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Case Report

Near-Infrared Spectroscopy (NIRS) in the Assessment of Cerebral Tissue Oxygenation (rSO2): Methodological Issues and Dilemmas

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Abstract: Introduction: Monitoring cerebral perfusion in patients with brain injury is a major clinical challenge. Monitoring cerebral oxygenation (rSO2) via NIRS was introduced in the early 1980s, and many clinicians believed it to be a valuable method for assessing cerebral perfusion and subsequent measures to optimize cerebral flow. The main problem with the use of NIRS is the presence of intermediate structures—the skin, skull, meninges, cerebrospinal fluid—and their influence on the test result. Therefore, it seems that NIRS assessment performed on a patient during brain death can give an idea of the magnitude of the influence of these intermediate structures on the monitoring result. Case presentation: We present a case study of cerebral oxygenation measurements in a patient undergoing a brain death diagnostic procedure. A clinical situation in which cerebral blood flow is stopped can give an idea of the specificity of this method, in particular of the influence of intermediate structures on the monitoring result. In this case, the result obtained using NIRS is increased by the patient's oxygenation before the apnea test. The influence of chromophores in the tissues surrounding the CNS and reflections and scattering of the light wave spectrum have a very significant effect on the final result of cerebral saturation measurement. Discussion: The majority of observations in existing research describing changes in cerebral perfusion or its optimization may be burdened by the problem described here, i.e., by the significant influence of measured intermediate structure oxygenation. The specificity of NIRS in assessing cerebral perfusion requires careful analysis. The therapeutic implications of monitoring cerebral oxygenation with NIRS are of great importance, and based on the example presented and the literature provided, this method should be used with caution. It has been shown that in a patient with brain death, the result of NIRS oxygenation measurements depends on the structures surrounding the brain.

Keywords: NIRS; cerebral perfusion; autoregulation; chromatophores

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1. Introduction

Monitoring cerebral oxygenation (rSO2) using near-infrared spectroscopy (NIRS) was introduced at the turn of the 1980s, and many clinicians believed it to be a valuable method and a dynamic tool for assessing cerebral perfusion and subsequent measures to optimize cerebral flow in patients with brain damage [1–3]. The problem is extremely important because the assessment of cerebral perfusion is based on very invasive and sophisticated diagnostic methods, thus limiting their application. The most commonly used invasive methods include measurements of intracranial pressure (ICP), cerebral temperature (BT), cerebral oxygen tension (PbtO2), neurochemistry via microdialysis (MD), cerebral blood flow (CBF), and jugular venous oxygen saturation (SjvO2) [1,2].

The methods described above allow for the continuous monitoring of cerebral oxygenation and perfusion. The non-invasive study of cerebral vascular blood flow by transcranial Doppler is limited to the time of measurement in the patient. Therefore, the introduction of

cerebral tissue saturation monitoring by non-invasive continuous observation has become an optimal and simple tool for monitoring patients with brain damage [1]. However, the initial interest in this method and the peak of the resulting medical research and publications ended in 2014–2015 [2]. Despite many years of experience with using spectroscopy to measure cerebral oxygenation, the benefits of its use have not been clearly established. Therapy standards based on the measurement results and reference standards have not yet been established [4,5].

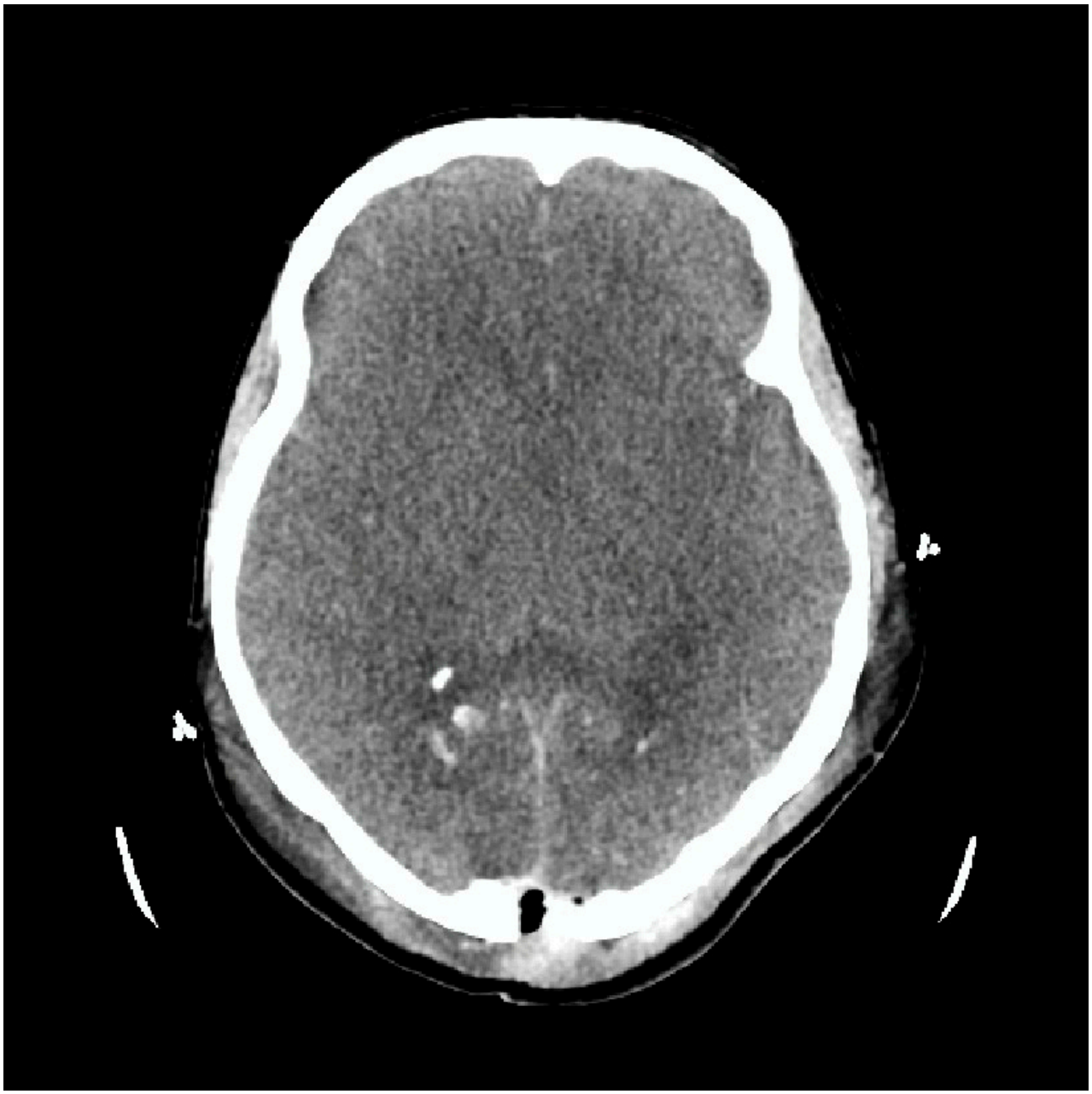
The main problem includes serious questions about the validation of this method, as its result depends on the presence of chromophores in intermediate structures. A very important argument for this statement is based on repeatedly published observations, but these are based on studies conducted on small groups of patients [6–8]. Another problem with NIRS measurements is the lack of established limits for saturation measurements.

The main problem is the presence of the described intermediate structures—the skin, skull, meninges, cerebrospinal fluid—and their influence on the test result. To eliminate the influence of chromatophores in superficial structures, two or more light detectors are used to obtain separate data from shallow and deep optical signals. This process is called spatial resolution [8,9]. There are a number of publications in the literature that show a significant effect of intermediate structures on the results of NIRS measurements. These publications use the phenomenon of orthostatic changes in blood flow in craniofacial structures, the effect of the Valsalva maneuver, the effect of vasoconstrictors, and even the mechanical restriction of flow through the skin using pressure bands [9–12]. We present a case in which the described dilemma of NIRS reading sensitivity is directly related to the diversification of CNS and craniofacial blood flow. A NIRS assessment performed on the patient during brain death in a clinical situation in which cerebral flow has stopped can give an idea of the magnitude of the influence of these intermediate structures on the monitoring result.

2. Case

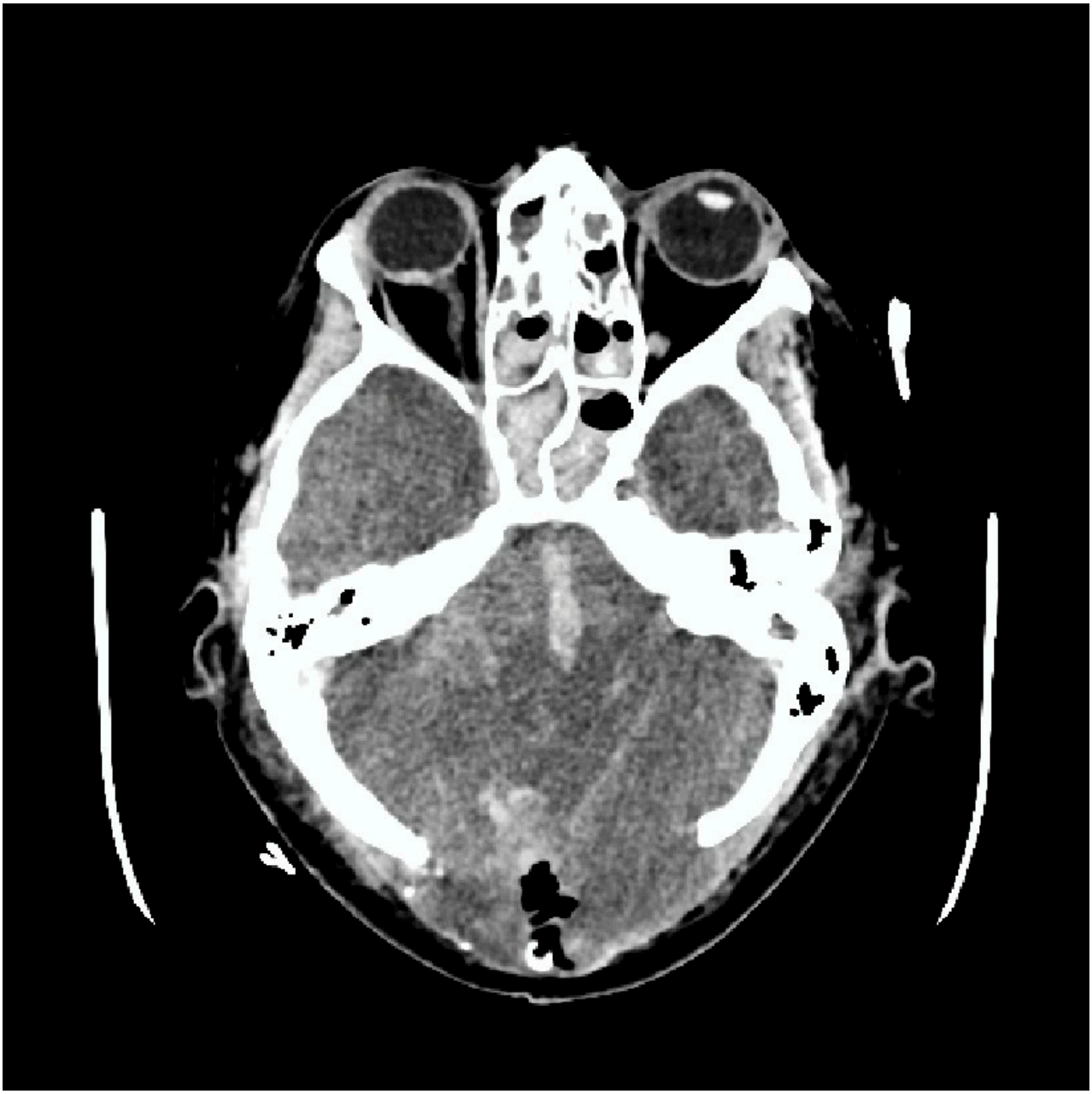
We present the case of a female patient diagnosed with AML (Acute Myeloid Leukemia). The patient was transferred from the hematology unit to the intensive care unit (ICU) after neurological deterioration. Based on the CT imaging studies performed, the diagnosis was acute intracranial hemorrhage. A diagnosis of posterior fossa hematoma requiring urgent neurosurgical intervention was confirmed. The patient was referred to surgery and underwent neurosurgery immediately after the CT scan. Suboccipital decompression was performed and the hematoma was evacuated. After surgery, the patient was transferred directly to the intensive care unit. The cornerstone of the treatment of patients with brain injury is the optimization of cerebral perfusion. Basically, this optimization is achieved by modulating intracranial pressure (ICP) and mean arterial pressure (MAP). As a concept, cerebral oxygenation monitoring, which measures mixed blood saturation (ratio of venous to arterial blood of 75%:25%) in brain tissue, corresponds to the parameter of oxygen supply to neural tissue. Therefore, NIRS measurement indirectly illustrates the hemodynamics of cerebral blood flow [1–3]. Monitoring cerebral oxygenation somewhat allows for maneuvers and interventions that increase the NIRS score. In cardiac surgery, the most common maneuvers used to improve spectroscopically measured oxygenation include improving venous drainage by raising the headgear, correcting morphologic deficits, increasing perfusion pressure, and increasing oxygenation, among others. However, these measures do not clearly improve patient outcomes [5].

In the presented case, hemodynamic and cerebral oxygenation monitoring was performed with NIRS to optimize cerebral perfusion. Despite therapy, the patient was diagnosed with an absence of brain reflexes. Imaging studies, including a CT scan of the CNS (Figure 1a,b) and CTA (Figure 2a,b), showed catastrophic brain damage. Then, according to our institution's brain death guidelines, clinical evaluations and apnea tests were performed at defined intervals (current AAN brain death guidelines do not require multiple evaluations) [13–15].



(**a**)

Figure 1. *Cont.*



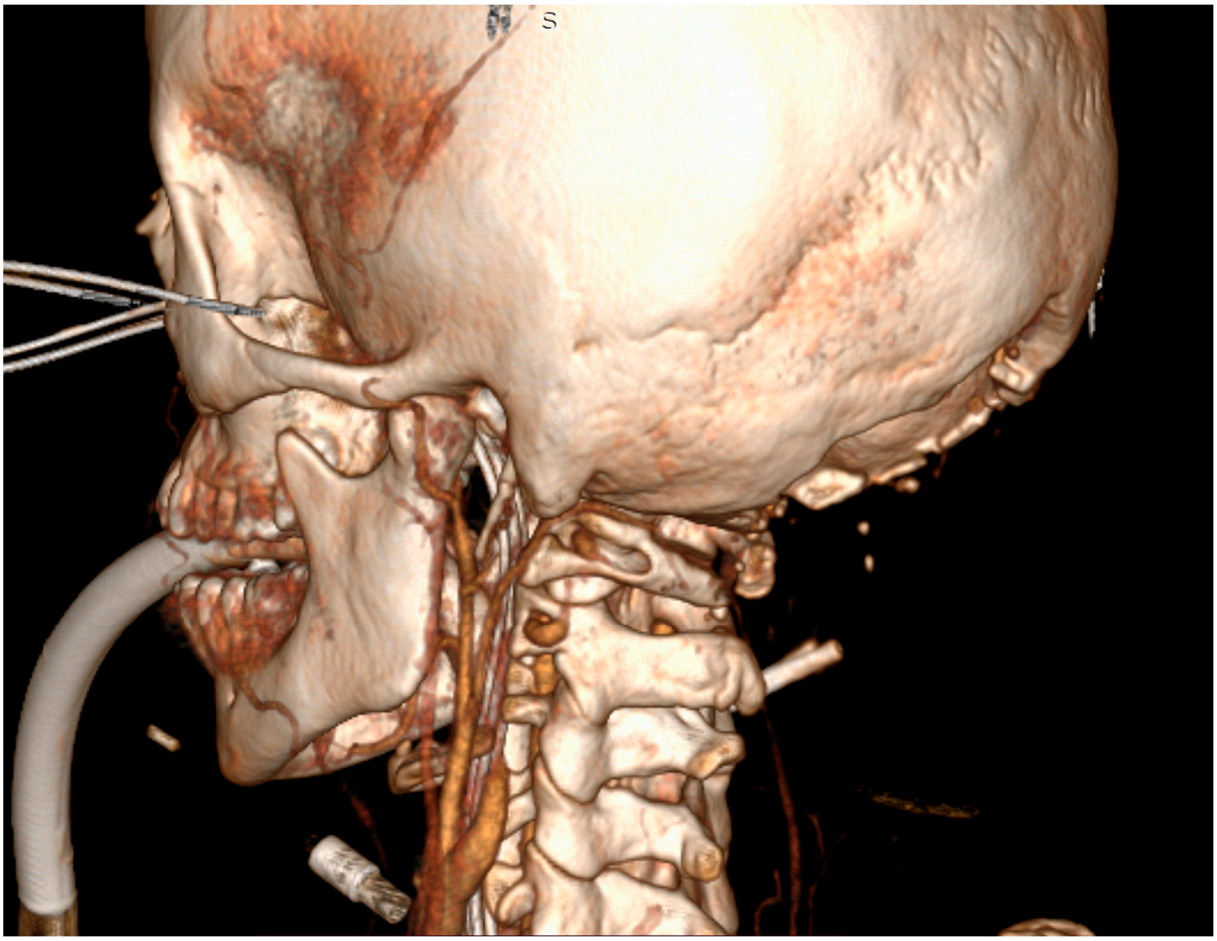
(**b**)

Figure 1. Head CT. The examination shows intermediate features of severe cerebral ischemia. (**a**) Loss of grey/white matter differentiation in the supratentorial space with a sign of pseudosubarachnoid hemorrhage. (**b**) Severe edema of the posterior fossa structures (despite suboccipital decompression) with completely obliterated basal cisterns and ischemic–hemorrhagic changes in the brainstem.

We present an analysis of cerebral oxygenation measurements using the INVOS™ Regional Oximeter in the presented case of a patient undergoing brain death diagnosis. A clinical situation in which cerebral blood flow is stopped can give an idea of the specificity of the method, in particular of the effect of the influence of intermediate structures on the monitoring result.

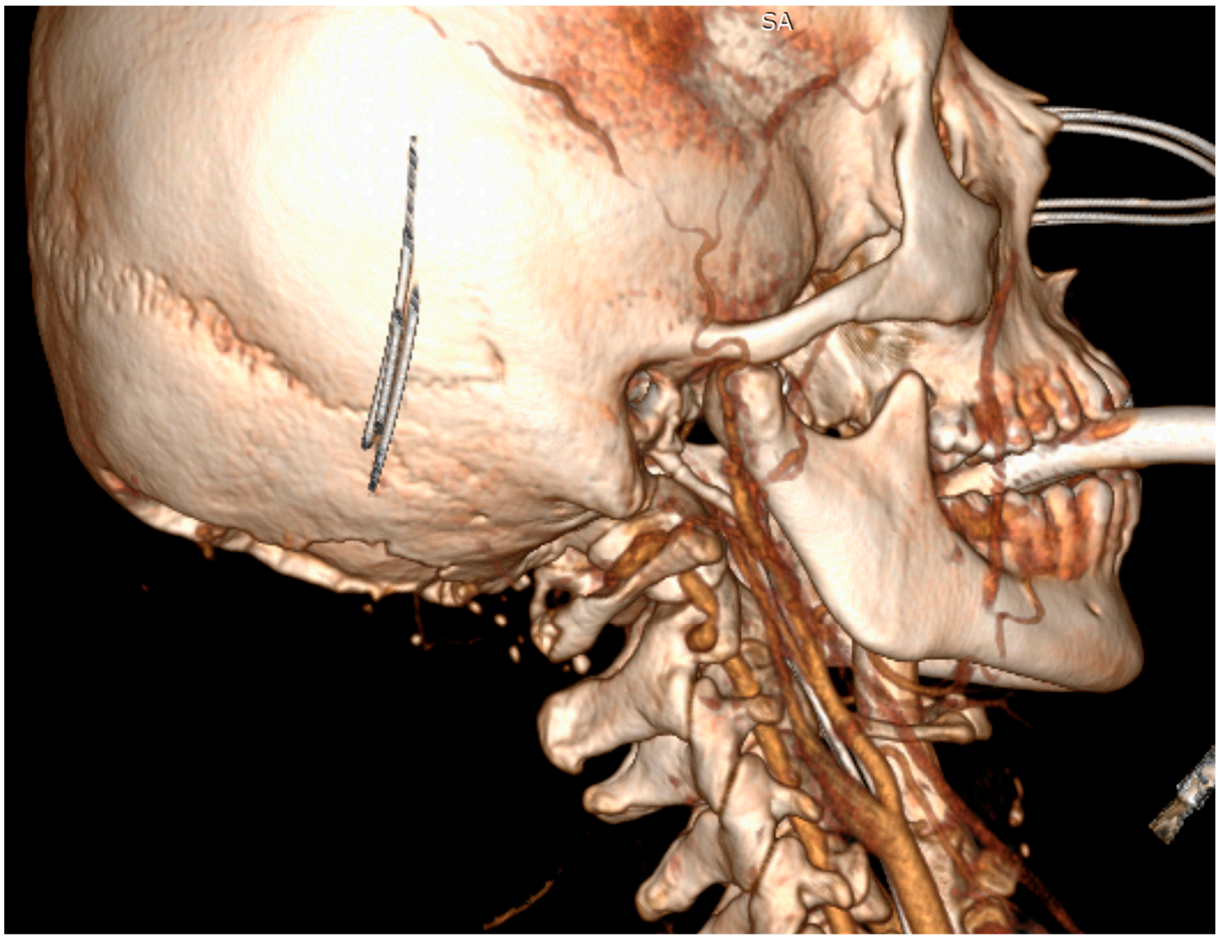
The determination of brain death was performed according to an internationally accepted protocol. The protocol for the diagnosis of brain death (BD) includes the following steps: prerequisites for the determination of BD, examinations, apnea tests, ancillary tests, communication of BD, and declaration of BD. The initial assessment includes a series of confirmations and exclusions for the assessment of brain death. If the initial assessment

and imaging findings are consistent with permanent CNS damage (prerequisites), neurological tests (examinations) are performed. These tests are the basis for the diagnosis of brain death and the patient's death. If the examinations have limitations or correcting metabolic disorders poses a problem, additional tests are performed. The accepted ancillary diagnostic methods are as follows: four-vessel catheter angiography, radionuclide cerebral blood flow scan, and, in adult patients, transcranial Doppler ultrasonography. The entire clinical evaluation process and standard observation times are strictly defined in the AAN criteria [15]. Specifically, the brain death protocol consists of a sequential series of tests to determine irreversible brainstem damage, including apnea tests. The respiratory center activity test is considered positive if there is no respiratory activity during a 5 min apnea observation of the patient with normal baseline gasometry during apnea observation and if there is an increase in CO2 level to a value above 60 mmHg, at least 20 mmHg from baseline. The diagnosis is made according to a protocol supervised by a brain death committee [13–15]. In our case, the clinical diagnosis was made without any interference. No clinical or metabolic problems interfered with the procedure. There were no clinical limitations to performing the apnea test on the patient, so no ancillary diagnostics were needed. Brain death was diagnosed.



(**a**)

Figure 2. *Cont.*



(**b**)

Figure 2. Head Computer Tomography Angiography (CTA). Three-dimensional reconstruction of the CTA study. (**a**) Left-hand side: left carotid arteries showing contrast flow obstruction in the extracranial segment of the C1 LICA (just behind the LCCA division) and in the extracranial segment of the V3/V4 LVA. (**b**) Right-hand side: right cerebral arteries showing contrast occlusion in the extracranial segment of the C1 RICA (before entering the RTCA) and in the extracranial segment of the V.4 RVA.

The patient was monitored with NIRS (INVOS™ Regional Oximeter, Minneapolis, MN, USA) throughout the procedure, from the diagnosis of areflexia until the patient was pronounced dead. As can be seen, the level of cerebral oxygenation was relatively constant, symmetrical from both cerebral hemispheres, and reached values close to 50%, both before and between the tests (Figure 3). Before the respiratory center drive test, the patient was first provided with 100% FiO2. The prerequisite for starting the apnea test is a normocapnic result in the baseline gas test (paCO2 35–45 mmHg). In the graph of NIRS measurement shown, a significant increase in rSO2 value can be observed, reaching 60–70% (improvement up to 20%). Increased saturation to a value close to rSO2 = 70% was maintained throughout the apnea test and then, after the patient was ventilated again, a further increase in the NIRS result is observed. Subsequently, a reduction in FiO2 to a baseline of 50% was followed by the return of NIRS to baseline values. A similar pattern was observed in both apnea tests (Figure 3).

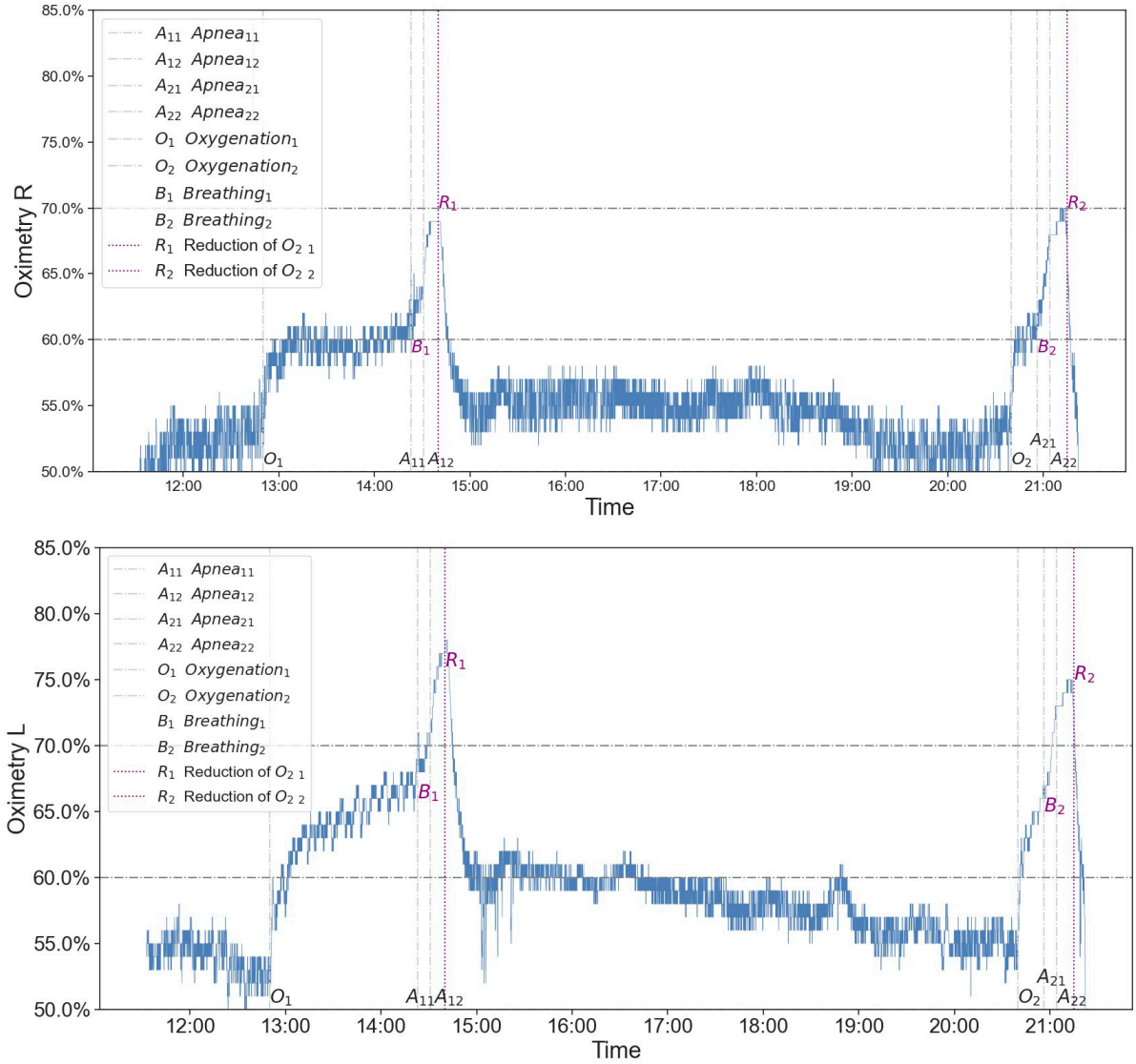


Figure 3. Measurements of cerebral oxygenation (rSO2) (right and left hemisphere) in the patient during diagnosis of brain death.

3. Discussion

The case of a patient with cerebral oxygenation monitored by NIRS spectrometry presented here vividly demonstrates the bias of the measurement method. The use of NIRS monitoring in a patient with a confirmed lack of intracranial flow clearly demonstrates the influence of extracranial structures on the measurement result. Despite many years of experience, it has not been possible to clearly define the norms of cerebral oxygenation or to standardize the management and treatment of patients according to the results obtained [5]. The basic problem with using NIRS in the treatment of patients does not arise from a general experience in which statistics would favor this measurement method. In the treatment of each individual patient, it is very important to determine the specificity of the diagnostic method, because the individual choice of therapy and the course of treatment depend on the method's results. Here, we present graphs of cerebral oxygenation obtained during the apnea test included in the procedure recommended by the brain death commission. Our observations coincide with experiments already described in the literature in the presented bibliography, but the value of this publication is the graphical illustration of the error in the measurement of cerebral oximetry. In the presented case, the NIRS result is increased due to the oxygenation of the patient before the apnea test. Chromophores in the tissues

surrounding the CNS and that of reflections and scattering of the light wave spectrum have a very significant effect on the final result of cerebral saturation measurement. A very important argument for this statement is based on observations that have been repeatedly published in studies conducted on small groups of patients [6–8,16]. This is exemplified by a publication by Tatli and colleagues, who confirmed the lack of sensitivity of NIRS diagnoses for confirming brain death in patients [7]. Attempts to explain these observations have already been described in the literature, but the magnitude of the changes in oxygenation in NIRS measurements in our study, i.e., an increase of more than 20% from the baseline, shows the importance of the measurement artifacts described. The problem of variability of cerebral oximetry measurements and its dependence on the ratio of intracranial and extracranial arterio-venous flow is complex. It is possible that the subsequent increase in NIRS measurements, which appears to be initiated when pressure ventilation with PEEP is initiated, is related to the phenomenon of venous outflow resistance. Respiration may lead to a redistribution of venous blood, a predominance of the arterial component, and an increase in the level of oxygenation in the measurements. The described dependence also shows a possible bias in the interpretation of NIRS measurements [16].

The majority of research observations describing changes in cerebral perfusion or its optimization may be burdened by the problem described, i.e., the significant influence of measured oxygenation from intermediate structures. Despite the described dilemmas, studies continue to confirm the usefulness of this method without considering the pitfalls presented here [17–20]. Numerous examples of the described dilemma can be found in papers using NIRS monitoring in cardiac surgery. Often, the issue of cerebral flow autoregulation is not considered, and the increase in arterial pressure and improvement in surface saturation are translated into a positive effect of the applied hemodynamic maneuvers. A publication by Takegawa et al. provides an example of the ambiguity of the problem [21]. A significant decrease in cerebral oximetry was observed in patients with induced hypothermia. According to the authors, this contradicts the logic of reduced CNS oxygen consumption. On the other hand, the authors do not link the result of reduced rSO2 with a possible reduction in blood flow through the described superficial structures, which depends precisely on the extrinsic temperature. They explain this phenomenon with an increase in cerebral vascular resistance and a decrease in cerebral blood flow, which is precisely the opposite of the intended effects of hypothermia.

The specificity of NIRS in assessing cerebral perfusion requires careful analysis. Despite the use of spatial resolution and multiple light emitters and detectors, commercially available spectroscopes do not provide a pure cerebral oxygenation signal [4]. The therapeutic implications of monitoring cerebral oxygenation with NIRS are of great importance, and from the example presented and the literature provided, this method should be used with caution. It has been shown that in a patient with brain death, the result of NIRS oxygenation measurements depends on the surrounding structures of the brain. Their influence can be so significant that, after oxygenation of the patient, it is possible to obtain NIRS measurements of rSO2 in a patient without cerebral flow that are comparable to measurements in a healthy person. This example vividly confirms the data from the literature and illustrates how large the margin of error of the measurements and the subsequent misinterpretation of the results obtained can be.

In a review published by the Nature Publishing Group in 2022, describing the experiences with NIRS to date, we did not find clear conclusions [22]. After the initial enthusiasm, the introduction of cerebral oxygenation monitoring poses serious problems. It is difficult to be guided by statistical results in individual cases, knowing the limitations of this method. The problem remains unsolved due to the complexity of the physiology of cerebral flow and its correlation or lack thereof with flow through structures surrounding brain tissue.

Perhaps solving all the problems that limit this method and taking into account artifacts that can affect the measurement result will increase its specificity.

4. Summary

We describe the case of a patient undergoing the brain death protocol and the recording of the obtained NIRS measurements which confirm the limitations of this method in diagnosing brain death. We show the extent to which the results are contaminated by intermediate structures. The extent of measurement contamination can be related to other cases of monitored patients. This problem is reflected in numerous publications in which NIRS monitoring does not lead to improved patient outcomes. The described example of continuous monitoring of a patient during supposed brainstem death is very illustrative and also gives an insight into the limitations of infrared spectrophotometry in its broad application. The management of patients with brain damage should be based on complex monitoring and test results, and only the analysis of all observed measurements and test results should be the basis for the direction of medical action.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

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