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Clinical Investigation

CLINICAL INVESTIGATION

Ultrasound-tagged near-infrared spectroscopy does not disclose absent cerebral circulation in brain-dead adults

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Abstract

Background: Near-infrared spectroscopy, a non-invasive technique for monitoring cerebral oxygenation, is widely used, but its accuracy is questioned because of the possibility of extra-cranial contamination. Ultrasound-tagged near-infrared spectroscopy (UT-NIRS) has been proposed as an improvement over previous methods. We investigated UT-NIRS in healthy volunteers and in brain-dead patients.

Methods: We studied 20 healthy volunteers and 20 brain-dead patients with two UT-NIRS devices, CerOx™ and c-FLOW™ (Ornim Medical, Kfar Saba, Israel), which measure cerebral flow index (CFI), a parameter related to changes in cerebral blood flow (CBF). Monitoring started after the patients had been declared brain dead for a median of 34 (range: 11–300) min. In 11 cases, we obtained further demonstration of absent CBF.

Results: In healthy volunteers, CFI was markedly different in the two hemispheres in the same subject, with wide variability amongst subjects. In brain-dead patients (median age: 64 yr old, 45% female; 20% traumatic brain injury, 40% subarachnoid haemorrhage, and 40% intracranial haemorrhage), the median (inter-quartile range) CFI was 41 (36–47), significantly higher than in volunteers (33; 27–36).

Conclusions: In brain-dead patients, where CBF is absent, the UT-NIRS findings can indicate an apparently perfused brain. This might reflect an insufficient separation of signals from extra-cranial structures from a genuine appraisal of cerebral perfusion. For non-invasive assessment of CBF-related parameters, the near-infrared spectroscopy still needs substantial improvement.

Keywords: brain death; brain monitoring; cerebral blood flow; near-infrared spectroscopy; ultrasound-tagged near-infrared spectroscopy

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Editor's key points

- Near-infrared spectroscopy (NIRS) is a widely used noninvasive technique for monitoring cerebral oxygenation, but its accuracy may be impaired by extracranial contamination.
- Ultrasound-tagged near-infrared spectroscopy (UT-NIRS), which has been proposed as an improvement over previous methods, was studied in 20 healthy volunteers and 20 brain-dead patients.
- Two devices tested both showed inter-hemispheric differences in cerebral flow index, a parameter related to cerebral blood flow, and higher values in brain-dead patients than in volunteers.
- Further refinements are necessary to make NIRS a reliable technique for monitoring cerebral perfusion free of extracranial interference.

Non-invasive neuromonitoring tools without risk of brain damage are advantageous. Near-infrared spectroscopy (NIRS), a system that emits near-infrared light and detects the returning light that has passed through extra-cranial and cerebral tissues, has been widely used for decades for measuring haemoglobin saturation in cerebral tissue.[1–4] Its validity in adults, however, has been questioned, mainly because of risk of extra-cranial contamination.[2,5–7]

Conventional NIRS extracts regional oxygen saturation in tissue by analysing the attenuation of light by oxygenated and deoxygenated haemoglobin within the microvasculature underneath the probe.[1] This analysis involves measuring the intensity of light backscattered from tissue using at least two wavelengths (commonly one wavelength is below and another is above 800 nm). Changes in regional oxygen saturation in the volume illuminated by the light are calculated from the intensity of light reaching two detectors using the Beer–Lambert law and spatially resolved spectroscopy.[1]

Ultrasound-tagged NIRS (UT-NIRS), introduced recently, combines NIRS and ultrasound, aiming at selective detection of the signal originating from changes in light passing through grey matter. Unlike conventional NIRS, UT-NIRS assesses localised Doppler broadening of coherent light at a single wavelength (808 nm) around the ultrasound frequency as a measure for changes in microvascular blood flow.[8] This technology is more closely related to laser Doppler flowmetry[9] than to conventional NIRS, as it does not calculate regional oxygen saturation. Unlike laser Doppler, the broadening is assessed around the frequency of the ultrasound wave, which is used to modulate the light (around 1 MHz). Therefore, UT-NIRS provides a regional measure of changes in blood flow underneath the sensor.

Earlier versions of the technology were tested in animal models, and found to correspond to laser Doppler readings during haemodynamic manipulations.[10] The broadening is calculated in arbitrary units (0–100), so the results are provided without calibration and do not reflect the absolute quantity of blood flow underneath the sensor. To what extent UT-NIRS technology focuses better on intracerebral signals requires confirmation.

Brain death is a condition of irreversible loss of brain function as a result of cessation of circulation in structures cranial to the *foramen magnum*. Different criteria are used to define patients as brain dead depending on national legislation, but global, complete, and irreversible brain ischaemia is a defining feature. We examined whether UT-NIRS properly detects the absence of cerebral blood flow (CBF) in brain-dead patients in comparison to healthy volunteers.

Methods

Data were collected from February 2014 to June 2017 at the Neurointensive Care Unit, and the study was approved by the Ethics Committee of the Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy. Healthy volunteers signed a consent form, whilst for the subset of patients declared brain dead no consent was sought, because the Ethics Committee agreed that a purely observational data collection in brain-death cases did not require specific consent. Families were informed, but no consent form was used.

Noninvasive CBF

Cerebral perfusion was measured with UT-NIRS using the CerOx™ device (Ornim Medical, Kfar Saba, Israel) up until December 2015, when a new model (c-FLOW™; Ornim Medical) became available. In February 2016, the c-FLOW software was upgraded to a later version. As claimed by the manufacturer, 'this technology allows a noninvasive and continuous check of deep tissue blood flow used to measure relative changes in blood flow that monitors regional microcirculatory blood flow in tissues'.[11] The device, connected to two probes, displays cerebral flow index (CFI) as a 'pure' number that ranges from 0 to 100. The normal CFI range is not known, and the manufacturer suggests considering relative changes in blood flow rather than absolute numbers. Each probe illuminates tissue of the right or left cerebral lobe with laser light, and collects light scattered back. The probes also incorporate a small ultrasound transducer that provides low-power waves to induce the UT-NIRS signal,[12] and the monitors display an indicator of the signal quality.

Preparation of subjects (volunteer or patient) and set-up of the device were completed according to the c-FLOW User Manual.[13] After selecting a flat, intact, hairless area on the forehead, cleaned with sterile alcohol wipes, two disposable adhesive pads (Smart Pads, supplied by Ornim) were applied, one on the right and one on the left. With care to avoid creating air bubbles, we applied a small amount of ultrasound gel to the UT-NIRS probes, which were then firmly pressed onto the adhesive pads. During the first measurements on volunteers, an Ornim representative supervised the placement of the frontal probes and correct set-up of the machine.

For healthy volunteers, data from the UT-NIRS were acquired for variable lengths of time (15–20 min) after having obtained a stable value with full signal quality. Peripheral capillary oxygen saturation, end-tidal CO_2, respiration rate, and cardiac frequency were recorded, and data stored for analysis. In brain-dead patients, UT-NIRS data acquisition started after the criteria for brain death had been fulfilled and after obtaining a good-quality signal from the device. At the beginning of this investigation, UT-NIRS measurement was continued for several hours (up to 6 h) to verify stability of the CFI. Measurements in the first five cases were consistent and stable, so the duration of monitoring was reduced, and the median recording time for all brain-dead patients was 34 min. All data were acquired directly from the Ornim devices in digital format and archived. In consideration of the stability of the data, two values were recorded for each patient with an interval of 5 min, and used for the analysis.