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Diagnostic Accuracy of a Near-Infrared Spectroscopy Device for Detecting Intracranial Hemorrhage in Mild Closed Traumatic Brain Injury at a Philippine Trauma Center

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Objective: This study aimed to evaluate the sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio, and negative likelihood ratio of a handheld Near Infrared Spectroscopy (NIRS) device (Infrascanner 2000®) in detecting intracranial hemorrhage in mild, closed traumatic brain injury patients in the emergency room setting.

Methods: This prospective study evaluated the diagnostic validity of a NIRS device in hemodynamically stable patients with mild, closed traumatic brain injury. The authors included patients aged 15 to 65 years who were consecutively admitted to the Emergency Department of the Philippine General Hospital from June 2017 to September 2017. Patients were scanned by a trained research assistant with the NIRS device in the frontal, temporal, parietal, and occipital areas of the brain bilaterally. A cranial computed tomography scan was used as a reference standard for comparison.

Results: A total of 83 participants with mild, closed traumatic brain injury were included in the final analysis. There were 68 (82%) males, and the mean age was 29.52 years old. Of the 83 participants, 41 had intracranial hemorrhages (23 subdural, 13 epidural, 5 intraprenchymal). The NIRS device exhibited a sensitivity, 85.37% [55-96.19%]; specificity, 92.86% [85.07-100.00%]; PPV, 92.12% [83.53-100.00%]; NPV, 86.67% [76.74-96.60%]; PLR, 11.96 [3.99-35.82]; and NLR, 0.16 [0.07-0.33].

Conclusion: The NIRS device can reliably screen for hemorrhages in patients with mild, closed traumatic brain injury using CT scan results as the gold standard. These diagnostic values suggest the potential role of the NIRS device in the early evaluation of patients with traumatic brain injury requiring urgent care.

Key words: near-infrared spectroscopy, intracranial hemorrhage, mild traumatic brain injury

Traumatic brain injury (TBI) is a leading cause of death and disability worldwide, constituting a considerable portion of the global injury burden at 27.08 million cases in 2016.[1,2] Locally, the mortality of trauma patients in the Philippine General Hospital (PGH) has been reported to be 18.6% (4,947 admissions) of patients admitted from January 2004 to May 2007. Specifically, TBI accounted for 63.4% of central nervous system-related deaths,[3] making the early identification of TBI essential. One hallmark pathological process in TBI is intracranial hemorrhage, which occurs in 45% of severe trauma cases.[4]

In 2015, 73 cases of TBIs were recorded at the PGH Emergency Department (ED).[5] Headache, vomiting, loss of consciousness, post-traumatic seizure, or a Glasgow Coma Score (GCS) below 15 were the usual presenting symptoms. All these patients were subjected to cranial computed tomography (CT) scan. Of 73 patients, 40% (n=29) were reported to have an intracranial hemorrhage or hematoma. In a study conducted by Syed et al. (2007), patients with GCSs of 13 to 15 were subjected to a cranial CT scan, but only 15% of patients had abnormal results, and only 4% needed surgical intervention.[6] In a setting with limited access to CT machines, it would be beneficial for patients suspected to require an immediate cranial CT scan to be screened and prioritized through an objective diagnostic procedure.

According to Leon-Carrion, et al. (2010), compared to urban areas, TBI patients in rural areas will require more time to be assessed and are more likely to encounter difficulties in gaining access to resources for diagnosis and treatment. Likewise, early surveillance of TBI is necessary to formulate a triage plan in mass casualty and the prioritization of more advanced imaging in the hospital, especially in the low-resource setting.[7]

Robertson, et al. reported promising results using a Near-Infrared Spectroscopy (NIRS) device in screening for intracranial hematomas among TBI patients. Good sensitivity (88%) and high specificity (90.7%) were observed.[8] The NIRS is a practical adjunct that can improve the identification of intracranial hematomas in the field and in the ED.[8] This valuable tool may enable early diagnosis and prompt surgical management of traumatic hematomas.[8]

In this study, the authors examined the Infrascanner 2000® (Infrascanner, InfraScan Inc., Philadelphia, PA, USA), a handheld NIRS device that detects brain hematomas based on the differential absorption pattern of a hematoma and normal brain tissue. The minimum detectible quantity of blood is 3.5 ml at a depth of not more than 2.5 cm from the surface of the cerebral cortex (Figure 1).[9,10] Specifically, this study aimed to determine the diagnostic validity of the Infrascanner 2000® device in detecting hematoma formation among patients with a closed head injury in a tertiary trauma center in the Philippines. Specifically, it seeks to determine the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), and negative likelihood ratio (NLR) of the device using a plain cranial CT scan as reference.

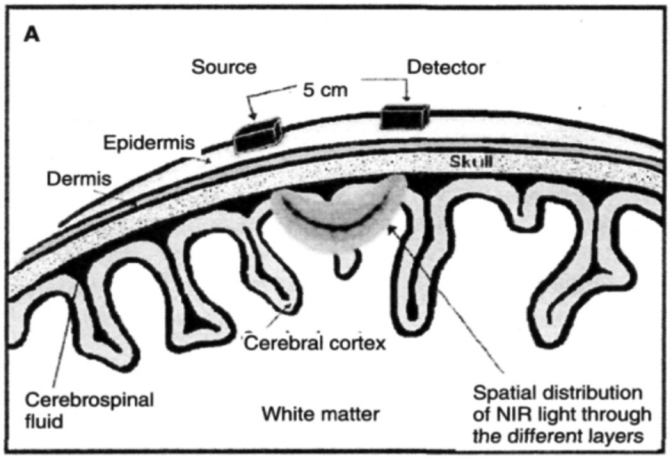

Figure 1. Schematic representation of NIR light travelling through the head. Spatial distribution of the light flux through the different tissue layers of the head is illustrated. The detected signal comes mainly from hemoglobin in small vessels (<1 mm diameter), such as capillary, arteriolar, and venular beds (Picture from the Infrascanner Manual).[10]

Methods

Study Design and Selection of Participants

This was a single-center prospective study designed to determine the diagnostic validity of the Infrascanner 2000® device in closed-head injuries by determining its sensitivity, specificity, PPV, NPV, PLR, and NLR using cranial CT scan as the gold standard. The analyses were performed using a "per-protocol" population.

The inclusion and exclusion criteria were based on the Canadian CT Head Rule.[11] All patients presenting in the ED with a history of head trauma from May to September 2017 were enrolled in the study if they met the following inclusion criteria: 1) had a Glasgow Coma Score (GCS) of 13-15; 2) age > 15 years old; 3) had no known coagulopathies; and 4) was not taking anticoagulation (warfarin) or antiplatelet (aspirin) medication. On the other hand, the exclusion criteria for the study were as follows: 1) age > 64 years; 2) with suspected open or depressed skull fracture; 3) had signs suggesting a basal skull fracture (e.g., hemotympanum, raccoon eyes, cerebrospinal fluid otorrhea/rhinorrhea); 4) demonstrated the Battle's sign (i.e., bruising around the mastoid process); 5) GCS < 15 at 2 hours post-injury; 6) had retrograde amnesia > 30 minutes duration; 7) was involved in mechanisms dangerous (e.g., pedestrian struck by a vehicle, ejection from a motor vehicle, fell from elevation >3 feet or five stair treads); 8) was hemodynamically unstable; and 9) had associated injuries. The STARD flow diagram for the study is illustrated in Figure 2.

Data Collection

Prospective participants who came to the surgery bay in the PGH ED were referred to the investigator to determine their inclusion in the study. Informed consent was obtained from all participants. The study was approved by the University of the Philippines – Manila Review Ethics Board (SUR 2016-482-01). All patients underwent NIRS device assessment upon admission to the ED and were immediately scheduled for CT scan evaluation.

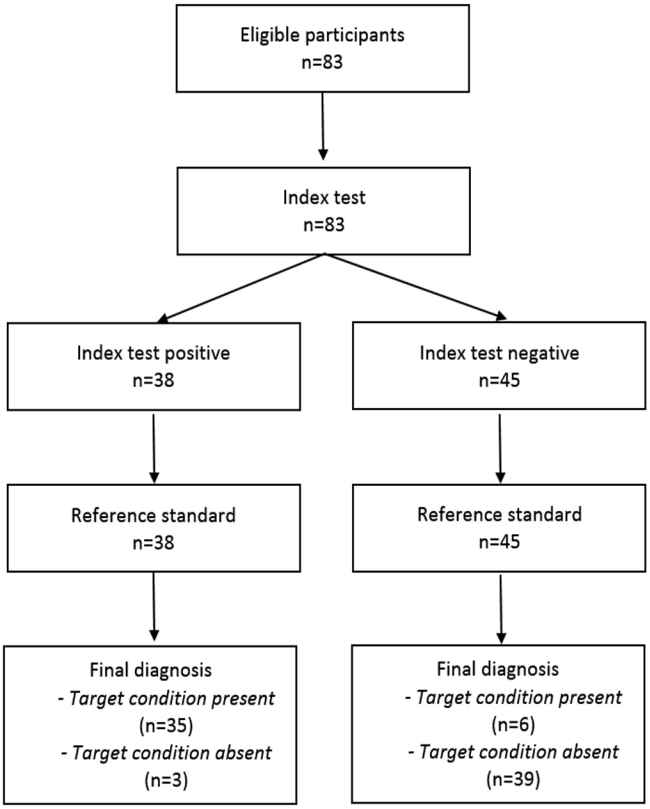

Figure 2. STARD flow diagram of the study participants.

A blinded and trained personnel scanned all the patients using the NIRS device. To obtain measurements, the Infrascanner 2000® standard examination was performed on four pre-determined pairs of locations in the head, as shown in Figure 3: 1) bilateral frontal areas above the frontal sinus; 2) bilateral temporal areas on the temporal fossa; 3) bilateral parietal areas, midway between the ear and the midline of the skull; and 4) bilateral occipital areas, midway between the ear and the occipital protuberance areas of the head. The read-out of the scan provides a difference in optical density (ΔOD) reading, which correlates to the severity of the hematoma and identifies which region of the brain is bleeding. The presence of hematoma was defined as a ΔODmax at any location ≥ 0.2.[8] The CT scans were read by a senior resident of the Department of Radiology in PGH. A 64-slice CT machine (GE Healthcare, Chicago, Illinois, US) was used.

Sample Size Calculation

The sample size needed for this study was computed following the methodological review of Hajian-Tilaki, et al.[12] for studies with binary test outcomes and known disease status. The formula is as follows:

$$n = \frac{Z^2_{\frac{\alpha}{2}} x \hat{P}(1-\hat{P})}{d^2 x (Prev)}$$

Where $\hat{P}$ is 74.6%, the pre-determined sensitivity based on the primary analysis of Infrascanner 2000®, as obtained from the operation manual of the instrument [15]; $Z_{\frac{\alpha}{2}}$ is 1.96 at α=0.05; Prev is 40% (29/73), the prevalence of intracranial hemorrhage among GCS 13-15 closed traumatic brain injury patients at the PGH in 2015.[5] d is 15%, the clinically presumed precision. The determined sample size of the study was 83.

Results

A total of 83 patients with duly accomplished informed consent forms were enrolled in the study. All patients underwent NIRS assessment at the time of admission and were then scheduled for an immediate CT scan. The cohort included mostly males (82%) and had a mean age of 29.52 years (range: 16-64 years). The majority of the injuries resulted from a vehicular crash (77%), followed by falls (16%), and mauling (7%). Patients came from Cavite (55%), Manila (14%), Batangas (11%), Laguna (10%), and Paranaque (10%). Upon admission, patients presented with the following levels of consciousness: GCS 15 (65%), GCS 14 (30%), and GCS 13 (5%). Vomiting (48%), headache (48%), brief loss of consciousness (20%), and seizures (9%) were noted as associated symptoms. The average time from injury to CT scan was 15.34 hours, while the average time from NIRS scanning to CT scan was 11.34 hours. The average NIRS scanning time was 8.24 minutes (Table 1).

Out of 83 cases, 4 cases (5%) were operative due to an epidural hemorrhage, requiring a burr hole evacuation

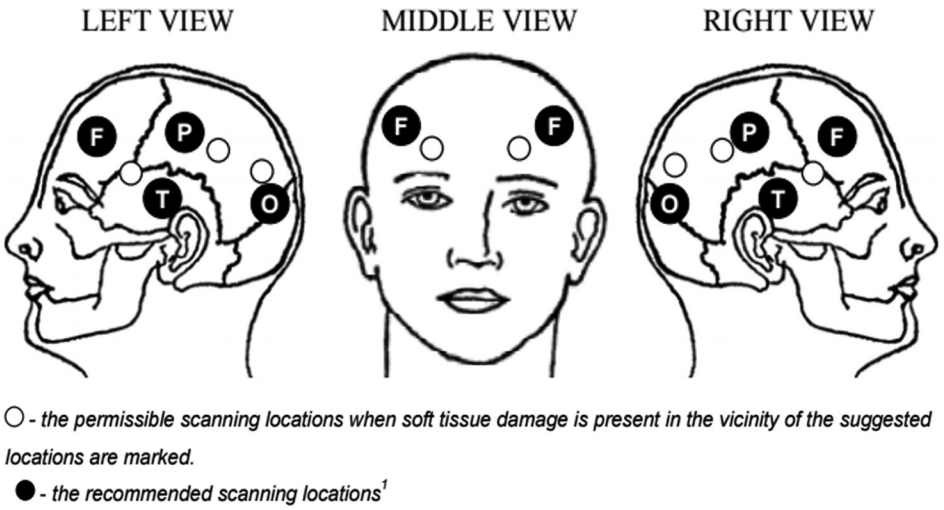

Figure 3. Schematic diagram for the placement of the NIRS device (Picture from the Infrascanner Manual).[10]

of the hematoma. In this study, subdural hematoma (28%) was the most common type of hemorrhage observed, presenting as a solitary condition or concomitant with other types of hematoma, such as epidural hematoma (16%), intraparenchymal hematoma (6%), and diffuse brain injury (4%) (Table 1).

Table 2 shows the performance of the Infrascanner 2000® in determining the presence of hemorrhage compared to CT scan findings. There were 35 patients noted to have true positive findings on CT scan, while 3 patients were false positive. There were 39 patients who had true negative results, while 6 patients were false negative. The diagnostic validity of the NIRS device yielded the following: sensitivity, 85.37% [95% confidence interval (CI): 74.55-96.19%]; specificity, 92.86% [95% CI: 85.07-100.00%]; PPV, 92.12% [95% CI: 83.53-100.00%]; NPV, 86.67% [95% CI: 76.74-96.60%]; PLR, 11.96 [95% CI: 3.99-35.82]; and NLR, 0.16 [95% CI: 0.07-0.33].

Discussion

This study is the first clinical trial that assessed the diagnostic validity of the Infrascanner 2000® in the Philippines. This study confirms previous studies supporting the ability of the Infrascanner 2000® device to screen and detect intracranial hematoma in acute and closed head injury patients needing immediate objective diagnostic triaging. Only patients with mild TBIs were included in the study because they are the subset of patients who require adjunct objective diagnostics to reach a more reliable working impression. Additionally, they are also the subset of patients where CT scan may or might not be warranted, depending on the Canadian CT rule. Investigating this gray area would provide insight regarding the potential utility of a NIRS device in TBI cases in rural areas and communities, which are comprised of this subset of patients.

The average time from injury to CT scan of 15.34 hours was comparable with the study done by Robertson, et al.,[8] which reported a 12-hour delay. The time from NIRS scanning to the scheduled CT scan had an average 11.34-hour delay because the Radiology Department prioritized patients needing more immediate evaluation, such as those with acute intracranial hemorrhage from cerebrovascular accidents, complete gut obstruction, and open head trauma. The timing for data collection is crucial to note because the NIRS method relies on the absorption characteristics of acute blood. As previous

Table 1. Demographics of study participants.

Parameter	Number	Percentage
Total sample (n)	83	100%
Male	68 (82%)	82%
Female	15 (18%)	18%
Mean age	29.52	
Age distribution		
15-20 years old	10	12%
21-30 years old	35	42%
31-40 years old	22	27%
41-50 years old	11	13%
51-60 years old	3	4%
61-65 years old	2	2%
Mechanism of Injury		
Vehicular Crash	64	77%
Fall	13	16%
Mauling	6	7%
Point of Origin		
Cavite	46	55%
Manila	12	14%
Batangas	9	11%
Paranaque	8	10%
Laguna	8	10%
Symptoms		
Vomiting	48	58%
Headache	48	58%
Seizure	13	16%
Others	20	24%
GCS Score		
15	54	65%
14	25	30%
13	4	5%
Operability		
Operative	4	5%
Non-operative	79	95%
CT Scan Results		
Subdural	23	28%
Epidural	13	16%
Intraparenchymal	5	6%
Diffuse Axonal Injury	3	4%
Negative	39	47%
Average NIRS scanning time	8.24 mins	
Average time from time of incident to CT scan	15.34 hours	
Difference NIRS Scan and Cranial CT-Scan	11.34 hours	

Table 2. Results of diagnostic accuracy testing of the NIRS device and the cranial CT scan.

		Cranial CT scan	
		+	-
NIRS	+	35 True positive	3 False positive
	-	6 False negative	39 True negative
Specificity		85.27% [85.07-100.00%]	
Sensitivity		92.86% [55-96.19%]	
Positive Predictive Value		92.10% [83.53-100.00%]	
Negative Predictive Value		86.67% [76.74-96.60%]	
Positive Likelihood Ratio		11.96 [3.99-35.82]	
Negative Likelihood Ratio		0.16 [0.07-0.33]	

studies have suggested, chronic subdural hematomas cannot be reliably detected by the NIRS device.[13] Notably, PGH patients usually come from the southern parts of Metro Manila to the proximal provinces of Region 4 (i.e., Cavite, Laguna, and Batangas). These areas usually take 3-4 hours of land travel with heavy traffic, suggesting that NIRS screening may still be useful in these patients. The process of NIRS assessment entails a learning curve that the assigned research assistant for scanning had to be attuned to. There may be difficulty in the placement of the device, particularly in prone and uncooperative patients. These factors may have contributed to variations in the average NIRS scanning time.

In comparison to Robertson, et al., present data revealed overlapping specificity (92.86% [95% CI: 85.07-100.00] vs. 90.70% [95% CI: 86.40-93.70]), sensitivity (85.37% [95% CI: 74.55-96.19] vs. 68.70 [95% CI: 58.30-77.60]), and NPV (86.67% [95% CI: 76.74-96.60] vs. 89.00% [95% CI: 84.60-92.3. However, present study found an increased PPV (92.12% [95% CI: 83.53-100.00] vs. 72.50% [95% CI: 62.00-81.10]) compared to Robertson, et al.[8] The PLR of 11.96 signifies that positive results in the Infrascanner 2000® device may adequately predict the presence of a hematoma on CT scan with a >45% approximate change in probability. Conversely, the NLR of 0.16 signifies that the negative results in the Infrascanner 2000® device adequate predict

that there is no hematoma formation on CT scan with a 30-45% approximate change in probability.[14]

Given these findings, objective evidence in ruling in or ruling out acute intracranial hematoma in patients with GCS 13-15 could be provided by the device. However, it is important to be wary of possible sources of false positives and negatives for the NIRS assessment. Presence of scalp hematomas may result in false positives while small hematomas may not be within the detection limit of the NIRS device. The ΔOD is directly proportional to the amount of hematoma present and inversely proportional to the distance of the hematoma from the scalp.[15,16] This was supported by the study findings as the consistency of detecting hematomas >3 ml and within 2.5 cm from the scalp was observed. Additionally, three small intra-axial hematomas (i.e., diffuse axonal brain injury) were falsely negative in the Infrascanner 2000® device but were detected by CT scan. Moreover, the four operative patients with a surgically significant amount (>30 cc) of epidural hematoma on CT scan yielded higher ΔOD values upon NIRS assessment. In this regard, the Infrascanner 2000® device may also be used at regular intervals, especially in epidural hematomas in which close monitoring should be performed to detect changes in size over time.

The authors found that the Infrascanner 2000® is an appropriate tool for screening closed head injury patients in emergency situations. However, the output of the Infrascanner 2000® does not outweigh the amount of information provided by a CT scan. Data from NIRS would not be sufficient to formulate a detailed plan for patients with TBI. Surgical decisions require additional information about the location, type, and size of the hematoma, as well as the presence of a midline shift and other indications of mass effect.[17] The Infrascanner 2000® device is also limited in its ability to detect traumatic processes such as diffuse axonal injury or cerebral edema, which can appear normal in a NIRS assessment. Positive findings in a NIRS examination might suggest a higher priority for imaging, even in an otherwise low-risk patient.[13]

This study has several limitations. First, thick and darkly colored hair may complicate the use of NIRS technology to detect intracranial hematoma. However, shaving areas of the head to obtain a more accurate NIRS examination would be an impediment to the clinical application of the device. The fiber optic light guides of the NIRS device were designed to minimize the significance of this confounding factor.[8] Second, in scalp injuries, the blood contained within the scalp hematoma can alter the ΔOD and result in a false-positive result. Thus, patients with a scalp laceration or hematoma were excluded from this study.[8,13] Patients with scalp injuries need to be evaluated for head injury and other pathologies. Low diagnostic parameters obtained from the occipital area could be attributed to these confounding variables. Third, the significant difference in scanning time with the Infrascanner 2000® device and the CT scan could have yielded false negatives and false positives. According to the product operation manual, a 30-minute interval between the CT scan and NIRS scanning (before or after the CT scan) may yield more accurate results reflective of the CT scan interpretation.

Conclusion

The sensitivity (85.37%), specificity (92.86%), PPV (92.12%), NPV (86.67%), PLR (11.96), and NLR (0.16) of the Infrascanner 2000® supports that this NIRS device may be a valid tool to objectively supplement clinical information in closed head injury patients with mild neurologic deficits. Its portable nature is an advantage in the field and acute traumatic settings in the ED. The rapidly available feedback makes it useful in triaging patients and objectively determining the urgency of the need for subsequent imaging. However, the Infrascanner 2000® device is only an adjunct to gold standard imaging, especially when a CT scan is readily available. Future studies regarding the use of the Infrascanner 2000® in the surveillance of progressing epidural hematoma and in pediatric low-risk TBI are recommended.

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