Published in final edited form as:
Neurosurgery. 2012 June ; 70(6): 1492–1503. doi:10.1227/NEU.0b013e31824ce933.

Position of Probe Determines Prognostic Information of Brain Tissue PO_2 in Severe Traumatic Brain Injury

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Abstract

BACKGROUND—Monitoring brain tissue PO_2 ($PbtO_2$) is part of multimodality monitoring of patients with traumatic brain injury (TBI). However, $PbtO_2$ measurement is a sampling of only a small area of tissue surrounding the sensor tip.

OBJECTIVE—To examine the effect of catheter location on the relationship between $PbtO_2$ and neurological outcome.

METHODS—A total of 405 patients who had $PbtO_2$ monitoring as part of standard management of severe traumatic brain injury were studied. The relationships between probe location and resulting $PbtO_2$ and outcome were examined.

RESULTS—When the probe was located in normal brain, $PbtO_2$ averaged 30.8 ± 18.2 compared with 25.6 ± 14.8 mm Hg when placed in abnormal brain ($P < .001$). Factors related to neurological outcome in the best-fit logistic regression model were age, $PbtO_2$ probe position, postresuscitation motor Glasgow Coma Scale score, and $PbtO_2$ trend pattern. Although average $PbtO_2$ was significantly related to outcome in univariate analyses, it was not significant in the final logistic model. However, the interaction between $PbtO_2$ and probe position was statistically significant. When the $PbtO_2$ probe was placed in abnormal brain, the average $PbtO_2$ was higher in those with a favorable outcome, 28.8 ± 12.0 mm Hg, compared with those with an unfavorable outcome, 19.5 ± 13.7 mm Hg ($P = .01$). $PbtO_2$ and outcome were not related when the probe was placed in normal-appearing brain.

CONCLUSION—These results suggest that the location of the $PbtO_2$ probe determines the $PbtO_2$ values and the relationship of $PbtO_2$ to neurological outcome.

Keywords

Brain tissue PO_2; Head injury; PO_2 monitoring; Traumatic brain injury

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Disclosures
This work was funded by National Institutes of Health grant P01-NS38660. The authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

Progress in the management of severe traumatic brain injury (TBI) has largely been through improvements in prehospital care, development of imaging techniques, and improved neurocritical care management. No specific therapies have been shown to improve neurological recovery. The major goal of neurocritical care management is to prevent secondary brain injury.

Present strategies in the management of patients with brain injury revolve around maintaining and improving cerebral oxidative metabolism.[1] Monitoring brain tissue PO_2 ($PbtO_2$) is part of multimodality monitoring of patients with TBI and is becoming more widely used in the management of patients with TBI, subarachnoid hemorrhage, and other acute neurological problems.[2,3] $PbtO_2$ monitoring in patients with TBI may help optimize cerebral perfusion pressure (CPP) by providing continuous data regarding regional or global brain oxygenation, and $PbtO_2$-directed therapies may improve outcome.[4,5]

However, $PbtO_2$ measurement is a localized sampling of only a small area of tissue immediately surrounding the sensor tip. Because of the heterogeneous nature of the brain injury in TBI and such localized measurement of the $PbtO_2$ with this technique, probe position is a critical aspect in correctly interpreting the resulting data. In general, placement of the $PbtO_2$ probe in normal brain is thought to give a measure of global brain tissue oxygenation, whereas the probe placed in or near injured brain reflects only local oxygenation in the surrounding brain tissue. Probe location (within normal brain vs injured brain) can therefore influence the detection of cerebral hypoxia and consequently patient management. There has been no general consensus on which position is the best strategy for brain tissue oxygen monitoring after severe TBI, and often the probe is placed on the basis of convenience (ie, at the site of the intracranial pressure [ICP] monitor) rather than as a result of a strategic clinical decision.

The purpose of this study was to examine the effect of catheter location on the relationship between $PbtO_2$ and long-term neurological outcome.

PATIENTS AND METHODS

The study design was a database review of deidentified research data that had been collected prospectively as a part of Institutional Review Board–approved research studies.

Patient Characteristics

A total of 405 patients who were admitted to Ben Taub General Hospital between July 1995 and March 2009 and had $PbtO_2$ monitoring as part of their standard monitoring of a severe TBI were studied. Inclusion criteria were the following: TBI, motor component of the Glasgow Coma Scale (GCS) score ≤5 (either after resuscitation or after subsequent deterioration), valid $PbtO_2$ data collected as a part of an ongoing research protocol, and demographic and injury characteristics and neurological outcome collected as a part of an ongoing research protocol. Exclusion criteria included GCS score of 3 with fixed, dilated pupils and loss to follow-up before 3 months after injury.

Clinical Management

The patients were managed by a standard protocol that emphasized the prevention of secondary insults and the prompt evacuation of intracranial masses. General management goals were PaO_2 > 100 mm Hg, $PaCO_2$ of 35 to 40 mm Hg, systolic blood pressure > 120 mm Hg, central venous pressure of 5 to 10 mm Hg, and urine output > 0.5 to 1 $mL \cdot kg^{-1} \cdot h^{-1}$. Phenytoin was given for 7 days as prophylaxis for seizures.

Invasive multimodal continuous monitoring included an ICP monitor, usually a ventriculostomy, a $PbtO_2$ probe, a jugular bulb catheter for jugular venous oxygen saturation ($SjvO_2$) monitoring, an arterial line for blood sampling and blood pressure monitoring, and a central venous catheter.

When the $PbtO_2$ probe was placed at the time of surgery for an intracranial mass lesion, it was positioned in the brain in what the neurosurgeon thought would be normal but vulnerable brain tissue based on the computed tomography (CT) scan appearance on admission. In diffuse injuries and with nonsurgical mass lesions, the $PbtO_2$ probe was usually placed at the site of the ICP monitor. When there was a unilateral parenchymal lesion, the $PbtO_2$ probe was placed on that side targeting perilesional tissue. When there was no parenchymal lesion, the $PbtO_2$ probe was usually placed on the right side. Regardless of the location, all $PbtO_2$ probes were positioned without the use of a bolt device. Confirmation of the location of the monitor was obtained on a follow-up CT scan usually within 24 hours after insertion.

The goals of management were ICP < 20 mm Hg and CPP > 60 mm Hg, unless $SjvO_2$ was < 50% or $PbtO_2$ was < 10 mm Hg, indicating the need for higher CPP. This threshold for $PbtO_2$ treatment was chosen because alterations in metabolism have been observed only when $PbtO_2$ drops < 10 mm Hg.[6,7] Treatment of intracranial hypertension was managed with the principles in the Brain Trauma Foundation guidelines for management of severe TBI[8] and involved surgical removal of mass lesions, use of cerebrospinal fluid drainage via ventriculostomy, sedation, neuromuscular paralysis, mannitol, and mild to moderate hyperventilation. Barbiturate coma, moderate hypothermia, and decompressive craniectomy were treatment options used for refractory intracranial hypertension. Forty-five patients (11.1%) underwent decompressive craniectomy. In 15 cases, the primary surgery was decompressive craniectomy for refractory intracranial hypertension with no evacuation of hematoma, and in 30 cases, the bone flap was left off at end of surgery for evacuation of a hematoma.

Low cerebral oxygenation ($PbtO_2$ < 10 mm Hg) was treated with the algorithm shown in Figure 1. This management algorithm was intended first to normalize factors that might impair cerebral oxygen delivery, including intracranial hypertension, hypotension, hypoxia, hypocarbia, and anemia. If $PbtO_2$ remained low after correction of these factors, normobaric hyperoxia or induced hypertension was used to try to improve oxygenation.

Monitoring of ICP, $PbtO_2$, and $SjvO_2$ was continued until both the ICP and brain oxygenation were normal for about 24 hours without treatment. At the end of the monitoring period, the $PbtO_2$ probes were removed and calibration drift was determined by measuring a stable PO_2 in room air, in blood gas standard calibration solutions, and in a no-oxygen “zero” solution.

Data Analysis

The demographic and clinical data collected included age, sex, mechanism of injury, type of intracranial injury, extent and severity of all injuries, and surgical procedures required. Trauma scores collected included the GCS score and pupil size/reactivity at the accident scene and in the emergency center and the Injury Severity Score. Cerebral oxygenation values and the other physiological parameters were recorded hourly within a few hours after intensive care unit admission and for the duration of the monitoring. The admission CT scan and a follow-up CT scan when the location of the $PbtO_2$ probe could be confirmed were available for analysis.

The Marshall CT category[9] was used to describe the admission CT scan findings, and the results were collapsed into the following 3 groups: mild diffuse injury (diffuse injury 1 and 2), severe diffuse injury (diffuse injury 3 and 4), and mass lesions (evacuated and unevacuated mass lesions). The GCS score on admission was also classified into the following 2 categories according to the motor GCS score: motor GCS score 4 to 6 and of 1 to 3. Pupil reactivity was classified as both pupils reactive, 1 unreactive pupil, or both pupils unreactive.

The patients had long-term Glasgow Outcome Scale (GOS) scores available (320 patients [79%] at 6 months and an additional 85 patients [21%] at 3 months). The analyses were performed for both the 320 patients with 6-month GOS scores and the 405 patients with the last known GOS score with similar results. In the data reported here, the last known GOS score was used for long-term outcome so that the data from all 405 patients could be used. The long-term GOS scores were dichotomized as favorable recovery (good recovery or moderate disability) and unfavorable recovery (severe disability, vegetative, or dead).

$PbtO_2$ findings were characterized for analysis in several different ways. The trend pattern of $PbtO_2$ over time was classified as a benign pattern when the values were always ≥ 10 mm Hg or only transiently, < 10 mm Hg at the onset of monitoring and as a tissue hypoxia pattern when the values were persistently < 10 mm Hg or decreased to < 10 mm Hg during the hospital course. In addition, the average $PbtO_2$ values for the entire monitoring period and for the duration of time that $PbtO_2$ was less than various thresholds (< 10, < 15, and < 20 mm Hg) were calculated for each patient. Follow-up CT scans were reviewed, and the position of the $PbtO_2$ probe within the brain was classified into one of the following 4 positions: in normal-appearing brain, near contused brain, in brain under an evacuated hematoma, or within contused brain (Figure 2). The last 3 probe positions were collapsed for the analysis as being in vulnerable or abnormal brain.

The relationship of demographic/injury characteristics (including age, GCS score, injury type, and the relationship of the $PbtO_2$ parameters described above) to GOS score was studied. For categorical data, the χ^2 test was used. For numerical data, the *t* test was used when the data were normally distributed; otherwise, the rank-sum test was used. Factors found to be significantly related to outcome in the univariate analyses were further studied with logistic regression analysis. The final logistic regression model was fit by use of a backward stepwise procedure. The final model was used to generate graphic representations of the effects of different variables.

RESULTS

Patient Characteristics

$PbtO_2$ data from 405 patients were available for analysis. Demographic and injury characteristics of all 405 patients, which are summarized in Table 1, were typical for a severe TBI population. Men predominated in the group, 327 (80.7%) compared with 78 women (19.3%). The mean age for the group was 34.2 ± 14.1 years, and the mean Injury Severity Score was 30.5 ± 8.0. The mechanism of injury was motor vehicle collision in 268 (66.2%), assault in 41 (10.1%), fall/jump in 58 (14.3%), and other in 21 (5.2%). In 17 patients (4.2%), the mechanism was unknown. Prehospital hypoxia and hypotension occurred in 29.4% and 12.8% of the patients, respectively.

An admission GCS score was available for 403 of the patients. The motor component of the GCS score was 1 to 3 in 188 patients (46.4%) and 4 to ± in 215 patients (53.1%). In 2 patients (0.5%), an admission GCS score could not be obtained because of pharmacological paralysis. A small fraction of patients (3.6%) had a motor score of 6 on their

postresuscitation examination but subsequently deteriorated to < 6. Pupils were reactive on admission in 236 patients (58.3%), 1 pupil was unreactive in 43 patients (10.6%), and both pupils were unreactive in 105 patients (25.9%). For 19 patients (4.7%), the pupils could not be assessed because of eye swelling or injury. The CT scan of the head on admission was classified as diffuse injury 1 or 2, diffuse injury 3 or 4, and mass lesion in 135 patients (33.3%), 87 patients (21.5%), and 183 patients (45.2%), respectively.

The GOS score was assessed at 3 and 6 months. A total of 129 patients (31.9%) had a favorable outcome, whereas 276 patients (68.1%) had an unfavorable outcome. Eighty-six of the 405 patients (21.2%) died.

$PbtO_2$ Variables

$PbtO_2$ was measured with a Licox sensor in almost all of the patients (396 patients [97.7%]). Alternative catheters (either Paratrend 7 or Neurotrend catheters) were used in 9 patients (2.2%). The $PbtO_2$ sensor was positioned in normal brain in 159 patients (39.3%) and in abnormal brain in 246 patients (60.7%). The average time for start of $PbtO_2$ monitoring was 10.5 ± 0.6 hours in patients who required surgery on admission and 10.4 ± 0.5 hours in patients who were taken directly from the emergency center to the intensive care unit. As might be expected from the nature of traumatic injuries, the type of injury strongly influenced the position of the $PbtO_2$ probe (Figure 3). The position of the probe was divided evenly between normal and abnormal brain only in patients with diffuse injury 3 or 4. In patients with mild diffuse injuries (Marshall CT category diffuse injury 1 or 2), 71.1% of the patients had the $PbtO_2$ probe placed in normal-appearing brain. In contrast, in patients with mass lesions, the probe was placed in normal-appearing brain in only 11.5%.

ICP and $PbtO_2$ were monitored for an average of 163.5 ± 118.9 and 96.8 ± 48.2 hours, respectively. Data were analyzed from a total of 39 097 hours of continuous $PbtO_2$ monitoring. Summary values for ICP, mean arterial pressure, CPP, $SjvO_2$, $ETCO_2$, and SaO_2 are listed in Table 2.

Trend graphs for $PbtO_2$ over time (median ± interquartile ranges) for the different catheter positions are illustrated in Figure 4. When the $PbtO_2$ probe was placed in normal-appearing brain (Figure 4, top left), the median values for $PbtO_2$ were > 20 mm Hg throughout the monitoring period. Very few values were < 10 mm Hg. When the $PbtO_2$ probe was placed in normal-appearing brain underlying an evacuated hematoma (Figure 4, top right), median $PbtO_2$ values were slightly lower but remained above 20 mm Hg throughout the monitoring period. More $PbtO_2$ values were around 10 mm Hg during the first day after injury. In patients in whom the $PbtO_2$ probe was placed near a contusion (Figure 4, bottom left), the median $PbtO_2$ values tended to decrease over the first few hours after injury, and a substantial portion of the $PbtO_2$ values were < 10 mm Hg during the first 24 hours after injury. When the $PbtO_2$ probe was placed in contused brain (Figure 4, bottom right), the median $PbtO_2$ values decreased after admission and were near or < 10 mm Hg throughout the first 30 hours after injury.

Several methods for summarizing the $PbtO_2$ data were examined to try to capture the information observed in Figure 4. These variables are summarized in Tables 2 and 3 and are described below first for all patients and then by $PbtO_2$ probe position.

The average $PbtO_2$ was 27.6 ± 14.4 mm Hg for the whole monitoring period in all patients. When the probe was located in normal brain, the average $PbtO_2$ was 30.8 ± 18. compared with 25.6 ± 14.8 mm Hg when then probe was placed in abnormal brain ($P < .001$). The cumulative hours that $PbtO_2$ stayed below the thresholds of 20, 15, and 10 mm Hg were a median of 24 (5-50.25), 11 (1-34), and 1 (0-18), respectively, in all patients. The time that

$PbtO_2$ was below each threshold was significantly longer in patients in whom the $PbtO_2$ probe was placed in abnormal brain (Table 3).

Four characteristic patterns for the change in $PbtO_2$ over time were observed in the individual patients. Trends in which $PbtO_2$ was always ≥ 10 mm Hg or $PbtO_2$ was only transiently decreased < 10 mm Hg at the beginning of the monitoring period were considered benign patterns. Most patients (343 [84.7%]) had such a pattern (Table 2). The remaining patients had a $PbtO_2$ pattern in which values were persistently < 10 mm Hg (15 [3.7%]) or decreased to < 10 mm Hg during the monitoring period after initially being normal (47 [11.6%]). These trend patterns were also strongly related to the $PbtO_2$ probe position (Table 3), with the probe being in abnormal brain in most of the patients (86%) having the abnormal $PbtO_2$ trends over time.

Relationship of $PbtO_2$ Variables to Outcome

In the univariate analyses, the factors that were significantly related to outcome included age, sum GCS score, the motor component of the GCS score from the neurological examination in the emergency center after resuscitation, pupil reactivity, type of injury, all of the $PbtO_2$ variables, and the ICP and CPP summary variables (Table 4). Patients who had a favorable recovery were younger, had a higher GCS score on admission, and were less likely to have unreactive pupils. Patients with an admission Marshall CT scan category of diffuse injury 1 or 2 were also more likely to be in the favorable outcome group ($P = .01$) than those patients with diffuse injury 3 or 4 or a mass lesion.

For the $PbtO_2$ variables (Table 4), the average $PbtO_2$, the duration of time that $PbtO_2$ was less than each of the 3 thresholds, and the $PbtO_2$ trend pattern were all significantly related to neurological outcome. Patients with a favorable outcome had an average $PbtO_2$ of 32.2 ± 16.3 compared with 25.1 ± 13.5 in the patients with an unfavorable outcome ($P < .001$). Patients with a favorable outcome were also more likely to have a $PbtO_2$ trend pattern in which $PbtO_2$ was never < 10 mm Hg (65.9% vs 46.7% for those with an unfavorable outcome) and less likely to have a pattern in which $PbtO_2$ was persistently < 10 mm Hg or decreased to < 10 mm Hg after initially being normal (3.9% vs 20.7%). The median duration of time that $PbtO_2$ was < 10 mm Hg was 0 hours for patients with a favorable recovery compared with 6 hours in patients with an unfavorable outcome ($P< .001$).

The position of the $PbtO_2$ was also significantly related to neurological outcome ($P = .03$), with patients having an unfavorable outcome more likely to have the probe placed in abnormal brain. Because the probe position was not randomly assigned in this study but was dependent on the type of injury and because the probe position was not a therapeutic intervention per se, it is most likely that this association with outcome reflects prognostic information from the type of injury.

In the final best-fit logistic regression model (Table 5), the factors that were related to neurological outcome were age, $PbtO_2$ probe position, initial motor GCS score, and the $PbtO_2$ trend pattern. Although the type of injury was significantly related to outcome in univariate analyses, this factor fell out of the final logistic model. It is possible that the prognostic information from type of injury was contained in the probe position, which was closely related to type of injury. Although the average $PbtO_2$ was significantly related to outcome in the univariate analyses, it was not significant in the final logistic model. However, the interaction between $PbtO_2$ and probe position was statistically significant. In patients in whom the $PbtO_2$ probe was placed in abnormal brain, the average $PbtO_2$ was higher in those with a favorable outcome, 28.8 ± 12.0, compared with those with an unfavorable outcome, 19.5 ± 13.7 mm Hg ($P = .01$). There was no significant difference in $PbtO_2$ with outcome when the probe was placed in normal-appearing brain: 33.8 ± 19.4 mm

Hg for patients with favorable outcome vs 31.4 ± 13.1 mm Hg for patients with unfavorable outcome. The odds ratio for average $PbtO_2$ to be associated with a favorable outcome was 0.988 when the $PbtO_2$ probe was in normal brain but 1.033 when the $PbtO_2$ probe was in abnormal brain. This odds ratio indicates that for every increase in average $PbtO_2$ of 1 mm Hg, the chance of having a favorable outcome was 1.033 times greater. Figure 5 shows this interaction relationship for average $PbtO_2$ and probe position in graphical form.

DISCUSSION

The local nature of the $PbtO_2$ values that are obtained with currently available probes is both a potential advantage and a problem. The advantage is that unlike global measurements of oxygenation or cerebral blood flow, the $PbtO_2$ probe has the possibility of being able to monitor focal regions of the brain. The problem is that the probe has to be placed strategically in the brain tissue of interest to take advantage of this monitoring characteristic. The critical importance of probe location is underemphasized in most studies reporting $PbtO_2$ data. In addition, the common practice of placing the $PbtO_2$ probe at the same site as the ICP monitor limits the ability to choose the optimal location for the $PbtO_2$ probe.

A number of previous studies have shown a relationship between $PbtO_2$ values and neurological outcome. Most of these studies have reported that their monitoring strategy was to place the probe in normal-appearing brain. Not all of the studies adjusted the $PbtO_2$ findings for other injury severity indicators. In 1998, Bardt et al[10] reported that a $PbtO_2 < 10$ mm Hg for > 30 minutes reduced the percent of favorable long-term outcomes from 73% to 22%, and Valadka et al[11] found that increasing durations of $PbtO_2 < 15$ mm Hg were associated with increasing risk of death. The Valadka et al model included age and duration of monitoring but not other important injury severity indicators. Van den Brink et al[12] also saw that a $PbtO_2 < 10$ mm Hg for > 30 minutes was associated with a greater chance of a poor outcome. $PbtO_2$ remained a significant predictor of outcome even when adjusted for clinical characteristics and CT scan findings.

Likewise, several previous studies have examined differences in $PbtO_2$ and other metabolic parameters in normal and pericontusional brain. A few have even compared different tissues in the same patient using 2 different probes simultaneously.[13,14] Longhi et al[15] compared $PbtO_2$ in pericontusional tissue with values obtained in normal-appearing brain after diffuse brain injury. Like the present study, they observed significantly lower $PbtO_2$ and longer durations of low $PbtO_2$ in pericontusional tissue. They also found different trends over time, with $PbtO_2$ recovering to normal over time in pericontusional tissue. One difference in methods was that the data collection started on day 2 after injury and the relationship to outcome was not studied. Extending these types of observations by adding measurements of extracellular biochemistry using microdialysis, Timofeev et al[6] reported higher levels of lactate, glycerol, lactate/pyruvate ratio, and lactate/glucose ratio in pericontusional tissue, even when adjusted for other factors including the $PbtO_2$.

The logical follow-up to these observational studies and others that relate $PbtO_2$ findings to neurological outcome is to determine whether $PbtO_2$ monitoring can direct therapy to maximize neurological outcome by preventing or treating early cerebral hypoxia. To date, such studies have been primarily comparisons with historical or concurrent controls that can reflect differences in injury severity and/or changes in other management practices over time. Compared with historical controls, several studies have found that $PbtO_2$-directed management has resulted in improved neurological recovery and/or mortality rate.[4,5,16] In contrast, Martini et al[17] found that $PbtO_2$-directed therapy performed at the discretion of the neurosurgeon resulted in no improvement in mortality rate but instead a worse neurological recovery and greater hospital resource use. The $PbtO_2$-monitored group in this study was

more severely injured, however, which may have affected the decision to monitor $PbtO_2$. The probe placement strategy was described in these observational studies was normal-appearing brain[5] or normal-appearing brain on the side of the most severe injury.[4,16,17] A phase II randomized clinical trial examining the value of $PbtO_2$-directed therapy to improve neurological outcome is planned (www.ClinicalTrials.gov; identifier NCT00974259). This may provide a more definite answer to these questions about whether $PbtO_2$-directed therapy can alter outcome.

Although the strategy for placing the probes was described in most of these previous studies, the final location of the probe is not commonly characterized or analyzed. In the present study, the placement strategy was to target normal-appearing tissue on the side of the most severe injury, which was thought to be the most vulnerable brain tissue. However, this description was not found to adequately characterize the actual location of the probes. Therefore, the final placement of the probe was examined on a follow-up CT scan, characterized, and included in the analysis. Four different descriptions of the final location were used, and different $PbtO_2$ trends over time were observed with each different location that described increasingly more severe injury of the brain.

Because of the retrospective nature of the study design, there are some limitations to the present study. The location of the $PbtO_2$ probe is inherently related to the nature of injury. That is, in patients with a diffuse injury, there would not always be an abnormal area to monitor. In some patients with mass lesions, there may be very limited normal brain that can be selected for monitoring. In addition, the placement of the probe in this study was not randomized but rather directed by the nature of the injury in many cases. For these reasons, the conclusions that can be drawn are limited. However, the present study clearly demonstrates how critical the location of the $PbtO_2$ probe is in determining the PO_2 values that will be obtained.

In addition, the present study showed that additional prognostic information from the $PbtO_2$ values was available only in patients in whom the probe was located in abnormal brain tissue, perhaps because there were fewer episodes of cerebral hypoxia in the patients in whom the probe was located in normal brain tissue. It might be also be that normal tissue is more resistant to cerebral hypoxia, and thresholds for hypoxic injury might be different in normal and abnormal brain tissue. This finding should not be interpreted to mean that monitoring $PbtO_2$ in normal brain tissue is not useful because all tissue hypoxia events, regardless of location, were treated in this study. Because the probe location cannot be completely controlled by the strategy used for monitor placement, the present findings suggest that the final probe location will affect $PbtO_2$ values and should be included in analyses.

The threshold for treatment of tissue hypoxia in this study was a $PbtO_2$ of < 10 mm Hg. The optimal treatment threshold has not been clearly established for TBI patients, and it is even possible that thresholds for injury may differ in normal and injured brain tissue. Early studies observed a relationship between the duration of time $PbtO_2$ was < 10 to 15 mm Hg and a poor neurological outcome.[10-12] Others have recommended maintaining $PbtO_2 > 15$ or even 20 mm Hg. Although the analysis included examination of time below several different thresholds, the results of this analysis might have been different if a higher treatment threshold had been used in managing the patients.

The PO_2 catheter technology evolved significantly over the period of this study. There are small inherent differences in the performance of the various catheters used in the study.[18] These differences are probably not clinically significant but could have introduced some variability into the analysis.

The GOS score at 6 months was not available in 85 patients and was imputed from the 3-month GOS score. Neurological recovery continues to improve over time, although the number of patients who would be expected to improve from unfavorable to favorable outcome between 3 and ± months is relatively small. It is possible that the results would have been different if the 6-month GOS score had been available in all patients. However, when the analyses were performed on only the 320 patients with 6-month GOS scores, the results were similar.

CONCLUSION

The purpose of this study was to examine the effect of catheter location on the relationship between $PbtO_2$ and long-term neurological outcome. The results showed that the location of the probe determined both the $PbtO_2$ values that were obtained and whether the $PbtO_2$ values were related to long-term neurological outcome. The location of the $PbtO_2$ probe must be kept in mind during the interpretation of data from individual patients and should be reported in publications that analyze $PbtO_2$ data.

ABBREVIATIONS

CPP	cerebral perfusion pressure
GCS	Glasgow Coma Scale
GOS	Glasgow Outcome Scale
TBI	traumatic brain injury

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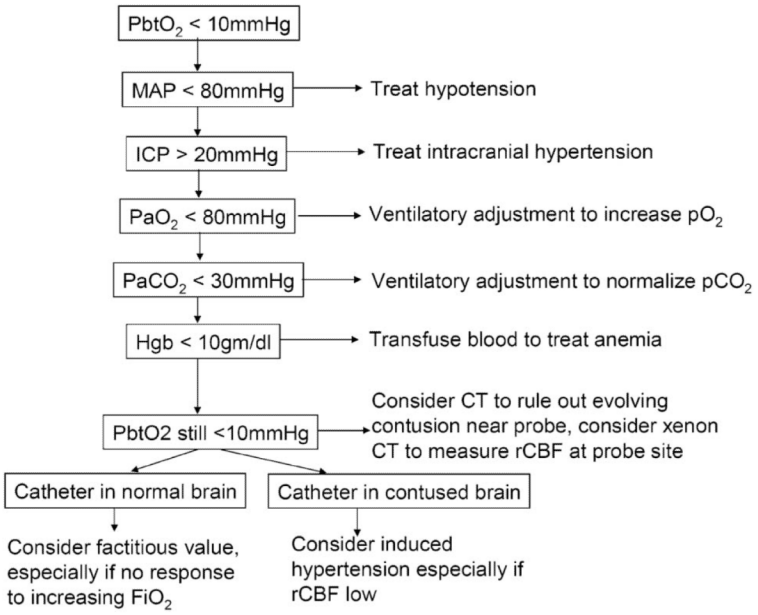

FIGURE 1.

Algorithm for treatment of a low brain tissue PO_2 ($PbtO_2$) used throughout the study period. CT, computed tomography; Hgb, hemoglobin; ICP, intracranial pressure; MAP, mean arterial pressure; rCBF, regional cerebral blood flow.

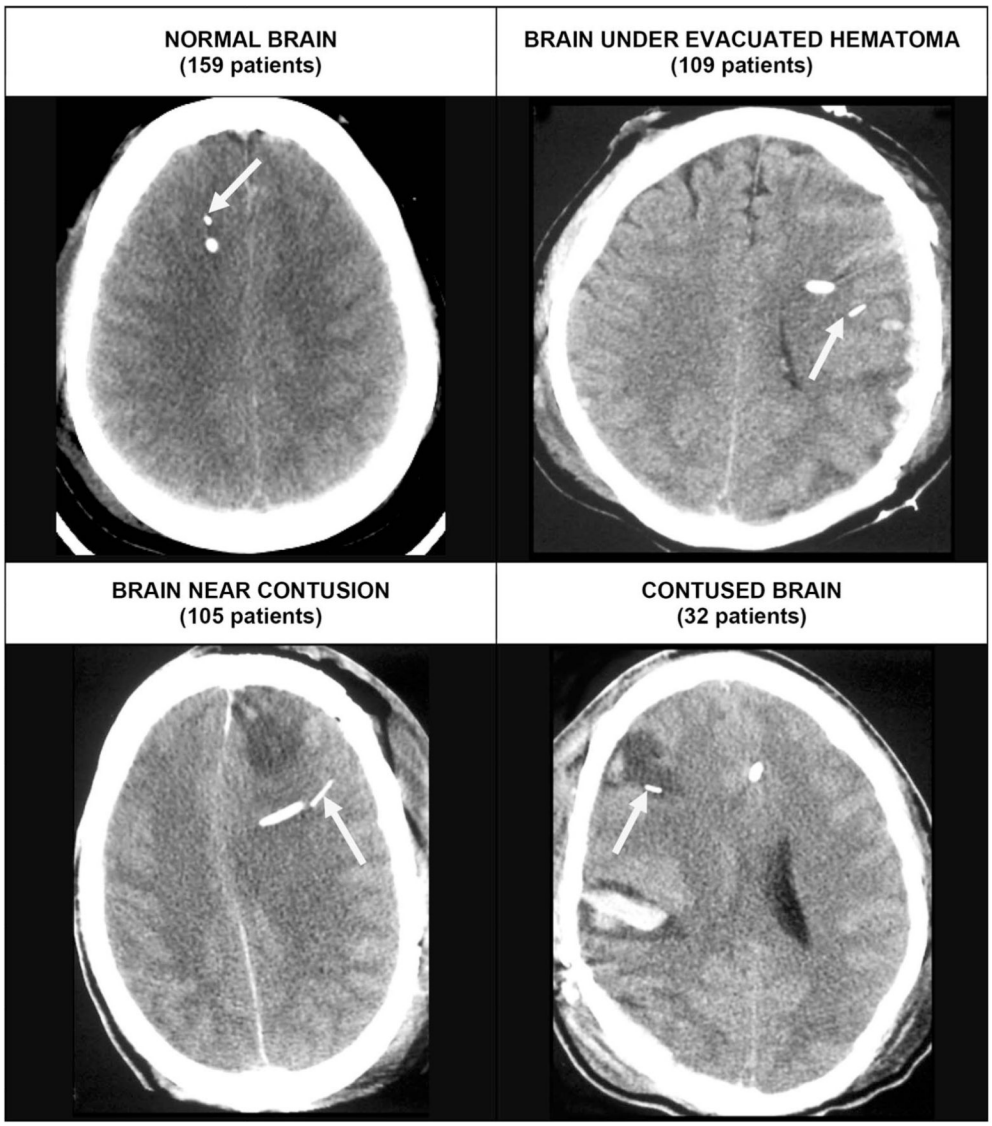

FIGURE 2.

Computed tomography scans illustrate typical appearance of the different catheter positions. The arrow identifies the brain tissue PO_2 ($PbtO_2$) probe in each case. **Top left,** the $PbtO_2$ probe in normal-appearing right frontal lobe in a patient with a diffuse brain injury. **Top right,** the $PbtO_2$ probe in brain after evacuation of a subdural hematoma. The probe was placed at the time of surgery in brain tissue. The brain appears normal but has been compressed by the subdural hematoma. **Bottom left,** a $PbtO_2$ probe in the left frontal lobe near a contusion. If the contusion expands, this tissue is likely to become involved or to be compressed. **Bottom right,** a $PbtO_2$ within a contusion in the right frontal lobe.

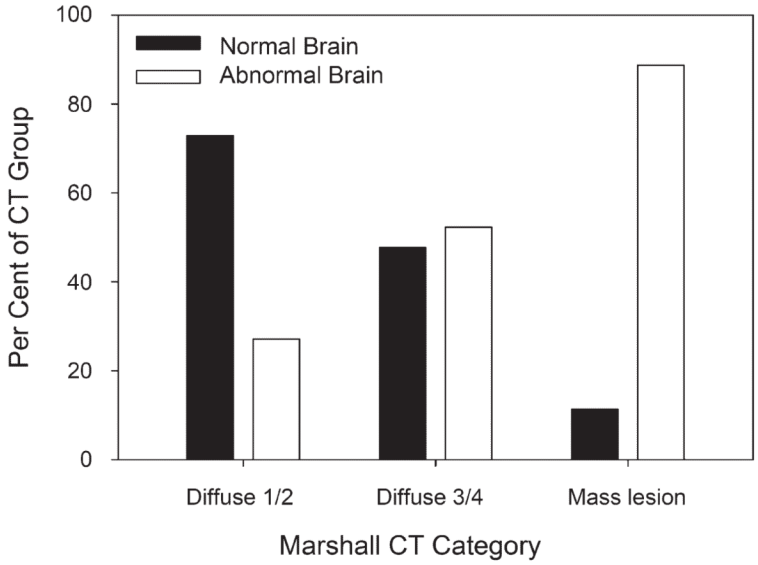

FIGURE 3.

The position of the brain tissue PO_2 ($PbtO_2$) probe was significantly influenced by the type of computed tomography (CT) scan lesion ($P < .001$).

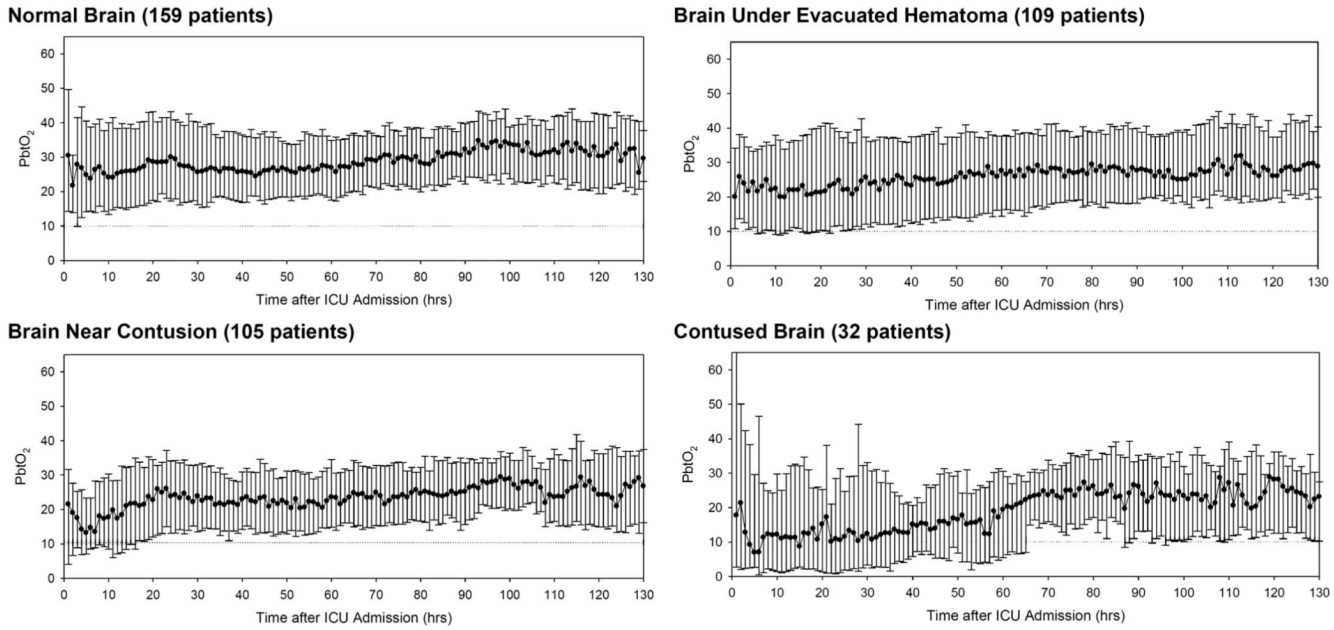

FIGURE 4.

Trend graphs of brain tissue PO_2 ($PbtO_2$) over time (median ± interquartile range) for the different catheter positions. ICU, intensive care unit.

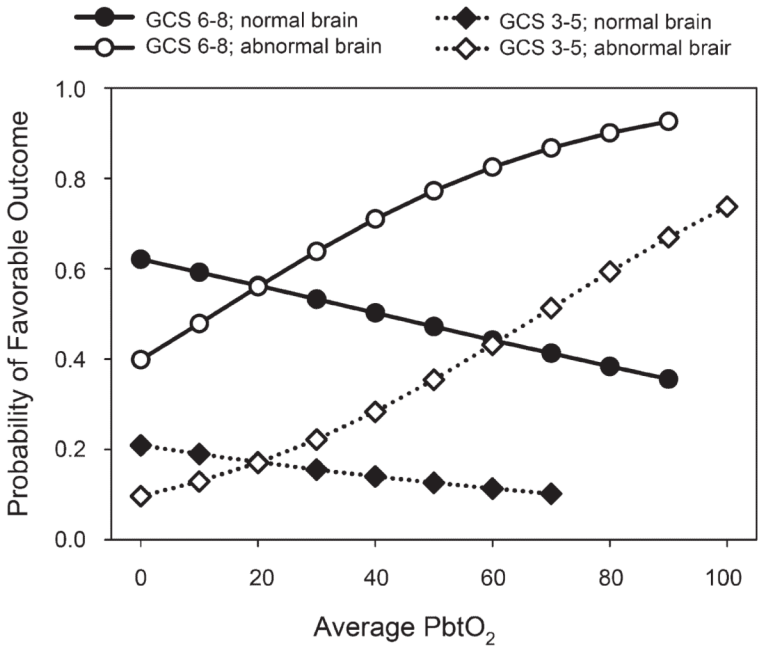

FIGURE 5.

Results of logistic regression model for the relationship of average brain tissue PO_2 ($PbtO_2$) and neurological outcome. The chances for a favorable outcome are generally less in patients with poor admission neurological status (diamonds) than in patients with better admission neurological status (circles). The open symbols show the chances of favorable outcome significantly improving with increasing $PbtO_2$ when the probe is placed in abnormal tissue; the solid symbols show no significant relationship between outcome and $PbtO_2$ when the probe is placed in normal brain. GCS, Glasgow Coma Scale.

TABLE 1

Demographic and Injury Severity Characteristics of 405 Patients With $PbtO_2$ Monitoring and Long-term Neurological Outcome[a]

Variable	Mean ± SD or n (%)
Age, y	34.2 ± 14.1
Sex	
Male	327 (80.7)
Female	78 (19.3)
Race	
White	112 (27.6)
Black	98 (24.2)
Hispanic	186 (45.9)
Asian	9 (2.2)
Mechanism of injury	
Motor vehicle collision	268 (66.2)
Fall/jump	58 (14.3)
Assault	41 (10.1)
Other	21 (5.2)
Unknown	17 (4.2)
Motor GCS	
1-3	188 (46.4)
4-6	215 (53.1)
Untestable	2 (0.5)
Pupils	
Both reactive	236 (58.3)
1 Unreactive	43 (10.6)
Both unreactive	105 (25.9)
Untestable	19 (4.7)
Injury Severity Score	30.5 ± 8.0
Apache II Score	20.8 ± 6.6
Prehospital hypotension	
Yes	52 (12.8)
No	353 (87.2)
Prehospital hypoxia	
Yes	119 (29.4)
No	286 (70.6)
Type of injury (Marshall CT category)	
Diffuse injury 1 or 2	135 (33.3)
Diffuse injury 3 or 4	87 (21.5)
Mass lesion	183 (45.2)

Variable	Mean ± SD or n (%)
Glasgow Outcome Scale	
Good recovery	62 (15.3)
Moderate disability	67 (16.5)
Severe disability	162 (40.0)
Vegetative	28 (6.9)
Dead	86 (21.2)

[a] CT, computed tomography; GCS, Glasgow Coma Scale.

TABLE 2

Brain Tissue Po_2 Catheter Information and Physiology in 405 Patients[a]

Variable	Mean ± SD, Median (Interquartile Range), or n (%)
Type of catheter	236 (58.3)
Licox Po_2 and Licox temperature probes	
Licox Po_2/temperature combination probe	160 (39.5)
Neurotrend Po_2, Pco_2, pH probe	7(1.7)
Paratrend 7 Po_2, Pco_2, pH probe	2 (0.5)
Location of catheter	
Normal brain	159 (39.3)
Brain underlying evacuated hematoma	109 (26.9)
Brain near contusion	105 (25.9)
Contused brain	32 (7.9)
Average $Pbto_2$, mm Hg	
All patients	27.6 ± 14.4
Duration of $Pbto_2$ monitoring, h	
Time < 10 mm Hg	1 (0-18)
Time < 15 mm Hg	11 (1-34)
Time < 20 mm Hg	24 (5-50.25)
$Pbto_2$ trend pattern	
Always ≥ 10 mm Hg	214 (52.8)
Transiently < 10 mm Hg at start	129 (31.9)
Persistently < 10 mm Hg	15 (3.7)
Decreased to < 10 mm Hg after normal at start	47 (11.6)
Average ICP, mm Hg	19.0 ± 9.5
Average MAP, mm Hg	91.6 ± 9.2
Average CPP, mm Hg	72.6 ± 14.2
Average $Sjvo_2$, %	73.9 ± 5.5
Average $ETco_2$, mm Hg	31.3 ± 3.9
Average Sao_2, %	99.0 ± 0.9

[a] CPP, cerebral perfusion pressure; ICP, intracranial pressure; MAP, mean arterial pressure; $Pbto_2$, brain tissue Po_2; $Sjvo_2$, jugular venous oxygen saturation.

TABLE 3

Brain Tissue Po_2 Variables by Probe Position in 405 Patients With Long-term Neurological Outcome[a]

Variable	Probe in Normal Brain, Mean ± SD or Median (Interquartile Range)	Probe in Abnormal Brain, Mean ± SD or Median (Interquartile Range)	*P*
Patients, n	159	246	
Average $Pbto_2$	30.8 ± 18.2	25.6 ± 14.8	<.001
$Pbto_2$ duration below thresholds, h			
Time < 10 mm Hg	0 (0-6.0)	5 (0-23.0)	<.001
Time < 15 mm Hg	4.0 (0-20.8)	15 (3-43)	<.001
Time < 20 mm Hg	16 (2-36)	30 (9-58)	<.001
$Pbto_2$ trend pattern	<.001		
Always ≥ 10 mm Hg	108 (50.5)	106 (49.5)	
Transiently < 10 mm Hg at start	42 (32.6)	87 (67.4)	
Persistently < 10 mm Hg	2 (13.3)	13 (86.7)	
Decreased to < 10 mm Hg after normal at start	7 (14.9)	40 (85.1)	

[a] $Pbto_2$, brain tissue Po_2.

TABLE 4

Relationship of Demographic, Injury Severity, Brain Tissue Po_2 and Other Hemodynamic Variables to Neurological Outcome (405 Patients With Outcome Data)[a]

Variable	Favorable Outcome, Mean ± SD, Median (Interquartile Range), or n (%)	Unfavorable Outcome, Mean ± SD, Median (Interquartile Range), or n (%)	Univariate Analysis *P*
Patients, n	129	276	
Demographic and injury severity variables			
Age	29.4 ± 12.6	37.4 ± 14.7	<.001
$Pbto_2$ catheter position			.03
Normal brain	61 (47.3)	98 (35.5)	
Abnormal brain	68 (52.7)	178 (64.5)	
Sum GCS			.006
9-15	35 (27.1)	39 (14.1)	
3-8	93 (72.1)	236 (85.5)	
Untestable	1 (0.8)	1 (0.4)	
Initial motor GCS			<.001
1-3	32 (24.8)	156 (56.5)	
4-6	96 (74.4)	119 (43.1)	
Untestable	1 (0.8)	1 (0.4)	
Pupil reactivity			<.001
Both pupils reactive	98 (76.0)	138 (50.0)	
1 or Both pupils nonreactive	27 (20.9)	123 (44.6)	
Untestable	4(3.1)	15 (5.4)	
Injury Severity Score	30.1 ± 7.4	30.7 ± 8.3	.46
Apache II Score	18.2 ± 6.2	21.9 ± 6.4	<.001
Prehospital hypotension			.33
Yes	13 (10.1)	39 (14.1)	
No	116 (89.9)	237 (85.9)	
Prehospital hypoxia			
Yes	30 (23.3)	89 (32.3)	.008
No	99 (76.7)	187 (67.7)	
Type of injury (Marshall CT category)			.01
Diffuse injury 1 or 2	56 (43.4)	79 (28.6)	
Diffuse injury 3 or 4	22 (17.1)	65 (23.6)	
Mass lesion	51 (39.5)	132 (47.8)	
$Pbto_2$ Variables			
Average $Pbto_2$, mm Hg	32.2 ± 16.3	25.1 ± 13.5 31.4 ± 13.1	<.001
Average $Pbto_2$ × catheter position			
Normal brain	33.8 ± 19.4		

Variable	Favorable Outcome, Mean ± SD, Median (Interquartile Range), or n (%)	Unfavorable Outcome, Mean ± SD, Median (Interquartile Range), or n (%)	Univariate Analysis *P*
Abnormal brain	28.8 ± 12.0	19.5 ± 13.7	
Tme $Pbto_2$ < 10 mm Hg, h	0 (0-6.25)	6 (0-25.5)	<.001
Tme $Pbto_2$ < 15 mm Hg, h	3 (0-19.25)	16 (3-42)	<.001
Time $Pbto_2$ < 20 mm Hg, h	11 (1.75-39.25)	31 (9.0-56.75)	<.001
$Pbto_2$ trend pattern			<.001
Never < 10 mm Hg	85 (65.9)	129 (46.7)	
Transiently < 10 mm Hg at start	39 (30.2)	90 (32.6)	
Persistently < 10 mm Hg or decreasing	5 (3.9)	57 (20.7)	
Other hemodynamic variables			
Average ICP (mm Hg)	16.5 ± 4.6	20.0 ± 10.9	<.001
Tme ICP > 25 mm Hg, h	6 (1-37.5)	17 (2-45)	.004
Tme ICP > 30 mm Hg, h	1 (0-7)	4 (0-17)	.002
Tme ICP > 40 mm Hg, h	0 (0-1)	0 (0-3)	.006
Highest ICP, mm Hg	35.5 ± 12.7	44.0 ± 24.1	<.001
Average MAP, mm Hg	91.8 ± 7.1	91.4 ± 10.0	.70
Tme MAP < 70 mm Hg, h	1 (0-5)	1 (0-5)	.17
Tme MAP < 80 mm Hg, h	14 (3.75-30)	14 (5-33.5)	.51
Tme MAP < 90 mm Hg, h	49 (22-81.2)	48.5 (20.5-88)	.60
Average CPP, mm Hg	75.3 ± 7.4	71.4 ± 16.3	.009
Time CPP < 50 mm Hg, h	1 (0-4)	2 (0-11)	.007
Time CPP < 60 mm Hg, h	11 (2-24.5)	13 (3-42.5)	.08
Time CPP < 70 mm Hg, h	34 (10.75-74.5)	40.5 (16-89)	.15
Average $Sjvo_2$, %	72.9 + 5.6	74.4 + 5.5	.02
Time $Sjvo_2$ < 50%, h	0 (0-2)	0 (0-2)	.37
Time $Sjvo_2$ < 40%, h	0 (0-0)	0 (0-0)	.86
Time $Sjvo_2$ < 30%, h	0 (0-0)	0 (0-0)	.21

[a] CPP, cerebral perfusion pressure; CT, computed tomography; GCS, Glasgow Coma Scale; ICP, intracranial pressure; MAP, mean arterial pressure; $Pbto_2$, brain tissue Po_2.

TABLE 5

Best-Fit Logistic Regression Model[a]

Variable	Best-Fit Logistic Model *P*
Age	<.001
$PbtO_2$ catheter position	.03
Initial motor GCS	<.001
Motor GCS × catheter position interaction	.14
Average $PbtO_2$	.33
Average $PbtO_2$ × catheter position interaction	.01
$PbtO_2$ trend pattern	.04

[a]GCS, Glasgow Coma Scale; $PbtO_2$, brain tissue PO_2.