Clinical Policy Bulletin:  
Near-Infrared Vascular Imaging and Near-Infrared Fluorescence Imaging  
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Policy

Aetna considers the use of near-infrared vascular imaging systems (e.g., AccuVein AV300 or VeinViewer) for 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 tumor angiogenesis and monitoring of response to anti-tumor vasculature therapy
- Facilitation of selective arterial clamping during partial nephrectomy
- Identification of vulnerable atherosclerotic plaques
- Navigation of laparoscopic anatomy during gastro-intestinal surgery.

See also CPB 0796 - Near-Infrared (NIR) Spectroscopy and CPB 111 - Indocyanine Green Angiography.

Background

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
In near-irreversible vascular imaging and near-infrared fluorescence imaging (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.

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 (2013) 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-risk 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 vascularization 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 superfamily, 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 prokaryotic 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.

**CPT Codes / HCPCS Codes / ICD-9 Codes**

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

No specific code
The above policy is based on the following references:
