EXPERIMENTAL RESEARCH

Brain tissue oxygen monitoring: a study of in vitro accuracy and stability of Neurovent-PTO and Licox sensors

Karlis Purins · Per Enblad · Bo Sandhagen · Anders Lewén

Abstract

Object Periods of brain tissue ischemia are common after severe head injury, and their occurrence and duration are negatively correlated with outcome. Accurate and reliable measurement of brain tissue oxygenation ($B_{ti}pO_2$) may be a key to improve patient outcome after severe head injury. Knowledge of stability and accuracy of the $B_{ti}pO_2$ systems is crucial. We have therefore conducted a bench test study of new Neurovent-PTO® (NV) and Licox® (LX) oxygen tension catheters to evaluate the sensor accuracy, response time to different oxygen tensions, response to temperature changes and long-term stability.

Methods For all experiments five new fluorescent NV sensors and five new electrochemical LX sensors were used. The catheter probes were placed into a container filled with a buffer solution. The solution was equilibrated with five high precision calibration gases. The accuracy of the probes was recorded after an equilibration period of 20 min in O_2 concentrations of 5, 10, 20, 30 and 40 mmHg at $37.0\pm0.2°C$. The probe response to an increase in temperature from 37.0°C to 38.5°C to 40.0°C in two different gases with O_2 concentrations of 10 and 20 mmHg were analysed. We also recorded the time for reaching 90% of a new oxygen concentration level when switching from one concentration to another. Finally, to test if there was a time-dependant drift in pO_2 recordings, all sensors were left in 10 mmHg O_2 solution for 10 days, and recordings were taken every 24 h.

Results In all gas concentrations, NV and LX sensors measured pO_2 with high accuracy and stability in vitro (mean differences from calculated values were for NV 0.76–1.6 mmHg and for LX −0.46–0.26 mmHg). Both sensors showed a shorter response time to pO_2 increase (for NV 56 ± 22 s and for LX 78 ± 21 s) compared to pO_2 decrease (for NV 131 ± 42 s and for LX 215 ± 63 s). NV pO_2 values were more stable for changes in temperature, while LX sensors showed larger standard deviations with increasing temperature (the difference from the calculated values in 19.7 mmHg O_2 at 40°C were for NV probes between 0.5 and 1.7 mmHg and LX between −2.3 and 1.9 mmHg). Both sensors gave stable results with low standard deviations during long-term (10 days) use, but with a slight elevation of measured pO_2 levels by time.

Conclusions Both NV and LX were accurate in detecting different oxygen tensions, and they did not deviate over longer recording times. However, LX needed a significantly longer time to detect changes in pO_2 levels compared to NV. Furthermore, LX probes showed an increased standard deviation with higher temperatures.

K. Purins · P. Enblad (✉) · A. Lewén
Department of Neuroscience, Section of Neurosurgery,
Uppsala University Hospital,
751 85 Uppsala, Sweden
e-mail: per.enblad@neuro.uu.se

B. Sandhagen
Department of Medical Sciences, Section of Clinical Physiology,
Uppsala University Hospital,
Uppsala, Sweden

Introduction

Periods of brain tissue ischemia are common after severe head injury, and their occurrence and duration are nega-

tively correlated with patient outcome [4–7, 11, 15, 22, 23]. Continuous measurement of intracranial pressure (ICP) is a standard monitoring procedure in patients suffering from severe traumatic brain injury (TBI) [1, 13]. Current management of severe head injury is based on reduction of elevated ICP. Elevated ICP is observed in about half of the patients with traumatic brain injury [1, 16, 18–20]. Brain tissue partial oxygen pressure ($B_{ti}pO_2$) sensors, introduced by the Rotterdam group, have been used for the last decades [14]. These sensors provide additional information of brain pathophysiology allowing detection of critical brain ischemic episodes [10, 11]. Multimodality monitoring and targeting of both ICP and $B_{ti}pO_2$ is associated with reduced patient mortality rate after severe TBI [19].

Accurate and reliable measurements of brain tissue oxygenation may be one of the keys to improve patient outcome after severe head injury [8, 17, 19]. However, reliability of probe accuracy, long-term drift and response time needs to be determined. Two types of sensors are available based on different technologies: a Clark type of electrochemical probe (Licox®, LX) and a fluorescent fibre optic sensor (Neurovent-PTO®, NV). The Licox system measures $B_{ti}pO_2$ and temperature, whereas the NV sensors additionally measures ICP.

The performance of the LX and NV sensors under standardised in vitro conditions are not very extensively described in the literature, with only a few studies in vitro for the LX and no studies for the NV sensor. Therefore, we have conducted a bench test study of the new Neurovent-PTO and Licox catheters to confirm the sensor accuracy, response time, response to temperature changes and long-term drift.

Materials and methods

For all experiments five fluorescent sensors (Neurovent-PTO®, Raumedic multiparameter sensor, Munchberg, Germany) and five electrochemical (Licox® ($n=3$) and Licox-PMO® ($n=2$), brain oxygen catheter-micro-probe, Integra Neurosciences Ltd., Hampshire, UK) sensors were used.

The fluorescent multiparameter NV sensor contains three optical sensors for oxygen tension (pO_2), ICP and temperature in one catheter probe. The NV probe has a diameter of 1.65 mm and pO_2 sensitivity area ~22 mm^2 (data provided by manufacturer). The electrochemical Clark type LX sensors has a diameter of 0.8 mm, sensor length of 150 mm and a pO_2 sensitive area of 13 mm^2 (data provided by manufacturer). The NV sensors do not need to be calibrated. For LX probes an individual chip card for each probe was used for calibration.

The catheter probes were placed into a liquid filled container (Equilibrator Tonometer, RNA Medical, Devens, MA, USA) filled with a buffer solution (Equil plus, RNA Medical). The solution was equilibrated with five high precision calibration gases (AGA, Enköping, Sweden), containing different O_2 concentrations (Table 1). Barometric pressure was recorded daily before each test by using a blood gas machine (ABL 800 Flex, Radiometer Copenhagen, Brønshøj, Denmark). The solution was kept at 37.0 ± 0.2°C for the complete monitoring time except for during the response to temperature experiments. Temperature was measured by two precision temperature probes (Equilibrator Tonometer integrated probe, RNA Medical and Physitemp TH-5, Clifton, NJ, USA). Temperature was raised using a warming box (Innova 4300, New Brunswick Scientific, NJ, USA) as shown in Fig. 1. NV and Licox-PMO sensors measure temperature from its multiparameter probe and calculate pO_2 automatically. Licox probes have an additional probe for temperature measurements.

Accuracy tests

The equilibrator was filled with buffer solution and bubbled with each calibration gas for a 30-min equilibration. After each equilibration all sensors were left in the buffer solution for 20 min with continuous measurements of pO_2. The value of pO_2 obtained at the end of the 20-min period was used to determine the accuracy of the probe. The solution was kept at 37.0 ± 0.2°C for the complete monitoring time.

Response time

The time for the sensors to reach a new level after a change in pO_2 gas concentration was defined as the response time. At first the sensors were kept for 20 min in pre-equilibrated liquid solution with 10 mmHg pO_2 gas and then placed in solution equilibrated with 40 mmHg pO_2 gas for another 20 min. The time it took for the sensor to change from 10 mmHg to 90% of 40 mmHg was recorded, denoted the 90% response time. After reaching the 90% level (i.e. 36 mmHg) the sensor was replaced in the 10 mmHg gas solution, and the 90% response time was again recorded, i.e. the time it took the sensor to reach 11 mmHg. The

Table 1 Gas concentrations used in the study

Calibration gas	pO_2mmHg	% O_2	% CO_2	% N_2
1	5	0.687	5.6	93.7
2	10	1.42	5.6	93
3	20	2.81	5.6	91.6
4	30	4.2	5.6	90.2
5	40	5.6	5.6	88.8

Fig. 1 The experimental setup for the in vitro pO_2 study showing the NV (*1*) and LX (*2*) monitors collecting the data from oxygen sensors. Two temperature probes (*3*) measured the temperature in the equilibrator (*4*), which was inserted in the warming box (*5*) and bubbled with high precision O_2 gases (*6*)

temperature was kept constant at 37.0±0.2°C during the experiment.

Response to temperature changes

To measure the sensor response to temperature changes two calibration gases were used (with 10 and 20 mmHg O_2). After the equilibration period the probes were left in the buffer for 20 min for both gases. For each gas concentration the temperature in the solution was changed starting from 37.0°C to 38.5°C and 40.0°C. At each temperature the pO_2 was measured for an additional 20 min.

Long-term drift test

To test if there was a time-dependant drift in pO_2 recordings two NV and two LX sensors were used, and readings were recorded after 24, 48, 72, 96, 120, 144, 168, 192, 216 and 240 h in pre-equilibrated gas with 10 mmHg O_2. The solution was bubbled continuously and kept at 37.0±0.2°C for the complete monitoring time.

Statistical methods

Data are presented as means ± standard deviation. A *t* test for dependant samples was run to assess the significances of any differences. For all the results the threshold of significance was set at a *p* value of 0.05. The calculations were done using Statistica® 8.0. Regarding the long-term drift test, an overall test for the effect of time was made with an analysis of variance model, for NV and LX separately. Factors in the model were probe and time.

Results

Accuracy of pO_2 sensors

There was no technical failure during the calibration of any of the probes. The pO_2 accuracy measurements for the sensors using five different oxygen concentrations are shown in Fig. 2 and Table 2. In low (~5 mmHg) oxygen gas concentration (the exact O_2 was calculated to 4.86 mmHg, depending on the barometric pressure), the mean readings for NV probes were 5.62±0.14 mmHg, which was 0.76±0.14 mmHg higher than the calculated O_2 value. LX probes showed a more accurate mean value of 5.12±0.71 mmHg, i.e. 0.26±0.71 mmHg higher than the reference value. When comparing the probe that gave the lowest oxygen value with the probe that gave the highest oxygen value, the spread was 8% of the true oxygen partial pressure for NV, whereas for LX the spread between the probes was 35% at this oxygen concentration. In ~10 mmHg oxygen concentration (10.02 mmHg calculated), the readings were for NV 10.82±0.50 mmHg and for LX 10.20± 1.04 mmHg. When measured in ~20 mmHg oxygen (with a calculated value of 19.78 mmHg), the NV showed 20.74± 0.76 mmHg and the LX probes gave 19.36±0.99 mmHg. In higher oxygen concentrations (with a calculated oxygen value of 29.76 mmHg), NV showed 31.16±0.62 mmHg and LX 29.92±1.33 mmHg. With oxygen concentration of
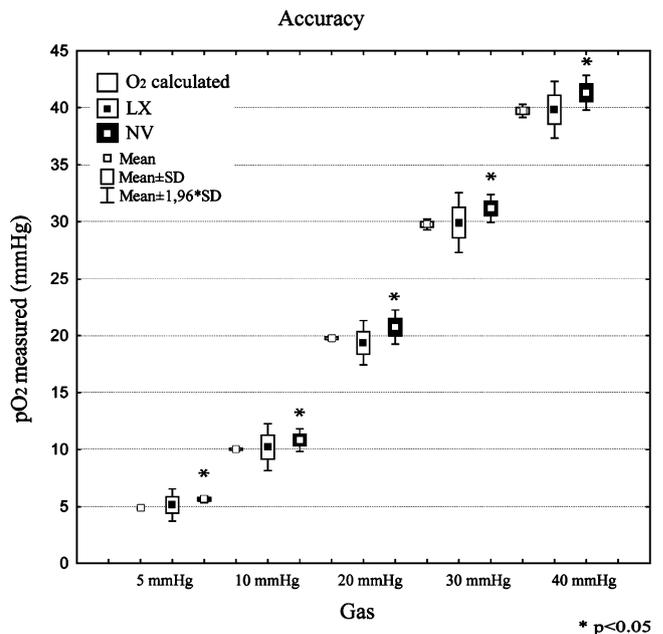
Fig. 2 The accuracy test for LX and NV sensors was performed with five high precision oxygen gases. The figure show measured oxygen tension in mmHg with LX and NV sensors compared with the reference (calculated) value. LX and NV values are shown as mean ± standard deviation and mean±1.96×SD. Statistically significant difference between measured and calculated O_2 value (**p*<0.05)

Table 2 Calculated and measured pO_2 values using the NV and LX oxygen sensors

Gas	pO_2calculated (mmHg)	pO_2measured (mmHg)	
		NV	LX
1	4.85±0.05	5.62±0.14	5.12±0.71
2	10.0±0.08	10.82±0.50	10.2±1.04
3	19.78±0.10	20.74±0.76	19.36±0.99
4	29.76±0.24	31.16±0.62	29.9±1.33
5	39.72±0.29	41.32±0.77	39.82±1.26

~40 mmHg (39.72 mmHg calculated), the NV mean readings were 41.32±0.77 mmHg and for LX 39.82±1.26 mmHg. Thus, in all gases the mean deviation from the calculated pO_2 was very small, for NV 0.76–1.6 mmHg and for LX −0.46–0.26 mmHg. For all gas concentrations, the small difference between NV readings and the calculated value were significant ($p<0.05$). For LX sensors, there were no significant difference between the calculated value and the recorded value. However, this was mainly an effect of the larger variation and spread in LX sensors, making the standard deviation larger.

Response time

When changing from low (10 mmHg) to high (40 mmHg) oxygen concentration, the NV sensors reacted fast in four of five probes, within 36–55 s. In one NV probe it took 95 s for the 90% response time. For all five probes the mean was 56±22 s (Fig. 3). The LX probes reacted somewhat slower in the same test, ranging from 45 to 103 s (mean 78±21 s; Fig. 3).

Figure 3b reflects the 90% response time when switching sensors from high oxygen concentration (40 mmHg) to low (10 mmHg). This test took longer time for both types of sensors. NV sensors needed 131±42 s and LX sensors 215±63 s; this difference was significant ($p<0.05$).

Long-term drift

For long-term measurements (240 h), probes were inserted in the equilibrated tonometer containing gas with 10 mmHg oxygen concentration, and readings were taken every 24 h. The pO_2 in the equilibration gas was calculated depending on the barometric pressure for each day (mean value ± SD= 10.02±0.11 mmHg, in absolute values ranging between 9.8 and 10.2 mmHg).

Individual NV sensors read pO_2 between 9.6 and 11.8 mmHg (mean value ± SD=10.83±0.59 mmHg), as shown in Fig. 4. Individual LX sensors read between 10.0 and 13.0 mmHg pO_2 (mean value ± SD=11.09±0.74 mmHg).

There was a significant difference between the calculated value and the NV probe measured values ($p=0.0003$). However, there was no trend towards a time-dependant increase or decrease in estimations. Instead, we observed only minimal fluctuations over time. For LX probes there were no statistical difference ($p=0.36$) between calculated and measured oxygen values due to larger variations between the probes.

Response to temperature changes

To detect the sensor response to temperature changes, the tonometer was equilibrated with two different oxygen concentrations (10 and 20 mmHg), and the temperature was raised from 37.0°C to 38.5°C and to 40.0±0.2°C. With the oxygen concentration of 10 mmHg, the pO_2 value for NV probes were slightly higher at all temperatures (ranging between 10.82 and 10.94 mmHg) compared to the calculated value (9.92–10.02 mmHg; Fig. 5a). For LX sensors the mean value of 10.0±0.63 mmHg was equal to the calculated value. At higher temperatures (38.5–40.0°C), the standard deviations increased for LX probes up to 1.20 mmHg.

With 20 mmHg oxygen concentration, the pO_2 measured was different for both NV ($p<0.05$) and LX (NS; Fig. 5b). In all measurements, the LX probes read lower mean values
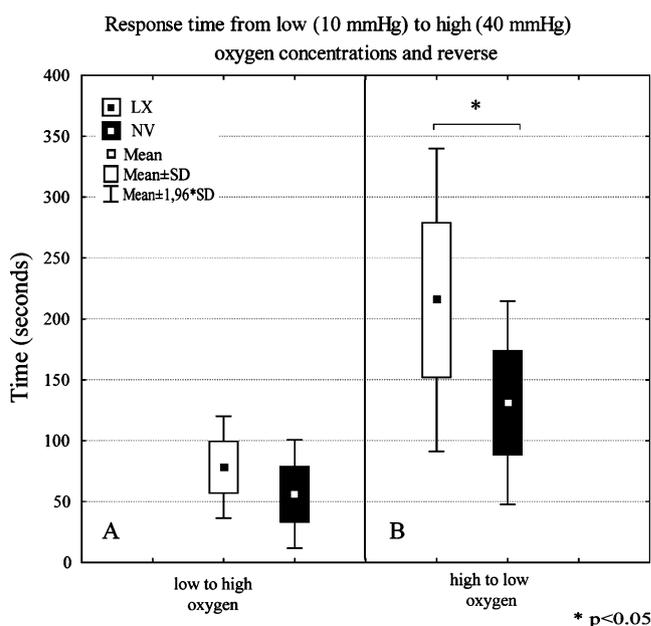
Fig. 3 The response time for LX and NV sensors. Time (seconds) needed to reach 90% of expected (calculated) pO_2 value when switching probes from **a** low (10 mmHg) to high (40 mmHg) oxygen concentration and from **b** high (40 mmHg) to low (10 mmHg) oxygen concentration. NV was significantly faster than LX in the response from high to low oxygen concentration. Data of LX and NV are shown as mean ± standard deviation (SD) and mean±1.96×SD. Statistically significant difference between LX and NV response time (*$p<0.05$)

Fig. 4 Long-term drift test for LX and NV sensors. The accuracy of the sensors in pO_2 (mmHg) measurement was evaluated continuously for 10 days in stable conditions (temperature 37.0±0.2°C, with equilibrated tonometer solution of 10±0.2 mmHg pO_2 corrected for atmospheric pressure changes)
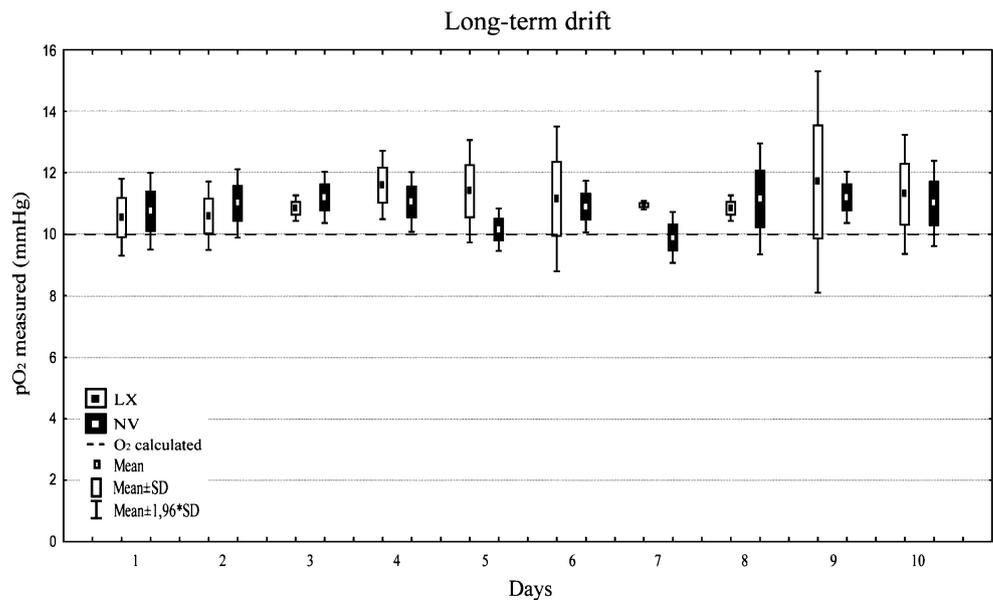
(18.9 to 19.14 mmHg), and the NV probes read higher mean values (20.74–20.78 mmHg), compared to the calculated value (19.7±0.1 mmHg). As temperature became higher, LX sensors standard deviation increased from 0.4 to 1.55 mmHg, while the NV probes standard deviation decreased from 0.76 to 0.44 mmHg.

Discussion

Measurement of brain tissue oxygenation may be an important contribution to the neurointensive care of head injured patients. In order to safely use and interpret data from commercial available systems for $B_{ti}pO_2$ measurements, we wanted to test the sensors regarding accuracy of absolute values, drift over time, variation with temperature and response time of changes in pO_2.

There are some clinical and experimental studies regarding the reliability of local brain tissue pO_2 sensors showing accurate, safe and stable measurements [2, 3, 8, 9, 12, 20, 22, 23]. However, there are only a few in vitro studies for electrochemical LX sensors [2, 8] and no studies for fiberoptic NV sensors. In clinical practice it is crucial to safely differentiate ischemic (5–15 mmHg) from normal (20–50 mmHg) pO_2 values [18, 21, 22], and therefore there is a need for in vitro validation studies of the monitoring devices.

To determine pO_2 system accuracy, sensitivity drift, response time and response to temperature changes, we used the same experimental setup for both sensors (LX and NV), similar to previous studies [2, 8]. To avoid technical errors, high precision O_2 gases were used, temperature was controlled, and the pO_2 value in the tonometer solution was calculated depending on atmospheric pressure.

Accuracy

Our tests confirmed that both LX and NV oxygen probes were highly accurate in measuring the oxygen partial pressure at different clinically relevant oxygen concentrations. In all gas concentrations, the LX sensors mean value were the closest (0.1–0.42 mmHg) to the reference value, though with relatively high standard deviations (0.71–1.33 mmHg). On the other hand, NV probes read slightly higher values (0.76–1.6 mmHg), not significantly different from LX, but with higher precision, i.e. less standard deviations (0.14–0.77 mmHg). We conclude that both sensors, even though based on different technologies, read partial oxygen pressure ranging from low to high concentration satisfactorily good and both systems are clinically eligible. The results from the LX sensors are comparable with recent data from Hoelper et al. [8]. To our knowledge, there is no previous independent report using NV sensors.

When the measured values were compared with the calculated oxygen values in low oxygen concentrations (5 and 10 mmHg), our data for the electrochemical LX probes showed a difference between 2.1% and 5.3%, which should be compared with previous data from the study by Dings et al. [2] where the difference was between −4.5% and 9.0%. For the NV probes in our study the difference from calculated values ranged between 4.0% and 10.2%. Neurotrend® (NT), another fibre optic oxygen sensor system, showed differences between 4.8% and 25.87% in the study by Dings et al. [2]. However, the experimental setup was quite different between ours and their study. For example, Dings et al. evaluated the sensors in a pO_2 of 0 and 42.7 mmHg but without using a buffer solution and not correcting pO_2 for local barometric pressure [2].

Fig. 5 The LX and NV sensors accuracy in different temperatures. The temperature in the buffer solution was raised from 37.0°C to 38.5°C and to 40.0±0.2°C. The tonometer was equilibrated with two different oxygen concentrations. In the *upper graph* (**a**) the response to temperature was performed with 10 mmHg oxygen concentration. Data of LX and NV sensors are shown in mean ± Standard deviation. In the *lower graph* (**b**) the test was performed with 20 mmHg and the same conditions. There was a larger variation with LX probes compared to NV

a Response to temperature changes at 10 mmHg oxygen

* p<0.05

b Response to temperature changes at 20 mmHg oxygen

* p<0.05
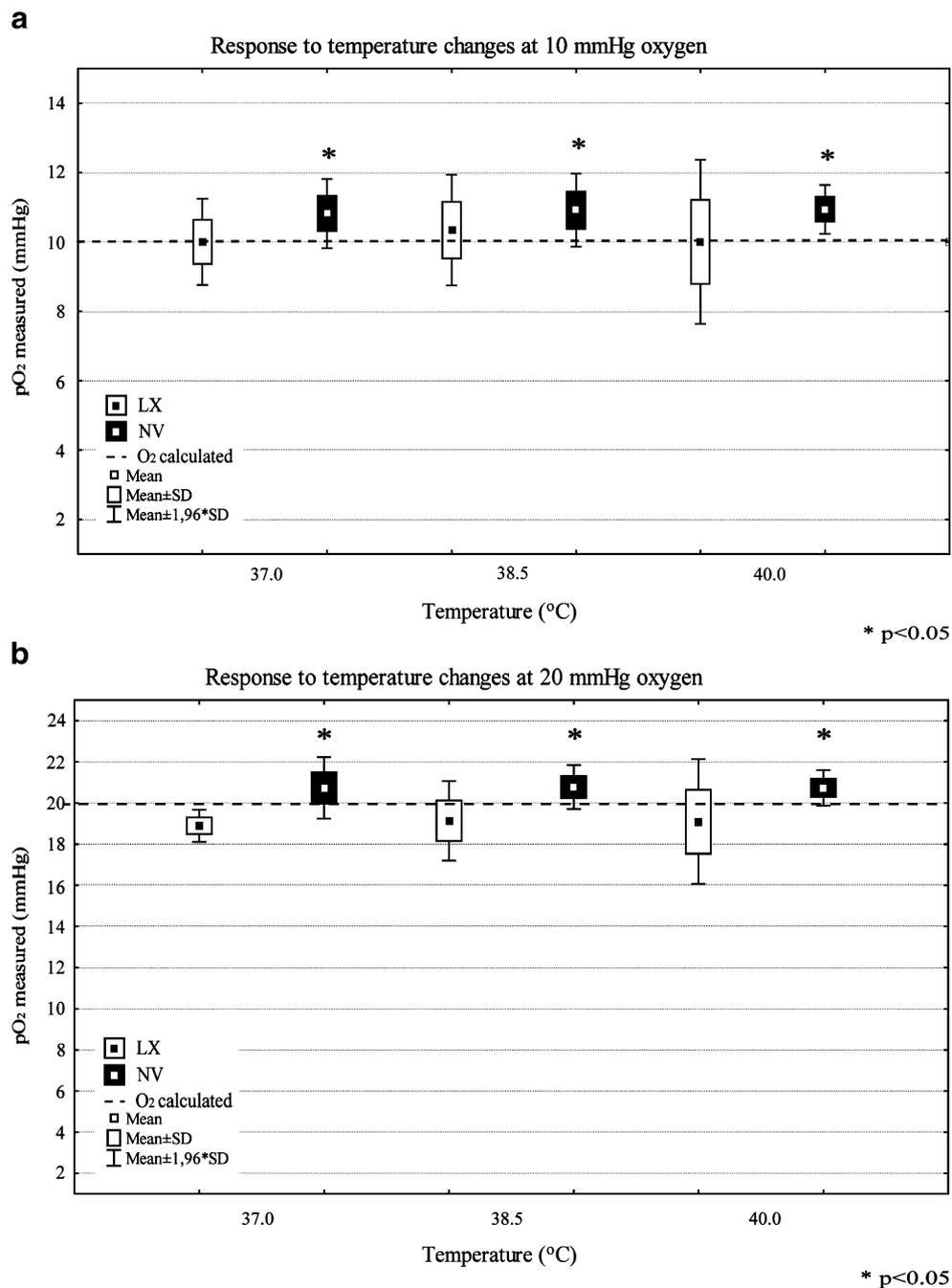
Response time

The pO_2 sensor response time is an important clinical factor. We analysed the response time to reach the pO_2 level from low (10 mmHg) to high (40 mmHg) oxygen concentration. The experimental setup was similar to the study reported by Hoelper et al. [8], but different oxygen concentrations were used (7.13 to 57.03 mmHg) in their study. In the low to high oxygen response test, the LX sensors (in our study) required 78.2±21 s compared to 129± 27 s in the study by Hoelper et al. [8]. The fibre optic

sensor response time was practically the same for NV in our study (56.2±22 s) and NT used in the other study (55±19 s) [8]. When going from high to low oxygen concentration in our study, both LX and NV sensors needed longer response time, LX sensors 215±63 s and NV 131±42 s. In Hoelper et al. [8], LX needed 174±26 s and NT 98±39 s.

The results from the two studies cannot be compared directly due to different oxygen concentrations used, but the results are relatively consistent and illustrate the magnitude of the response time needed for the different systems, that the response time is shorter for NV and NT (fiberoptic

systems) compared to LX (electrochemical system) and that the response time is longer from high to low oxygen concentration for all systems. It is obvious that the response time is good enough for the clinical situation for all systems.

Long-term drift

Of major clinical importance is the question whether there is a drift in sensor accuracy over time. In clinical practice, an observation period for $B_{ti}pO_2$ of 7–10 days is to be expected. In our test of long-term drift we measured the accuracy for 10 days under stable conditions. We found that both LX and NV catheters performed well during this period, with a mean pO_2 difference from the calculated value of less than 1 mmHg, which is supported by the results from Hoelper et al. [8] who did a 5-day long-term drift test in ~20 mmHg oxygen concentration. Although the in vitro long-term drift tests showed stable levels, the stability after long-term use in patient needs to be assessed.

Response to temperature changes

In clinical studies using the LX system, Stocchietti et al. [21] observed brain tissue pO_2 changes related to changes in brain temperature. We therefore wanted to study the influence of temperature in the range between 37.0°C and 40.0°C in two different oxygen levels. The results showed that there was no temperature effect on NV probes. With the LX system an increased standard deviation was observed with increasing temperature. In the clinical situation, this must be considered when the brain tissue oxygen value approaches the assumed critical threshold level.

Conclusions

LX and NV sensors measured pO_2 with high accuracy and stability in vitro, but the precision was higher for NV sensors. Both sensors showed a shorter response time to pO_2 increase compared to pO_2 decrease. LX sensors needed a significantly longer time to detect changes in pO_2 levels compared to NV. NV pO_2 values were stable for changes in temperature, while LX sensors showed less accuracy with increasing temperature. LX and NV sensors gave stable results with low deviations during long-term (10 days) use.

References

1. Bratton SL, Chestnut RM, Ghajar J, McConnell Hammond FF, Harris OA, Hartl R, Manley GT, Nemecek A, Newell DW, Rosenthal G, Schouten J, Shutter L, Timmons SD, Ullman JS, Videtta W, Wilberger JE, Wright DW (2007) Guidelines for the management of severe traumatic brain injury. VI. Indications for intracranial pressure monitoring. J Neurotrauma 24(Suppl 1):S37–S44
2. Dings J, Meixensberger J, Jager A, Roosen K (1998) Clinical experience with 118 brain tissue oxygen partial pressure catheter probes. Neurosurgery 43:1082–1095
3. Fandino J, Stocker R, Prokop S, Imhof HG (1999) Correlation between jugular bulb oxygen saturation and partial pressure of brain tissue oxygen during CO2 and O2 reactivity tests in severely head-injured patients. Acta Neurochir (Wien) 141:825–834
4. Gopinath SP, Valadka AB, Uzura M, Robertson CS (1999) Comparison of jugular venous oxygen saturation and brain tissue Po2 as monitors of cerebral ischemia after head injury. Crit Care Med 27:2337–2345
5. Haitsma IK, Maas AI (2002) Advanced monitoring in the intensive care unit: brain tissue oxygen tension. Curr Opin Crit Care 8:115–120
6. Haitsma IK, Maas AI (2007) Monitoring cerebral oxygenation in traumatic brain injury. Prog Brain Res 161:207–216
7. Hlatky R, Valadka AB, Gopinath SP, Robertson CS (2008) Brain tissue oxygen tension response to induced hyperoxia reduced in hypoperfused brain. J Neurosurg 108:53–58
8. Hoelper BM, Alessandri B, Heimann A, Behr R, Kempski O (2005) Brain oxygen monitoring: in-vitro accuracy, long-term drift and response-time of Licox- and Neurotrend sensors. Acta Neurochir (Wien) 147:767–774 discussion 774
9. Imberti R, Bellinzona G, Langer M (2002) Cerebral tissue PO2 and SjvO2 changes during moderate hyperventilation in patients with severe traumatic brain injury. J Neurosurg 96:97–102
10. Kiening KL, Schoening WN, Stover JF, Unterberg AW (2003) Continuous monitoring of intracranial compliance after severe head injury: relation to data quality, intracranial pressure and brain tissue PO2. Br J Neurosurg 17:311–318
11. Kiening KL, Unterberg AW, Bardt TF, Schneider GH, Lanksch WR (1996) Monitoring of cerebral oxygenation in patients with severe head injuries: brain tissue PO2 versus jugular vein oxygen saturation. J Neurosurg 85:751–757
12. Lang EW, Mulvey JM, Mudaliar Y, Dorsch NW (2007) Direct cerebral oxygenation monitoring—a systematic review of recent publications. Neurosurg Rev 30:99–106 discussion 106-107
13. Maas AI, Dearden M, Teasdale GM, Braakman R, Cohadon F, Iannotti F, Karimi A, Lapierre F, Murray G, Ohman J, Persson L, Servadei F, Stocchetti N, Unterberg A (1997) EBIC—guidelines for management of severe head injury in adults. European Brain Injury Consortium. Acta Neurochir (Wien) 139:286–294
14. Maas AI, Fleckenstein W, de Jong DA, van Santbrink H (1993) Monitoring cerebral oxygenation: experimental studies and preliminary clinical results of continuous monitoring of cerebrospinal fluid and brain tissue oxygen tension. Acta Neurochir Suppl (Wien) 59:50–57
15. Menzel M, Doppenberg EM, Zauner A, Soukup J, Reinert MM, Bullock R (1999) Increased inspired oxygen concentration as a factor in improved brain tissue oxygenation and tissue lactate levels after severe human head injury. J Neurosurg 91:1–10
16. Narayan RK, Kishore PR, Becker DP, Ward JD, Enas GG, Greenberg RP, Domingues Da Silva A, Lipper MH, Choi SC, Mayhall CG, Lutz HA 3rd, Young HF (1982) Intracranial pressure: to monitor or not to monitor? A review of our experience with severe head injury. J Neurosurg 56:650–659
17. Reinert M, Barth A, Rothen HU, Schaller B, Takala J, Seiler RW (2003) Effects of cerebral perfusion pressure and increased

fraction of inspired oxygen on brain tissue oxygen, lactate and glucose in patients with severe head injury. Acta Neurochir (Wien) 145:341–349 discussion 349-350

18. Sarrafzadeh AS, Sakowitz OW, Callsen TA, Lanksch WR, Unterberg AW (2000) Bedside microdialysis for early detection of cerebral hypoxia in traumatic brain injury. Neurosurg Focus 9:e2

19. Stiefel MF, Spiotta A, Gracias VH, Garuffe AM, Guillamondegui O, Maloney-Wilensky E, Bloom S, Grady MS, LeRoux PD (2005) Reduced mortality rate in patients with severe traumatic brain injury treated with brain tissue oxygen monitoring. J Neurosurg 103:805–811

20. Stiefel MF, Udoetuk JD, Spiotta AM, Gracias VH, Goldberg A, Maloney-Wilensky E, Bloom S, Le Roux PD (2006) Conventional neurocritical care and cerebral oxygenation after traumatic brain injury. J Neurosurg 105:568–575

21. Stocchetti N, Protti A, Lattuada M, Magnoni S, Longhi L, Ghisoni L, Egidi M, Zanier ER (2005) Impact of pyrexia on neurochemistry and cerebral oxygenation after acute brain injury. J Neurol Neurosurg Psychiatry 76:1135–1139

22. van den Brink WA, van Santbrink H, Steyerberg EW, Avezaat CJ, Suazo JA, Hogesteeger C, Jansen WJ, Kloos LM, Vermeulen J, Maas AI (2000) Brain oxygen tension in severe head injury. Neurosurgery 46:868–876 discussion 876-868

23. van Santbrink H, Maas AI, Avezaat CJ (1996) Continuous monitoring of partial pressure of brain tissue oxygen in patients with severe head injury. Neurosurgery 38:21–31