# The Accuracy of Transcutaneous $P_{CO_2}$ in Subjects With Severe Brain Injury: A Comparison With End-Tidal $P_{CO_2}$

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**BACKGROUND: In patients suffering from brain injury, end-tidal $P_{CO_2}$ ($P_{ETCO_2}$) monitoring is controversial, but transcutaneous $P_{CO_2}$ ($P_{tcCO_2}$), which is noninvasive and utilizes immediate display, may be an alternative method. We hypothesized that $P_{tcCO_2}$ would be more accurate than $P_{ETCO_2}$ for monitoring $P_{aCO_2}$ in patients with severe brain injury. METHODS: A prospective observational study included consecutive mechanically ventilated adult subjects who had acute brain injury and an arterial catheter in place. When an arterial blood gas analysis was required, the $P_{ETCO_2}$ and $P_{tcCO_2}$ values were simultaneously recorded. The agreement between the $P_{ETCO_2}$, $P_{tcCO_2}$, and $P_{aCO_2}$ measurements (reference) was determined using the Bland-Altman method. The number of outliers defined by the formula ([$P_{ETCO_2}$ or $P_{tcCO_2}$] − $P_{aCO_2}$) > ± 4 mm Hg indicated the proportion of measurements that were considered clinically unacceptable. RESULTS: A total of 25 subjects were included in the study, and 85 simultaneous measurements of $P_{aCO_2}$, $P_{tcCO_2}$, and $P_{ETCO_2}$ were obtained. The bias and precision between $P_{aCO_2}$ and $P_{tcCO_2}$ were −0.75 and 6.23 mm Hg, respectively. The limits of agreement ranged from −12.97 to 11.47 mm Hg. The bias and precision between $P_{aCO_2}$ and $P_{ETCO_2}$ were 0.68 and 5.82 mm Hg, respectively. The limits of agreement ranged from −10.72 to 12.08 mm Hg. There were 34 (40%) outliers for the $P_{tcCO_2}$ sensor and 34 (40%) outliers for the $P_{ETCO_2}$ sensor (*P* > .99). CONCLUSIONS: The accuracy of $P_{tcCO_2}$ was not superior to that of $P_{ETCO_2}$ for assessing $P_{CO_2}$ levels and should not be used to monitor these levels in subjects with severe brain injury.** *Key words: respiratory monitoring; end-tidal $p_{co_2}$; transcutaneous $p_{co_2}$; brain injury; accuracy.* [Respir Care 2014;59(8):1242–1247. © 2014 Daedalus Enterprises]

## Introduction

Patients who suffer from a brain injury require maintenance of blood carbon dioxide pressure ($P_{CO_2}$) within the physiological range to avoid cerebral spinal fluid pH change and prevent cerebral vasodilatation and vasoconstriction.[1] The accepted standard technique for monitoring $P_{CO_2}$ is the determination of $P_{aCO_2}$ using arterial blood gas. However, the arterial blood gas test is time-consuming, requires a significant amount of blood, must be repeated (particularly in patients with brain injury), and does not display immediate data.

Therefore, techniques that can avoid these pitfalls are needed. End-tidal $P_{CO_2}$ ($P_{ETCO_2}$) is a noninvasive tool that allows for the continuous monitoring of $P_{CO_2}$. However, in subjects with severe brain injuries, the use of $P_{ETCO_2}$ as a

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surrogate of $P_{aCO_2}$ has been disappointing.[2-5] Therefore, $P_{ETCO_2}$ is only recommended for use in out-of-hospital settings when arterial blood gas is not available.[6-8]

New devices that measure transcutaneous $P_{CO_2}$ ($P_{tcCO_2}$) have become available. The general principle of $P_{tcCO_2}$ measurement is that $CO_2$ diffuses from capillaries through tissue and across the semipermeable membrane of the device sensor, which is a modified Severinghaus electrode.[9] The agreement between the measured $P_{tcCO_2}$ and $P_{aCO_2}$ is dependent on the high tissue solubility of $CO_2$, which is further promoted by warming of the skin under the electrode. However, studies of this technology in intensive care units have produced conflicting results, with accuracy varying between studies according to the type of subjects who were evaluated.[10-14] In studies that have compared both $P_{tcCO_2}$ and $P_{ETCO_2}$ to blood gas-measured $P_{aCO_2}$, the former technology does appear to be more accurate.[15,16]

In this study, we hypothesized that $P_{tcCO_2}$ would be more accurate than $P_{ETCO_2}$ in predicting $P_{aCO_2}$ in patients with brain injury. Therefore, we compared simultaneous $P_{tcCO_2}$ and $P_{ETCO_2}$ values to the reference $P_{aCO_2}$ value in subjects with brain injury.

**QUICK LOOK**

**Current knowledge**

Control of arterial carbon dioxide in mechanically ventilated patients with traumatic brain injury prevents both cerebral vasodilatation and vasoconstriction which may alter intracranial pressure. The optimum range of arterial carbon dioxide in head injury is not known. Monitoring arterial carbon dioxide is a standard of care.

**What this paper contributes to our knowledge**

Neither transcutaneous carbon dioxide or end-tidal carbon dioxide monitoring accurately predicted arterial carbon dioxide in a population of mechanically ventilated subjects with brain injury. Accurate control of arterial carbon dioxide requires arterial blood gas analysis.

## Methods

This prospective observational study was performed at the surgical ICU of a university hospital from June 2011 to January 2012. The study was approved by the Centre Hospitalier Universitaire ethics committee, which waived the requirement for informed consent from subjects or their relatives (law relative to French public health policy 2004-806; ethics committee approval 12.03).

Consecutive mechanically ventilated subjects who were $> 15$ y of age, had a brain injury (Glasgow coma scale $\leq 8$), had an arterial catheter in place, and required arterial blood gases were included.

All subjects with brain injury were managed according to standardized protocols to maintain a mean arterial pressure $\geq 85$ mm Hg, an intracranial pressure $\leq 20$ mm Hg, and a cerebral perfusion pressure $\geq 65$ mm Hg.[1] Other types of therapy to avoid secondary insults were applied as recommended.[1] In subjects who suffered from subarachnoid hemorrhage, mean arterial pressure was maintained $\geq 90$ mm Hg. All subjects were in a semirecumbent position ($> 30°$) and received sedative agents but none were paralyzed.

The following data were recorded during the first 24 h of admission to the ICU: age, sex, body weight, the nature of the brain injury, the Glasgow coma scale upon admission, the simplified acute physiology score II, and the sequential organ failure assessment score. Norepinephrine was administered when necessary, and the dose was recorded. For each comparison, the following variables were reported: core body temperature, tidal volumes, breathing frequencies, use and level of PEEP, presence of mottling on the legs, capillary refilling time, arterial pH, and hemoglobin level provided by the arterial blood gas analysis.

When the inclusion criteria were met and arterial blood gas measurement was ordered, the $P_{tcCO_2}$ and $P_{ETCO_2}$ were simultaneously recorded.

### Carbon Dioxide Measurement

Arterial blood was sampled using an arterial catheter (Seldicath 3F, Plastimed-Prodimed, Le Plessis Bouchard, France) in a heparinized syringe and assessed using an analyzer (700/800 series, Radiometer Medical ApS, Brønshøj, Denmark). $P_{tcCO_2}$ was measured using the SenTec monitor via a V-Sign sensor (SenTec, Therwil, Switzerland) according to the manufacturer's instructions. All of the measurements were taken at the right or left earlobe. The V-sign sensor was inserted into the docking station of the monitor, and the calibration was automatically performed. Then, the V-sign sensor was clipped into the multisite attachment at the earlobe ring. Earlobe measurement was chosen because it appeared more accurate than forehead or cheek measurement.[13] The quality of the signal was estimated by the pulsatility index provided by the SenTec monitor (normal range: 1–2). As a warm-up period ($\approx$30 min) is necessary for the electrode to reach its optimal working conditions, all of the measurements were performed after this period.

$P_{ETCO_2}$ was measured via a nonaspirated infrared capnograph (M1460A, Hewlett Packard, Andover, Massachusetts), which was inserted at the tip of the tracheal tube and connected to a multiparameter monitor (SC 9000 XL, Siemens Elema AB, Solna, Sweden). The quality of the $P_{ETCO_2}$ measurement was the visualization on the monitor of a typical waveform with rapid and abrupt inspiratory/expiratory segments separated by a near horizontal alveolar plateau. All of the measurements were taken at least 30 min after any modifications in the mechanical ventilation parameters and/or changes in the norepinephrine rate.

## Statistical Analysis

To demonstrate the superiority of $P_{tcCO_2}$ compared with $P_{ETCO_2}$, at least 82 measurements were required (NQuery Advisor 6.0, Statistical Solutions Ltd., Cork, Ireland) assuming an $\alpha$-risk of .05, a $\beta$-risk of .2, and a proportion of outliers of 40% and 20% in the $P_{ETCO_2}$ and$P_{tcCO_2}$ groups, respectively.[4] The $P_{aCO_2}$ value obtained by arterial blood gas was the reference value. Statistical analysis was performed using SAS version 9.3 software (SAS Institute, Cary, North Carolina). Data were expressed as the mean ± SD and median (interquartile range) for the non-normally distributed variables and as the number (percentage). The agreement between the 2 measurement methods was assessed using a Bland-Altman analysis.[17] The study design included several measurements per subject; therefore, a correction was used in the limits of agreement calculation.[18] The outliers were defined as the differences $P_{aCO_2} - P_{tcCO_2}$ or $P_{aCO_2} - P_{ETCO_2}$ that strictly exceeded ± 4 mm Hg.

In addition, variables that may explain the outliers for $P_{aCO_2} - P_{tcCO_2}$ and $P_{aCO_2} - P_{ETCO_2}$ were studied and compared using a Student *t* test or a Kruskal-Wallis test when necessary. Body temperature, hemodynamic parameters (capillary refilling time, presence of mottling on the legs, and norepinephrine dose), arterial pH, and hemoglobin level were compared between $P_{aCO_2} - P_{tcCO_2}$ nonoutliers and outliers. The body temperature, the ventilation parameters (breathing frequencies, tidal volumes, PEEP), the hemodynamic parameters (capillary refilling time, mottling on the legs, and norepinephrine dose), the arterial pH, and the hemoglobin level were compared between $P_{aCO_2} - P_{ETCO_2}$ nonoutliers and outliers.

## Results

Twenty-five subjects were included, and 85 simultaneous measurements of $P_{aCO_2}$, $P_{tcCO_2}$, and $P_{ETCO_2}$ were obtained. The baseline subject characteristics are provided in Table 1. The median number of measurements per subject was 4 (range: 1–5), and all the measurements were performed at the acute phase in the first 48 h after admission in ICU. Body core temperature, ventilation parameters, arterial pH, and hemoglobin level measured at each comparisons are provided in Table 2. During the measurements, all of the subjects received a norepinephrine infusion at a mean dose of 0.4 ± 0.5 $\mu$g/kg/min.

Table 1. Subject Characteristics

| | |
|---|---|
| Subjects, *n* | 25 |
| Age (y) | 46 (31–52) |
| Sex (male) | 13 (52) |
| Nature of the brain injury | |
| Trauma | 16 (64) |
| Subarachnoid hemorrhage | 3 (12) |
| Other* | 6 (24) |
| SAPS II | 43 (36–52) |
| SOFA score | 8 (7–9) |
| Glasgow coma scale upon admission | 6 (4–7) |

The data are presented as the median (interquartile 25–75) or number (%).
* Other includes stroke (*n* = 2), intracranial hemorrhage (*n* = 2), brain abscess (*n* = 1), and tumor (*n* = 1).
SAPS II = simplified acute physiology score II
SOFA = sequential organ failure assessment

Table 2. Core Body Temperature, Ventilation Parameters, Hemodynamic Parameters, Arterial pH, and Hemoglobin Level for Each Comparison (*n* = 85)

| | |
|---|---|
| Core body temperature (°C) | 37.8 ± 0.8 (36.7–40.7)* |
| Ventilation parameters | |
| Tidal volume (mL/kg) | 7.8 ± 1.2 |
| Breathing frequency (breaths/min) | 13 ± 3 |
| PEEP, *n* (%) | 59 (69) |
| Level of PEEP (cm $H_2O$) | 3 ± 2 |
| Mottling, *n* (%) | 40 (47) |
| Capillary refilling time (s)† | 2 (1–3) |
| Arterial pH | 7.41 ± 0.06 |
| Hemoglobin (g/dL) | 9.5 ± 1.4 |

Values are expressed as mean ± SD unless indicated otherwise.
* Minimum to maximum.
† Missing data (*n* = 2).

A comparison of the $P_{CO_2}$ measurements using arterial blood gas and the $P_{ETCO_2}$ and $P_{tcCO_2}$ measurements is presented in Table 3. The number of outliers did not vary between the $P_{tcCO_2}$ and $P_{ETCO_2}$ measurements. The regression analysis and the results of the Bland-Altman analysis are provided in Table 2 and Figure 1.

Variables that may explain the outliers for $P_{aCO_2} - P_{tcCO_2}$ and $P_{aCO_2} - P_{ETCO_2}$ are provided in Tables 4 and 5, respectively. There were no differences between nonoutliers and outliers.

## Discussion

In this population of subjects with severe brain injury, $P_{tcCO_2}$ was not superior to $P_{ETCO_2}$ and could not be used as a surrogate of $P_{aCO_2}$. The percentage of outliers was high and did not vary between the 2 measurement methods.

The use of $P_{ETCO_2}$ as a surrogate of $P_{aCO_2}$ in the ICU is controversial. Kerr et al[3] compared $P_{ETCO_2}$ with $P_{aCO_2}$ in

Table 3. Arterial, Transcutaneous and End-Tidal Carbon Dioxide Pressure Values, Linear Regression, and the Bland-Altman Analysis Results ($P_{tcCO_2}$ or $P_{ETCO_2}$ vs $P_{aCO_2}$) and Number of Outliers

| | $P_{CO_2}$ Values (mm Hg) | Linear Regression | | Bland-Altman Analysis | | | Outliers $n$ (%) |
|---|---|---|---|---|---|---|---|
| | | Correlation Coefficient | P | Bias* (mm Hg) | Precision (mm Hg) | Limits of Agreement (mm Hg) | |
| $P_{aCO_2}$ | 37.0 ± 6.2 (23.0; 53.0) | | | | | | |
| $P_{tcCO_2}$ | 37.7 ± 7.2 (24.1; 61.3) | 0.60 | < .001 | –0.75 | 6.23 | –12.97; 11.47 | 34 (40) |
| $P_{ETCO_2}$ | 36.3 ± 6.7 (22.0; 52.0) | 0.58 | < .001 | 0.68 | 5.82 | –10.72; 12.08 | 34 (40) |

The data are presented as the mean ± SD (min; max) or number (%).
* Bias was the difference between $P_{aCO_2}$ and $P_{tcCO_2}$ or $P_{ETCO_2}$.
$P_{tcCO_2}$ = transcutaneous $P_{CO_2}$
$P_{ETCO_2}$ = end-tidal $P_{CO_2}$

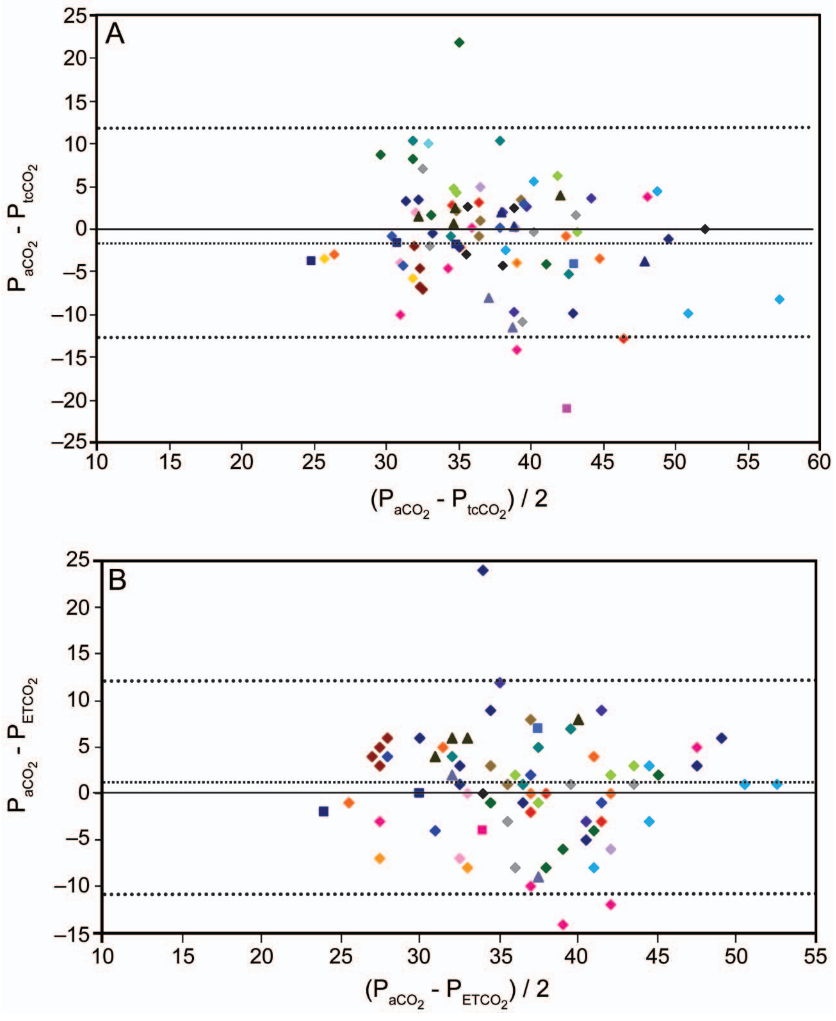


Fig. 1. Bland-Altman agreement between arterial $P_{CO_2}$ and $P_{tcCO_2}$ (A) and between arterial $P_{CO_2}$ and $P_{ETCO_2}$ (B). The dotted lines denote the limits of agreement. Each color and shape of data points refer to one subject.

traumatic brain injury subjects and found a bias of 1 mm Hg and limits of agreement that ranged from −5.2 to 17.2 mm Hg, but no clinical limits of agreement were defined. In 21 traumatic brain injury subjects, the bias was 5.5 mm Hg, and the limits of agreement ranged from −4.5 to 15.5 mm Hg.[4] The values that were considered clinically relevant were ± 4 mm Hg; therefore, $P_{ETCO_2}$ could not be used to substitute for $P_{aCO_2}$. Moreover, the

Table 4. Core Body Temperature, Hemodynamic Parameters, Arterial pH, and Hemoglobin Level in $P_{aCO_2}$ – $PtcCO_2$ Nonoutliers vs Outliers

| | Nonoutliers ($n$ = 51)* | Outliers ($n$ = 34)* | $P$ |
|---|---|---|---|
| Core body temperature (°C) | 37.7 ± 0.6 | 37.9 ± 0.9 | .63 |
| Hemodynamic parameters | | | |
| Capillary refilling time† (s) | 2 (1–3) | 2 (1–3) | .35 |
| Mottling, $n$ (%) | 23 (45) | 16 (47) | > .99 |
| Norepinephrine (μg/kg/min) | 0.46 ± 0.65 | 0.24 ± 0.3 | .39 |
| Arterial pH | 7.41 ± 0.06 | 7.40 ± 0.05 | .48 |
| Hemoglobin (g/dL) | 9.7 ± 1.4 | 9.3 ± 1.4 | .20 |

Values are expressed as mean ± SD unless indicated otherwise.
* Number of pair data.
† Data are expressed as median (interquartile range).

Table 5. Core Body Temperature, Ventilation and Hemodynamic Parameters, and Arterial pH in $P_{aCO_2}$ − $P_{ETCO_2}$ Nonoutliers vs Outliers

| | Nonoutliers ($n$ = 51)* | Outliers ($n$ = 34)* | $P$ |
|---|---|---|---|
| Core body temperature (°C) | 37.9 ± 0.9 | 37.7 ± 0.6 | .48 |
| Ventilation parameters | | | |
| Breathing frequency (breaths/min) | 13 ± 2 | 14 ± 4 | .53 |
| Tidal volume (ml/kg) | 7.9 ± 1.3 | 7.6 ± 1.0 | .48 |
| PEEP ( cm $H_2O$) | 3 ± 2 | 4 ± 2 | .33 |
| Hemodynamic parameters | | | |
| Capillary refilling time† (s) | 2 (1–3) | 2 (1–3) | .31 |
| Mottling, $n$ (%) | 21 (41) | 18 (53) | .40 |
| Norepinephrine (μg/kg/min) | 0.39 ± 0.58 | 0.35 ± 0.51 | .96 |
| Arterial pH | 7.41 ± 0.06 | 7.4 ± 0.05 | .41 |

Values are expressed as mean ± SD unless indicated otherwise.
* Number of pair data.
† Data are expressed as median (interquartile range).

$P_{aCO_2}$ – $P_{ETCO_2}$ differences in 40% of the cases were outside of the previously defined limit. Lee et al[5] found values that were outside of the limit of ± 5 mm Hg in 23% of traumatic brain injury subjects.

The use of the SenTec monitor in ICUs has produced contrasting data. Rodriguez et al[10] evaluated this monitor in 50 ICU subjects who were hospitalized for various reasons. The bias was −0.2 mm Hg, and the limits of agreement ranged from −9.4 mm Hg to 9.0 mm Hg. The authors concluded that the $P_{tcCO_2}$ measurement was an acceptable tool for monitoring $P_{CO_2}$, but they did not consider predefined limits. Bolliger et al[11] compared the SenTec and Tosca 500 monitors in 50 ICU subjects. For the SenTec and Tosca 500 monitors, the bias was −2.60 and −2.75 mm Hg, and the limits of agreement ranged from −14.1 to 8.8 mm Hg and −11.5 to 7.2 mm Hg, respectively. According to the predefined limit of ± 7.5 mm Hg, the authors concluded that the 2 devices were inaccurate. Baulig et al[12] evaluated the SenTec monitor in cardiac surgery subjects. The bias was 0.37 mm Hg, and the limits of agreement ranged from −9.0 to 9.75 mm Hg. Using a new available sensor, they found a bias of 1.1 mm Hg and limits of agreement that ranged from −3.4 to 5.5 mm Hg, with a predefined limit of ± 5 mm Hg.[13] In a study that evaluated the Tosca 500 monitor including 55 subjects, of whom 10 were multiple traumatic and neurosurgical subjects, the bias was 1.2 mm Hg, and the limits of agreement ranged from −10.5 to 13.0 mm Hg.[14] Nevertheless, in the subgroup of subjects with brain injury, the authors concluded that $P_{tcCO_2}$ should be used with caution.[14]

Few studies have evaluated simultaneous measurements of $P_{ETCO_2}$ and $P_{tcCO_2}$ using the $P_{aCO_2}$ measurement as a reference.[15,16] During general anesthesia, the values obtained with the transcutaneous $P_{CO_2}$ monitor had a lower bias and narrower limits of agreement than those obtained with the end-tidal $P_{CO_2}$ monitor (0.19 vs −4.40 mm Hg and −4.6 to 4.9 mm Hg vs −10.7 to 2.9 mm Hg, respectively).[15] In mechanically ventilated subjects who required interhospital transport, Hinkelbein et al[16] found that the bias for the end-tidal measurement was higher than that obtained with $P_{tcCO_2}$ (−5.3 vs −0.6 mm Hg).

According to the a priori better performance of $P_{tcCO_2}$, we expected that $P_{tcCO_2}$ would be more accurate than $P_{ETCO_2}$. We considered that acceptable differences between $P_{tcCO_2}$ or $P_{ETCO_2}$ and $P_{aCO_2}$ would not exceed ± 4 mm Hg, as previously considered to be clinically relevant in studies of subjects with brain injury.[4,5,19] The percentage of outliers using the SenTec monitor did not differ from those that were associated with the $P_{ETCO_2}$ measurement and the limits of agreement were significant, which suggests that the $P_{tcCO_2}$ measurement should not be used in subjects suffering from brain injury.

Our study has some limitations that must be pointed out. Indeed, it may be argued that norepinephrine may have modified the skin perfusion and $P_{tcCO_2}$ values. These subjects often require such medication at the acute phase to maintain adequate cerebral perfusion pressure and/or mean arterial pressure.[1] Nevertheless, the relationship between vasopressor use and an alteration in the bias and precision has not been demonstrated, and, in our study, no relationship was found between the norepinephrine dose and the difference between $P_{aCO_2}$ and $P_{tcCO_2}$.[14,20] We measured $P_{tcCO_2}$ at the earlobe, and we cannot exclude regional hypoperfusion, although the earlobe site was found to provide better accuracy.[13]

## Conclusions

$P_{tcCO_2}$ measured at the earlobe with the SenTec monitor was not superior to $P_{ETCO_2}$ in subjects who were suffering from brain injury and should not be used to monitor $P_{CO_2}$ in these subjects.


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