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Review

# NIRS in clinical neurology — a 'promising' tool?

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ABSTRACT

Near-infrared spectroscopy (NIRS) has become a relevant research tool in neuroscience. In special populations such as infants and for special tasks such as walking, NIRS has asserted itself as a low resolution functional imaging technique which profits from its ease of application, portability and the option to co-register other neurophysiological and behavioral data in a 'near natural' environment. For clinical use in neurology this translates into the option to provide a bed-side oximeter for the brain, broadly available at comparatively low costs. However, while some potential for routine brain monitoring during cardiac and vascular surgery and in neonatology has been established, NIRS is largely unknown to clinical neurologists. The article discusses some of the reasons for this lack of use in clinical neurology. Research using NIRS in three major neurologic diseases (cerebrovascular disease, epilepsy and headache) is reviewed. Additionally the potential to exploit the established position of NIRS as a functional imaging tool with regard to clinical questions such as preoperative functional assessment and neurorehabilitation is discussed.



**Contents**



*Abbreviations:* ABP, arterial blood pressure; AD, Alzheimer's disease; ALS, amyotrophic lateral sclerosis; BCI, brain computer interface; CSD, cortical spreading depression; CSF, cerebrospinal fluid; CT, computed tomography; CVT, cerebral venous thrombosis; DBS, deep brain stimulation; dwI, diffusion weighted imaging; ECD, extracranial Doppler sonography; ECT, electroconvulsive therapy; EP, evoked potential; ICU, intensive care unit; LP, lumbar puncture (spinal tap); MCA, middle cerebral artery; MCI, mild cognitive impairment; MEP, motor evoked potential; PFO, patent foramen ovale; pwI, perfusion weighted imaging; $SpO_2$, partial oxygen saturation; SWI, susceptibility weighted imaging; TCD, transcranial Doppler sonography; VEP, visually evoked potential.

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## Introduction

A methodology providing continuous readings of cerebral oxygenation, applicable non-invasively at the bed side and relying on comparatively inexpensive technology should have overcome the stage of a 'promising tool' with regard to its routine application in neurology. However, over 35 years after its first description (Jobsis, 1977) and 25 years after the development of the first commercial monitors (Cope and Delpy, 1988), Near-infrared spectroscopy (NIRS) is largely unknown to clinicians even in specialized neurological departments.

Ironically one reason for this apparent discrepancy may be related to the versatility of the method. The list of parameters derived from changes in optical properties of brain tissue is long (Table 1). It reaches from the most straight forward assessment of concentration changes in oxygenated, deoxygenated and total hemoglobin (HbO, HbR, HbT) over the less reliable estimation of redox-changes in cytochrome oxidase (cyt-ox) (Tisdall et al., 2007) to a number of derivations yielding oxygenation indices such as regional oxygen saturation ($rSaO_2$) or the tissue oxygenation index (TOI) (Al-Rawi and Kirkpatrick, 2006; Pocivalnik et al., 2011). Application of an optical contrast agent (indocyanine green, ICG) extends the spectrum to an index of perfusion (Terborg et al., 2004), also targeted by DCS (diffuse correlation spectroscopy) a methodology sharing many features with NIRS (Durduran et al., 2004). Finally some groups still advocate the sensitivity of non-invasive approaches to very fast changes in optical properties in response to neuronal signaling (Gratton and Fabiani, 2010). The cornucopia of parameters may be scientifically rewarding but strongly limits comparability between studies from different groups and is unsuited for clinical use. This may hold in particular for neurology, a field where diagnosis and therapy evaluation strongly rely on conflating the patient's history and neurological status with the results of a large number of established instrument-based results.

A second issue hampering the introduction of NIRS in clinical neurology is the fact that in adults at best half of the cerebral cortex can be interrogated. Mesial, insular and even cortex in deep sulci plus all subcortical and infratentorial parts of the brain cannot be reached (Fig. 1). Interestingly clinical use and its critical evaluation may be most advanced in brain-monitoring during cardiac and carotid artery surgery (Pennekamp et al., 2009; Vohra et al., 2009; Zheng et al., 2012) and in critical care settings (Smith, 2011). In this field NIRS studies largely rely on a 'pars pro toto' approach, correlating drops in cerebral oxygenation measured in a quite limited area of the cerebral cortex to the occurrence of any post-interventional neurological deficit. On the contrary neurological differential diagnosis of diseases affecting the central nervous system (CNS) usually aims at identifying a more or less circumscribed localization of the lesion or dysfunction to then differentiate between the underlying pathology.

A third challenge to the establishment of any novel methodology for routine clinical use is the necessity to demonstrate a specific advantage over existing diagnostic procedures. Listing the most common diseases

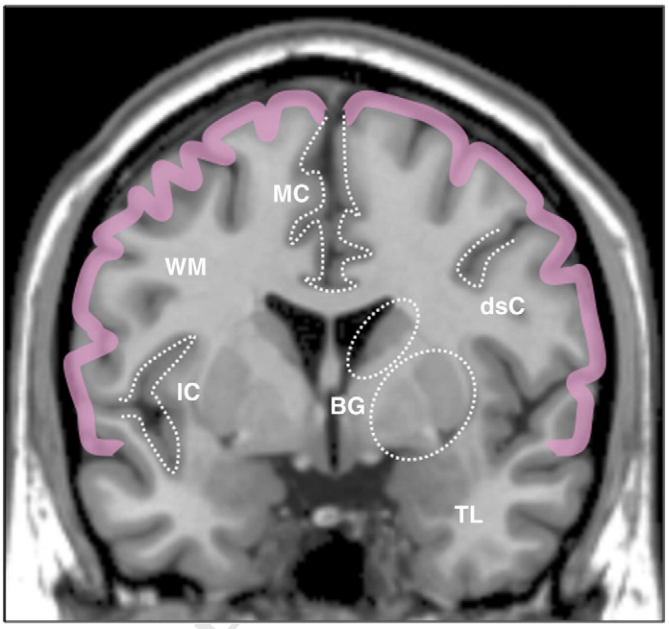


**Fig. 1.** Coronal slice illustrating brain structures accessible to NIRS. Neocortex at the brain's surface can be interrogated by NIRS (pink ribbon). Note that besides deep brain structures (e.g. basal ganglia, BG) and white matter (WM) substantial neocortical areas cannot be reliably reached (TL: temporal lobe; IC: insular cortex; MC: mesial cortex in the interhemispheric cleft; dsC: cortex in deep sulci). The brain areas reached account to roughly half of the neocortex. Infratentorial structures such as the cerebellum and brainstem cannot be assessed.

**Table 1**
List of the most commonly reported parameters in studies using NIRS (near-infrared spectroscopy) and their potential in clinical neurology. Though the assessment is based on a similar principle, values may substantially differ (Pocivalnik et al., 2011). Results may support a somewhat greater sensitivity to deep layers (Liebert et al., 2006).

| Abbreviation | Parameter | Assessment principle | Potential for clinical use | Limitations |
|---|---|---|---|---|
| HbO | Oxygenated hemoglobin concentration | Direct assessment by modified Beer–Lambert approach; dual-wavelength approach sufficient | Changes in cerebral hemodynamics and blood oxygenation | No absolute values; combination of HbO/HbR/HbT responses may result in 12 different response patterns |
| HbR | Deoxygenated hemoglobin concentration | | | |
| HbT | Total Hb concentration (=HbO + HbR) | | | |
| HbD | Hemoglobin difference (=HbO − HbR) | Simple derivation | | Reported in few publications |
| Cyt-ox | Cytochrome-oxidase redox state | Requires ≥3 wavelengths | Marker for cellular oxygenation and energy metabolism | Low concentration, liable to crosstalk From Hb changes |
| $rSaO_2$ | Regional oxygen saturation | Requires multi-distance | Single value to assess oxygenation, reported by many studies on intraoperative/ICU applications | Strong assumptions on background optical properties[a] |
| TOI | Tissue oxygenation index | | | |
| $BFI^{ICG}$ | Blood flow index | I.V. application of indocyanine green (ICG); bolus renders transit time based on absorption or fluorescence; | Perfusion in analogy to perfusion-weighted MRI | Requires I.V. bolus |
| $ICG^{fluo}$ | Fluorescence after injection | | Perfusion and potentially extravasation in superficial tumors or inflammation | I.V. application, complex modeling of fluorescence in layered tissue, as yet only feasibility study[b] |
| EROS | 'Event related optical signals' — fast optical changes | High frequency sampling mandatory; mostly reported for frequency domain monitors | May be sensitive to neuronal changes related to electrophysiological signal | A number of groups doubt transcranial detectability |

[a] Note that rSaO2 and TOI are provided by different commercial monitors.
[b] Single feasibility study with a time resolved NIRS system.

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