Near-Infrared (NIR) Spectroscopy

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*

Aetna considers near-infrared (NIR) spectroscopy experimental and investigational for the following indications (not an all-inclusive list) because of insufficient evidence of its effectiveness.

- Assessing pain
- Detecting carotid or coronary vulnerable plaques
- Detecting traumatic intracranial hematoma/traumatic brain injury
- Evaluating anesthetic depth
- Evaluating autism spectrum disorder
- Evaluating gait disorders
- Evaluating lower extremity wounds/predicting wound healing (e.g., for measurement of oxy-hemoglobin)
- Evaluating mitochondrial disorder
- Evaluating psychiatric disorders (e.g., bipolar disorder, depression, dysthymic disorder, major depressive disorder, obsessive compulsive disorder, panic disorder, psychotic disorder, schizophrenia, and social anxiety disorder)
- Evaluating risk of developing post-operative deep vein thrombosis
- Guiding peripheral intravenous catheterization
- Intra-operative localization, lymph node sampling, and margin assessment of lung cancer

Policy History

Last Review
10/29/2019
Effective: 03/12/2010
Next Review: 08/27/2020

Definitions

Additional Information
Clinical Policy Bulletin
Notes
- Monitoring cerebral perfusion in the management of individuals with acute neurological disorders (e.g., head injury, subarachnoid hemorrhage, stroke, or following neurosurgery)
- Monitoring cerebral perfusion during cardiac surgery
- Monitoring cerebral perfusion during non-cardiac surgery (e.g., abdominal surgery, orthopedic surgery including shoulder arthroscopy, and thoracic surgery)
- Monitoring of post-operative cognitive dysfunction
- Neonatal therapeutic hypothermia (e.g., identifying infants suitable for studies of adjuvant neuroprotective therapies, or modifying the duration of cooling and/or re-warming)
- Post-operative monitoring of free flap
- Predicting cardiovascular outcome in persons with coronary artery disease
- Treatment of restless legs syndrome
- Use in the intensive care or neonatal intensive care setting
- Use in pediatric cardiac critical care.

Aetna considers near-infrared spectroscopy (NIRS) using spatial frequency domain imaging (SFDI) technology (e.g., the Ox-Imager CS device, Modulated Imaging, Inc) experimental and investigational for the identification and evaluation of vascular tissue compromise (e.g., for measurement of oxy- and deoxy-hemoglobin), and for all other indications, because of a lack of clinical studies demonstrating that this approach improves clinical outcomes.

Aetna considers near-infrared intravascular ultrasound coronary imaging (e.g., the InfraReDx LipiScan™ IVUS Imaging System) experimental and investigational for all indications (e.g., for detecting lipid-rich plaques and guiding cholesterol-lowering therapy).

See also CPB 0382 Intravascular Ultrasound (../300_399/0382.html), CPB 0520 - Magnetic Resonance Imaging of the Cardiovascular System - Cardiac MRI (../500_599/0520.html), and CPB 0846 - Near-Infrared Vascular Imaging and Near-Infrared Fluorescence Imaging (../800_899/0846.html)

Background
Many heart attacks occur when a fatty coronary plaque ruptures, forming dangerous blood clots. Lipid content within coronary artery plaques are believed to correlate with the probability of plaque rupture as well as with the rate of progression of atherosclerosis. Pathologic studies of patients who died from a heart attack have identified a large lipid core among features of coronary artery disease that were associated with plaque rupture and thrombosis.

García-García et al (2008) stated that detection of coronary vulnerable plaques in-vivo is essential for studying their natural history and assessing potential treatment modalities and, therefore, may have an important impact on the prevention of acute myocardial infarction and death. Research is currently underway to determine how coronary artery plaques that are prone to rupture can best be identified before they cause a heart attack and several invasive and non-invasive techniques have been developed to assess the vulnerable plaque. Most of the techniques show exciting features, but none have proven their value in an extensive in-vivo validation study and all have a lack of prospective data (Schaar et al, 2007).

Near-infrared (NIR) spectroscopy (e.g., LipiScan Coronary Imaging System) is a catheter-based technique that is currently under investigation for detecting coronary vulnerable plaques (Lau et al, 2004). It identifies the chemical composition of substances based on the differential absorption of light in the NIR spectrum by different molecules. An important feature of NIR light is that it can penetrate tissue and can therefore identify a tissue despite the presence of blood between the detector and the target. This is an important advantage for imaging within the human coronary artery. The application of NIR spectroscopy to identify lipid deposition within coronary arteries has shown promising results in pre-clinical ex-vivo studies (Moreno et al, 2002; Gardner et al, 2008). A limitation of NIR spectroscopy is that it is influenced by flowing blood, and its lack of structural definition restricts its independent use in vulnerable plaque detection (Cassis, 1993; Lau et al, 2004).

Waxman et al (2009) reported their initial results from the SPECTACL (SPECTroscopic Assessment of Coronary Lipid) trial, a parallel first-in-human multi-center, phase II-III study designed to demonstrate the applicability of the lipid core-containing plaques (LCP) detection algorithm in living patients. Intra-coronary NIR spectroscopy was performed in patients undergoing percutaneous coronary intervention. Acquired spectra were blindly compared with autopsy NIR spectroscopy signals with multi-variate statistics. To meet the end point of spectral similarity, at least 2/3 of the scans were required to have greater than 80 % of spectra similar to the autopsy spectra. A total of 106 patients were enrolled. Spectroscopic data could not be obtained in 17 (16 %) patients due to technical limitations, leaving 89 patients for analysis. Spectra from 30 patients were un-blinded to test the calibration of the LCP detection algorithm. Of the remaining 59 blinded cases, after excluding 11 due to inadequate data, spectral similarity was demonstrated in 40 of 48 spectrally adequate scans (83 % success rate, 95 % confidence
interval: 70 % to 93 %, median spectral similarity/pullback: 96 %, inter-quartile range 10 %). The LCP was detected in 58 % of 60 spectrally similar scans from both cohorts. There were no serious adverse events attributed to NIR spectroscopy. The authors concluded that the intra-vascular NIR spectroscopy system safely obtained spectral data in patients that were similar to those from autopsy specimens and that the results demonstrate the feasibility of invasive detection of coronary LCP with this novel system.

The LipiScan Coronary Imaging System (InfraReDx, Inc., Burlington, MA) uses intra-vascular NIR spectroscopy during coronary angiography to take images of lesions within coronary arteries in order to detect the lipid content within coronary artery plaques. It was cleared for marketing through the U.S. Food and Drug Administration (FDA) 510(k) process in April 2008. The system measures light delivered through the blood and reflected from the artery wall and produces a map of the artery’s chemical composition. The reflected wavelengths vary depending on how much fat and other substances are in the plaque in the illuminated portion of the wall.

Although initial results from the SPECTACL trial showed that signals obtained in patients were spectrally similar to those obtained in autopsy-validated lesions, there is insufficient evidence of how NIR spectroscopy impacts the clinical outcomes of patients with coronary artery disease. Prospective studies demonstrating the effectiveness of NIR spectroscopy in improving clinical outcomes are needed.

In a review on imaging the vulnerable carotid artery plaque, Hermus and colleagues (2009) stated that imaging plays a key role in the selection of patients for carotid artery surgery. Indication for carotid endarterectomy or stenting is based on symptomatology and degree of stenosis as determined by angiography, duplex ultrasonography or computed tomographic angiography. Degree of stenosis has long time been assumed the most reliable predictor of stroke-risk in patients with carotid artery stenosis and accordingly, traditional imaging methods were focused on luminal stenosis. There is, however, growing evidence that other factors than degree of stenosis determine whether a carotid plaque will result in acute neurologic events or not. Various morphological characteristics and molecular processes have proven to be highly related to carotid plaque instability and symptomatology. As a result, the focus of imaging techniques in carotid artery disease is more and more shifting towards identification of the vulnerable plaque rather than the high-grade stenosis. In traditional imaging modalities, new insights of imaging beyond degree of stenosis have been explored and may be able to detect morphological characteristics of plaque vulnerability. In addition, advanced molecular imaging methods have been developed and are able to identify molecular and cellular processes in the vulnerable carotid artery plaque. It is clear that recent developments in carotid imaging are of great potential in the identification of the vulnerable carotid plaque. Near-infrared spectroscopy was not mentioned as a modality for imaging carotid plaques.
Yamaki et al (2011) examined whether the pre-operative level of deoxygenated hemoglobin (HHb) in the calf muscle during light-intensity exercise is useful for identifying patients at risk of developing deep vein thrombosis (DVT) after total knee or hip arthroplasty. A total of 68 patients undergoing total knee or total hip arthroplasty were enrolled. The Caprini risk assessment model was used to stratify patients into Caprini 5 to 6, Caprini 7 to 8, and Caprini greater than 8 groups. The pre-operative diameter of each venous segment was measured, and the time-averaged velocity (TAV) and time-averaged flow (TAF) of the popliteal vein (POPV) were assessed. Moreover, the prevalence of venous reflux in the POPV was evaluated pre-operatively. Near-infrared spectroscopy was used to measure the calf muscle HHb level. The calf venous blood filling index (FI-HHb) was calculated on standing, and then the calf venous ejection index (EI-HHb) was obtained after 1 tip-toe movement and the venous retention index (RI-HHb) after 10 tip-toe movements. All patients received low-dose unfractionated heparin pre-operatively and fondaparinux for post-operative thrombo-prophylaxis. Patients with arterial insufficiency, those who had pre-operative DVT, and those who developed bilateral DVT after surgery were excluded from the study. Four patients were excluded on the basis of the exclusion criteria. Among the 64 patients evaluated, 14 (21.9 %) were found to have DVT post-operatively. Among the risk factors for DVT, only the previous DVT was significantly predominant in patients who developed DVT (p = 0.001). The diameter of the popliteal vein was significantly smaller in patients who developed post-operative DVT than in those who did not (p = 0.001).

Similarly, the diameter of the gastrocnemius vein was significantly larger in patients with post-operative DVT than in those without (p = 0.010). TAV and TAF were significantly increased in the popliteal vein in patients who developed post-operative DVT (p = 0.043, 0.046, respectively). Both groups showed a similar prevalence of reflux in the POPV (p = 0.841). The pre-operative NIR spectroscopy-derived RI was significantly increased in patients who developed DVT relative to those who did not (p = 0.004). The RI increased as the Caprini score progressed; however, there were no statistically significant differences between the 3 categories. Using ultrasound-and NIR spectroscopy-derived parameters of significance as a unit of analysis, an optimal RI cut-off point of greater than 2.3 showed the strongest ability to predict post-operative DVT, followed by a cut-off point greater than 0.25 cm for the diameter of the gastrocnemius vein (GV). The authors concluded that NIR spectroscopy-derived RI greater than 2.3 may be a promising parameter for identifying patients at risk of developing post-operative DVT despite pharmacologic DVT prophylaxis. A GV diameter of greater than 0.25 cm also seems to contribute to the development of post-operative DVT. The authors stated that these results might be helpful to physicians for deciding which patients require more intensive thrombo-prophylaxis.

Aries et al (2012) noted that there is uncertainty whether bilateral NIR spectroscopy can be used for monitoring of patients with acute stroke. In a pilot study, these researchers examined the NIR spectroscopy responsiveness to systemic and stroke-related changes over-night by assessing the effects of brief peripheral arterial oxygenation and mean arterial pressure alterations in the
affected versus non-affected hemisphere in 9 patients with acute stroke. Significantly more NIR spectroscopy drops were registered in the affected compared with the non-affected hemisphere (477 drops versus 184, p < 0.001). In the affected hemispheres, nearly all peripheral arterial oxygenation drops (n = 128; 96 %) were detected by NIR spectroscopy; in the non-affected hemispheres only 23 % (n = 30; p = 0.17). Only a few mean arterial pressure drops were followed by a significant NIR spectroscopy drop. However, this was significantly different between both hemispheres (32 % versus 13 %, p = 0.01). The authors concluded that this pilot study found good responsiveness of NIR spectroscopy signal to systemic and stroke-related changes at the bedside; however, these findings require confirmation in a larger sample.

Cross et al (2009) examined if NIR could detect water concentration changes or edema formation in acute partial-thickness burn injuries. Adult burn patients within 72 hours post-injury, thermal etiology, partial-thickness burn depth, and less than 20 % total body surface area (TBSA) were included. Burn wounds were stratified into partial-thickness superficial or deep wounds based on histology and wound healing time. NIR devices were used to quantify edema in a burn and respective control sites. The sample population consisted of superficial (n = 12) and deep (n = 5) partial-thickness burn injuries. The patients did not differ with respect to age (40 +/- 15 years), TBSA (5 +/- 4 %), and mean time for edema assessment (2 days). Water content increased 15 % in burned tissue compared with the respective control regions. There were no differences in water content at the control sites. At 48 hours, deep partial-thickness injuries showed a 23 % increase in water content compared with 18 % superficial partial-thickness burns. NIR could detect differences in water content or edema formation in partial-thickness burns and unburned healthy regions. The authors concluded that NIR holds promise as a non-invasive, portable clinical tool to quantify water content or edema in burn wounds.

In a pilot study, Weingarten et al (2010) examined the effectiveness of in-vivo diffuse NIR spectroscopy in predicting wound healing in diabetic foot ulcers. A total of 16 chronic diabetic wounds were followed and assessed for subsurface oxy-hemoglobin concentration using the NIR device. Weekly measurements were conducted until there was wound closure, limb amputation, or 20 completed visits without healing. Digital photography measured wound size, and the degree of wound contraction was compared with the NIR results. In the 16 patients followed, 7 wounds healed, 6 limbs were amputated, and 3 wounds remained opened after 20 visits. The initial values in subsurface hemoglobin concentration in all wounds were higher than the non-wound control sites. Healed wounds showed a consistent reduction of hemoglobin concentration several weeks before closure that approached control site values. In wounds that did not heal or resulted in amputation of the limb, the hemoglobin concentration remained elevated. In some cases, these non-healing wounds appeared to be improving clinically. A negative slope for the
rate of change of hemoglobin concentration was indicative of healing across all wounds. The authors concluded that evaluation of wounds using NIR may provide an effective measurement of wound healing. These preliminary findings need to be validated by well-designed studies.

In June 2010, NIR-intravascular ultrasound (IVUS) coronary imaging (e.g., the InfraReDx LipiScan™ IVUS Imaging System [InfraReDx, Inc., Burlington, MA]) was cleared by the FDA for marketing via the 510(k) process. The system combines both NIR and IVUS technologies. According to the 510(k) summary the modifications from the LipiScan Coronary Imaging System to the LipiScan IVUS Imaging System are the inclusion of ultrasound imaging within the same dimensions of the catheter and an expanded indication for use (ultrasound examination of coronary intravascular pathology). The InfraReDx LipiScan IVUS imaging system utilizes the same basic catheter design and the same operating principle as the predicate LipiScan Coronary Imaging system, while the ultrasound capabilities are functionally equivalent to the iLab™ Ultrasound Imaging System (Boston Scientific Corp., Fremont, CA). However, there is currently insufficient evidence to support the clinical value of near-infrared intravascular ultrasound imaging systems. Well designed studies are needed to ascertaining the effectiveness of near-infrared intravascular ultrasound coronary imaging in improving clinical outcomes.

Mallas et al (2011) stated that the use of intravascular imaging modalities for the detection and assessment of atherosclerotic plaque is becoming increasingly useful. Current clinical invasive modalities assess the presence of plaque using anatomical information and include IVUS and optical coherence tomography (OCT). However, such modalities cannot take into account underlying functional biological information, which can however be revealed with the use of molecular imaging. Consequently, intravascular molecular imaging is emerging as a powerful approach. These researchers have developed such a near-infrared fluorescence (NIRF) imaging system and showcased, in phantom as well as in-vivo (rabbit) experiments, its potential to successfully detect inflamed atherosclerotic plaques, using appropriate fluorescent probes. In this article, the authors discussed some limitations of the current system and suggested the combined use of the NIRF and IVUS imaging systems as a means for more accurate assessment of atherosclerotic plaque. They included some results and models that showcase the potential power of this kind of hybrid imaging.

Madder et al (2013) noted that recent studies emphasized the importance of direct intra-coronary imaging techniques that provide insights regarding not only lesion architecture but also plaque composition, especially the presence or absence of lipid-core plaque (LCP). A recently introduced catheter provides simultaneous near-infrared spectroscopy (NIRS) spectral data co-registered with standard IVUS images in a single intra-coronary pullback. The case-series study illustrated the data obtained by this combined NIRS-IVUS device and highlighted its potential clinical applications.
Zynda et al (2013) examined if there was a relationship between angiographic lesion complexity and the extent of LCP identified by catheter-based NIRS. A total of 78 patients who underwent coronary angiography and target-vessel NIRS were selected from the Chemometric Observations of Lipid Core Containing Plaques of Interest in Native Coronary Arteries Registry, an industry sponsored registry to collate clinical findings in all patients undergoing NIRS evaluation. A lipid-core burden index (LCBI) was obtained from the scan of the proximal 50 mm of the target vessel. Three-vessel SYNTAX (total, tSYN) and target single-vessel (only NIRS-interrogated vessel) SYNTAX (1vSYN) scores were calculated and compared to LCBI. High LCBI was defined as (greater than 110) and was compared to tertile scores for 1vSYN score (low: 0 to 5, intermediate: 6 to 10, high: greater than or equal to 11) and previously established tertiles for tSYN score (low: 0 to 22, intermediate: 23 to 32, high: greater than or equal to 33).

Patients had mean age of 63 years with prevalence of females (10 %), diabetes mellitus (28 %), hypertension (88 %), and smoking history (72 %); 1vSYN and tSYN scores correlated poorly with LCBI \( (r(2) = 0.25; p = 0.02; n = 78) \) and \( (r(2) = 0.24; p = 0.04; n = 78) \), respectively. Mean LCBI did not differ significantly across all tertiles of 1vSYN or tSYN scores. The authors concluded that angiographic SYNTAX score only weakly correlated with LCBI. It is of interest as well that high LCBI was also present in cases of low SYNTAX scores. The disparity between the degree of angiographic complexity and the amount of LCP supports postulated mechanisms of the adverse event propensity even in patients who demonstrate low angiographic complexity. They stated that future studies are needed to ascertain the clinical significance of high LCBI in patients with low-to-intermediate angiographic complexity and their potential for percutaneous coronary intervention-related complications.

Pu et al (2012) tested the hypothesis that NIRS combined with IVUS would provide novel information of human coronary plaque characterization. Greyscale-IVUS, virtual histology (VH)-IVUS, and NIRS were compared in 131 native lesions (66 vessels) that were interrogated during catheterization by all 3 modalities. Greyscale-IVUS detected attenuated and echo-lucent plaques correlated with NIRS-detected lipid-rich areas. Attenuated plaques contained the highest NIRS probability of lipid core, followed by echo-lucent plaques. By VH-IVUS, 93.5 % of attenuated plaques contained confluent necrotic core (NC) and were classified as VH-derived fibro-atheromas (FAs). Although 75.0 % of echo-lucent plaques were classified as VH-FAs, VH-NC was seen surrounding an echo-lucent zone, but not within any echo-lucent zone.

Furthermore, echo-lucent zones themselves contained fibro-fatty and/or fibrous tissue. All calcified plaques with arc greater than 90° contained greater than 10 % VH-NC (range of 16.0 % to 41.2 %) and were classified as calcified VH-FAs, but only 58.5 % contained NIRS-detected lipid core. A positive relationship between VH-derived % NC and NIRS-derived LCBI was found in non-calcified plaques, but not in calcified plaques. The authors concluded that combining
NIRS with IVUS contributes to the understanding of plaque characterization in-vivo. They stated that further studies are needed to examine if combining NIRS and IVUS will contribute to the assessment of high-risk plaques to predict outcomes in patients with coronary artery disease.

Nishikawa (2009) noted that non-invasive monitoring of regional cerebral oxygen saturation has been introduced in clinical settings for estimation of cerebral perfusion and cerebral blood flow (CBF). The author described several issues regarding the usefulness and clinical limitations associated with the use of NIRS or NIRS cerebral oximetry, as well as relevant information on basic principles of monitoring. The author concluded that there is currently insufficient clinical data concerning critical levels of measured variables that are essential for safe peri-operative management of patients susceptible for cerebral ischemia.

Transcranial Doppler for the identification of patients at risk for cerebral hyperperfusion syndrome (CHS) following carotid endarterectomy (CEA) can not be performed in 10 to 15% of patients because of the absence of a temporal bone window. Pennekamp and colleagues (2009) stated that NIRS may be of additional value in these patients. These researchers compared (i) the value of NIRS related to existing cerebral monitoring techniques in prediction of peri-operative cerebral ischemia, and (ii) the relation between NIRS and the occurrence of CHS. A systematic literature search relating to NIRS and CEA was conducted in PubMed and EMBASE databases. Those included were: (i) prospective studies; (ii) on NIRS for brain monitoring during CEA; (iii) including comparison of NIRS to any other intra-operative cerebral monitoring systems; and (iv) on either symptomatic or asymptomatic patients. These investigators identified a total of 16 studies, of which 14 focused on the prediction of intra-operative cerebral ischemia and shunt indication. Only 2 studies discussed the ability of NIRS in predicting CHS. Values obtained from NIRS correlated well with those from transcranial Doppler and electroencephalography indicating ischemia. However, a threshold for post-operative cerebral ischemia could not be determined. Neither could a threshold for selective shunting be determined since shunting criteria varied considerably across studies. The evidence suggesting that NIRS is useful in predicting CHS is modest. The authors concluded that NIRS seems a promising monitoring technique in patients undergoing CEA. Yet the evidence to define clear cut-off points for the presence of peri-operative cerebral ischemia or identification of patients at high risk of CHS is limited. They stated that a large prospective cohort study addressing these issues is urgently needed.

Mittnacht (2010) summarized recent developments and available data on the use of NIRS in children at risk for low perfusion. During states of low cardiac output, CBF and thus cerebral NIRS may be better preserved than in somatic tissue sites. Consequently, sites other than the frontal cerebral cortex have been investigated for a possible correlation with invasive measures
of systemic perfusion and oxygenation (e.g., abdomen, flank, and muscle). The abdominal site seems preferable to the flank site NIRS (kidney region) application. In order to increase the sensitivity, specificity, and positive predictive value of tissue oximetry to detect systemic hypoperfusion, multi-site NIRS such as a combination of cerebral and somatic site NIRS has been suggested. Near-infrared spectroscopy has also been used to evaluate systemic perfusion in patients undergoing first-stage palliation for hypoplastic left heart syndrome. The authors concluded that despite shortcomings in the ability of NIRS technology to accurately reflect validated and directly measured parameters of systemic oxygen delivery and blood flow, NIRS can certainly assist in the detection of low-flow states (low cardiac output). They stated that large, randomized, prospective studies with well defined outcome parameters are still missing and warranted in order to clearly define the role of NIRS in children at risk for low perfusion.

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The American College of Cardiology Foundation/American Heart Association clinical practice guideline on coronary artery bypass graft surgery (2011) stated that the effectiveness of routine use of intra-operative or early post-operative monitoring of cerebral oxygen saturation via NIRS to detect cerebral hypo-perfusion in patients undergoing CABG is uncertain.

Aries et al (2012) noted that there is uncertainty whether bilateral NIRS can be used for monitoring of patients with acute stroke. In a pilot study, the NIRS responsiveness to systemic and stroke-related changes was studied over-night by assessing the effects of brief peripheral arterial oxygenation and mean arterial pressure alterations in the affected versus non-affected hemisphere in 9 patients with acute stroke. Significantly more NIRS drops were registered in the affected compared with the non-affected hemisphere (477 drops versus 184, p < 0.001). In the
affected hemispheres, nearly all peripheral arterial oxygenation drops (n = 128; 96 %) were detected by NIRS; in the non-affected hemispheres only 23 % (n = 30; p = 0.17). Only a few mean arterial pressure drops were followed by a significant NIRS drop. This was however significantly different between both hemispheres (32 % versus 13 %, p = 0.01). The authors concluded that this pilot study found good responsiveness of NIRS signal to systemic and stroke-related changes at the bedside but requires confirmation in a larger sample.

Lipcey et al (2012) stated that near infrared spectroscopy of the thenar eminence (NIRSth) is a non-invasive bedside method for assessing tissue oxygenation. The NIRS probe emits light with several wavelengths in the 700- to 850-nm interval and measures the reflected light mainly from a predefined depth. Complex physical models then allow the measurement of the relative concentrations of oxy and deoxyhemoglobin, and thus tissue saturation (StO2), as well as an approximation of the tissue hemoglobin, given as tissue hemoglobin index. These investigators reviewed the current knowledge of the application of NIRSth in anesthesia and intensive care. They performed an analytical and descriptive review of the literature using the terms "near-infrared spectroscopy" combined with "anesthesia," "anesthesiology," "intensive care," "critical care," "sepsis," "bleeding," "hemorrhage," "surgery," and "trauma" with particular focus on all NIRS studies involving measurement at the thenar eminence. They found that NIRSth has been applied as clinical research tool to perform both static and dynamic assessment of StO2. Specifically, a vascular occlusion test (VOT) with a pressure cuff can be used to provide a dynamic assessment of the tissue oxygenation response to ischemia. StO2 changes during such induced ischemia-reperfusion yield information on oxygen consumption and microvascular reactivity. Some evidence suggested that StO2 during VOT can detect fluid responsiveness during surgery. In hypovolemic shock, StO2 can help to predict outcome, but not in septic shock. In contrast, NIRS parameters during VOT increase the diagnostic and prognostic accuracy in both hypovolemic and septic shock. Minimal data are available on static or dynamic StO2 used to guide therapy. The authors concluded that although the available data are promising, further studies are necessary before NIRSth can become part of routine clinical practice.

Clark et al (2012) stated that brain injury remains a source of morbidity associated with congenital heart surgery. Intra-operative neuro-monitoring is used by many centers to help minimize neurologic injury and improve outcomes. Neuro-monitoring at the authors’ institution is performed using a combination of NIRS, transcranial Doppler ultrasound, electroencephalography (EEG), and somatosensory evoked potentials. Adverse or concerning parameters instigate attempts at corrective intervention. A review of the literature regarding neuro-monitoring studies in pediatric cardiac surgery showed that evidence is limited to
demonstrate that intra-operative neuro-monitoring is associated with improved neurologic outcomes. The authors concluded that further clinical research is needed to assess the utility and cost-effectiveness of intra-operative neuro-monitoring for pediatric heart surgery.

Zheng et al (2013) noted that NIRS is used during cardiac surgery to monitor the adequacy of cerebral perfusion. These investigators evaluated available data for adult patients to determine (i) whether decrements in cerebral oximetry during cardiac surgery are associated with stroke, post-operative cognitive dysfunction (POCD), or delirium; and (ii) whether interventions aimed at correcting cerebral oximetry decrements improve neurologic outcomes. They searched PubMed, Cochrane, and Embase databases from inception until January 31, 2012, without restriction on languages. Each article was examined for additional references. A publication was excluded if it did not include original data (e.g., review, commentary) or if it was not published as a full-length article in a peer-reviewed journal (e.g., abstract only). The identified abstracts were screened first, and full texts of eligible articles were reviewed independently by 2 investigators. For eligible publications, these researchers recorded the number of subjects, type of surgery, and criteria for diagnosis of neurologic end points. They identified 13 case reports, 27 observational studies, and 2 prospectively randomized intervention trials that met inclusion criteria. Case reports and 2 observational studies contained anecdotal evidence suggesting that regional cerebral oxygen saturation (rSO2) monitoring could be used to identify cardiopulmonary bypass cannula malposition. Six of 9 observational studies reported an association between acute rSO2 desaturation and POCD based on the Mini-Mental State Examination (n = 3 studies) or more detailed cognitive testing (n = 6 studies). Two retrospective studies reported a relationship between rSO2 desaturation and stroke or type I and II neurologic injury after surgery. The observational studies had many limitations, including small sample size, assessments only during the immediate post-operative period, and failure to perform risk adjustments. Two randomized studies evaluated the effectiveness of interventions for treating rSO2 desaturation during surgery, but adherence to the protocol was poor in one. In the other study, interventions for rSO2 desaturation were associated with less major organ injury and shorter intensive care unit hospitalization compared with non-intervention. The authors concluded that reductions in rSO2 during cardiac surgery may identify cardiopulmonary bypass cannula malposition, particularly during aortic surgery. Only low-level evidence links low rSO2 during cardiac surgery to post-operative neurologic complications, and data are insufficient to conclude that interventions to improve rSO2 desaturation prevent stroke or POCD.

Shellhaas et al (2013) evaluated the utility of amplitude-integrated EEG (aEEG) and rSO2 measured using NIRS for short-term outcome prediction in neonates with hypoxic ischemic encephalopathy (HIE) treated with therapeutic hypothermia. Neonates with HIE were monitored with dual-channel aEEG, bilateral cerebral NIRS, and systemic NIRS throughout cooling and...
rewarming. The short-term outcome measure was a composite of neurologic examination and brain MRI scores at 7 to 10 days. Multiple regression models were developed to assess NIRS and aEEG recorded during the 6 hours before re-warming and the 6-hour re-warming period as predictors of short-term outcome. A total of 21 infants, mean gestational age 38.8 ± 1.6 weeks, median 10-minute Apgar score 4 (range of 0 to 8), and mean initial pH 6.92 ± 0.19, were enrolled. Before re-warming, the most parsimonious model included 4 parameters (adjusted R(2) = 0.59; p = 0.006): lower values of systemic rSO2 variability (p = 0.004), aEEG bandwidth variability (p = 0.019), and mean aEEG upper margin (p = 0.006), combined with higher mean aEEG bandwidth (worse discontinuity; p = 0.013), predicted worse short-term outcome. During re-warming, lower systemic rSO2 variability (p = 0.007) and depressed aEEG lower margin (p = 0.034) were associated with worse outcome (model-adjusted R(2) = 0.49; p = 0.005). Cerebral NIRS data did not contribute to either model. The authors concluded that during day 3 of cooling and during re-warming, loss of physiologic variability (by systemic NIRS) and invariant, discontinuous aEEG patterns predicted poor short-term outcome in neonates with HIE. The authors concluded that these parameters, but not cerebral NIRS, may be useful to identify infants suitable for studies of adjuvant neuroprotective therapies or modification of the duration of cooling and/or re-warming. Moreover, they stated that “additional work is required before these findings could be applied directly at the bedside …. However, the value of cerebral NIRS monitoring remains uncertain in this patient population”.

Brugaletta and Sabate (2014) stated that atherosclerosis is the main cause of coronary artery disease (CAD), which is today the leading cause of death worldwide and will continue to be the first in the world in 2030. Vulnerable coronary plaques are usually characterized by a high content of necrotic core, a thin inflamed fibrous cap (intense accumulation of macrophages) and scarce presence of smooth muscle cells. None of these characteristics can be estimated by coronary angiography, which on the contrary under-estimates the magnitude of atherosclerotic burden, particularly in earlier stage disease when positive vascular remodeling may allow "normal" lumen caliber despite substantial vascular wall plaque. The recognition of the ubiquity of substantial but non-flow limiting lesions that may be at high-risk for subsequent plaque rupture has resulted in a paradigm shift in thinking about the pathophysiology of CAD, with the focus no longer solely on the degree of arterial luminal narrowing. This growing need for more information about coronary atherosclerosis in order to identify patients and lesions at risk for complications during percutaneous coronary intervention (PCI) and for future adverse cardiac events has been the primary impetus for the development of novel intra-coronary imaging methods able to detect plaque composition, in particular presence of a necrotic core/lipid pool, such as IVUS virtual histology and NIRS.
Ranger et al (2014) stated that nurses play a crucial role in the evaluation and treatment of pain in the critically ill patient. This responsibility is all the more critical with this particular population because many may not be able to self-report their pain level and the typical behavioral signs of pain may be subtle or absent. According to recent recommendations, vital signs should not be used as primary indicators of pain but rather considered as a cue to begin further assessment. Other than vital signs, human brain reactivity to pain has been extensively studied with the use mainly of MRI and positron-emission tomography (PET). However, the use of these sophisticated methods may be unrealistic in the critically ill. Of interest to assessing these patients in a clinical setting is the non-invasive measurement of regional cerebral tissue oxygenation with NIRS technique. There are indications that NIRS is capable of detecting the cerebral hemodynamic changes associated with sensory stimuli, including pain. The objective of this review paper was to provide nurses with a better understanding of NIRS technology, including a review of the literature on functional studies that have used NIRS in critically ill populations, and how it could be used in both research and practice. The authors concluded that current NIRS techniques have well recognized limitations that must be considered carefully during the measurement and interpretation of signals. Thus, its clinical use is yet to be fully established. Nonetheless, cerebral NIRS technique as an approach to assess brain activity in response to pain should not be abandoned.

Neshat Vahid and Panisello (2014) noted that the decreasing post-operative mortality in patients with congenital heart disease (CHD) has enabled an increasing interest in preventing morbidity, especially from the central nervous system; and the use of NIRS in the intensive care unit has gained popularity over the last decade. This review aimed to ascertain its ability to affect outcome. Recent studies have started to incorporate cerebral NIRS in the assessment, evolution, and outcomes of surgical patients with CHD. These studies often represent small single-center high-risk cohorts who were evaluated in a retrospective or an observational manner. Nevertheless, new data are starting to indicate that NIRS may be helpful not only in the assessment of critical care parameters, such as cardiac output performance or likelihood of adverse events, but, most notably, in the long-term neurological outcome. The authors concluded that in addition to additional corroborative trials from different centers, a critical question that remains to be answered is whether targeting cerebral NIRS values, as part of goal-directed therapy protocols, can help to improve outcome overall.

Nielsen (2014) determined non-cardiac surgical procedures that provoke a reduction in rScO2 and evaluated whether an intra-operative reduction in rScO2 influences post-operative outcome. The PubMed and Embase database were searched from inception until April 30, 2013 and inclusion criteria were intra-operative NIRS determined rScO2 in adult patients undergoing non-cardiac surgery. The type of surgery and number of patients included were recorded; a total of 113 articles and evidence suggested that rScO2 is reduced during thoracic surgery involving...
single lung ventilation, major abdominal surgery, hip surgery, and laparoscopic surgery with the patient placed in anti-Trendelenburg's position. Shoulder arthroscopy in the beach-chair position (BCP) and carotid endarterectomy with clamped internal carotid artery (ICA) also cause pronounced cerebral desaturation. A greater than 20 % reduction in rScO2 coincided with indices of regional and global cerebral ischemia during carotid endarterectomy. Following thoracic surgery, major orthopedic surgery, and abdominal surgery the occurrence of post-operative cognitive dysfunction (POCD) might be related to intra-operative cerebral desaturation. The authors concluded that certain non-cardiac surgical procedures were associated with an increased risk for the occurrence of rScO2. Moreover, they stated that evidence for an association between cerebral desaturation and post-operative outcome parameters other than cognitive dysfunction needs to be established.

Pant and colleagues (2014) examined the risks of shoulder arthroscopy in the BCP as opposed to the lateral decubitus position. The challenge during general anesthesia, particularly with the patient in the BCP, has been to ascertain the lower limit of blood pressure auto-regulation, correctly measure mean arterial pressure, and adequately adjust parameters to maintain cerebral perfusion. There is increasing concern about the BCP and its association with intra-operative cerebral desaturation events (CDEs). Assessment of CDEs intra-operatively remains difficult; the emerging technology NIRS may provide non-invasive, inexpensive, and continuous assessment of cerebral perfusion, offering an "early warning" system before irreversible cerebral ischemia occurs. These investigators performed a systematic review to determine the incidence of intra-operative CDEs as measured by NIRS and whether it is possible to risk-stratify patients for intra-operative CDEs, specifically the degree of elevation in the BCP. Searching Medline, Embase, and the Cochrane Central Register of Controlled Trials from inception until December 30, 2013, these researchers found 9 studies (n = 339) that met the search criteria. The Level of Evidence was III or IV. The authors concluded that there remains a paucity of high-level data. The mean incidence of CDEs was 28.8 %. They found a strong positive correlation between CDEs and degree of elevation in the BCP (p = 0.056). Emerging evidence (Level IV) suggested that it may be able to stratify patients on the basis of age, history of hypertension and stroke, body mass index, diabetes mellitus, obstructive sleep apnea, and height. The challenge remains, however, in defining the degree and duration of cerebral desaturation, as measured by NIRS, required to produce measureable neurocognitive decline post-operatively.

Guiding Peripheral Intravenous Catheterization

In a randomized clinical trial, de Graaff and colleagues (2014) evaluated the clinical utility of a near-infrared vascular imaging device (VascuLuminator) in pediatric patients who were referred to the anesthesiologist because of difficult cannulation. There were 226 consecutive children referred to pediatric anesthesiologists by the treating pediatrician of the in- and out-patient clinic,
because of difficulties with intravenous cannulation, were included in this cluster randomized clinical trial. The presence and use of the near-infrared vascular imaging device for peripheral intravenous cannulation (PIC) was randomized in clusters of 1 week. Success at first attempt (Fisher exact test) and time to successful cannulation (Log-rank test) were assessed to evaluate differences between groups. Success at first attempt in the group with the VascuLuminator (59 %) was not significantly different from the control group (54 %, p = 0.41), neither was the median time to successful cannulation: 246 s and 300 s, respectively (p = 0.54). The authors concluded that visualization of blood vessels with near-infrared light and with near-infrared vascular imaging device did not improve success of PIC in pediatric patients who are known difficult to cannulate.

Curtis and associates (2015) stated that peripheral intravenous catheterization in children is challenging, and success rates vary greatly. These researchers conducted a pragmatic randomized controlled trial (RCT) to examine if the use of ultrasound or near-infrared vascular imaging to guide catheterization would be more effective than the standard approach in achieving successful catheter placement on the first attempt. These investigators enrolled a convenience sample of 418 children in a pediatric emergency department who required peripheral intravenous catheterization. They stratified them by age (less than or equal to 3 years and greater than 3 years) and randomly assigned them to undergo the procedure with the standard approach, or with the help of either ultrasound or near-infrared vascular imaging. The primary outcome was the proportion of patients who had successful placement of a catheter on the first attempt. The rate of successful first attempts did not differ significantly between either of the 2 intervention groups and the standard approach group (differences in proportions -3.9 %, 95 % confidence interval [CI]: -14.2 % to 6.5 %, for ultrasound imaging; -8.7 %, 95 % CI: -19.4 % to 1.9 %, for near-infrared imaging). Among children 3 years and younger, the difference in success rates relative to standard care was also not significant for ultrasound imaging (-9.6 %, 95 % CI: -29.8 % to 10.6 %), but it was significantly worse for near-infrared imaging (-20.1 %, 95 % CI: -40.1 % to -0.2 %). Among children older than 3 years, the differences in success rates relative to standard care were smaller but not significant (-2.3 %, 95 % CI: -13.6 % to 9.0 %, for ultrasound imaging; -4.1 %, 95 % CI: -15.7 % to 7.5 %, for near-infrared imaging). None of the pair-wise comparisons was statistically significant in any of the outcomes. The authors concluded that neither technology improved first-attempt success rates of peripheral intravenous catheterization in children, even in the younger group. These findings do not support investment in these technologies for routine peripheral intravenous catheterization in children.

In a systematic review and meta-analysis, Park and colleagues (2016) examined the use of NIR devices for peripheral intravenous cannulation (PIVC) in pediatric patients. These investigators searched 3 databases (Medline, Embase, and the Cochrane CENTRAL); RCTs that compared PIVC using NIR devices and the "traditional" method (with no assistive device) were included. The primary outcome was a failure rate at the 1st attempt, and the effect size was measured by
the risk ratio for failure. Subgroup analysis was performed according to control group risk for failure at 1st attempt as an indicator of difficult procedure (low versus high). A total of 11 studies were included in the meta-analysis. There was no significant difference in the primary outcome between the 2 methods (risk ratio 1.03, CI: 0.89 to 1.20, I^2 = 48 %). In a subgroup analysis, the subgroup difference between subsets of low and high control group risk was significant (I^2 = 83 %). In the subset of the high control group risk, using NIR light devices showed a lower risk for failure than the traditional method (risk ratio 0.81, CI: 0.64 to 1.01, I^2 = 0 %). The authors concluded that using NIR light devices did not have an impact on overall failure rate at the 1st attempt at PIVC in pediatric patients. The findings of this study indicated that there was no overall benefit of using NIR light devices for pediatric peripheral intravenous cannulation; however, this device might be useful for the patients in a difficult condition of successful cannulation.

Post-Operative Monitoring of Free Flap

Chen and colleagues (2016) noted that although free flaps have become a reliable technique, vascular occlusion remains a significant risk. Flap survival is closely linked to the time interval between the onset and surgical repair of a microvascular problem. The newly emerged NIRS showed the characteristics of being non-invasive, continuous, easy to use, objective, and immediately reflective, possibly making it an ideal candidate for post-operative flap monitoring. These investigators performed a systemic review to determine the clinical value of NIRS in the early detection of vascular crisis associated with a free flap. A literature search was conducted using PubMed (MEDLINE), the Cochrane Library, and Web of Science from database inception through October 2013. Studies were selected strictly according to the inclusion/exclusion criteria by 2 independent reviews. A total of 8 studies were finally included in this review. A total of 710 free flap procedures were performed in 629 patients using NIRS for monitoring. At the same time, 433 free flaps performed in 430 patients without the use of NIRS were included as the control group. No significant differences in the rates of vascular crisis (p = 0.917) and re-exploration (p = 0.187). However, there were significant differences in the salvage rates (p < 0.001) and flap failure rates (p = 0.003). For the free flaps monitored by NIRS that were not associated with vascular crisis, no alarms were raised by NIRS, giving 100 % sensitivity and specificity. The authors concluded that NIRS appeared to be a highly suitable candidate for post-operative flap monitoring. Moreover, they stated that larger-scale, randomized, multi-centric clinical trials are needed in the future.

Predicting Cardiovascular Outcome in Persons with Coronary Artery Disease
In a prospective, observational study, Oemrawsingh et al (2014) determined the long-term prognostic value of intra-coronary NIRS as assessed in a non-culprit vessel in patients with coronary artery disease (CAD). Near-infrared spectroscopy was performed in a non-culprit coronary artery in 203 patients referred for angiography due to stable angina pectoris (SAP) or acute coronary syndrome (ACS). The primary end-point was the composite of all-cause mortality, non-fatal ACS, stroke, and unplanned coronary re-vascularization. The 1-year cumulative incidence of the primary end-point was 10.4%. Cumulative 1-year rates in patients with a LCBI equal to and above the median (43.0) versus those with LCBI values below the median were 16.7% versus 4.0% (adjusted hazard ratio [HR]: 4.04; 95% CI: 1.33 to 12.29; p = 0.01). The relation between LCBI and the primary end-point was similar in SAP and ACS patients (p value for heterogeneity = 0.14). Similar differences between high and low LCBI were observed in pre-specified secondary end-points. The authors concluded that CAD patients with an LCBI equal to or above the median of 43.0, as assessed by NIRS in a non-culprit coronary artery, had a 4-fold risk of adverse cardiovascular events during 1-year follow-up. Moreover, they stated that this observation warrants confirmation by larger studies with extended follow-up.

Near-Infrared Intravascular Ultrasound Coronary Imaging

Erlinge and associates (2015) stated that ischemic heart disease is the leading cause of death worldwide. The common denominator for plaques causing acute coronary syndrome (ACS) is lipid accumulation, either as a lipid core or lipid pools. An intra-coronary imaging device to detect lipid-rich plaques (LRPs) could therefore identify most of the plaques causing ACS and sudden death. Near-infrared spectroscopy combined with intra-vascular ultrasound is a promising new intracoronary imaging method that is able to specifically quantify lipid accumulation measured as the LCBI. NIRS-IVUS is highly specific for the identification of ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) culprit plaques usually in the form of a circular LRP. NIRS-IVUS may assist in defining the etiology of coronary events. The effect of cholesterol-lowering therapy on the lipid core can be measured in coronary plaques in patients, and NIRS-IVUS may be a useful tool for drug development in phase II studies as a surrogate end-point for future ACS. Plaques with a high LCBI have an increased risk of peri-procedural events. NIRS-IVUS can help to define the diameter and length of stents to avoid procedure-related complications. Increased coronary LCBI predicts a higher risk of future cardiovascular events. The authors concluded that lipid core detection using NIRS may help to identify vulnerable plaques to treat them before they cause ACS or sudden death.

Evaluation of Anesthetic Depth
Curtin et al (2014) stated that endoscopic procedures performed in the United States routinely involve the use of conscious sedation as standard of care. The use of sedation reduces patient discomfort and anxiety while improving the technical quality of the procedure, and as a result, over 98 % of clinicians have adopted the practice. The tremendous benefits of sedation are offset by heightened costs, increased patient discharge time, and cardio-pulmonary complication risks. The inherent liabilities of putting patients under sedation have necessitated a large number of physiological monitoring systems in order to ensure patient comfort and safety.

Currently, the American Society of Anesthesiologist (ASA)'s guidelines recommend monitoring of pulse oximetry, blood pressure, heart rate, and end-tidal CO2; although important safeguards, these physiological measurements do not allow for the reliable assessment of patient sedation. Proper monitoring of patient state ensures procedure quality and patient safety; however no "gold-standard" is available to determine the depth of sedation which is comparable to the anesthesiologist's professional judgment. Developments in functional NIRS (fNIRS) over the past 20 years have introduced cost-effective, portable, and non-invasive neuroimaging tools that measure cortical hemodynamic activity as a correlate of neural functions. Anesthetic drugs, such as propofol, operate by suppressing cerebral metabolism. Functional NIRS imaging methods have the ability to detect these drug-related effects as well as neuronal activity through the measurement of local cerebral hemodynamic changes. In the present study, a total of 41 patients were continuously monitored using fNIRS while undergoing out-patient elective colonoscopy with propofol sedation. The authors concluded that these preliminary results indicated that oxygenated Hb changes in the dorsolateral pre-frontal cortex, as assessed by fNIRS were correlated with changes in response to bolus infusions of propofol, whereas other standard physiological measures were not significantly associated. These preliminary findings need to be validated by well-designed studies.

Hernandez-Meza et al (2015) noted that the standard-of-care guidelines published by the ASA recommend monitoring of pulse oximetry, blood pressure, heart rate, and end tidal CO2 during the use of anesthesia and sedation. This information can help to identify adverse events that may occur during procedures. However, these parameters are not specific to the effects of anesthetics or sedatives, and therefore they offer little, to no, real-time information regarding the effects of those agents and do not give the clinician the lead-time necessary to prevent patient "awareness". Since no "gold-standard" method is available to continuously, reliably, and effectively monitor the effects of sedatives and anesthetics, such a method is greatly needed.

Investigation of the use of fNIRS as a method for anesthesia or sedation monitoring and for the assessment of the effects of various anesthetic drugs on cerebral oxygenation has started to be conducted. The authors provided a thorough review of the currently available published scientific studies regarding the use of fNIRS in the fields of anesthesia and sedation monitoring, commented on their findings, and discussed the future work needed for the translation of this technology to the clinical setting.
Becerra et al (2016) examined if a nociceptive signal elicited by colonic insufflation could be measured from the brain. A total of 17 otherwise healthy patients (age of 54.8 ± 9.1 years; 6 females) undergoing routine colonoscopy (i.e., no history of significant medical conditions) were monitored using NIRS. Moderate sedation was produced using standard clinical protocols for midazolam and meperidine, titrated to effect. Near-infrared spectroscopy data captured during the procedure was analyzed offline to evaluate the brains’ responses to nociceptive stimuli evoked by the insufflation events (defined by physician or observing patients' facial responses). Analysis of NIRS data revealed a specific, reproducible pre-frontal cortex activity corresponding to times when patients grimaced. The pattern of the activation was similar to that previously observed during nociceptive stimuli in awake healthy individuals, suggesting that this approach may be used to evaluate brain activity evoked by nociceptive stimuli under sedation, when there is incomplete analgesia. Although some patients reported recollection of procedural pain after the procedure, the effects of repeated nociceptive stimuli in surgical patients may contribute to post-operative changes including chronic pain. The authors concluded that the findings of this study indicated that NIRS may be a suitable technology for continuous nociceptive afferent monitoring in patients undergoing sedation and could have applications under sedation or anesthesia.

Kussman et al (2016) assessed the feasibility of fNIRS to measure cortical responses to noxious stimulation during general anesthesia. A multi-channel continuous wave near-infrared imager was used to measure somatosensory and frontal cortical activation in patients undergoing catheter ablation of arrhythmias under general anesthesia. Anesthetic technique was standardized and intra-operative NIRS signals recorded continuously with markers placed in the data set for the timing and duration of each cardiac ablation event. Frontal cortical signals only were suitable for analysis in 5 of 8 patients studied (mean age of 14 ± 1 years, weight of 66.7 ± 17.6 kg, 2 males); 30 ablative lesions were recorded for the 5 patients. Radiofrequency or cryoablation was temporally associated with a hemodynamic response function in the frontal cortex characterized by a significant decrease in oxyhemoglobin concentration (paired t-test, p < 0.05) with the nadir occurring in the period 4 to 6 seconds after application of the ablative lesion. Cortical signals produced by catheter ablation of arrhythmias in patients under general anesthesia mirrored those seen with noxious stimulation in awake, healthy volunteers, during sedation for colonoscopy, and functional MRI activations in response to pain. The authors concluded that the findings of this study demonstrated the feasibility and potential utility of fNIRS as an objective measure of cortical activation under general anesthesia.

Evaluating Psychiatric Disorders
Akashi and associates (2015) noted that studies on major depressive disorder (MDD) showed that the degree of correlation between the Beck Depression Inventory (BDI) and Hamilton Depression Rating Scale (HAMD) varies widely. These researchers examined if this discrepancy reflects specific functional abnormalities in the fronto-temporal cortex. Mildly depressed or euthymic patients with MDD (n = 52), including 21 patients with MDD with the discrepancy, i.e., those with low HAMD17 scores (less than or equal to 13) but high BDI-II scores (greater than 28), and 31 patients without the discrepancy, i.e., those with low HAMD17 scores and low BDI-II scores (less than or equal to 28), participated in the study along with 48 control subjects.

Regional changes of oxygenated Hb (oxy-Hb) levels during a verbal fluency task (VFT) were monitored using a 52-channel NIRS device. In the fronto-temporal regions, mean oxy-Hb changes induced by the VFT were significantly smaller in patients with MDD than in control subjects. In 5 channels within frontal regions, the increase in mean oxy-Hb levels was significantly greater in MDD patients with the BDI-HAMD discrepancy than in those without the discrepancy. In 6 channels within the frontal region of the patients with MDD, significant positive correlations were observed between mean oxy-Hb changes and BDI total scores (\( \rho = 0.38 \) to 0.59; \( p < 0.05 \), false discovery rate corrected). The authors concluded that the distinct pattern of activation of the pre-frontal cortex suggested that MDD with the BDI-HAMD discrepancy is pathophysiologically different from MDD without the discrepancy. Moreover, they stated that these findings need replication in severely depressed patients, particularly those with melancholia.

Mikawa and co-workers (2015) clarified differences in oxy-Hb activation between depressive and euthymic states as well as regional brain dysfunction in relation to symptom severity in bipolar disorder (BD). A total of 55 patients with BD, including 30 with bipolar depression (BPD) and 25 with euthymic bipolar disorder (BPE), and 28 healthy controls (HCs) participated in the study.

Regional hemodynamic changes during a VFT were monitored using a 52-channel NIRS apparatus. The mean oxy-Hb changes induced by VFT were significantly smaller in the BD patients than in the HCs in 18 channels in the fronto-temporal regions (false-discovery rate \( p < 0.05 \), \( p = 0.000 \) to 0.011). The BPD group exhibited significantly smaller changes in mean oxy-Hb compared with the BPE group in 3 channels of the left temporal region (\( p = 0.005 \) to 0.014). In the BD patients, significant negative correlations were observed between mean oxy-Hb changes in the left temporal regions and the severity of depression. The authors concluded that BD patients have persistent hypo-function of the fronto-temporal cortical regions. Moreover, the hemodynamic response in the left temporal regions was associated with symptom severity. The major drawback of this study was its small sample size, making the results susceptible to type II errors.
Kawano and colleagues (2016) stated that the search for objective biomarkers of psychiatric disorders has a long history. Despite this, no universally accepted instruments or methods to detect biomarkers have been developed. One potential exception is NIRS, although interpreting the measures of blood flow recorded with this technique remains controversial. In this study, these researchers examined the relationship between recorded blood flow and depression severity assessed using the Hamilton depression scale in patients with various psychiatric disorders. Enrolled patients (n = 43) had DSM-IV diagnoses of MDD (n = 25), BD (n = 5), schizophrenia (n = 3), dysthymic disorder (n = 3), psychotic disorder (n = 3), panic disorder (n = 2), and obsessive compulsive disorder (n = 2). The VFT was administered during blood flow recording from the frontal and temporal lobes. These investigators found that severity of depression was negatively correlated with the integral value of blood flow in the frontal lobe, irrespective of psychiatric diagnosis (F = 5.94, p = 0.02). The authors concluded that these findings supported blood flow in the frontal lobe as a potential biomarker of depression severity across various psychiatric disorders. The major drawbacks of this study were its limited sample size and no replication in the second set.

Kawashima and colleagues (2016) noted that patients with social anxiety disorder (SAD) experience unusual fear in normal social situations. In this study, the verbal fluency task (VFT) was administered while subjects were undergoing NIRS scanning. The purpose of VFT was to examine the functions of the frontal and temporal lobes. Subjects included 145 drug-naïve patients with SAD and 152 healthy controls (HCs). All subjects underwent psychological testing to determine levels of anxiety and depression and to evaluate cognition. The scores of patients with SAD indicated significantly higher anxiety and depressive states than those in HCs on several measures: Leibowitz Social Anxiety Scale (LSAS), Profile of Mood States (POMS), Spielberger Anxiety Inventory (STAI), Beck Depression Inventory (BDI), and Social Adaptation Self-evaluation Scale (SASS). Patients with SAD also had higher scores on the future denial, threat prediction, self-denial, past denial, and inter-personal threat sections of the Depression and Anxiety Cognition Scale (DACS). NIRS scanning revealed hyperactivity in the left frontal cortex of patients with SAD. Threat prediction scores on DACS were negatively correlated with oxyhemoglobin responses in the right frontal cortex. The authors concluded that the findings of this study demonstrated the different mechanisms of the right and left frontal cortex in situations of SAD. Moreover, they stated that further studies with a larger sample size are needed to verify these findings.

Intensive Care Setting

Wally and Velik-Salchner (2015) stated that NIRS allows continuous measurement of cerebral rSO2. It is a weighted saturation value derived from approximately 70 to 75% venous, 20 to 25% arterial and 2.5 to 5.0% capillary blood. In contrast to pulse oximetry, NIRS is independent of
pulsatile flow. Thus, it is also applicable during extra-corporeal circulation, cardio-pulmonary resuscitation (CPR), and hypothermia. These researchers described the application of cerebral and somatic NIRS in cardiology and cardiac surgery patients in the operation room, during and after CPR, and during the intensive care unit (ICU) stay. This article was based on peer-reviewed literature from PubMed. Interventions based on decline of cerebral NIRS values during on-pump cardiac surgery can reduce major organ morbidity and mortality; however, the appearance of a post-operative cognitive dysfunction is scarcely influenced. Persisting of low cerebral oximetry values during resuscitation is a marker for not achieving return of spontaneous circulation under normothermia; and NIRS is an additional method for monitoring that can be used during extra-corporeal circulation. The authors concluded that NIRS is a rapidly available, user-friendly, and non-invasive method for continuous measurement of rSO2. It provides additional information about tissue oxygenation especially during resuscitation and extra-corporeal circulatory assist support. The authors concluded that recommendations concerning the use of NIRS for standard monitoring during resuscitation and mechanical circulatory support are not currently available. Moreover, they stated that further studies are needed to show if use of NIRS can reduce pulse control and hands-off times during resuscitation and if use of NIRS can improve outcome after CPR and mechanical circulatory support.

Green and colleagues (2016) noted that standard hemodynamic monitoring such as blood pressure and pulse oximetry may only provide a crude estimation of organ perfusion in the critical care setting. Near-infrared spectroscopy is based on the same principle as a pulse oximeter and allows continuous non-invasive monitoring of Hb oxygenation and deoxygenation and thus tissue saturation "StO2". These investigators provided an overview of NIRS technology principles and discussed its current clinical use in the critical care setting. The study selection was performed using the PubMed database to find studies that investigated the use of NIRS in both the critical care setting and in the ICU. Currently, NIRS in the critical care setting is predominantly being used for infants and neonates. A number of studies in the past decade have shown promising results for the use of NIRS in surgical/trauma ICUs during shock management as a prognostic tool and in guiding resuscitation. It is evident that over the past 2 decades, NIRS has gone from being a laboratory fascination to an actively employed clinical tool. The authors concluded that even though the benefit of routine use of this technology to achieve better outcomes is still questionable, the fact that NIRS is a low-cost, non-invasive monitoring modality improves the attractiveness of the technology. However, they stated that more research is needed before recommending its routine use in the critical care setting.

A consensus on circulatory shock and hemodynamic monitoring from the European Society of Intensive Care Medicine (Cecconi, et al., 2014) noted that the use of metabolic parameters for the assessment of regional microcirculatory perfusion is promising. An occlusion test with near-infrared spectroscopy may help to evaluate indirectly the dynamic response of the
microcirculation to an occlusion, even if the link between vasoreactivity, microcirculation and tissue oxygenation is still not clearly established. The consensus suggests techniques to assess regional circulation or microcirculation for research purposes only.

Critical Care of Neonates

Holler and colleagues (2015) performed a systematic qualitative review on peripheral muscle NIRS measurements in the clinical care of term and pre-term neonates. A systematic search of PubMed and Ovid Embase was performed using the following terms: neonate, neonates, newborn, newborns, infant, infants, near-infrared spectroscopy, NIRS, oxygenation, perfusion, oxygen extraction, peripheral, tissue, muscle, calf, forearm and thigh. Additional articles were identified by a manual search of the cited references. Only human studies were included. A total of 21 studies were identified to use peripheral muscle NIRS measurements as a single method, 17 studies combined cerebral and peripheral muscle NIRS measurements, and 1 study used multi-site NIRS measurements in human neonates, 2 randomized studies were identified; and 2 additional publications were included because they provided important general information about peripheral muscle NIRS measurements. The authors concluded that in the care of critically ill neonates peripheral muscle NIRS measurements, alone or in combination with cerebral or multi-site NIRS measurements, provided useful additional information about peripheral circulation and oxygenation. They stated that this method is a promising tool in the recognition of early states of centralization (compensated shock) in this vulnerable group of patients. However, they noted that further studies are needed before this method can be used in the clinical routine.

Detection of Traumatic Intracranial Hematoma / Traumatic Brain Injury

In a systematic review and meta-analysis, Brogan and colleagues (2017) evaluated the evidence regarding the use of NIRS for detection of traumatic intracranial hematoma. These investigators noted that head injury is the most common trauma presentation to UK emergency departments, with around 1.2 million patients each year. The key management principal for this time-critical illness remains early surgical intervention. With the development of hand-held NIRS devices, there is now the possibility of triaging and diagnosing these patients immediately, where computed tomography (CT) scanner is unavailable. These researchers stated that NIRS has 2 related but distinct potential uses within clinical medicine: (i) as a triage tool both in hospital and pre-hospital settings by doctors, nurses or paramedics as determined by its negative predictive value (NPV), and (ii) as a diagnostic aid as determined by its positive predictive value (PPV). NIRS technology has a cross-study sensitivity of 78 %, specificity of 90 %, PPV of 77 %, and a NPV of 90 %, which does not meet current standards as a diagnostic/triage tool in the populations studied. Additionally, its use is limited to those without extracranial injuries and
may also be complicated by long scan times. The authors concluded that larger and more heterogeneous studies are needed to specifically evaluate NIRS performance in detecting intracranial lesions requiring emergency evacuation.

Peters and associates (2017) stated that early identification of traumatic brain injury (TBI) is essential; NIRS can be used in pre-hospital settings for non-invasive monitoring and the diagnosis of patients who may require surgical intervention. The hand-held NIRS Infrascanner (InfraScan Inc.; Philadelphia, PA) uses 8 symmetrical scan points to detect intracranial bleeding. A scanner was tested in a physician-staffed helicopter Emergency Medical Service (HEMS).

The results were compared with those obtained using in-hospital CT scans. Scan time, ease-of-use, and change in treatment were scored. A total of 25 patients were included. Complete scans were performed in 60% of patients. In 15 patients, the scan was abnormal, and in 1 patient, the scan resulted in a treatment change. Compared with the results of CT scanning, the Infrascanner obtained a sensitivity of 93.3% and a specificity of 78.6%. Most patients had severe TBI with indication for transport to a trauma center prior to scanning. In 1 patient, the scan resulted in a treatment change. Evaluation of patients with less severe TBI is needed to support the usefulness of the Infrascanner as a pre-hospital triage tool. The authors concluded that promising results were obtained using the InfraScan NIRS device in pre-hospital screening for intracranial hematomas in TBI patients. High sensitivity and good specificity were found. They stated that further research is needed to determine the beneficial effects of enhanced pre-hospital screening on triage, survival, and quality of life in TBI patients.

Schober and co-workers (2017) noted that in HEMS, the pre-hospital detection of intracranial hematomas should improve patient care and the triage to specialized neurosurgical hospitals. Recently, non-invasive detection of intracranial hematomas became possible by applying transcranial NIRS; and 2nd-generation devices are currently available (e.g., the Infrascanner 2000 (InfraScan)) that appear suited also for pre-hospital HEMS applications. Since HEMS operations are time-critical, these researchers studied the Infrascanner 2000 as a "first-time-right" monitor in healthy volunteers (n = 17, hospital employees, no neurologic history). In addition, they studied the implementation of the Infrascanner 2000 in a European HEMS organization (Lifeliner 1, Amsterdam, the Netherlands). The principal results of the study were as follows: The screening for intracranial hematomas in healthy volunteers with first-time-right intention resulted in a marked rate of virtual hematomas (false positive results, i.e., 12/17), rendering more time consuming repeat measurements advisable. The results of the implementation of the Infrascanner in HEMS suggested that NIRS-based intracranial hematoma detection is feasible in the HEMS setting; however, some drawbacks exist and their possible solutions were discussed. The authors concluded that future studies are needed to demonstrate how NIRS-based intracranial hematoma detection will improve pre-hospital decision making in HEMS and ultimately patient outcome.
Mathieu and colleagues (2019) stated that NIRS may provide a non-invasive way to monitor cerebral oxygenation in patients with TBI, thus, allowing for timely intervention aimed at reversing regional brain tissue hypoxia. These researchers conducted a systematic review of NIRS-based oximetry measurements and their association with patient functional outcome and other neurophysiological parameters. They searched Medline, Embase, SCOPUS, BIOSIS, GlobalHealth and Cochrane Databases from inception to December 2018 and relevant conference proceedings published over the last 5 years. A total of 42 studies meeting inclusion criteria were found (37 prospective observational, 5 retrospective designs); 7 studies reporting on the association between NIRS-based cerebral oxygenated hemoglobin measurements, mortality, modified Rankin Scale (mRS), Glasgow Outcome Scale, or Extended Glasgow Outcome Scale were identified; 42 studies exploring associations with neurophysiological parameters were included. Notwithstanding significant gaps in the currently available literature, this analysis suggested a link between NIRS-detected cerebral hypoxia during the acute phase of TBI and poor functional outcome. NIRS measurements appeared to reflect changes in intracranial pressure, invasively monitored brain tissue oxygen tension and various cerebrovascular reactivity indices although low quality contradicting data exist. The authors concluded that the findings of this review highlighted the need for more prospective work before routine integration of NIRS-based techniques into multi-modality monitoring regimen.

Evaluation of Gait Disorders

Gramigna and colleagues (2017) stated that many neurological diseases (e.g., Parkinson’s disease and stroke) are characterized by gait disorders whose neuro-functional correlates are poorly investigated. Indeed, the analysis of real walking with the standard neuroimaging techniques poses strong challenges, and only a few studies on motor imagery or walking observation have been performed so far. Functional NIRS (fNIRS) is becoming an important research tool to assess functional activity in neurological populations or for special tasks, such as walking, because it allows investigating brain hemodynamic activity in an ecological setting, without strong immobility constraints. These investigators performed a systematic review following PRISMA guidelines on fNIRS-based examination of gait disorders; 12 of the initial yield of 489 articles were included in this review. The lesson learnt from these studies suggested that oxyhemoglobin levels within the prefrontal and premotor cortices are more sensitive to compensation strategies reflecting postural control and restoration of gait disorders. The authors concluded that although this field of study is in its relative infancy, the evidence provided encourages the translation of fNIRS in clinical practice, as it offers an unique opportunity to examine in depth the activity of the cortical motor system during real walking in neurological patients.
Intra-Operative Localization, Lymph Node Sampling, and Margin Assessment of Lung Cancer

Keating and colleagues (2017) stated that complete tumor resection is the most important predictor of patient survival with non-small cell lung cancer. Methods for intra-operative margin assessment after lung cancer excision are lacking. In an animal-model, these researchers evaluated NIR intra-operative imaging with a folate-targeted molecular contrast agent (OTL0038) for the localization of primary lung adenocarcinomas, lymph node sampling, and margin assessment. A total of 10 dogs with lung cancer underwent either video-assisted thoracoscopic surgery or open thoracotomy and tumor excision after an intravenous injection of OTL0038. Lungs were imaged with an NIR imaging device both in-vivo and ex-vivo. The wound bed was re-imaged for retained fluorescence suspicious for positive tumor margins. The tumor signal-to-background ratio (SBR) was measured in all cases. Next, 3 human patients were enrolled in a proof-of-principle study; tumor fluorescence was measured both in-situ and ex-vivo. All canine tumors fluoresced in-situ (mean Fluoptics SBR, 5.2 [range of 2.7 to 8.1]; mean Karl Storz SBR 1.9 [range of 1.4 to 2.6]). In addition, the fluorescence was consistent with tumor margins on pathology; 3 positive lymph nodes were discovered with NIR imaging. In addition, a positive retained tumor margin was discovered upon NIR imaging of the wound bed. Human pulmonary adenocarcinomas were also fluorescent both in-situ and ex-vivo (mean SBR of greater than 2.0). The authors concluded that NIR imaging can identify lung cancer in a large-animal model. In addition, NIR imaging can discriminate lymph nodes harboring cancer cells and also bring attention to a positive tumor margin. In humans, pulmonary adenocarcinomas fluoresced after the injection of the targeted contrast agent. These preliminary findings need to be further investigated in well-designed studies.

Treatment of Restless Legs Syndrome

American Academy of Neurology’s practice guideline summary on “Treatment of restless legs syndrome in adults” (Winkelman et al, 2016) stated that “Near-infrared spectroscopy is possibly effective in treating primary moderate to severe RLS (1 Class II study versus sham and 1 Class II study showing no difference between 2 devices)”. Level C recommendation: Physicians may consider prescribing near-infrared spectroscopy. The use of NIR for the treatment of restless legs syndrome needs to be further investigated.

Spatial Frequency Domain Imaging (SFDI)

Spatial Frequency Domain Imaging (SFDI) is a non-contact imaging modality that provides rapid wide-field imaging that non-invasively yields quantitative spatial maps, utilizing spatially modulated light patterns of visible and/or near-infrared (NIR) light, to extract intrinsic tissue optical properties and biochemical composition. These include concentration of chromophores,
such as oxy and deoxy hemoglobin, total hemoglobin (related to blood volume), tissue oxygen saturation, water content, and scattering coefficient (related to tissue structure). SFDI is capable of rendering quantitative two-dimensional maps of the concentration of chromophores. The technique works by shining different patterns of light on the tissue, recording a video of the remitted light, and processing the movie acquired (Burmeister et al., 2015; Cuccia, 2012; Durr, 2018; Tabassum et al, 2016).

Recent applications based on SFDI technology for skin imaging to evaluate for tissue compromise have included in vivo monitoring of burn wounds, determining flap perfusion during surgical procedures, and assessing cutaneous vascular abnormalities.

On January 18, 2017, Modulated Imaging, Inc. (Irvine, CA) announced that it had received clearance from the U.S. Food and Drug Administration (FDA) for its Ox-Imager CS device, which was designed to assist clinicians with the identification of vascular compromise. The Ox-Imager CS is a non-invasive, non-contact tissue oxygenation measurement system that is cleared for use by a healthcare professional to map and report an approximate value of oxygen saturation (StO2), oxy-hemoglobin (HbO2) and deoxy-hemoglobin (HbR) in superficial tissue for patients with potential circulatory compromise (Modulated Imaging, 2018).

The Ox-Image CS device visualizes spatially-resolved optical and functional parameters of biological tissue. Spectral analysis is used to measure oxygen saturation (StO2), oxyhemoglobin (HbO2), deoxyhemoglobin (HbR) and determine tissue optical properties (absorption and scattering) using specific LED wavelengths and patterns. The Ox-Imager CS uses both visible (VIS) and near-infrared (NIR) wavelengths between 450 and 1000 nm and a CCD camera for collecting hyperspectral images. Tissue oximetry exposes tissue to optical radiation of known wavelengths and captures the remitted light or reflectance. The remitted back scattered light is then used to calculate the tissue constituents based on principles of multispectral imaging and Spatial Frequency Domain Imaging (SFDI) (FDA, 2016).

Yafi et al. (2017) state that spatial frequency domain imaging (SFDI) has the potential to provide a means for pressure ulcer (PU) risk stratification, healing and staging. The authors present 4 preliminary cases demonstrating feasibility of SFDI to assess skin status in high-risk populations and pre-existing wounds. Patients at risk for PU were imaged using a near-infrared SFDI system. SFDI-derived images of tissue function (tissue hemoglobin, tissue oxygen saturation) and structure (tissue scattering) were then compared to each other as well as a blinded dermatologist's clinical impressions. In all 4 cases, the authors observed spatial changes in tissue constituents (decrease in tissue oxygen saturation, increased blood pooling, decreased scattering). The authors state that their preliminary study demonstrates the feasibility of optical technology to assess tissue oxygen saturation and blood volume status in a quantitative manner.
Ponticorvo et al. (2014) state that changes in the reduced scattering coefficient can differentiate superficial partial, deep partial and full thickness burns at one hour after injury. Burns can be challenging to classify based on clinical appearance alone, therefore, the authors investigated spatial frequency domain imaging (SFDI) and laser speckle imaging (LSI) in controlled burn wounds in a pig model. Burn wounds were imaged starting at one hour after the initial injury and daily at approximately 24, 48 and 72 hours post burn. Biopsies were taken on each day in order to correlate the imaging data to the extent of burn damage as indicated via histological analysis. A prototype clinical imaging system (v100, Modulated Imaging Inc., Irvine, CA) was used to acquire the burn data. The instrument consisted of a near-infrared camera with cross-polarizers to reduce specular reflection. A light source with LEDs centered at 658, 730, and 850 nm was projected off of a spatial light modulator, Digital Micromirror Device (DMD Discovery 1100, Texas Instruments Inc., Dallas, TX). It took approximately 12 seconds to collect one sequence of data, and this process was repeated every 30 seconds. Custom C# software (Modulated Imaging Inc., Irvine, CA) was used to control the hardware. A surface profilometry calibration measurement of a sample with known optical properties was used to correct the effects of surface curvature and day to day instrument variations. The absorption maps at each wavelength were used to estimate chromophore concentration maps of oxygenated and deoxygenated hemoglobin that could be converted to tissue oxygen saturation (stO2) by dividing oxygenated hemoglobin by the sum of oxygenated and deoxygenated hemoglobin. Maps of the reduced scattering coefficient at each of the wavelengths were also generated using this technique. The LSI instrument consisted of three main hardware components: a laser source, CCD camera, and computer. The authors found that, in a pig model, changes in reduced scattering coefficient and blood flow could be used to categorize burn severity as soon as one hour after the burn injury. The authors concluded that their findings suggest that SFDI and LSI information have the potential to provide useful metrics for quantifying the extent and severity of burn injuries.

Nguyen et al. (2013) conducted an initial human pilot study which suggests that SFDI has the potential to provide intraoperative oxygenation images in real-time during surgery. The authors state that early detection of vascular complications improves rate of flap salvage, and that SFDI is a promising new technology that provides oxygenation images over a large field of view. A pilot study of 3 women undergoing unilateral breast reconstruction after mastectomy were evaluated using SFDI technology over the course of the operation. Time points included images of each hemiabdominal skin flap before elevation, the selected flap after perforator dissection, and after microsurgical transfer. The authors found that SFDI was able to measure tissue oxy-hemoglobin concentration (ctO2Hb), tissue deoxyhemoglobin concentration, and tissue oxygen saturation (stO2). Images were created for each metric to monitor flap status and the results quantified throughout the various time points of the procedure. For 2 of 3 patients, the chosen flap had a higher ctO2Hb and stO2. For 1 patient, the chosen flap had lower ctO2Hb and stO2. There were no perfusion deficits observed based on SFDI and clinical follow-up. The authors
concluded that with the use of this technology, surgeons can obtain tissue oxygenation and hemoglobin concentration maps to assist in intraoperative planning, which can potentially prevent complications and improve clinical outcome.

Pharaon et al. (2012) state that SFDI can be used to quantify and detect physiologic changes that occur after arterial and venous occlusion in a rodent tissue transfer flap model. SFDI is a novel, noninvasive, wide-field imaging technology capable of quantifying oxygenated and deoxygenated hemoglobin levels, as well as, total hemoglobin and tissue saturation. The authors investigated SFDI (before and after selective vascular occlusion) on pedicled fasciocutaneous flaps on Wistar rats. The investigation was conducted using a prototype device, call the Tissue OxImager (by Modulated Imaging, Inc. Irvine, CA), which is a new optical imaging technology to detect vascular occlusion based on the SFDI technology. Three flap groups (control, selective arterial occlusion, and selective venous occlusion) and a fourth group composed of native skin between the flaps was measured. The authors found no statistically significant differences between the control flap group and the experimental flap groups before selective vascular occlusion: oxyhemoglobin (p = 0.2017), deoxyhemoglobin (p = 0.3145), total hemoglobin (p = 0.2718), and tissue saturation (p = 0.0777). In the selective arterial occlusion flap group, percentage change in total hemoglobin was statistically different from that of the control flap group (p = 0.0218). The remaining parameters were not statistically different from those of the control flap: percentage change in oxyhemoglobin (p = 0.0888), percentage change in deoxyhemoglobin (p = 0.5198), and percentage change in tissue saturation (p = 0.4220). The selective venous occlusion flap group demonstrated changes statistically different compared with the control flap group: percentage change in oxyhemoglobin (p = 0.0029) and deoxyhemoglobin, total hemoglobin, and tissue saturation (p < 0.0001). The authors concluded that their results indicate that SFDI can be used to quantify and detect physiologic changes that occur after arterial and venous occlusion in a rodent tissue transfer flap model. This device may have a high clinical applicability in monitoring postoperative patients.

Evaluation of Autism Spectrum Disorder

Zhang and Roeyers (2019) noted that a growing body of research has examined the functional development of the brain in autism spectrum disorder (ASD). Functional NIRS (fNIRS) is increasingly being used in this respect. This method has several advantages over other functional neuroimaging techniques in studying brain functions in ASD, including portability, low cost, and availability in naturalistic settings. These researchers evaluated 30 empirical studies, published in the past 10 years, that used fNIRS in individuals with ASD or in infants with a high risk of developing ASD. These studies examined either brain activation using multiple tasks (e.g., face processing, joint attention and working memory) or functional organization under a resting-state condition in ASD. The majority of these studies reported atypical brain activation in
the prefrontal cortex, inferior frontal gyrus, middle and superior temporal gyrus. Some studies revealed altered functional connectivity, suggesting an inefficient information transfer between brain regions in ASD. The authors concluded that these findings suggested that fNIRS is a promising tool to investigate neurodevelopment in ASD from an early age.

Liu and associates (2019) reviewed a relatively new method for studying the developing brain in children and infants with ASD. Despite advances in behavioral screening and brain imaging, due to paradigms that do not easily allow for testing of awake, very young, and socially-engaged children -- i.e., the social and the baby brain -- the biological underpinnings of this disorder remain a mystery. These investigators introduced an approach based on fNIRS, which offers a non-invasive imaging technique for studying functional activations by measuring changes in the brain's hemodynamic properties. This further enables measurement of brain activation in upright, interactive settings, while maintaining general equivalence to fMRI findings. The authors reviewed the existing studies that have used fNIRS for ASD, discussing their promise, limitations, and their technical aspects, gearing this study to the researcher who may be new to this technique and highlighting potential targets for future research.

Evaluation of Mitochondrial Disorder

In a case-series study, Niemi and Chock (2019) examined the use of NIRS to evaluate neonates with mitochondrial disorders. These investigators observed abnormally high cerebral oxygen saturation levels indicating insufficient tissue oxygen utilization. The authors proposed that NIRS may be an additional tool in the diagnostic evaluation of a suspected mitochondrial disorder.

Evaluation of Major Depressive Disorder

Akiyama and associates (2018) stated that previous functional neuroimaging studies of depression have demonstrated fronto-temporal dysfunction, including the dorsolateral prefrontal cortex, while patients performed working memory and language comprehension tasks. Recent NIRS studies have shown fronto-temporal hypofunction in depression by verbal fluency task, but the regions of impairment affecting respective depressive symptoms still remain unclear. These investigators examined fronto-temporal function during word production task in depression with multi-channel NIRS. Further, they examined if any depressive symptoms affect fronto-temporal dysfunction. A total of 177 major depressive patients and 50 healthy control volunteers participated in this study. Their cerebral activations were compared during verbal fluency task. Although performance was not significantly different, hypo-activation in the bilateral fronto-temporal regions was significantly observed in depressed patients, compared with controls. Left lateral fronto-temporal activation was significantly reduced in the group with mandatory symptom, which was depressed mood, or loss of interest or pleasure, compared with the group
that still had residual depressive symptoms in spite major depressive disorder (MDD) having
been remitted. The authors concluded that these findings indicated hypofunction of the bilateral
fronto-temporal regions in depression during verbal fluency task. Further, hypofunction of these
regions in the left hemisphere by this task could reflect whether the subjects recovered from
depressed mood, or loss of interest or pleasure. The main drawback of this study was that the
MDD group had significantly higher age and education level than the controls.

Satomura and colleagues (2019) noted that long-term longitudinal studies are needed to
establish neuroimaging indicators that contribute to the detection of severity changes over time
in patients with MDD. A total of 165 patients with MDD underwent clinical assessments and
NIRS examination at the initial evaluation (T0). After 1.5 years, 45 patients who visited for the
follow-up evaluation (T1.5) were included in the analysis. These researchers conducted
analyses using the 17-item Hamilton Rating Scale for Depression (HAMD) scores and mean oxy-
hemoglobin concentration ([oxy-Hb]) changes during a cognitive task in NIRS at T0 (T0_HAMD,
T0_[oxy-Hb]) and at T1.5 (T1.5_HAMD, T1.5_[oxy-Hb]), and their intra-individual longitudinal
changes (∆HAMD = T1.5_HAMD - T0_HAMD, ∆[oxy-Hb] = T1.5_[oxy-Hb] - T0_[oxy-Hb]). For
severity-dependent regions, the ∆[oxy-Hb] in the right inferior frontal gyrus (IFG) was negatively
correlated with the ∆HAMD. For severity-independent regions, the intra-class correlation
coefficients between T0_ and T1.5_[oxy-Hb] were moderate in the bilateral middle frontal gyri
(MFG). The authors concluded that brain activation in the right IFG and the bilateral MFG as
measured by NIRS may differentially indicate clinical severity and trait-related abnormalities in
MDD. These findings need to be validated by well-designed studies. The main drawback of this
study was that the percentage of patients included in the follow-up examination was relatively
small.

Monitoring of Post-Operative Cognitive Dysfunction

Yu and colleagues (2018) stated that various techniques have been employed for the early
detection of peri-operative cerebral ischemia and hypoxia. Cerebral NIRS is increasingly used in
this clinical scenario to monitor brain oxygenation. However, it is unknown whether peri-
operative cerebral NIRS monitoring and the subsequent treatment strategies are of benefit to
patients. These researchers examined the effects of peri-operative cerebral NIRS monitoring
and corresponding treatment strategies in adults and children, compared with blinded or no
cerebral oxygenation monitoring, or cerebral oxygenation monitoring based on non-NIRS
technologies, on the detection of cerebral oxygen desaturation events (CDEs), neurological
outcomes, non-neurological outcomes and socioeconomic impact (including cost of
hospitalization and length of hospital stay [LOS]). They searched the Cochrane Central Register
of Controlled Trials (CENTRAL 2016, Issue 12), Embase (1974 to 20 December 2016) and
Medline (PubMed) (1975 to December 20, 2016). They also searched the World Health
Organization (WHO) International Clinical Trials Registry Platform for ongoing studies on December 20, 2016. These investigators updated this search in November 2017, but these results have not yet been incorporated in the review; they imposed no language restriction. The authors included all relevant RCTs dealing with the use of cerebral NIRS in the peri-operative setting (during the operation and within 72 hours after the operation), including the operating room, the post-anesthesia care unit and the intensive care unit (ICU). Two authors independently selected studies, assessed risk of bias and extracted data. For binary outcomes, they calculated the risk ratio (RR) and its 95 % CI. For continuous data, they estimated the mean difference (MD) between groups and its 95 % CI. As these researchers expected clinical and methodological heterogeneity between studies, they employed a random-effects model for analyses and examined the data for heterogeneity (I2 statistic). They created a “Summary of findings” table using GRADEpro. These investigators included 15 studies in the review, comprising a total of 1,822 adult participants. There were 12 studies awaiting classification, and 8t ongoing studies. None of the 15 included studies considered the pediatric population; 4 studies were conducted in the abdominal and orthopedic surgery setting (lumbar spine, or knee and hip replacement), 1 study in the carotid endarterectomy setting, and the remaining 10 studies in the aortic or cardiac surgery setting. The main sources of bias in the included studies related to potential conflict of interest from industry sponsorship, unclear blinding status or missing participant data; 2 studies with 312 participants considered post-operative neurological injury, however no pooled effect estimate could be calculated due to discordant direction of effect between studies (low-quality evidence); 1 study (n = 126) in participants undergoing major abdominal surgery reported that 4/66 participants experienced neurological injury with blinded monitoring versus 0/56 in the active monitoring group. A second study (n = 195) in participants having coronary artery bypass surgery reported that 1/96 participants experienced neurological injury in the blinded monitoring group compared with 4/94 participants in the active monitoring group. The authors were uncertain whether active cerebral NIRS monitoring had an important effect on the risk of post-operative stroke because of the low number of events and wide confidence interval (RR 0.25, 95 % CI: 0.03 to 2.20; 2 studies, 240 participants; low-quality evidence). They were uncertain whether active cerebral NIRS monitoring had an important effect on post-operative delirium because of the wide confidence interval (RR 0.63, 95 % CI: 0.27 to 1.45; 1 study, 190 participants; low-quality evidence); 2 studies with 126 participants showed that active cerebral NIRS monitoring may reduce the incidence of mild post-operative cognitive dysfunction (POCD) as defined by the original studies at 1 week after surgery (RR 0.53, 95 % CI: 0.30 to 0.95, I2 = 49 %, low-quality evidence). Based on 6 studies with 962 participants, there was moderate-quality evidence that active cerebral oxygenation monitoring probably did not decrease the occurrence of POCD (decline in cognitive function) at 1 week after surgery (RR 0.62, 95 % CI: 0.37 to 1.04, I2 = 80 %). The different type of monitoring equipment in 1 study could potentially be the cause of the heterogeneity. The authors were uncertain whether active cerebral NIRS monitoring had an important effect on intra-operative mortality or
post-operative mortality because of the low number of events and wide confidence interval (RR 0.63, 95 % CI: 0.08 to 5.03, I²= 0 %; 3 studies, 390 participants; low-quality evidence). There was no evidence to determine whether routine use of NIRS-based cerebral oxygenation monitoring causes adverse effects. The authors concluded that the effects of peri-operative active cerebral NIRS monitoring of brain oxygenation in adults for reducing the occurrence of short-term, mild POCD were uncertain due to the low quality of the evidence. There was uncertainty as to whether active cerebral NIRS monitoring had an important effect on post-operative stroke, delirium or death because of the low number of events and wide confidence intervals. The conclusions of this review may change when the 8 ongoing studies are published and the 12 studies awaiting assessment are classified. These researchers stated that more RCTs performed in the pediatric population and high-risk patients undergoing non-cardiac surgery (e.g. neurosurgery, carotid endarterectomy and other surgery) are needed.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT codes covered if selection criteria are met:</td>
<td></td>
</tr>
<tr>
<td>0493T</td>
<td>Near-infrared spectroscopy studies of lower extremity wounds (e.g., for oxyhemoglobin measurement)</td>
</tr>
<tr>
<td>CPT codes not covered for indications listed in the CPB:</td>
<td></td>
</tr>
<tr>
<td>Ox-Imager CS device: no specific code:</td>
<td></td>
</tr>
<tr>
<td>+ 0205T</td>
<td>Intravascular catheter-based coronary vessel or graft spectroscopy (e.g., infrared) during diagnostic evaluation and/or therapeutic intervention including imaging supervision, interpretation, and report, each vessel (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>Other CPT codes related to the CPB:</td>
<td></td>
</tr>
<tr>
<td>+ 92978</td>
<td>Intravascular ultrasound (coronary vessel or graft) during diagnostic evaluation and/or therapeutic intervention including supervision, interpretation and report; initial vessel</td>
</tr>
<tr>
<td>+ 92979</td>
<td>each additional vessel</td>
</tr>
<tr>
<td>ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):</td>
<td></td>
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<tr>
<td>C34.00 - C34.92</td>
<td>Malignant neoplasm of bronchus and lung</td>
</tr>
<tr>
<td>E88.40 - E88.49</td>
<td>Mitochondrial metabolism disorders</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>----------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>F01.50 - F99</td>
<td>Mental behavioral and neurodevelopmental disorders</td>
</tr>
<tr>
<td>G25.81</td>
<td>Restless legs syndrome</td>
</tr>
<tr>
<td>G31.84</td>
<td>Mild cognitive impairment, so stated [post-operative cognitive dysfunction]</td>
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<tr>
<td>G45.0 - G45.9</td>
<td>Transient cerebral ischemic attacks and related syndromes</td>
</tr>
<tr>
<td>G89.0 - G89.4</td>
<td>Pain, not elsewhere classified</td>
</tr>
<tr>
<td>G97.31 - G97.32</td>
<td>Intraoperative hemorrhage and hematoma of a nervous system organ or structure complicating a nervous system or other procedure</td>
</tr>
<tr>
<td>I25.10 - I41</td>
<td>Coronary atherosclerosis</td>
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<tr>
<td>I60.00 - I62.9</td>
<td>Nontraumatic subarachnoid and intracranial hemorrhage</td>
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<tr>
<td>I65.01 - I66.29</td>
<td>Occlusion and stenosis of precerebral arteries, occlusion of cerebral arteries</td>
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<td>I67.89</td>
<td>Other cerebrovascular disease</td>
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<tr>
<td>I82.401 - I82.429</td>
<td>Acute venous embolism and thrombosis of deep vessels of lower extremity</td>
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<tr>
<td>I97.810 - I97.821</td>
<td>Intraoperative or postprocedural cerebrovascular infarction during cardiac or other surgery</td>
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<tr>
<td>L89.000 - L89.95</td>
<td>Pressure ulcers</td>
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<tr>
<td>O22.30 - O22.33, O87.1</td>
<td>Deep phlebothrombosis in pregnancy and the puerperium</td>
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<td>P81.8 - P81.9</td>
<td>Disturance of temperature regulation of newborn</td>
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<tr>
<td>P91.60 - P91.63</td>
<td>Hypoxic ischemic encephalopathy [HIE]</td>
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<td>R26.0 - R26.9</td>
<td>Abnormalities of gait and mobility</td>
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<td>R52</td>
<td>Pain, unspecified</td>
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<td>S06.0xA - S06.6x9S</td>
<td>Intracranial injury</td>
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<td>S09.0xA+ - S09.93x+</td>
<td>Other and unspecified injuries of head</td>
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<td>S70.211+ - S71.159+</td>
<td>Open wound of lower limb</td>
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<td>S80.211+ - S81.859+</td>
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<tr>
<td>S90.411+ - S91/359+</td>
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<td>Code Description</td>
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<td>T81.72x+</td>
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<td>Z01.810</td>
<td>Encounter for preprocedural cardiovascular examination</td>
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<tr>
<td>Z01.811</td>
<td>Encounter for preprocedural respiratory examination</td>
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<td>Z01.818</td>
<td>Encounter for other preprocedural examination</td>
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<td>Z13.6</td>
<td>Encounter for screening for cardiovascular disorders</td>
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<tr>
<td>Z13.89</td>
<td>Encounter for screening for other disorders [evaluating risk of developing post-operative deep vein thrombosis]</td>
</tr>
<tr>
<td>Z98.89</td>
<td>Other specified postprocedural states [neurosurgery]</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:


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Amendment to
Aetna Clinical Policy Bulletin Number: 0796 Near-Infrared (NIR) Spectroscopy

There are no amendments for Medicaid.