Near-Infrared Spectroscopy (NIRS) to detect traumatic intracranial haematoma: A systematic review and meta-analysis

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Abstract

Head injury is the most common trauma presentation to UK emergency departments with around 1.2 million patients seen each year. The key management principal for this time critical illness remains early surgical intervention to prevent secondary injury. With the development of handheld near-infrared spectroscopy (NIRS) devices there is now the possibility of triaging and diagnosing these patients immediately where a computed tomography (CT) scanner is not available. NIRS has two related but distinct potential uses within clinical medicine. **Firstly, as a triage tool both in hospital and pre-hospital settings by doctors, nurses or paramedics as determined by its negative predictive value (NPV). Secondly, it may be used as a diagnostic aid as determined by its positive**

predictive value (PPV). The aim of this systematic review and meta-analysis is therefore to interrogate the current literature on NIRS in detecting intracranial haematomas.

NIRS technology has a cross study sensitivity of 78%, specificity of 90%, PPV of 77% and a NPV of 90%.

At present, NIRS does not meet current standards as a diagnostic aid or triage tool in the populations studied. Its diagnostic accuracy is limited to those without extracranial injuries and may also be complicated by long scan times.

Larger and more heterogeneous studies are required specifically evaluating how NIRS performs in detecting intracranial lesions requiring emergency evacuation.

Key Words: Traumatic brain injury, head trauma, near infrared spectroscopy, intracranial haemorrhage, intracranial haematoma

Introduction

Head injury is the most common trauma presentation to UK emergency departments with around 1.2 million patients seen each year. [1] The key management principal for this time critical illness remains early surgical intervention to prevent secondary injury from brain compression.[2,3] With the development of handheld near-infrared spectroscopy (NIRS) devices there is now the possibility of triaging and diagnosing these patients immediately where a computed tomography (CT) scanner is not available.

Near-infrared light was first utilised in 1977, by F.F. Jobsis, on the brain and exposed heart of a feline to monitor hypoxic events.[4] This is possible due to the transparency of biological tissues through which photons can be transmitted. The light used in the near infrared spectrum, especially between 700 to 1000nm, is able to penetrate the human tissues "optical window".[5] Once the light has penetrated into the tissue it is either scattered or absorbed. The light is mostly scattered by the bones, skin and cerebral white matter. However, red blood cells, which represent roughly 1.5% of the solid tissue, have a low scattering effect and high absorption. Utilising this principle, the portable near-infrared device (http://infrascanner.com) (http://www.bytecmed.com/en/produkte/crainscan) is placed on the cranium where one probe emits near-infrared light and the other detects light that is scattered by the tissue. The '*optical density'* of the tissue is calculated and by comparing the left and right hemispheres in the frontal, parietal, temporal and occipital areas lesions with extravascular accumulation of haemoglobin can be detected, unless of course, there are bilateral pathologies.

NIRS has two related but distinct potential uses within clinical medicine. Firstly as a triage tool as determined by its negative predictive value (NPV) to exclude lesions in patients where computed tomography (CT) scanning is not immediately available and ultimately deciding whether or not patients are transferred to a major trauma centre. Secondly as a diagnostic aid as determined by its positive predictive value (PPV) allowing clinicians to diagnose and instigate early treatment in intracranial haematomas requiring urgent evacuation. This could include burr holes in a hospital without CT imaging or even in the prehospital setting if transfer times were significant.

In a systematic review, Dieters *et al* concluded that NIRS required further refinement before use in clinical contexts due to concerns regarding accuracy.[6] Subsequent studies have demonstrated 93% sensitivity in detecting intracranial haematomas over 25ml and 100% over 75ml.[7] **Studies have suggested that clot volumes of 20-80ml should be managed surgically.[8] However, the management largely depends on the site, type, dominance and depth of haematoma as well as co-morbidities and neurological status.** By combining clinical examination and NIRS it may now be possible to reach a diagnosis of extra-axial haematoma safely and accurately without CT. The aim of this systematic review is therefore to interrogate the current literature on NIRS in detecting intracranial haematomas.

Methods

Search strategy and selection and criteria

The protocol for this systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[9] The review protocol is registered on the PROSPERO international prospective register of systematic reviews and can be viewed at http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015020064#.VVXfSVyDSng (CRD42015020064).

The search terms '*near infrared spectroscopy OR infrascanner'* and *'haematoma OR hematoma OR haemorrhage OR hemorrhage'* were used to search the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, LILACS, http://www.opengrey.eu, Science Citation Index, ClinicalTrials.gov and Current Controlled Trials from 01/01/1990 to 01/01/2015. Only articles in English were considered for review. Two independent reviewers (RJB, BG) identified articles from the above search, which was then checked by a third (HJM).

Studies were included if they assessed the sensitivity and specificity of NIRS in identifying intracranial haematomas in humans. All article titles and abstracts were screened and full articles were then assessed for eligibility. Article references were also screened for eligibility. Two authors performed data extraction independently (RJB, BG).

Our primary outcomes were PPV, NPV and accuracy of NIRS in detecting intracranial lesions warranting emergency evacuation using CT scan results for comparison. Acceptable PPV and NPV cut offs were set at 95% for assessment of primary outcomes. Secondary outcomes were sensitivity, specificity and advantages and limitations of NIRS. Where the sensitivity, specificity, PPV, NPV or 95% confidence limits were not given these were calculated by RB and HJM.[10] Subgroup analysis was performed on patients requiring surgical intervention and also on paediatric cohorts due to anatomical differences and the negative correlation between age and accuracy of NIRS.[11] Forest plots were used to allow for comparison of outcomes.

Studies were individually assessed for risk of bias.

All analysis was performed in Microsoft® Excel® for Mac 2011 Version 14.5.5.

Results

In all, 192 studies were returned from the databases and one article from a reference list. Four duplicates were removed. Title and abstracts were screened and 175 articles were excluded from further analysis. Fourteen articles were then retrieved **and a further six were excluded from review, as they were not assessing sensitivity/specificity in humans**. ***Figure 1*** demonstrates the PRISMA flowchart of screening/selection process.

Table 1 presents the characteristics of all eight included studies.

Two studies were performed in children aged <15 giving a combined sensitivity of 100% (CI 75.3-100).[12,13] ***(Table 2)*** Both studies (n=46) used the Infrascanner© 1000 by InfraScan (http://infrascanner.com). Bressen et al. list one true positive but do not disclose the pathology from CT.[12] Salonia et al. describe twelve lesions including subdurals, extradurals and subarachnoid haemorrhages.[13] Reducing radiation exposure was viewed as the main benefit from NIRS technology in children and can be confirmed by a combined negative predictive value of 100% (CI 88-100) between studies. The combined PPV was 81% (CI 54-96). One major disadvantage in infants and toddlers is compliance resulting in long scan times of up to 14 minutes and n=6 exclusions due to uncooperative behaviour.[12,13] However, given the symptomatology of traumatic brain injury this fact also applies to adults and is described by Leon-Carrion et al.[14]

Six studies were performed in adults between 2005 and 2010 with two researchers using the Infrascanner© 1000 (http://infrascanner.com), two using CrainScan© by ByTech (http://www.bytecmed.com/en/produkte/crainscan), one using “smartscan” and one using a NIRS device developed by the research team. Authors using “smartscan” and the in house device were unavailable for comment regarding their near-infrared spectroscopy devices. One study did not state which device it used. There are no published studies comparing sensitivity/specificity between

portable NIRS devices. ***Table 3*** displays the diagnostic accuracy between devices with all devices performed similarly. The best PPV of 100% was from "Smartscan" (n=60) and the best NPV of 97% was by Francis et al's own device (n=50).[15]

Table 4 displays the inter-study sensitivity, specificity, PPV and NPV in adults. On combining data from all studies, NIRS technology has a sensitivity of 78%, specificity of 90%, PPV of 77% and a NPV of 90% but these values vary greatly between studies as demonstrated by ***figure 2.1***, ***figure 2.2***, ***figure 2.3***, and ***figure 2.4***. PPV and NPV ranges from 67% to 100% and 87% to 98% respectively. Kahraman et al. quote a PPV of 100%, however the clinicians were not blinded.[16]

In three studies, 44 cases required emergency evacuation of intracranial haematomas.[7,15,16] Authors only reported true positives (n=42) and false negatives (n=2) within this subgroup giving a combined sensitivity of 96% (CI 85-1) in detecting intracranial haematomas requiring emergency evacuation. Calculation of PPV and NPV were not possible due to lack of subgroup analysis within articles. Authors were contacted but did not reply within timeframes.

A potential source of bias was identified with one study being industry funded by InfraScan Inc.[7]

Discussion

Near-infrared spectroscopy is a potentially invaluable for clinicians both as a diagnostic and triage tool for intracranial haemorrhage. Pre-hospital and emergency medicine are among the main specialities that would benefit greatly from its clinical application. With a cross study NPV of 0.9 (CI 0.88-0.93), NIRS may be of significance as a triage tool in the near future ***(Figure 2.4)***. However, with a PPV of 0.77 (CI 0.71-0.82) ***(Figure 2.3)*** it appears that, at present, NIRS cannot be used as a diagnostic aid for intracranial haemorrhage or to aid placement of burrholes in the broad population as studied.

The potential use of NIRS's as a triage tool could be diverse - from the remote medical practitioner to prehospital ambulance staff in an urban environment – essentially any situation where CT scanning is not immediately available. At present, NIRS does not meet our NPV requirements of 0.95 in adults. However, Robertson et al show an increase in the NPV from 0.89 (CI 0.85-0.92) to 0.97 (CI 0.95-0.99) when limiting their analysis to subdurals, extradurals and intracerebral haematomas/contusions >3.5mls and <2.5cm from the brain surface.[7] This data suggests that NIRS may be used to exclude haematomas requiring emergency surgical evacuation. It must be noted that InfraScan Inc. funded this study introducing potential bias. As for paediatric cohorts, our NPV requirements initially appear to be met with a combined NPV of 1 (CI 0.88-1). However, one must consider the cohort from which this NPV is derived. Bressen et al enrolled one-hundred and three paediatric patients into their study, all of which were evaluated using the Infrascanner© 1000.[12] Only eighteen of the one-hundred and three patients subsequently underwent CT scanning detecting one pathological lesion. This results in a small sample size for calculating the NPV even when combed with the twenty-eight subjects from Salonia et

al.[13] Additionally, there were seven positive infrascans with no further evaluation by CT. Four of these scans can be explained by the large scalp haematomas but there is no explanation for the remaining three. Therefore, we conclude that further evaluation of NPV is required.

There once was an era when rural doctors performed "exploratory" trephination without the aid of any imaging modality with a significant reduction in mortality.[16] The World Health Organization state that *'CT scans facilitate such treatment, but they are not mandatory. It should be noted that increase survival with drainage of intracranial haematoma was widely documented in the era before CT scans'.* [2] If near-infrared spectroscopy has acceptable diagnostic accuracy then practitioners may perform targeted, rather than exploratory burr holes. However, with an overall positive predictive value of 0.771, near-infrared spectroscopy does not meet our current standards as a diagnostic tool for this life threatening condition. In fact, Robertson et al actually demonstrate a decrease in PPV from 0.725 to 0.637 when applying the same criteria described in the last paragraph of *"subdurals, extradurals and intracerebral haematomas/contusions >3.5mls and <2.5cm from the brain surface"*.[7] This suggests a high proportion of false positives but unfortunately the authors do no provide any further explanation for this. They do, however, demonstrate that the volume of blood within the cranium is proportional to sensitivity. For example, for haematomas >70mls sensitivity is 1 and lesions 25mls-70mls sensitivity is 0.93. In all eight studies included in our meta-analysis there were forty-nine reported cases of extradural/subdural haematomas requiring emergency evacuation. In three of these studies, 44 cases were analysed separately allowing us to calculate a combined sensitivity of 0.96 (CI 0.85-1) in detecting intracranial haematomas requiring emergency evacuation.[7,15,16] We were unable to calculate the PPV or NPV due to false positives and true negatives not being reported in the paper. Of particular interest, Karhaman et al. quote a PPV of 1 (CI 0.87-1) ***(Figure 2.3)*** in detecting acute and chronic intracranial haematomas in twenty-six patients requiring surgical intervention.[16] Unfortunately, the NIRS operator was not blinded so bias cannot be excluded but this does suggest a potential use for NIRS in detecting intracranial haematomas requiring emergency evacuation. These two conflicting studies by Karhaman and Robertson et al requires further investigation before NIRS is considered as a diagnostic aid for intracranial haematomas.[7,16]

A common criticism of NIRS technology is the fact that subgaleal haematomas impede the detection rates of intracranial pathology. Due to the mechanisms of injury resulting in traumatic brain injury a large proportion of these patients may not be suitable for NIRS examination. Robertson et al. excluded 11 subjects from their study due to this very reason.[7] In fact, anything altering NIRS path of light may affect the accuracy of the device, hence some authors have recorded hair type, hair pigment and skin pigment. Although these factors may well be significant there have been no published studies. NIRS manufacturers also document that ambient light and movement artifact may result in errors messages thus requiring repeat measurements and prolonged scan times. It is clear from the published evidence that the type and depth of lesion correlates well with sensitivity.[7] Deep lesions remain difficult to detect due to the longer path of light and old lesions due to the breakdown of haemoglobin and changing absorption spectra. Compliance also appears be a major issue in paediatric cohorts with

Salonia et al quoting long scan times of up to fifteen minutes, which may impede on rapid assessment and triage of patients.[13]

The manufacturers of both CrainScan© and Infrascanner© were contacted but only Infrascan Inc. were available for comment. Their responses regarding they key differences between devices are detailed below. The Infrascanner© emits near-infrared light at a wavelength of 808nanometers, whereas the CrainScan© emits light at 785nanometers. *'Both are close to the desired 805nm wavelength, where the system is sensitive only to the amount of blood and not to oxygen saturation in the blood'.* Measurement methods also differ between devices; CrainScan© use a wide angle light source and detector that is placed over hair thus compressing it under the light source, Infrascanner© on the other hand uses 1.6mm optical fibres that the user must manoeuvre between hair follicles to gain contact with the scalp. Due to hair follicles obstructing the path of light when using CrainScan© the Infrascanner© reportedly has a lower detection threshold thus detecting smaller and deeper bleeds. Infrascan Inc. then stated *'the Infrascanner is less affected by hair color as it mostly bypasses it. Crasinscan works only in light hair patients and in darker patients the hair has to be shaved locally to take a reading'*. BYTECH were unavailable to provide any further information regarding the CrainScan© and there has been no published studies comparing devices. The only such information we do have is provided above in ***table 3***.

In summary, with a cross study NPV of 0.9 (CI 0.88-0.93) and a PPV of 0.77 (CI 0.71-0.82) NIRS does not meet our requirements for a diagnostic or triage tool in the broad population studied. However, in a subset, for example GCS 3 with unilateral fixed dilated pupil, the PPV and NPV may well be greater enabling it to be used as such a tool and possibly guide the placement of prehospital burrholes.[17] The studies included in this systematic review, however, have not been powered to demonstrate this. Near-infrared spectroscopy has some limitations but as long as users understand the implications of these its portability and potential as a prehospital or rural medical triage tool may outweigh these. Near-infrared spectroscopy, currently, does not have a place in diagnosing intracranial haematomas where computed tomography is immediately available. Larger and more heterogeneous studies are required specifically evaluating how NIRS performs in detecting intracranial lesions requiring emergency evacuation in the emergency department and prehospital setting.

<u>Review Limitations</u>

All authors of papers included in this review were contacted, of which three replied and one provided further information that was included in our analysis. Additionally, to allow for cross-study comparisons we had to use data from different near-infrared spectroscopy manufacturers, which could possibly result in inconsistencies due to the calibration of devices.

<u>Contributions</u>

RJB performed literature search and data extraction, registered PROSPERO review, performed statistical analysis, constructed tables and graphs and lead paper write up. VK provided background

information on near-infrared spectroscopy. BG performed literature search and confirmed data extraction for table 1. HJM confirmed statistical analysis and reviewed drafts. MHW reviewed final draft and supervised paper write up.

Declaration of interest

The authors report no declarations of interest.

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