SAP: Infrascanner 2000 NCT03353246

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Project: Assessment of Accuracy, Precision, and Feasibility of a Handheld Near-Infrared Light Device (InfraScanner 2000™) in Detecting Subdural and Epidural Hematomas in Patients Admitted to Duke University Hospital: A Pilot Study

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Deadlines: N/A

Background:
Traumatic brain injury (TBI) is a global pandemic that affects over 10 million people annually, with the incidence expected to continue to mushroom in coming years (1). In industrialized nations, this is a trivial requirement, as CT scans are used ubiquitously to definitively diagnose epidural hematomas (EPH) and subdural hematomas (SDH), readily and reliably triaging patients to surgical versus medical management. In less developed countries, CT scanners are often nonexistent. When they are present, they are extremely meager in number, peppered across treacherous geography, with scant transportation and emergency infrastructure.

In 1997, the first ever handheld device that could definitively detect the presence and location of epidural and subdural hematomas was introduced (2). Initially named the Runman, the device was intended to detect intracranial hematomas in remote and military settings to triage which casualties should be airlifted to medical centers equipped to offer neurosurgery. After numerous iterations, the InfraScanner 1000™ was introduced in the mid 2000's. In 2010, the pivotal five-site double-blinded clinical trial was published, and ultimately led to FDA clearance of the InfraScanner 1000™. In the study, the Infrascanner 1000™ measurements were compared to CT scans of 365 patients, 96 of which were hematoma cases of various sizes, depths and locations. The study demonstrated high sensitivity (88%) in detecting hematomas > 3.5cc in volume and < 2.5 cm from the surface of the brain, and a specificity of 91%. Since then there have been numerous studies that have replicated these results and have substantiated that it is a capable tool for pre-hospital diagnosis of intracranial hematomas (2-12).

The goal of this study is to determine the sensitivity, specificity, and positive and negative predictive values of the portable near-infrared-based device (portable NIR-based device), the InfraScanner 2000™, to detect intracranial hematomas [EDH and/or SDH] in patients hospitalized at Duke University Hospital (DUH) who have sustained or who are suspected to have sustained head trauma and have consequently received a brain computed tomography (CT) scan(s).

Specific Aims:

Aim 1: Determine whether the InfraScanner 2000™ detects epidural and/or subdural hematomas with adequate precision relative to CT scans to be used as a diagnostic tool for epidural and/or subdural hematomas.

Aim 2: Use these findings to inform the feasibility of conducting a future trial in which the InfraScanner 2000™ is used as a stand-alone diagnostic tool for intracranial hematomas, and therein, to determine candidacy for decompressive craniotomies in patients who suffer traumatic brain injuries in places where CT scans are not available.

Primary Objective:

1. Estimate the test characteristics (sensitivity, specificity, and the false positive and false negative rates) of the portable NIR-based device (InfraScanner 2000™) in the identification of any size hematoma. The results of the CT scan(s) will serve as the gold standard.

Secondary Objective:

1. Estimate the test characteristics of the InfraScanner 2000™ in identification of hematomas within its detection limits (volume >3.5 mL and depth <2.5 cm) compared to CT scan results as the gold standard.

Study Population:

- Any patient who presents to DUH with suspected head trauma and receives a brain CT scan will be considered for this study. Our final sample size is 581 measurements for 500 patients.

Inclusion/Exclusion:

- Duke ER patient with suspected head trauma and received a brain CT scan

Data Management:

Explain multiple measurements for the same patients,
Sample size
If there are multiple scans on a single patient, define the presence of a hematoma per patient as the first hematoma detected by the Infrascanner on any assessment and compare results with the corresponding CT assessment (within 30 minutes on same date).

Variables:

1. Age: continuous
2. Sex: male/female
3. Skin color: white/light brown/dark brown/black/yellow
4. Hair thickness: bald/thin/medium/thick/MPB
5. Hair color: NA/white/grey/blond/light brown/dark brown/black/red
6. Hair length: bald/0-1 inch/1-3 inches/3-6 inches/>6 inches
7. Scalp hematoma present: Y/N, if yes, Y/N at 8 different locations (left/right frontal/temporal/parietal/occipital)
8. Scalp laceration present: Y/N, if yes, Y/N at 8 different locations (left/right frontal/temporal/parietal/occipital)
9. Scalp fracture present: Y/N, if yes, Y/N at 8 different locations (left/right frontal/temporal/parietal/occipital)

10. Positive infrascan: Y/N
11. Positive CT: Y/N, if yes, Y/N at 8 different locations (left/right frontal/temporal/parietal/occipital)
12. Ventricular effacement: Y/N
13. Midline shift: Y/N
14. CT blood location: Y/N, if yes, Y/N at 8 different locations (left/right frontal/temporal/parietal/occipital)
15. CT blood size: in cubic centimeters (cc) at 8 different locations (left/right frontal/temporal/parietal/occipital)
16. Distance-from-cranium: TBD

Statistical Analysis:

Definitions of the statistics of interest:

Let A+ denote the event that the test is positive for hematoma and B+ denote the event that a hematoma is present. Sensitivity, $P(A+/B+)$, will be defined for each patient (scan) as the probability that a true hematoma as determined by CT scan will be detected (14). Similarly, let A- denote the event that the test is negative for hematoma and B- denote the event that a hematoma is not present. Specificity, $P(A-/B-)$, will be defined as the probability of being negative for hematoma on the InfraScanner 2000™ scan within 30 minutes of CT given the patient has no hematoma present.

The false positive rate will be defined as $PF+ = P(B-/A+) = P(A+/B-)[1-P(B+)]/P(A+)$. Similarly, the false negative rate will be defined as $PF- = P(B+/A-) = [1-P(A+/B+)]P(B+)/[1-P(A+)]$. Estimates for the false positive and false negative rates will be provided for a range of values for the prevalence of hematomas.

1. Estimation of test characteristics with 90% confidence at the patient level using SAS 9.4;
2. Estimate test characteristics at the scan level (treat each measurement as independent sample) and 95% confidence intervals will be computed as a secondary analysis.
3. Estimating Receiver Operating Characteristic (ROC) curves with patient and scan as the units of analysis with 95% confidence interval.
4. Fit a logistics regression of correct and incorrect detection from InfraScanner, adjusting for age, gender, skin color, hair color, hair thickness, hair length, scalp hematoma, scalp laceration, scalp fracture, ventricular effacement and midline shift.

Analysis plan:

1. A baseline table (Table 1) will describe overall study cohort characteristics by hematoma status.
2. Hematoma characteristics will be summarized at the patient level and also at the scan level (Table 2 and Table 3).
3. A 2x2 table of CT and InfraScanner results. Sensitivity, specificity, false positive value, false negative value, and their 95% confidence intervals will be calculated at patient level using the contingency table and reported. Repeat the analysis at scan level.
4. 2x2 tables of CT and InfraScanner results by quadrant. Corresponding counts and test characteristics will be calculated for each quadrant (frontal, temporal, parietal, and occipital). Repeat the analysis at scan level.
5. 2x2 tables of CT and InfraScanner results for hematomas within the detection limit. Corresponding counts and test characteristics will be calculated for hematomas within the detection limit (blood volume > 3.5 cc and distance from cranium < 2.5 cm). Repeat the analysis at scan level.

6. 2x2 tables of CT and InfraScanner results by types of hematoma. Corresponding counts and test characteristics will be calculated for each type of hematoma (SDH, EDH, etc.). Repeat the analysis at scan level.
7. 2x2 tables of CT and InfraScanner results by types of hematoma for those within the detection limit. Corresponding counts and test characteristics will be calculated for each type of hematoma (SDH, EDH, etc.) for those within the detection limit (blood volume > 3.5 cc and distance from cranium < 2.5 cm). Repeat the analysis at scan level.
8. Minimum blood volume detected as positive by InfraScanner 2000 will be reported.
9. Distributions of Blood Volumes and Difference in Optical Density (ΔOD) will be plotted for patients with hematoma.
10. InfraScanner results for special cases will be reported. Special cases include: patients who died, or had surgeries (craniectomy or craniotomy), or had ventricular effacement or midline shift.
11. Logistic regression model will be fit to assess the association between InfraScanner result and potential confounders that include patient age, sex, hair length, hair thickness, hair color, skin color, scalp laceration, scalp fracture, and scalp hematoma. Odds ratios with 95% CI will be reported.

Table Shells:

Table 1: Study Population Characteristics

	Hematoma present on CT N=	**Hematoma not present on CT N=**	**Total N=**	**p-value**
Gender Female Male				
Age N Mean (SD) Median Q1, Q2				
Skin Color				
Hair Color				
Hair Thickness				
Hair Length				
Mechanism of Injury Fall from elevation MVC Etc.				
Mortality				
GCS N Mean (SD) Median Q1, Q2				
Blood volume Left frontal Right frontal Etc. (?)				
Loss of Consciousness Yes No				
Location Frontal Temporal Occipital Parietal				
Hematoma Type SDH EDH Etc.				

Table 2: 2x2 Contingency Table of CT and InfraScanner results

	Hematoma CT		
Hematoma InfraScanner	**No**	**Yes**	**Total N=**
No			
Yes			
Total N=			

Table 3: 2x2 Contingency Table of CT and InfraScanner Results for SDH

	Hematoma CT of SDH		
Hematoma InfraScanner of SDH	**No**	**Yes**	**Total N=**
No			
Yes			
Total N=			

Similarly, for EDH, etc.

Reference:

1. Hyder AA, Wunderlich CA, Puvanachandra P, Gururaj G, Kobusingye OC. The impact of traumatic brain injuries: a global perspective. NeuroRehabilitation. 2007;22(5):341-53.
2. Robertson CSGSPCB. Use of Near-Infrared Spectroscopy to Identify Traumatic Intracranial Hematomas. Journal of biomedical optics. 1997;2:33-41.
3. Braun T, Kunz U, Schulz C, Lieber A, Willy C. [Near-infrared spectroscopy for the detection of traumatic intracranial hemorrhage: Feasibility study in a German army field hospital in Afghanistan]. Der Unfallchirurg. 2015;118(8):693-700.
4. Bressan S, Daverio M, Martinolli F, Dona D, Mario F, Steiner IP, et al. The use of handheld near-infrared device (Infrascanner) for detecting intracranial haemorrhages in children with minor head injury. Child's nervous system : ChNS : official journal of the International Society for Pediatric Neurosurgery. 2013.
5. Francis SV, Ravindran G, Visvanathan K, Ganapathy K. Screening for unilateral intracranial abnormalities using near infrared spectroscopy: a preliminary report. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia. 2005;12(3):291-5.
6. Leon-Carrion J, Dominguez-Roldan JM, Leon-Dominguez U, Murillo-Cabezas F. The Infrascanner, a handheld device for screening in situ for the presence of brain haematomas. Brain injury. 2010;24(10):1193-201.
7. Peters J, Van Wageningen B, Hoogerwerf N, Tan E. Near-Infrared Spectroscopy: A Promising Prehospital Tool for Management of Traumatic Brain Injury. Prehospital and disaster medicine. 2017;32(4):414-8.

8. Robertson CS, Gopinath SP, Chance B. A new application for near-infrared spectroscopy: detection of delayed intracranial hematomas after head injury. Journal of neurotrauma. 1995;12(4):591-600.
9. Robertson CS, Zager EL, Narayan RK, Handly N, Sharma A, Hanley DF, et al. Clinical evaluation of a portable near-infrared device for detection of traumatic intracranial hematomas. Journal of neurotrauma. 2010;27(9):1597-604.
10. Salonia R, Bell MJ, Kochanek PM, Berger RP. The utility of near infrared spectroscopy in detecting intracranial hemorrhage in children. Journal of neurotrauma. 2012;29(6):1047-53.
11. Xu L, Tao X, Liu W, Li Y, Ma J, Lu T, et al. Portable near-infrared rapid detection of intracranial hemorrhage in Chinese population. Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia. 2017;40:136-46.
12. Zhang Q, Ma H, Nioka S, Chance B. Study of near infrared technology for intracranial hematoma detection. Journal of biomedical optics. 2000;5(2):206-13.
13. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology. 1982;143(1):29-36.
14. JL F. Statistical Methods for Rates and Proportions. Second ed. New York, New York: John Wiley & Sons; 1981. p. 1-18.