	RA, BA, PA	13	487	72.0	No	– (4.00/69.60)	–0.32	1.73	–2.8	13.2	– (2.50/11.00)	–0.39	1.04	– (7.23/7.55)	–0.04	0.06
Larson *et al.*, 1994[34]	OR/ICU: NS, CS	RA	29	552	6.0/46.0	No	15.06 (4.27/70.40)	–	–	1.0	30.0	4.93 (3.20/7.20)	0.17	0.88	7.39 (7.23/7.57)	0.01	0.08
Paolillo *et al*, 1994[52]	OR/ICU: CS, CVS	RA	27	283	25.0	–	– (8.80/55.33)	–0.36	3.24	–	–	– (3.20/8.00)	0.12	0.71	– (7.14/7.63)	–0.02	0.06
Uchida *et al.*, 1994[71]	OR: OLV, CVS	RA	17	196	46.0	No	– (8.00/73.33)	0.12	7.97	–	–	– (4.00/7.20)	–0.37	0.56	– (7.28/7.53)	0.00	0.06
	ICU			151		No	–	1.13	3.92	–	–	–	0.52	1.01		0.01	0.07
Kilger *et al*, 1995[31]	ICU	RA, BA, PA	10	320	205.0	No	– (6.13/57.73)	–0.57	3.17	–	–	– (3.33/10.53)	–0.37	1.20	– (7.25/7.55)	–0.03	0.08
Pappert *et al.*, 1995[53]	ICU	RA	10	596	281.0	No	– (6.67/79.33)	0.25	2.11	1.9	11.5	– (3.47/13.60)	0.08	0.67	– (7.24/7.67)	0.01	0.04
Kurahashi *et al.*, 1996[32]	OR/ICU: CS	RA	46	319	87.0	No	– (–/–)	0.60	4.56	–	–	– (–/–)	0.60	1.65	– (–/–)	0.01	0.07
Oropello *et al.*, 1996[51]	Animal, pigs	FA	7	98	4.0	No	– (6.40/15.73)	–0.77	2.58	–	–	– (2.93/5.73)	–0.55	0.78	– (7.21/7.50)	0.04	0.09
		SVC	6	86	4.0	No	– (2.53/13.20)	–1.05	2.28	–	–	– (3.47/6.93)	–0.49	0.66	– (7.17/7.48)	0.02	0.06
Roupie *et al.*, 1996[56]	ICU	RA	15	260	120.0	No	– (2.40/43.47)	0.21	2.99	–	–	– (3.60/14.67)	–0.04	0.93	– (6.84/7.57)	0.01	0.07

[a]This system was previously described by Gehrich and colleagues.[21] [b]No Bland–Altman analyses were done, but linear regression analysis (*r*, SEE, standard error of estimate in kPa): P_{O_2} (0.99, 0.48), P_{CO_2} (0.99, 0.25), pH (0.98, 0.03). [c]No Bland–Altman analyses were done, but linear regression analysis (*r*, SEE, standard error of estimate in kPa): P_{O_2} (0.93, 4.40), P_{CO_2} (0.96, –), pH (0.99, –).

Table 3 Evaluation studies of more recent and currently available multiparameter CIBM devices. Probes (CIBM): NT™=Neotrend™, PT7®=Paratrend7®, PT7+®=Paratrend 7+®. Setting: OR=operating room, ICU=intensive care unit, CVS=cardiovascular surgery, NS=neurosurgery, OLV=one lung ventilation, thoracic part of surgery, abdominal part of surgery, CPB=cardiopulmonary bypass, pre-, on-, post-bypass, ORTHO=orthopaedic surgery, LAP=laparoscopic surgery, CS=cardiac surgery. Insertion site: RA=radial artery, FA=femoral artery, CA=carotid artery, UA=umbilical artery, JV=jugular vein, ChA=chorionic artery, PV=peripheral vein. Application: mean in place duration in hours. Recalibration: adjusting the original calibration curve using *in vitro* measured laboratory blood gas determinations

	Probe (CIBM)	Setting	Insertion (site)	Subjects (*n*)	Samples (*n*)	Application (h)	Recalibration	P_{O_2}					P_{CO_2}			pH		
								Range (kPa) [mean (min/max)]	Bias	2 SD	Bias	2 SD	Range (kPa) [mean (min/max)]	Bias	2 SD	Range [mean (min/max)]	Bias	2 SD
Studies on animals																		
Clutton-Brock *et al.*, 1994[11]	PT7®	Juvenile pigs	CA	10	292	8.0	No	– (3.33/66.67)	–0.65	2.32	–3.8	11.6	– (2.67/10.67)	0.09	0.83	– (6.80/7.40)	–0.03	0.08
Devlieger *et al.*, 2000[17]	NT™	Adult rabbits	CA/JV	6	147	–	Yes	11.16 (2.02/22.53)	–0.56	2.91	–	–	7.95 (3.40/16.27)	0.21	2.19	7.30 (6.98/7.50)	–0.02	0.06
	NT™	Fetal lambs	ChA	4	20	2.1	Yes	4.39 (1.60/6.91)	–0.52	1.15	–	–	7.75 (6.59/8.85)	–0.10	0.98	7.21 (7.14/7.30)	0.00	0.04
Studies on adult patients																		
Clutton-Brock *et al.*, 1992[12]	PT7®	ICU	RA	25	461	47.0	–	– (–/–)	0.29	7.36	–	–	– (–/–)	0.18	1.40	– (–/–)	–0.01	0.12
Venkatesh *et al.*, 1994[75]	PT7®	ICU	FA	10	71	14.0	Yes	– (12.40/26.90)	0.80	5.40	5.1	28.6	– (3.30/6.80)	0.22	3.30	– (7.21/7.53)	0.01	0.14
Venkatesh *et al.*, 1994[77]	PT7®	ICU	RA	13	158	42.9	Yes	– (8.00/59.60)	0.38	6.84	4.7	54.7	– (3.50/6.90)	0.22	1.32	– (7.31/7.61)	0.01	0.12
Liem *et al.*, 1995[35]	PT7®	OR: LAP	RA	27	27	–	–	– (–/–)	–	–	–	–	– (–/–)	–0.31	0.55	– (–/–)	0.00	0.05
Venkatesh *et al.*, 1995[76]	PT7®	OR: CPB, pre	RA	20	72	–	–	– (17.33/61.87)	–0.93	9.07	–3.0	28.0	– (3.20/5.47)	0.20	0.53	– (7.36/7.57)	0.02	0.10
	PT7®	OR: CPB, on			157			– (18.27/68.00)	0.40	12.00	0.5	28.0	– (2.80/5.47)	0.07	0.53	– (7.28/7.53)	0.01	0.12
	PT7®	OR: CPB, post			174			– (8.13/40.00)	0.53	7.20	14.0	34.0	– (2.80/6.67)	0.20	1.07	– (7.10/7.55)	0.02	0.12
Abraham *et al.*, 1996[1]	PT7®	ICU	RA	19	341	69.9	Yes	– (–/–)	–	–	–1.2	25.1	– (–/–)	0.17	0.66	– (–/–)	0.01	0.05
Nunomiya *et al.*, 1996[49]	PT7®	ICU	RA	9	62	72.0	Yes	– (6.03/72.32)	–0.22	5.33	–	–	– (3.84/9.13)	0.07	0.54	– (7.19/7.60)	0.00	0.04
Venkatesh *et al.*, 1996[79]	PT7®	OR: ORTHO	RA	10	30	1.4	–	– (–/–)	0.16	5.20	0.4	28.0	– (–/–)	0.07	0.48	– (–/–)	0.02	0.06
Myles *et al.*, 1997[48]	PT7®	OR: CPB	RA	20	140	–	–	– (–/–)	–1.14	11.52	–	–	– (–/–)	–0.15	0.80	– (–/–)	0.02	0.07
Zollinger *et al.*, 1997[85]	PT7®	OR: OLV	RA	23	138	3.7	No	24.00 (6.10/61.10)	0.38	9.71	–	–	5.70 (4.10/9.50)	0.31	0.78	7.39 (7.19/7.50)	–0.02	0.07
Ishikawa *et al.*, 1998[29]	PT7®	OR: OLV, thorac	RA	12	84	–	Yes	– (6.27/59.87)	–0.13	10.67	0.8	43.2	– (3.31/7.65)	0.12	0.83	– (7.30/7.49)	0.00	0.04
	PT7®	OR: OLV, abdom						– (9.60/34.00)	0.00	5.60	–0.2	23.6	– (4.04/6.21)	0.08	0.83	– (7.34/7.47)	–0.01	0.08
Zaugg *et al.*, 1998[83]	PT7®	OR: OLV	RA	30	76	1.2	No	29.93 (4.93/83.33)	0.24	11.03	–	–	5.33 (3.60/7.47)	0.01	0.55	7.40 (7.24/7.51)	0.01	0.04
Myles *et al.*, 1999[47]	PT7®	OR: OLV	RA	11	55	7.1	No	– (–/–)	–2.93	14.40	–	–	– (–/–)	–0.21	1.57	– (–/–)	0.01	0.10
Endoh *et al.*, 2001[18]	PT7®	OR: CVS	JV	18	101	–	Yes	– (3.50/16.00)	–0.16	1.20	–	–	– (3.70/9.60)	0.00	0.92	– (7.12/7.59)	0.01	0.07

Table 3 *Continued*

	Probe (CIBM)	Setting	Insertion (site)	Subjects (*n*)	Samples (*n*)	Application (h)	Recalibration	P_{O_2}				P_{CO_2}				pH		
								Range (kPa) [mean (min/max)]	Bias	2 SD	Bias	Range (kPa) [mean (min/max)]	Bias	2 SD	Bias	Range [mean (min/max)]	Bias	2 SD
Menzel *et al.*, 2001[43]	PT7+®	OR: NS	FA	20	124	4.0	–	36.82 (10.00/50.00)	0.20	4.08	–	–	0.25	0.46	0.04	7.45 (–/–)	–0.02	
Studies on paediatric patients																		
Weiss *et al.*, 1996[81]	PT7®	ICU	FA	5	150	127.0	–	– (5.20/28.53)	–	–	1.9	34.2	–0.10	1.25	0.05	– (7.12/7.58)	0.01	
Hatherill *et al.*, 1997[27]	PT7®	OR/ICU: CS	FA	10	100	27.0	No	5.30 (2.50/8.20)	0.04	0.87	–	–	–0.44	0.74	0.06	7.39 (7.14/7.59)	0.02	
Tobias *et al.*, 1998[69]	PT7®	ICU	PV	4	17	99.0	–	– (–/–)	–	–	–	–	0.40	0.37	0.04	7.38 (7.16/7.50)	0.04	
Morgan *et al.*, 1999[46]	NT™	ICU	UA	27	753	120.7	Yes	– (–/–)	–0.19	1.98	–	–	0.26	1.04	0.04	– (–/–)	0.00	
Weiss *et al.*, 1999[82]	PT7®	ICU	RA/FA	24	414	101.0	Yes	– (–/–)	0.16	6.40	–	–	–0.24	1.68	0.06	– (–/–)	0.01	
Tobias *et al.*, 2000[68]	PT7®	ICU	PV	23	100	115.2	–	– (–/–)	–	–	–	–	–0.28	0.72	0.06	– (7.24/7.54)	0.03	
Coule *et al.*, 2001[14]	PT7®	ICU	RA/FA	50	1445	108.0	Yes	– (4.53/64.00)	0.10	6.60	–	–	–0.05	1.28	0.08	– (6.99/7.66)	0.00	

The CDI™ 1000 Blood Gas Monitoring System (CDI-3M Healthcare, Tustin, CA, USA; Table 2) consisted of fluorescent P_{O_2}, P_{CO_2} and pH sensors and a thermocouple. *In vitro* and *in vivo* animal studies by Miller and colleagues,[44] and Shapiro and colleagues[64] showed excellent results. High fragility and poor results in clinical studies, especially for P_{O_2}, attributable to adherence to blood vessel walls (wall effect), rendered the commercial production and wider use of the system impossible.[2 39 40]

Smith, King and Schlain,[66] and Zimmerman and Dellinger[84] studied another CIBM device, the Optex Biosentry® System (Optex Biomedical, The Woodlands, TX, USA; Table 2). Absorbance sensors were used for pH and P_{CO_2}, and a fluorescent sensor was used for P_{O_2} assessment. Flexible optical fibres allowed the indicator dye chamber to be located at the side of the probe, rather than at the tip, thus decreasing the wall effect problem. No further investigations or progress in marketing were made partly because of high costs and also because of poor accuracy of the probe in some studies.[39]

The PB 3300 (Puritan Bennett Corp., FoxS Division, Carlsbad, CA, USA; Table 2) was a different CIBM device which consisted entirely of fluorescent sensors. It was evaluated in laboratory, animal, and clinical studies (Table 2). Some improvements were made with this device by enabling circumferential sensing of gases which was associated with a reduced wall effect. The system has been withdrawn for economical reasons as a result of high costs and poor performance in some clinical investigations.[39 56]

Current state of continuous intravascular blood gas monitoring

Paratrend 7+®

At present, the Paratrend 7+® (PT7+®; Diametrics Medical Inc., High Wycombe, UK; distributed by Philips Medical Systems), and Neotrend™ (NT™) are the only commercially available multiparameter CIBM systems (Table 3). Clutton-Brock, Hendry and Fink[12] described the technology of the Paratrend 7® (PT7®) in 1992. Originally, the PT7® was a hybrid probe incorporating four different sensors: a miniaturized Clark electrode to measure P_{O_2}; optodes to determine P_{CO_2} and pH (absorbance sensors, phenol red in bicarbonate solution); and a thermocouple (copper, constantan) to measure temperature and allow temperature correction of the blood gas values. The sensors were housed in a heparin-coated microporous polyethylene tube that was permeable to the analytes to be measured. In 1999, the manufacturer modified the design of the PT7® and introduced a new probe, the PT7+®. The Clark electrode was replaced by an optical P_{O_2}-sensor (fluorescent quenching sensor, ruthenium dye in silicone matrix). The other sensors and the main characteristics of the probe remained unchanged. According to the manufacturer, the new P_{O_2}

Table 4 Applications of CIBM. OLV=one lung ventilation, LVRS=lung volume reduction surgery

	Operating room	Intensive care unit
Adults	Thoracic surgery with OLV Lung transplantation[33 47] Major thoracoscopic surgery (e.g. LVRS)[83 85 86] Cardiac, vascular surgery[18 33 48 76] Liver transplantation[33] Major surgery in critically ill patients[33]	Critically ill patients, requiring repeated blood gas measurements for at least 48–72 h
Paediatrics	High risk surgery, especially cardiac surgery[27]	Premature infants with congenital heart disease, respiratory distress, reactive pulmonary vascular resistance, and persistent fetal circulation[28] Critically ill patients, requiring repeated blood gas measurements for at least 48–72 h
Obstetrics	Fetal monitoring during fetal surgery[17 30 37]	
Animals	Experimental studies	

sensor measures P_{O_2} more precisely, with a faster response time and less artefacts. Unfortunately, most evaluation studies published thus far have been of the PT7®; only one study by Menzel and colleagues[43] has evaluated the new PT7+® probe (Table 3).

Neotrend™

Neotrend™ (NT™; Diametrics Medical Inc., High Wycombe, UK; distributed by Philips Medical Systems), a modification of the PT7+®, was designed for CIBM in the umbilical artery of newborn infants. As in the PT7+®, P_{O_2}, P_{CO_2} and pH are measured by fibreoptic sensors and the temperature is determined by a thermocouple (Table 3).

Current clinical use

Site of measurement

The most common site for CIBM measurement is the radial artery in adults and the femoral artery in children, particularly if they are <5 yr old. There are some disadvantages of the radial approach: it is more susceptible to motion and positional artefacts, vasospasm, and changes in peripheral blood flow. Nevertheless, this approach is chosen routinely in adults and older children, because of easy access, the double blood vessel supply of the hand, and low complication rates.[75 82] The umbilical artery is used for probe insertion in neonates.[46] The incidence of catheter-related complications with the NT™ is low and does not differ from that observed with a standard umbilical artery catheter.[13] Other sites of measurement are peripheral veins in children,[68 69] the jugular venous bulb in adults,[18] and carotid arteries, chorionic arteries and jugular veins in animal studies.[11 17]

Evaluation studies of current CIBM devices, and ranges of application

All the evaluation studies published with currently available commercial CIBM devices are listed in Table 3. CIBM has been applied in various clinical settings in the operating room and the intensive care unit, as well as in experimental studies (Table 4). Different study designs and different statistical analyses render comparison of these studies difficult. Moreover, there are methodological limitations. For example, several studies corrected a perceived bias during the study period by adjusting the original calibration curve using *in vitro* laboratory blood gas determinations ('recalibration'). This may be necessary after prolonged monitoring in the clinical setting, according to the recommendations of the manufacturer. However, the issue of 'recalibration' was not mentioned in all of the studies, and 'recalibration' was performed at different time points. Similarly, the temperature at which P_{O_2}, P_{CO_2} and pH were measured and compared was not mentioned in all the studies. Most authors did not address the issue of temperature correction (i.e. the use of alpha-stat or pH-stat). Furthermore, the number of measurements per patient varied in all the studies. Some performed a large number, others only a few measurements with a single probe or patient.

An animal study with the PT7® showed good performance (Table 3) over a wide range of blood gas values under laboratory conditions.[11] Another study on animals with an NT™ probe presented the feasibility and accuracy of fibreoptic multiparameter sensing in fetal monitoring. The NT™ probe showed good performance at low P_{O_2} levels (P_{O_2} <6.7 kPa; bias (2 SD): –0.2 (1.5) kPa). However, as a result of movement and interference by the endoscopic light, readings for all variables were only available for about 50% of the operating time. The authors concluded that extensive modification of the sensor design would be necessary before the sensor could be used routinely in this area.[17]

There are several clinical evaluation studies from the operating theatre and the intensive care unit. Most studies in the operating room are in adults undergoing one lung ventilation for major thoracic surgery (thoracoscopic surgery, lung transplantation),[47 83 85] or major thoracoabdominal surgery (oesophagectomy).[29] Studies in cardiac and/or vascular surgery,[18 27 48 76] major orthopaedic surgery,[79]

laparoscopic surgery,[35] and neurosurgery[43] have also been done. Blood gas values were measured over wide ranges (P_{O_2} 3.5–83.3 kPa, P_{CO_2} 1.8–15.2 kPa, pH 6.99–7.66). Overall performance in P_{O_2} measurement was relatively poor (bias –2.9 to 0.8 kPa, 2 SD of bias 0.5–14.4 kPa). However, looking at the clinically important lower range of P_{O_2}, much better results were obtained. Zaugg and colleagues[83] found a bias (2 SD) of –0.5 (2.2) kPa for P_{O_2} <13.3 kPa in patients undergoing thoracoscopic surgery; Nunomiya and colleagues[49] showed a bias (2 SD) of –0.3 (1.7) kPa for P_{O_2} <13.3 kPa; Coule and colleagues[14] measured a bias (2 SD) of 0.24 (2.18) kPa for P_{O_2} <8.0 kPa in children in the intensive care unit (in this article the term precision was used and assumed to be 1 SD of the bias); Weiss and colleagues[82] obtained a bias (2 SD) of 0.1 (2.5) kPa for P_{O_2} <9.3 kPa in children in the intensive care unit; and Hatherill and colleagues[27] presented a bias (2 SD) of 0.0 (0.8) kPa for P_{O_2} values ranging from 2.5 to 8.2 kPa (mean 5.3 kPa) in children with cyanotic heart disease. These results are comparable with the animal study by Devlieger and colleagues.[17] Performance of P_{CO_2} and pH measurement was acceptable over the whole ranges.

Studies in the intensive care unit were done in adults,[1 12 49 75 77] as well as in children and neonates.[14 27 46 68 69 81 82] Despite poor reporting, the ranges of measured blood gas values were smaller compared with the operating theatre studies, despite the probes being used over a much longer time period. The reported mean longest duration of use was 127 h (5.3 days),[81] and the single longest duration of use was 429 h (17.8 days).[46] Furthermore, the number of measurements per patient or probe, respectively, was much greater in the intensive care unit (17 measurements per patient or probe in the intensive care unit *vs* six in the operating room), and 'recalibrations' were done more frequently in the intensive care unit.

Two studies reported on the PT7® sensors inserted in a peripheral vein in paediatric patients.[68 69] Only the values for i.v. P_{CO_2} and pH were compared with the respective arterial values.

Reliability, accuracy and consistency

In the technical specification sheet of the PT7+® and the NT™, the manufacturer presents promising *in vitro* data with blood gases and temperature measured over wide ranges (P_{O_2} 2.6–66.6 kPa, P_{CO_2} 1.3–10.6 kPa, pH 6.80–7.80, temperature 10–42°C) with a good performance. Using gas-tonometered solutions, 95% confidence limits were: ±5% or ±0.4 kPa (whichever is greater) of the actual values for a P_{O_2} <16 kPa, and ±10% for a P_{O_2} ⩾16 kPa; ±0.4 kPa for P_{CO_2}; ±0.03 for pH; and ±0.3°C for temperature. At 37°C, it took <15 s for the sensor to start responding to a change in blood gases, and the 90% response time for the sensor was 180 s or less. Drifts of the sensors were <0.5% h^{-1} for P_{O_2} and P_{CO_2}, and <0.005 pH units h^{-1}.[1]

Comparison of blood gas variables from continuous intravascular sensors with those from laboratory blood gas analysers is a controversial issue. Blood gas variables vary substantially within short periods of time even in stable patients in the intensive care unit. The accuracy of laboratory blood gas analysers can be quantified in the laboratory where the values to be measured are known. However, this is not the case in clinical studies. Thus, the clinical performance of an optode-based intravascular probe must be judged in comparison with an electrode-based blood gas analyser, for which clinical performance cannot be specifically quantified.[62] Moreover, resulting values for bias (2 SD) of a CIBM device not only reflect the accuracy of the intravascular device, but also depend on the accuracy of the laboratory blood gas analyser used as a reference. Laboratory blood gas analysers (even between individual analysers of the same manufacturer), also have inconsistencies.[24 25] The bias of intravascular sensors could either be reduced or increased if the blood gas analysers also showed high levels of bias. Poor repeatability [bias (2 SD)] of variables obtained by the blood gas analyser would, in contrast, inherently result in poorer repeatability for the variables from the intravascular sensors.[11] Blood gas values measured by a laboratory blood gas analyser may also be affected by pre-analytic sample errors. Therefore, even with an ideal laboratory blood gas analyser, the measured blood gas values would never completely reflect the real blood gas values *in vivo*. Since intermittently drawn blood samples analysed by laboratory blood gas analysers are the clinical standard of care, all authors used this procedure as a reference method to assess the accuracy of CIBM.

No official recommendations concerning performance of continuous intravascular blood gas devices exist. However, several guidelines for laboratory blood gas analysers have been published by the Clinical Laboratory Improvement Amendment/Health Care Finance Administration (CLIA/HCFA), the College of American Pathologists (CAP), and the Emergency Care Research Institute (ECRI) (Table 5). If they are applied to the published evaluation studies of PT7® and NT™ (Table 3), most of the bias values lie within these recommended ranges. Concerning repeatability, the situation is less clear as a result of poor reporting of the distribution of the measured P_{O_2}, P_{CO_2} and pH values. P_{O_2} measurements met the recommendations least, although a much better performance was obtained in the clinically important lower P_{O_2} range as discussed above. In contrast, values for P_{CO_2} and pH were more acceptable and comparable to the given recommendations.

As temperature in the radial artery reflects an intermediate or even peripheral temperature, it is not surprising that values for temperature with the PT7® were lower (bias –0.5°C) than those recorded rectally.[85]

On the screen of CIBM devices, additional values such as oxygen saturation, bicarbonate concentration, and base excess are provided, which are continuously calculated based on algorithms and normograms. These variables

Table 5 Quality recommendations for laboratory blood gas analysers. ULA=upper limit of agreement, LLA=lower limit of agreement, CLIA/HCFA=Clinical Laboratory Improvement Amendment/Health Care Finance Administration, CAP=College of American Pathologists; ECRI=Emergency Care Research Institute

	P_{O_2}	P_{CO_2}	pH
Bias			
Shapiro *et al.*[65]	0.7 kPa	0.4 kPa	0.05
ULA, LLA (bias ± 2 SD)			
CLIA/HCFA[1 42 63 65]	± 3 SD[a]	± 1.3 kPa or ± 16%[b]	± 0.08
CAP[63 65]	± 15%	± 0.8 kPa	± 0.06
ECRI[19]	4.0–20.0 kPa: ± 7.5% or ± 0.6 kPa[b] >20.0 kPa: ± 12.5%	2.7–10.7 kPa: ± 7.5% or ± 0.6 kPa[b] >10.7 kPa: ± 12.5%	[c] [c]

[a]SD of a proficiency blood gas analyser used as reference; [b]whichever is greater; [c]there is no reference method for pH measurement for laboratory blood gas analysers.

agreed poorly with those calculated by laboratory blood gas analysers in a number of studies.[18 27 85] This may reflect differences in the built in algorithms.[73] Interestingly, the poor agreement between two different blood gas analysers for bicarbonate and base excess was similar.[22] Such variations between laboratory blood gas analysers render estimation of the accuracy of these calculated values impossible.

Response times were analysed and found to correlate well with the values in the manufacturer's figures for the PT7®. Mean 90% *in vitro* response time was 70 s for P_{O_2}, 143 s for P_{CO_2} and 78 s for pH.[77] Response times *in vivo* were comparable, as shown in clinical studies. The PT7® was also evaluated during cemented total hip replacement. As a result of the instantaneous effect of acetabular and femoral cementation, mean Pa_{O_2} values dropped significantly within 90 s (mean onset time) following the application.[79] Furthermore, response times from four sensors were investigated after using them in patients undergoing cardiopulmonary bypass. The mean 90% post-*in vivo* response time was 100 s for P_{O_2}, 122 s for P_{CO_2}, and 123 s for pH, respectively. Additionally, these sensors were exposed to known concentrations of enflurane, isoflurane and halothane. There was no interference with the pH and P_{CO_2} sensors by any of the anaesthetic gases tested, but halothane interfered with P_{O_2} measurement.[76] Other investigations exposed PT7® sensors to the fluorescent drug propofol as well as to bone cement (methyl methacrylate), and sterile polymer powder *in vitro*. No interference of these substances with blood gas measurement was found.[77 79] Halothane interference with P_{O_2} measurement in the PT7® probe was attributable to the electrochemical reduction of halothane by the Clark electrode used on the PT7® probe. None of the anaesthetic agents have any effect on the optical measurement of P_{O_2}, and so the PT7+® probe should be free from this interference.

Sensor drifts *in vivo* were reported in an early animal study. Mean variation of the bias per hour was acceptable at –0.59% for P_{O_2}, 0.42% for P_{CO_2} and –0.002 pH units, respectively.[11] These results were confirmed in humans undergoing cardiopulmonary bypass (i.e. mean variation of the bias per hour was –0.43% for P_{O_2}, 0.62% for P_{CO_2} and 0.001 pH units).[76]

Limitations and complications

Reliable intravascular blood gas measurement depends on a number of mechanical, electrical and physicochemical properties of the CIBM probe as well as the conditions of the vessel into which the probe is inserted. Blood flow in the vessel containing the probe is most critical. CIBM becomes unreliable if blood flow decreases or stops, for example during inflation of a sphygmomanometer cuff, because of vasospasm, or during cardiopulmonary resuscitation. P_{O_2} was shown to be the most flow-dependent variable. Insertion of the probe into a femoral artery yields more reliable results compared with those from the radial artery during low flow states.[74 75] If the sensor becomes attached to the wall of the vessel, thus measuring a combined blood and tissue P_{O_2}, the oxygen value may be falsely low. Hybrid probes (PT7®) are less susceptible, as the P_{O_2} electrode has a larger surface area. Arterial catheters are flushed *in vivo* with a continuous solution. If the sensing probe is not inserted for an adequate distance over the tip of the arterial catheter, it may measure the blood gas variables in the flush solution, resulting in errors known as the 'flush effect'.[78] Interference from electrocautery and ambient or endoscopic light may be another source of erroneous blood gas values.[17 82] Damping of the arterial pressure tracing or difficulty in withdrawing blood from the arterial catheter was reported in one study, and occurred after an average of 35.4 h of measurement in only four patients (15%).[1] However, even without an indwelling CIBM probe, the incidence of damping or difficulty in withdrawing blood from radial artery catheters was reported to be 17–26%.[58] Without any adverse events, clot formation (incidence 8–30%) was observed in three studies.[29 68 82] Poor robustness of the fibreoptic cables led to bending and kinking in up to 20% of patients, resulting in probe malfunctioning and a short user life.[1 27 68 82] Finally, before measurement, a 30 min warm-up time is mandatory for calibration. Hence, the device is not immediately available. The unit is also quite bulky.

Costs

Costs are important, and new monitoring devices are warranted only if cost effectiveness may be shown. Either reduction in overall cost or an improvement in patient outcome is required. Some cost–benefit analyses on CIBM have been done, but different results have been obtained. Some authors recommended the use of CIBM and presented cost-savings,[20 82] others argued against this technology because of high costs and low benefits (i.e. the monitoring system far exceeding the clinical needs).[28] This may be attributable to a differing basis for the analyses. Costs assumed for one conventional, intermittent laboratory blood gas analysis varied between 2.50 and 80.00 euros per sample. Some investigations assessed only the direct costs of CIBM, in other words, approximately 20 000 euros for the satellite monitor including a patient data module, 15 000 euros for the calibration unit, and 500 euros for each one way sensor. Others also took indirect costs into account, for example administrative costs, laboratory support, and specialized personnel. Therefore, no concluding data are currently available on the cost–benefit ratio of CIBM.

Outcome

The impact of undetected changes in arterial blood gases on patient outcome has not yet been investigated. Experimental studies reported myocardial ischaemia with a potential risk of myocardial damage even when the period of hypoxia was short, if coronary blood flow was limited.[59] Pa_{O_2} <8.0 kPa, as often observed during thoracic surgery with one lung ventilation, is thought to be the threshold that should be detected. It is associated with an increased risk of perioperative myocardial ischaemia in susceptible individuals.[45 83]

Although CIBM appears to be advantageous, there are no prospective, randomized, double-blind studies of its impact on morbidity and mortality, length of intensive care unit and hospital stay, or myocardial and cerebral ischaemia. Future outcome studies should focus on well-defined groups of selected patients who might benefit from CIBM (e.g. critically ill patients with potentially rapid and unexpected changes in blood gas values). Nevertheless, it may be difficult, if not impossible, to show a positive impact of CIBM on patient outcome.

Conclusions

Development of CIBM devices has resulted in the commercially available PT7+® probe for adults and NT™ probe for newborns. Changes in blood gas values may be immediately and reliably detected in the clinical setting without significant side-effects or complications. Indications for CIBM, in terms of evidence-based medicine, are still lacking since the cost–benefit ratio and the impact on patient outcome are unknown. Nevertheless, CIBM is being used by clinicians in selected patient groups in the operating theatre and the intensive care unit. It is useful during surgery where blood gas values can change rapidly and unexpectedly, for example during thoracic surgery with one lung ventilation, cardiovascular surgery and organ transplantation. CIBM is useful in critically ill patients needing a considerable number of blood gas determinations over a long period, for example premature infants with severe cardiopulmonary disease, and patients with acute respiratory distress syndrome, sepsis, and severe trauma.

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