Near-Infrared Vascular Imaging and Near-Infrared Fluorescence Imaging

Policy

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

Aetna considers the use of near-infrared vascular imaging systems (e.g., AccuVein AV300 or VeinViewer) for assessment of cutaneous wound, and guiding vascular access experimental and investigational because their effectiveness has not been established.

Aetna considers near-infrared fluorescence imaging experimental and investigational for the following indications (not an all-inclusive list):

- Confirmation and identification of the position of gastro-epiploic vessels during minimally invasive esophagectomy
- Detection of ovarian cancer metastases
- Detection of tumor angiogenesis and monitoring of response to anti-tumor vasculature therapy
- Diagnosis of rheumatoid arthritis
- Evaluation of coronary atherosclerosis

Policy History

Last Review 10/13/2016
Effective: 05/17/2013
Next Review: 10/12/2017

Definitions

Additional Information

Clinical Policy Bulletin Notes
Facilitation of selective arterial clamping during partial nephrectomy
Identification of vulnerable atherosclerotic plaques Intra-operative anatomy navigation during minimally invasive surgery
Lymphatic imaging in lymphangiomatosis
Mapping of microvascular circulation in ischemic diseases
Mapping of sentinel lymph nodes in endometrial cancer
Navigation of laparoscopic anatomy during gastro-intestinal surgery.

See also CPB 0111 - Indocyanine Green Angiography (.../100_199/0111.html), and CPB 0796 - Near-Infrared (NIR) Spectroscopy (.../700_799/0796.html).

Background
Near-Infrared Vascular Imaging:

Peripheral intravenous (PIV) catheter insertion is a common, painful, and sometimes difficult procedure for many infants and children in the pediatric emergency department (ED) because of the small caliber and impalpability of the veins. Changes in catheter design and adoption of new imaging techniques have been tried to facilitate line placement. Near-infrared (NIR) imaging is a non-invasive and non-ionizing modality that has been employed to improve the success rate of PIV catheter placement in pediatric patients (e.g., reduce the number of attempts, the number of needle redirections, and the overall time to catheter placement). The VeinViewer® (Luminetx Corporation, Memphis, TN) is a NIR light device that delineates the running course of subcutaneous veins.

In an observational feasibility study, Cuper et al (2011) evaluated for the first time the value of visualizing veins by a prototype of a NIR vascular imaging system for venipuncture in children. Participants were children (0 to 6 years) attending the clinical laboratory of a pediatric university hospital during a 2-month period without (n = 80) and subsequently during a 1-month period with a prototype of an NIR vascular imaging
system (n = 45). Failure rate (i.e., more than 1 puncture) and time of needle manipulation were determined. With the NIR vascular imaging system, failure rate decreased from 10/80 to 1/45 (p = 0.05) and time decreased from 2 seconds (1 to 10) to 1 second (1 to 4, p = 0.07). The authors concluded that the findings of this study showed promising results on the value of an NIR vascular imaging system in facilitating venipuncture.

Chapman et al (2011) examined the benefit of the VeinViewer, a device that delineates subcutaneous veins using NIR light and video technology, for PIV placement in children in the ED. A prospective, randomized sample of children aged 0 to 17 years who required a non-emergent PIV in a tertiary care pediatric ED were enrolled in this study. Subjects were randomized to standard PIV cannulation (SC) or PIV cannulation with the VeinViewer (VV). The primary outcome measure was time to PIV placement. Secondary outcome measures included number of PIV attempts and pain scores as reported by the child, parent or guardian, and nurse using a 100-mm visual analog scale (VAS). A total of 323 patients completed the study: 174 boys and 149 girls. Age, sex, and body mass index (BMI) were not different between groups. There were no differences in time to PIV placement, number of PIV attempts, or pain scores for the overall study group. However, a planned subgroup analysis of children age 0 to 2 years (n = 107) did yield significant results for the geometric mean time to place the PIV (121 seconds [VV] versus 167 seconds [SC], p = 0.047) and for nurses' perception of pain (median VAS 34 [VV] versus 46 [SC], p = 0.01). The authors concluded that while no results were significant for the overall study group, subgroup analysis of children age 0 to 2 years suggested that the VeinViewer may decrease the time to PIV placement.

In a randomized controlled trial, Perry et al (2011) examined if the use of a NIR light venipuncture aid (VeinViewer) would improve the rate of successful first-attempt placement of IV catheters in a high-volume pediatric ED. Patients younger than 20 years with standard clinical indications for IV access were randomized to have IV placement by ED nurses (in 3 groups
stratified by 5-year blocks of nursing experience) using traditional methods (standard group) or with the aid of the VeinViewer (device group). If a vein could not be cannulated after 3 attempts, patients crossed-over from one study arm to the other, and study nurses attempted placement with the alternative technique. The primary end point was first-attempt success rate for IV catheter placement. After completion of patient enrollment, a questionnaire was completed by study nurses as a qualitative assessment of the device. A total of 123 patients (median age of 3 years) were included in the study: 62 in the standard group and 61 in the device group. There was no significant difference in first-attempt success rate between the standard (79.0 %, 95 % confidence interval [CI]: 66.8 % to 88.3 %) and device (72.1 %, 95 % CI: 59.2 % to 82.9 %) groups. Of the 19 study nurses, 14 completed the questionnaire; 70 % expressed neutral or unfavorable assessments of the device in non-dehydrated patients without chronic underlying medical conditions and 90 % found the device a helpful tool for patients in whom IV access was difficult. The authors concluded that first-attempt success rate for IV placement was non-significantly higher without than with the assistance of the VeinViewer in a high-volume pediatric ED. They noted that nurses placing IVs did report several benefits to use of the device with specific patient groups, and future research should be carried out to demonstrate the role of the VeinViewer in these patients.

In a randomized controlled trial, Kim et al (2012) examined if the use of the VeinViewer in infants and children facilitated peripheral venous access, especially in difficult cases. Pediatric patients between the ages of 1 month and 16 years who required peripheral venous access in the pediatric ward were included in this study. Prior to randomization, difficult intravenous access (DIVA) score, a 4-variable clinical prediction rule for first-attempt success, was estimated. These investigators compared the first-attempt success rates and procedural times between the VeinViewer group and a control group. They evaluated 111 patients: 54 in the VeinViewer group and 57 in the control group. Patient demographics and factors related to the success of vein access were similar for
both groups. The overall first-attempt success rate was 69.4 % (77/111) in the VeinViewer group and 66.7 % (38/57) in the control group, a difference that was not statistically significant. However, the first-attempt success rate increased from (25 %) 5/20 in the control group to (58 %) 14/24 in the VeinViewer group for difficult veins with a DIVA score greater than 4 (p = 0.026). There were no significant differences in procedural time between the two groups. The authors concluded that the VeinViewer facilitated peripheral venous access for pediatric patients with difficult veins, which enhanced first-attempt success rates.

The AccuVein AV300 device was developed to assist venipuncture and IV cannulation by enhancing the visibility of superficial veins. It uses infrared light to highlight hemoglobin so that blood vessels are darkly delineated against a red background.

Sanchez-Morago et al (2010) stated that despite major advances that have occurred in medicine and biotechnology in recent years, advances to locate veins have been very limited. The AccuVein AV300 is a portable manual instrument that enables nurses to locate certain peripheral veins. This device does not substitute a nurse's traditional skill in locating veins by visual or feeling means, but rather this device supplements their skills and enhances them. This device is lightweight, intuitive, and does not require previous training for its use and hygiene since it never enters into contact with a patient's skin as it emits an infrared light on the skin, which reflects veins drawing them on the surface of the skin.

Kaddoum et al (2012) evaluated the effectiveness of the AccuVein AV300 in improving the first-time success rate of IV cannulation of anesthetized pediatric patients. Participants were randomized to cannulation with the AccuVein AV300 or standard insertion by experienced pediatric anesthesiologists. An observer recorded the number of skin punctures and cannulation attempts required, and the time between tourniquet application and successful cannulation or 4 skin
punctures, whichever came first. There were 146 patients with a median age of 4.6 years (range of 0.18 to 17.1 years), 46.6% were males, 80.8% were light skin colored, and 15.7% were younger than 2 years. The first-attempt success rates were 75% (95% CI: 63.8 to 84.2%) using AV300 and 73% (95% CI: 61.9 to 81.9%) using the standard method (p = 0.85). Patients with dark or medium skin color were 0.38 times less likely to have a successful first-attempt than patients with light skin color. The difference between the 2 treatment groups in number of skin punctures and the time to insertion was not significant.

Although the AV300 was easy to use and improved visualization of the veins, the authors found no evidence that it was superior to the standard method of IV cannulation in unselected pediatric patients under anesthesia.

de Graaff et al (2014) evaluated the clinical utility of a NIR 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 NIR 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 NIR light and with NIR vascular imaging device did not improve success of PIC in pediatric patients who are known difficult to cannulate.

In summary, there is currently insufficient evidence on the effectiveness of near-infrared vascular imaging for guiding vascular access. Well-designed studies are needed to validate
these preliminary findings.

**Assessment of Cutaneous Wound:**

Paul and colleagues (2015) stated that the ability to phenotype wounds for the purposes of assessing severity, healing potential and treatment is an important function of evidence-based medicine. A variety of optical technologies are currently in development for non-invasive wound assessment. To varying extents, these optical technologies have the potential to supplement traditional clinical wound evaluation and research, by providing detailed information regarding skin components imperceptible to visual inspection. These assessments are achieved through quantitative optical analysis of tissue characteristics including blood flow, collagen re-modeling, hemoglobin content, inflammation, temperature, vascular structure, and water content. Technologies that have, to this date, been applied to wound assessment include: NIR imaging, thermal imaging, optical coherence tomography (OCT), orthogonal polarization spectral imaging, fluorescence imaging, laser Doppler imaging, microscopy, spatial frequency domain imaging, photo-acoustic detection, and spectral/hyper-spectral imaging. The authors presented a review of the technologies in use or development for these purposes with 3 aims: (i) providing basic explanations of imaging technology concepts, (ii) reviewing the wound imaging literature, and (iii) providing insight into areas for further application and exploration. They stated that non-invasive imaging is a promising advancement in wound assessment and all technologies require further validation.

**Near-Infrared Fluorescence Imaging:**

Schols et al (2013) provided an overview of current developments in surgical optical imaging for improved anatomic identification and physiologic tissue characterization during laparoscopic gastro-intestinal surgery. A systematic literature search in the PubMed database was conducted. Eligible studies reported on any kind of novel optical imaging technique applied
for anatomic identification or physiologic tissue characterization in laparoscopic gastro-intestinal surgery. Gynecologic and urologic procedures also were included whenever vascular, nerve, ureter, or lymph node imaging was concerned. Various surgical imaging techniques for enhanced intra-operative visualization of essential tissue types (i.e., blood vessel, bile duct, ureter, nerve, lymph node) and for tissue characterization purposes such as assessment of blood perfusion were identified. An overview of pre-clinical and clinical experiences was given as well as the potential added value for intra-operative anatomic localization and characterization during laparoscopy. The authors concluded that implementation of new optical imaging methods during laparoscopic gastro-intestinal surgery can improve intra-operative anatomy navigation. This may lead to increased patient safety (preventing iatrogenic functional tissue injury) and procedural efficiency (shorter operating time). They stated that near-infrared fluorescence imaging seems to possess the greatest potential for implementation in clinical practice in the near future.

Harke et al (2014) presented a single-surgeon, matched-pair analysis to show the feasibility of combining the technique of selective clamping with usage of NIR fluorescence (NIRF) imaging in robot-assisted partial nephrectomy and to investigate short-term renal function outcomes. A total of 22 patients underwent selective clamping partial nephrectomy with the application of indocyanine green (ICG). Out of this cohort, a matched-pair analysis for R.E.N.A.L. nephrometry parameter was employed for 15 exactly matching partners. Demographic, surgical, pathological and kidney function data were collected for the initial cohort, and matched-pair comparison was made between the subgroups retrospectively. Robot-assisted partial nephrectomy without clamping of the hilum was possible in 21 patients; in 1 patient, main artery clamping was necessary due to bleeding. Mean clinical tumor size was 37.7 mm. Mean selective clamping ischemia time was 11.6 mins with an estimated blood loss of 347 ml. No intra-operative complications occurred, and post-operative
complications (n = 4), including 2 major urological (urinoma, late-onset acute hemorrhage) complications, were found. There were no side effects of ICG administration. Matched-pair analysis for 15 patients showed similar demographic and surgical data without any significant differences in tumor characteristics. Comparing short-term renal function outcomes, significantly decreased estimated glomerular filtration rate reduction in the selective clamping group with an absolute loss of 5.1 versus 16.1 ml/min in the global ischemia cohort (p = 0.045) could be observed. The authors concluded that robot-assisted partial nephrectomy with selective clamping of the tumor feeding vascular branches is a promising technique for reduced ischemic renal trauma. This may lead to improved kidney function preservation.

Press and Jaffer (2014) noted that coronary artery disease (CAD) is an inflammatory process that results in buildup of atherosclerosis, typically lipid-rich plaque in the arterial wall. Progressive narrowing of the vessel wall and subsequent plaque rupture can lead to myocardial infarction and death. Recent advances in intra-vascular fluorescence imaging techniques have provided exciting coronary artery-targeted platforms to further characterize the molecular changes that occur within the vascular wall as a result of atherosclerosis and following coronary stent-induced vascular injury. These investigators summarized recent developments in catheter-based imaging of coronary arterial-sized vessels; focusing on 2-dimensional NIRF molecular imaging technology as an approach to identify inflammation and fibrin directly within coronary artery-sized vessels. The authors concluded that intravascular NIRF is anticipated to provide new insights into the in-vivo biology underlying high-risk plaques, as well as high-risks stents prone to stent re-stenosis or stent thrombosis.

Sarkaria et al (2014) stated that during esophagectomy, identification and preservation of the right gastro-epiploic vascular arcade are critical and may be challenging with minimally invasive approaches. These researchers assessed the use of near-infrared fluorescence imaging fluorescence
angiography (NIFI-FA) during robotic-assisted minimally invasive esophagectomy (RAMIE) as an aid to visualize the gastric vasculature with mobilization. After intravenous administration of 10 mg of ICG, a robotic platform with NIR optical fluorescence capability was used to examine the gastric vasculature in patients undergoing RAMIE. A total of 30 (71%) of 42 patients undergoing RAMIE were assessed using NIFI-FA during mobilization of the greater gastric curve and fundus; 11 were excluded because the system was not available, and 1 was excluded because of documented allergy to iodinated contrast. The median time from ICG administration to detectable fluorescence was 37.5 seconds (range of 20 to 105 seconds). Near-infrared fluorescence imaging FA identified or confirmed termination of the vascular arcade in all 30 cases. Subjectively, NIFI-FA often identified otherwise unvisualized small transverse vessels between the termination of the vascular arcade and the first short gastric artery, as well as between the short gastric arteries. Identification and/or confirmation of the vascular arcade position during mobilization of the greater curve/omentum were also aided by NIFI-FA. The authors concluded that although there are limitations to the current technology, NIFI-FA may be a useful adjunct to confirm and identify the position of gastro-epiploic vessels, allow for safer and more confident dissections during gastric mobilization, as well as potentially decrease serious intra-operative vascular misadventures.

Ma et al (2014) stated that pathological angiogenesis is crucial in tumor growth, invasion and metastasis. Previous studies demonstrated that the vascular endothelial growth inhibitor (VEGI), a member of the tumor necrosis factor super-family, can be used as a potent endogenous inhibitor of tumor angiogenesis. Molecular probes containing the asparagine-glycine-arginine (NGR) sequence can specifically bind to CD13 receptor, which is over-expressed on neovasculature and several tumor cells. Near-infrared fluorescence optical imaging for targeting tumor vasculature offers a non-invasive method for early detection of tumor angiogenesis and efficient monitoring of response to anti-tumor vasculature therapy.
These researchers developed a new NIRF imaging probe on the basis of an NGR-VEGI protein for the visualization of tumor vasculature. The NGR-VEGI fusion protein was prepared from proaryotic expression, and its function was characterized in-vitro. The NGR-VEGI protein was then labeled with a Cy5.5 fluorophore to afford Cy5.5-NGR-VEGI probe. Using the NIRF imaging technique, these investigators visualized and quantified the specific delivery of Cy5.5-NGR-VEGI protein to subcutaneous HT-1080 fibrosarcoma tumors in mouse xenografts. The Cy5.5-NGR-VEGI probe exhibited rapid HT-1080 tumor targeting, and highest tumor-to-background contrast at 8 hours post-injection (pi). Tumor specificity of Cy5.5-NGR-VEGI was confirmed by effective blocking of tumor uptake in the presence of unlabeled NGR-VEGI (20 mg/kg). Ex-vivo NIRF imaging further confirmed in-vivo imaging findings, demonstrating that Cy5.5-NGR-VEGI displayed an excellent tumor-to-muscle ratio (18.93 ± 2.88) at 8 hours pi for the non-blocking group and significantly reduced ratio (4.92 ± 0.75) for the blocking group. The authors concluded that Cy5.5-NGR-VEGI provided highly sensitive, target-specific, and longitudinal imaging of HT-1080 tumors. They stated that as a novel theranostic protein, Cy5.5-NGR-VEGI has the potential to improve cancer treatment by targeting tumor vasculature.

Detection of Ovarian Cancer Metastases:

Tummers et al (2015) noted that in ovarian cancer, 2 of the most important prognostic factors for survival are completeness of staging and completeness of cytoreductive surgery (CRS). Therefore, intra-operative visualization of tumor lesions is of great importance. Pre-clinical data already demonstrated tumor visualization in a mouse-model using NIRF imaging and ICG as a result of enhanced permeability and retention (EPR). These researchers determined the feasibility of intra-operative ovarian cancer metastases imaging using NIRF imaging and ICG in a clinical setting. A total of 10 patients suspected of ovarian cancer scheduled for staging or CRS were included. Patients received 20 mg ICG intravenously after opening the abdominal cavity. The mini-FLARE NIR fluorescence imaging system was
used to detect NIRF lesions. These investigators reported that 6 out of 10 patients had malignant disease of the ovary or fallopian tube, of which 2 had metastatic disease outside the pelvis; 8 metastatic lesions were detected in these 2 patients, which were all NIR fluorescent. However, 13 non-malignant lesions were also NIR fluorescent, resulting in a false-positive rate of 62%. There was no significant difference in tumor-to-background ratio between malignant and benign lesions (2.0 versus 2.0; p = 0.99). The authors concluded that this was the first clinical trial demonstrating intra-operative detection of ovarian cancer metastases using NIRF imaging and ICG. Despite detection of all malignant lesions, a high false-positive rate was observed. Therefore, they stated that NIRF imaging using ICG based on the EPR effect is not satisfactory for the detection of ovarian cancer metastases.

Intra-Operative Anatomy Navigation during Minimally Invasive Surgery:

Schols et al (2015) stated that NIRF imaging, using contrast agents with fluorescent characteristics in the near-infrared (NIR: 700 to 900 nm) window, is considered to possess great potential for clinical practice in the future of minimally invasive surgery (MIS), given its capacity for intra-operative, real-time anatomical navigation, and identification. These researchers provided an overview of the literature concerning the current and potential future applications of fluorescence imaging in supporting anatomical guidance during MIS, and thereby guiding future research. A systematic literature search was performed in the PubMed and Embase databases. All identified articles were screened and checked for eligibility by 2 authors. In addition, literature was sought by screening references of eligible articles. After administration of a fluorescent dye (e.g., ICG), NIRF imaging can be helpful to improve the visualization of vital anatomical structures during MIS. Extra-hepatic bile ducts, arteries, ureters, sentinel lymph nodes, and lymph vessels have successfully been identified using NIRF imaging. A uniform approach regarding timing and route of dye administration has not yet been established. Optimization of
both imaging systems and fluorescent dyes is needed to improve current shortcomings. New pre-clinical dyes are considered for optimization of NIRF imaging. The authors concluded that future implementation of new intra-operative optical methods, such as NIRF, could significantly contribute to intra-operative anatomy navigation and facilitate critical decision-making in MIS. Moreover, they stated that further research (i.e., large multi-center randomized controlled trials) is needed to establish the true value of this innovative optical imaging technique in standard clinical practice.

*Lymphatic Imaging in Lymphangiomatosis:*

Rasmussen et al (2015) stated that lymphangiomatosis is a rare disorder of the lymphatic system that can impact the dermis, soft tissue, bone, and viscera and can be characterized by lymphangiomas, swelling, and chylous discharge. Whether disordered lymphangiogenesis in lymphangiomatosis affects the function and anatomy of the entire systemic lymphatic circulation or is localized to specific sites is not fully known. These researchers reported the case of a 35-year-old Caucasian female diagnosed with whole-body lymphangiomatosis at 2 months of age and who continued to present with progressive disease was imaged with NIRF lymphatic imaging. While the peripheral lymphatics in the extremities appeared largely normal compared to prior studies, these investigators observed tortuous lymphatic vessels, fluorescence drainage from the peripheral lymphatics into lymphangiomas, and extensive dermal lymphatics in the left thigh and inguinal regions where the subject had previously had surgical assaults, potentially indicating defective systemic lymphangiogenesis. The authors concluded that further research into anatomical and functional lymphatic changes associated with the progression and treatment of lymphangiomatosis could aid in understanding the pathophysiology of the disease as well as point to treatment strategies.

*Mapping of Microvascular Circulation in Ischemic Diseases:*
Namikawa and colleagues (2015) noted that NIRF imaging has better tissue penetration, allowing for the effective rejection of excitation light and detection deep inside organs. Indocyanine green generates NIRF after illumination by an NIR ray, enabling real-time intra-operative visualization of superficial lymphatic channels and vessels transcutaneously. The HyperEye Medical System (HEMS) can simultaneously detect NIR rays under room light to provide color imaging, which enables visualization under bright light. Thus, NIRF imaging using ICG can provide for excellent diagnostic accuracy in detecting SLNs in cancer and microvascular circulation in various ischemic diseases, to assist surgeons with intra-operative decision-making. Including HEMS in this system could further improve the SLN mapping and intra-operative identification of blood supply in reconstructive organs and ischemic diseases, making it more attractive than conventional imaging. Moreover, the development of new laparoscopic imaging systems equipped with NIR will allow fluorescence-guided surgery in a minimally invasive setting. The authors concluded that future directions, including the conjugation of NIR fluorophores to target specific cancer markers might be realistic technology with diagnostic and therapeutic benefits.

**Mapping of Sentinel Lymph Nodes in Endometrial Cancer:**

In a pilot study, Plante and associates (2015) reported their initial experience with ICG for sentinel lymph node (SLN) mapping in cervical and endometrial cancer using a new endoscopic fluorescence imaging system. These researchers reviewed all patients who underwent primary surgery for early-stage endometrial and cervical carcinoma with SLN mapping using fluorescence imaging followed by pelvic lymphadenectomy from February to July 2014. Intra-cervical injection of ICG at 3 and 9 o'clock was performed in all cases; SLNs were ultra-staged on final pathology. Sensitivity and specificity values were calculated. A total of 50 patients were included in the study (42 endometrial and 8 cervical cancers). The median age was 62 (24 to 88) years and median BMI was 29 (19 to 56). The median SLN count was 3.1 (0 to 7) and
median lymph node count was 15 (2 to 37). The overall and bilateral detection rate was 96 % (48/50) and 88 % (44/50). Positive SLNs were identified in 22 % of patients (11/50), including 8 isolated tumor cells (ITC), 2 micro‐metastasis and 1 macro‐metastasis. There was 1 side‐specific false negative case. Sensitivity, specificity and NPV were 93.3 %, 100 % and 98.7 %, per side, respectively. Para‐aortic node dissection was performed in 22 % of cases. Two had para‐aortic node metastasis both in patients with positive pelvic SLN. There were no allergic reactions to the ICG. The authors concluded that based on their experience in this pilot study, NIRF imaging with ICG is an excellent and safe tracer modality for SLN mapping with a very high overall (96 %) and bilateral (88 %) detection rate. The findings of this pilot study need to be validated by well‐deigned studies.

An UpToDate review on “Endometrial carcinoma: Pretreatment evaluation, staging, and surgical treatment” (Plaxe, 2015) states that “One of the most important prognostic factors for endometrial carcinoma is the presence of extrauterine disease, particularly pelvic and paraaortic lymph node metastases. The approach to lymph node assessment is controversial, particularly in women presumed to have early stage disease .... Sentinel lymph node biopsy for endometrial carcinoma is still investigational. A meta‐analysis of 26 studies including 1,101 sentinel node procedures found a sensitivity of 93 % for the detection of lymph node metastases in women with endometrial carcinoma. According to the sentinel lymph node hypothesis, tumor cells migrate from a primary tumor and colonize one or a few lymph nodes (i.e., the sentinel lymph node) before involving other lymph nodes. Peritumoral injection of a dye or tracer permits identification of a sentinel lymph node in most patients, and its status accurately predicts the status of the remaining regional nodes. The site of injection of the tracer for endometrial carcinoma is controversial. Studies have evaluated cervical, subserosal, and hysteroscopically‐guided endometrial injection. The meta‐analysis of 26 studies described above found that pericervical injection was associated with a significantly increased rate of detecting any
sentinel node and that hysteroscopic injection was associated with a significantly decreased detection rate”. This review does not mention near-infrared fluorescence imaging as a management tool.

Furthermore, National Comprehensive Cancer Network’s clinical practice guideline on “Endometrial carcinoma” (Version 2.2015) states that “The role of SLN mapping is currently being evaluated. No prospective randomized trials have been reported that evaluated this technique in endometrial cancer”.

**Diagnosis of Rheumatoid Arthritis:**

Krohn and colleagues (2015) stated that near-infrared fluorescence optical imaging (FOI) is a novel imaging technology in the detection and evaluation of different arthritides. Fluorescence optical imaging was validated in comparison to magnetic resonance imaging (MRI), grey-scale ultrasonography (GSUS), and power Doppler ultrasonography (PDUS) in patients with early rheumatoid arthritis (RA). Hands of 31 patients with early RA were examined by FOI, MRI, and US. In each modality, synovitis of the wrist, metacarpophalangeal joints (MCP) 2-5, and proximal interphalangeal joints (PIP) 2-5 were scored on a 4-point scale (0 to 3). Sensitivity and specificity of FOI were analyzed in comparison to MRI and US as reference methods, differentiating between 3 phases of FOI enhancement (P1-P3). Intraclass correlation coefficients (ICC) were calculated to evaluate the agreement of FOI with MRI and US. A total of 279 joints (31 wrists, 124 MCP and 124 PIP joints) were evaluated. With MRI as the reference method, overall sensitivity/specificity of FOI was 0.81/0.00, 0.49/0.84, and 0.86/0.38 for wrist, MCP, and PIP joints, respectively. Under application of PDUS as reference, sensitivity was even higher, while specificity turned out to be low, except for MCP joints (0.88/0.15, 0.81/0.76, and 1.00/0.27, respectively). P2 appeared to be the most sensitive FOI phase, while P1 showed the highest specificity. The best agreement of FOI was shown for PDUS, especially with regard to MCP and PIP joints (ICC of 0.57 and 0.53, respectively), while correlation with MRI was
slightly lower. The authors concluded that FOI remains an interesting diagnostic tool for patients with early RA, although this study revealed limitations concerning the detection of synovitis. They stated that further research is needed to evaluate its full diagnostic potential in rheumatic diseases.

**Evaluation of Coronary Atherosclerosis:**

Verjans and associates (2016) examined if ICG-enhanced NIRF imaging can illuminate high-risk histologic plaque features of human carotid atherosclerosis, and in coronary atheroma of living swine, using intra-vascular NIRF- OCT imaging. A total of 8 patients were enrolled in the BRIGHT-CEA (Indocyanine Green Fluorescence Uptake in Human Carotid Artery Plaque) trial; 5 patients were injected intravenously with ICG 99 ± 25 mins before clinically indicated carotid endarterectomy; 3 saline-injected endarterectomy patients served as control subjects. Excised plaques underwent analysis by intra-vascular NIRF-OCT, reflectance imaging, microscopy, and histopathology. Next, following ICG intravenous injection, in-vivo intra-coronary NIRF-OCT and intra-vascular ultrasound imaged 3 atheroma-bearing coronary arteries of a diabetic, cholesterol-fed swine. Indocyanine green was well-tolerated; no adverse clinical events occurred up to 30 days post-injection. Multi-modal NIRF imaging including intra-vascular NIRF-OCT revealed that ICG accumulated in all endarterectomy specimens. Plaques from saline-injected control patients exhibited minimal NIRF signal. In the swine experiment, intra-coronary NIRF-OCT identified ICG uptake in all intra-vascular ultrasound-identified plaques in-vivo. On detailed microscopic evaluation, ICG localized to plaque areas exhibiting impaired endothelial integrity, including disrupted fibrous caps, and within areas of neovascularization. Within human plaque areas of endothelial abnormality, ICG was spatially related to localized zones of plaque macrophages and lipid, and, notably, intra-plaque hemorrhage. The authors concluded that the findings of this study demonstrated that ICG targets human plaques exhibiting endothelial abnormalities and provided new insights into its targeting mechanisms in clinical and experimental atheroma. They stated that intra-coronary
NIRF-OCT of ICG may offer a novel, clinically translatable approach to image pathobiological aspects of coronary atherosclerosis.

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<th>CPT Codes / HCPCS Codes / ICD-10 Codes</th>
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<td>Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by &quot;+&quot;:</td>
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**ICD-10 codes will become effective as of October 1, 2015:**

Near-infrared vascular imaging systems (e.g., AccuVein AV300 or VeinViewer) for guiding vascular access:

CPT codes not covered for indications listed in the CPB:

<table>
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<th>CPT Code</th>
<th>Description</th>
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<td>0287T</td>
<td>Near-infrared guidance for vascular access requiring real-time digital visualization of subcutaneous vasculature for evaluation of potential access sites and vessel patency</td>
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**Near-infrared fluorescence imaging:**

No specific code

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

<table>
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<th>Code</th>
<th>Description</th>
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<tr>
<td>C00.0</td>
<td>Neoplasms [detection of tumor angiogenesis and monitoring of response to anti tumor vasculature therapy]</td>
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<tr>
<td>I70.0</td>
<td>Atherosclerosis [identification of vulnerable atherosclerotic plaques]</td>
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The above policy is based on the following references:

**Near-Infrared Vascular Imaging:**


Near-Infrared Fluorescence Imaging:


8. Plaxe SC. Endometrial carcinoma: Pretreatment evaluation, staging, and surgical treatment. UpToDate Inc., Waltham, MA. Last reviewed August 2015.


Amendment to
Aetna Clinical Policy Bulletin Number: 0846
Near-Infrared Vascular Imaging and Near-Infrared Fluorescence Imaging

There are no amendments for Medicaid.