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
- Evaluating anesthetic depth
- Evaluating lower extremity wounds/predicting wound healing (e.g., for measurement of oxy-hemoglobin)
- Evaluating psychiatric disorders (e.g., bipolar disorder depression, dysthymic disorder, obsessive compulsive disorder, panic disorder, psychotic disorder, and schizophrenia)
- Evaluating risk of developing post-operative deep vein thrombosis
- Guiding peripheral intravenous catheterization
- 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)
- 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
- Use in the intensive care or neonatal intensive care setting
- Use in pediatric cardiac critical care

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), and CPB 0520 - Magnetic Resonance Imaging of the Cardiovascular System - Cardiac MRI (../500_599/0520.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. Intracoronary 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-
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 to11) 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 coronary pullback. The case-series study illustrated the data obtained by this combined NIRS-IVUS device and highlighted its potential clinical applications.
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) cannot 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.

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 examined 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. 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). The author concluded 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.
parameters are still missing and warranted in order to clearly define the role of NIRS in children at risk for low perfusion.

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.

Lipcsey 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 micro-vasculatory 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 rewarming and the 6-hour rewarming 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 rewarming, 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-Tredelenburg'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 outpatient 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
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
 '''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.'''

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.
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 (p = 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.

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

**ICD-10 codes will become effective as of October 1, 2015:**

CPT codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ 0205T</td>
<td>Intravascular catheter-based coronary vessel or graft spectroscopy (eg, 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>0286T</td>
<td>Near-infrared spectroscopy studies of lower extremity wounds (e.g., for oxyhemoglobin measurement)</td>
</tr>
</tbody>
</table>

Other CPT codes related to the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<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>
</tbody>
</table>

**ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<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>
</tr>
<tr>
<td>I60.00 - I62.9</td>
<td>Nontraumatic subarachnoid and intracranial hemorrhage</td>
</tr>
<tr>
<td>I65.01 - I66.29</td>
<td>Occlusion and stenosis of precerebral arteries, occlusion of cerebral arteries</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>I67.89</td>
<td>Other cerebrovascular disease</td>
</tr>
<tr>
<td>I82.401 -</td>
<td>Acute venous embolism and thrombosis of deep vessels of lower extremity</td>
</tr>
<tr>
<td>I82.4z9</td>
<td></td>
</tr>
<tr>
<td>I97.810 -I97.821</td>
<td>Intraoperative or postprocedural cerebrovascular infarction during cardiac or other surgery</td>
</tr>
<tr>
<td>O22.30 - O22.33, O87.1</td>
<td>Deep phlebothrombosis in pregnancy and the puerperium</td>
</tr>
<tr>
<td>P81.8 - P81.9</td>
<td>Disturance of temperature regulation of newborn</td>
</tr>
<tr>
<td>P91.60 - P91.63</td>
<td>Hypoxic ischemic encephalopathy [HIE]</td>
</tr>
<tr>
<td>R52</td>
<td>Pain, unspecified</td>
</tr>
<tr>
<td>S06.4x0+ - S06.6x9+</td>
<td>Traumatic epidural, subdural and subarachnoid hemorrhage</td>
</tr>
<tr>
<td>S09.0xx+ - S09.93x+</td>
<td>Other and unspecified injuries of head</td>
</tr>
<tr>
<td>S70.211+ - S71.159+ - S80.211+ - S81.859+ - S90.411+ - S91/359+</td>
<td>Open wound of lower limb</td>
</tr>
<tr>
<td>T81.710+ - T81.72x+</td>
<td>Vascular complications following a procedure, not elsewhere classified</td>
</tr>
<tr>
<td>Z01.810</td>
<td>Encounter for preprocedural cardiovascular examination</td>
</tr>
<tr>
<td>Z01.811</td>
<td>Encounter for preprocedural respiratory examination</td>
</tr>
<tr>
<td>Z01.818</td>
<td>Encounter for other preprocedural examination</td>
</tr>
<tr>
<td>Z13.6</td>
<td>Encounter for screening for cardiovascular disorders</td>
</tr>
<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:


25. Mittnacht AJ. Near infrared spectroscopy in children at


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

There are no amendments for Medicaid.