

OMNIBUS CODES

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COVERAGE SUMMARY

All CPT/HCPCS codes/services addressed in this policy are noted in the table below. Click on the code to be directed to the full coverage rationale and clinical evidence applicable to each of the listed procedures.

Code	Description	Conclusion
0054T	Computer-assisted musculoskeletal surgical navigational orthopedic procedure, with image-guidance based on fluoroscopic images (List separately in addition to code for primary procedure)	Unproven
0055T	Computer-assisted musculoskeletal surgical navigational orthopedic procedure, with image-guidance based on CT/MRI images (List separately in addition to code for primary procedure)	Unproven
0085T	Breath test for heart transplant rejection	Unproven
0100T	Placement of a subconjunctival retinal prosthesis receiver and pulse generator, and implantation of intra-ocular retinal electrode array, with vitrectomy	Unproven
0103T	Holotranscobalamin, quantitative	Unproven

Code	Description	Conclusion
0174T	Computer-aided detection (CAD) (computer algorithm analysis of digital image data for lesion detection) with further physician review for interpretation and report, with or without digitization of film radiographic images, chest radiograph(s), performed concurrent with primary interpretation (List separately in addition to code for primary procedure)	Unproven
0175T	Computer-aided detection (CAD) (computer algorithm analysis of digital image data for lesion detection) with further physician review for interpretation and report, with or without digitization of film radiographic images, chest radiograph(s), performed remote from primary interpretation	Unproven
0182T	High dose rate electronic brachytherapy, per fraction	Proven for breast cancer; unproven for nonmelanoma skin cancer
0205T	Intravascular catheter-based coronary vessel or graft spectroscopy (e.g., infrared) during diagnostic evaluation and/or therapeutic intervention including imaging supervision, interpretation, and report, each vessel (List separately in addition to code for primary procedure)	Unproven
0206T	Computerized database analysis of multiple cycles of digitized cardiac electrical data from two or more ECG leads, including transmission to a remote center, application of multiple nonlinear mathematical transformations, with coronary artery obstruction severity assessment.	Unproven
0207T	Evacuation of meibomian glands, automated, using heat and intermittent pressure, unilateral	Unproven
0223T	Acoustic cardiography, including automated analysis of combined acoustic and electrical intervals; single, with interpretation and report	Unproven
0224T	Acoustic cardiography, including automated analysis of combined acoustic and electrical intervals; multiple, including serial trended analysis and limited reprogramming of device parameter - AV or VV delays only, with interpretation and report	Unproven
0225T	Acoustic cardiography, including automated analysis of combined acoustic and electrical intervals; multiple, including serial trended analysis and limited reprogramming of device parameter - AV and VV delays, with interpretation and report	Unproven
0233T	Skin advanced glycation end products (AGE) measurement by multi-wavelength fluorescent spectroscopy	Unproven
0239T	Bioimpedance Spectroscopy (SEAC SFB3, Impedimed)	Unproven
0243T	Intermittent measurement of wheeze rate for bronchodilator or bronchial-challenge diagnostic evaluation(s), with interpretation and report	Unproven
0244T	Continuous measurement of wheeze rate during treatment assessment or during sleep for documentation of nocturnal wheeze and cough for diagnostic evaluation 3 to 24 hours, with interpretation and report	Unproven

Code	Description	Conclusion
0263T	Intramuscular autologous bone marrow cell therapy, with preparation of harvested cells, multiple injections, one leg, including ultrasound guidance, if performed; complete procedure including unilateral or bilateral bone marrow harvest	Unproven
0264T	Intramuscular autologous bone marrow cell therapy, with preparation of harvested cells, multiple injections, one leg, including ultrasound guidance, if performed; complete procedure excluding bone marrow harvest	Unproven
0265T	Intramuscular autologous bone marrow cell therapy, with preparation of harvested cells, multiple injections, one leg, including ultrasound guidance, if performed; unilateral or bilateral bone marrow harvest only for intramuscular autologous bone marrow cell therapy	Unproven
0266T	Implantation or replacement of carotid sinus baroreflex activation device; total system (includes generator placement, unilateral or bilateral lead placement, intra-operative interrogation, programming, and repositioning, when performed)	Unproven
0267T	Implantation or replacement of carotid sinus baroreflex activation device; lead only, unilateral (includes intra-operative interrogation, programming, and repositioning, when performed)	Unproven
0268T	Implantation or replacement of carotid sinus baroreflex activation device; pulse generator only (includes intra-operative interrogation, programming, and repositioning, when performed)	Unproven
0269T	Revision or removal of carotid sinus baroreflex activation device; total system (includes generator placement, unilateral or bilateral lead placement, intra-operative interrogation, programming, and repositioning, when performed)	Refer to Coverage Rationale and Clinical Evidence
0270T	Revision or removal of carotid sinus baroreflex activation device; lead only, unilateral (includes intra-operative interrogation, programming, and repositioning, when performed)	Refer to Coverage Rationale and Clinical Evidence
0271T	Revision or removal of carotid sinus baroreflex activation device; pulse generator only (includes intra-operative interrogation, programming, and repositioning, when performed)	Refer to Coverage Rationale and Clinical Evidence
0272T	Interrogation device evaluation (in person), carotid sinus baroreflex activation system, including telemetric iterative communication with the implantable device to monitor device diagnostics and programmed therapy values, with interpretation and report (e.g., battery status, lead impedance, pulse amplitude, pulse width, therapy frequency, pathway mode, burst mode, therapy start/stop times each day)	Unproven

Code	Description	Conclusion
0273T	Interrogation device evaluation (in person), carotid sinus baroreflex activation system, including telemetric iterative communication with the implantable device to monitor device diagnostics and programmed therapy values, with interpretation and report (e.g., battery status, lead impedance, pulse amplitude, pulse width, therapy frequency, pathway mode, burst mode, therapy start/stop times each day); with programming	Unproven
0281T	Percutaneous transcatheter closure of the left atrial appendage with implant, including fluoroscopy, transseptal puncture, catheter placement(s), left atrial angiography, left atrial appendage angiography, radiological supervision and interpretation	Unproven
0286T	Near-infrared spectroscopy studies of lower extremity wounds (e.g., for oxyhemoglobin measurement)	Unproven
0287T	Near-infrared guidance for vascular access requiring real-time digital visualization of subcutaneous vasculature for evaluation of potential access sites and vessel patency	Unproven
0288T	Anoscopy with delivery of thermal energy to the muscle of anal canal (e.g., for fecal incontinence)	Unproven
0291T	Intravascular optical coherence tomography (coronary native vessel or graft) during diagnostic evaluation and/or therapeutic intervention, including imaging supervision, interpretation, and report; initial vessel (List separately in addition to primary procedure)	Unproven
0292T	Each additional vessel (List separately in addition to primary procedure)	Unproven
0293T	Insertion of left atrial hemodynamic monitor; complete system, includes implanted communication module and pressure sensor lead in left atrium including transseptal access, radiological supervision and interpretation, and associated injection procedures, when performed	Unproven
0294T	Pressure sensor lead at time of insertion of pacing cardioverter-defibrillator pulse generator including radiological supervision and interpretation and associated injection procedures, when performed (List separately in addition to code for primary procedure)	Unproven
0301T	Destruction/reduction of malignant breast tumor with externally applied focused microwave, including interstitial placement of disposable catheter with combined temperature monitoring probe and microwave focusing sensocatheter under ultrasound thermotherapy guidance	Unproven
0302T	Insertion or removal and replacement of intracardiac ischemia monitoring system including imaging supervision and interpretation when performed and intra-operative interrogation and programming when performed; complete system (includes device and electrode)	Unproven
0303T	Insertion or removal and replacement of intracardiac ischemia monitoring system including imaging supervision and interpretation when performed and intra-operative interrogation and programming when performed; electrode only	Unproven

Code	Description	Conclusion
0304T	Insertion or removal and replacement of intracardiac ischemia monitoring system including imaging supervision and interpretation when performed and intra-operative interrogation and programming when performed; device only	Unproven
0305T	Programming device evaluation (in person) of intracardiac ischemia monitoring system with iterative adjustment of programmed values, with analysis, review, and report	Unproven
0306T	Interrogation device evaluation (in person) of intracardiac ischemia monitoring system with analysis, review, and report	Unproven
0307T	Removal of intracardiac ischemia monitoring device	Refer to coverage regarding complications
0319T	Insertion or replacement of subcutaneous implantable defibrillator system with subcutaneous electrode	Unproven
0320T	Insertion of subcutaneous defibrillator electrode	Unproven
0321T	Insertion of subcutaneous implantable defibrillator pulse generator only with existing subcutaneous electrode	Unproven
0322T	Removal of subcutaneous implantable defibrillator pulse generator only	Unproven
0323T	Removal of subcutaneous implantable defibrillator pulse generator with replacement of subcutaneous implantable defibrillator pulse generator only	Unproven
0324T	Removal of subcutaneous defibrillator electrode	Unproven
0325T	Repositioning of subcutaneous implantable defibrillator electrode and/or pulse generator	Unproven
0326T	Electrophysiologic evaluation of subcutaneous implantable defibrillator (includes defibrillation threshold evaluation, induction of arrhythmia, evaluation of sensing for arrhythmia termination, and programming or reprogramming of sensing or therapeutic parameters)	Unproven
0327T	Interrogation device evaluation (in person) with analysis, review and report, includes connection, recording and disconnection per patient encounter; implantable subcutaneous lead defibrillator system	Unproven
0328T	Programming device evaluation (in person) with iterative adjustment of the implantable device to test the function of the device and select optimal permanent programmed values with analysis; implantable subcutaneous lead defibrillator system	Unproven
0330T	Tear film imaging, unilateral or bilateral, with interpretation and report	Unproven
0331T	Myocardial sympathetic innervation imaging, planar qualitative and quantitative assessment	Unproven
0332T	Myocardial sympathetic innervation imaging, planar qualitative and quantitative assessment; with tomographic SPECT (For myocardial infarct avid imaging, see 78466, 78468, 78469)	Unproven
0335T	Extra-osseous subtalar joint implant for talotarsal stabilization	Unproven

Code	Description	Conclusion
0338T	Transcatheter renal sympathetic denervation, percutaneous approach including arterial puncture, selective catheter placement(s) renal artery (ies), fluoroscopy, contrast injection(s), intraprocedural roadmapping and radiological supervision and interpretation, including pressure gradient measurements, flush aortogram and diagnostic renal angiography when performed; unilateral	Unproven
0339T	Transcatheter renal sympathetic denervation, percutaneous approach including arterial puncture, selective catheter placement(s) renal artery (ies), fluoroscopy, contrast injection(s), intraprocedural roadmapping and radiological supervision and interpretation, including pressure gradient measurements, flush aortogram and diagnostic renal angiography when performed; bilateral	Unproven
0340T	Ablation, pulmonary tumor(s), including pleura or chest wall when involved by tumor extension, percutaneous, cryoablation, unilateral, includes imaging guidance	Unproven
0341T	Quantitative pupillometry with interpretation and report, unilateral or bilateral	Unproven
0346T	Ultrasound, elastography (List separately in addition to code for primary procedure)	Unproven
0347T	Placement of interstitial device(s) in bone for radiostereometric analysis (RSA)	Unproven
0348T	Radiologic examination, radiostereometric analysis (RSA); spine, (includes, cervical, thoracic and lumbosacral, when performed)	Unproven
0349T	Radiologic examination, radiostereometric analysis (RSA); spine, (includes, cervical, thoracic and lumbosacral, when performed) upper extremity(ies), (includes shoulder, elbow and wrist, when performed)	Unproven
0350T	Radiologic examination, radiostereometric analysis (RSA); spine, (includes, cervical, thoracic and lumbosacral, when performed) lower extremity(ies), (includes hip, proximal femur, knee and ankle, when performed)	Unproven
0351T	Optical coherence tomography of breast or axillary lymph node, excised tissue, each specimen; real time intraoperative	Unproven
0352T	Optical coherence tomography of breast or axillary lymph node, excised tissue, each specimen; real time intraoperative interpretation and report, real time or referred	Unproven
0353T	Optical coherence tomography of breast, surgical cavity; real time intraoperative	Unproven
0354T	Optical coherence tomography of breast, surgical cavity; real time intraoperative interpretation and report, real time or referred	Unproven
0356T	Insertion of drug-eluting implant (including punctual dilation and implant removal when performed) into lacrimal canaliculus, each	Unproven

Code	Description	Conclusion
0358T	Bioelectrical impedance analysis whole body composition assessment, supine position, with interpretation and report	Unproven
20985	Computer-assisted surgical navigational procedure for musculoskeletal procedures, image-less	Unproven
28446	Open osteochondral autograft, talus (includes obtaining graft[s])	Unproven
29799	Unlisted procedure – Kinesio taping	Unproven
30999	Unlisted procedure, nose (Rhinophototherapy, intranasal application of ultraviolet and visible light, bilateral)	Unproven
31634	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with balloon occlusion, with assessment of air leak, with administration of occlusive substance (e.g., fibrin glue), if performed	Unproven
31647	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with balloon occlusion, when performed, assessment of air leak, airway sizing, and insertion of bronchial valve(s), initial lobe	Unproven
31648	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with removal of bronchial valve(s), initial lobe	Unproven
31649	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with removal of bronchial valve(s), each additional lobe (List separately in addition to code for primary procedure)	Unproven
31651	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with balloon occlusion, when performed, assessment of air leak, airway sizing, and insertion of bronchial valve(s), each additional lobe (List separately in addition to code for primary procedure[s])	Unproven
43206	Esophagoscopy, flexible, transoral; with optical endomicroscopy	Unproven
43252	Esophagogastroduodenoscopy, flexible, transoral; with optical endomicroscopy	Unproven
48160	Pancreatectomy, total or subtotal, with autologous transplantation of pancreas or pancreatic islet cells	Proven
48999	Unlisted procedure, pancreas	Proven in certain circumstances
53855	Insertion of a temporary prostatic urethral stent, including urethral measurement	Unproven
60659	Unlisted laparoscopy procedure, endocrine system	Proven in certain circumstances
64999	Unlisted procedure, Nervous system	Proven in certain circumstances
76120	Cineradiography/videoradiography, except where specifically included	Unproven
76125	Cineradiography/videoradiography to complement routine examination (List separately in addition to code for primary procedure)	Unproven
76496	Unlisted fluoroscopic procedure (e.g., diagnostic, interventional)	Unproven
76499	Unlisted diagnostic radiographic procedure	Unproven/Proven

Code	Description	Conclusion
77424	Intraoperative radiation treatment delivery, x-ray, single treatment session	Proven for breast cancer; unproven for nonmelanoma skin cancer
77425	Intraoperative radiation treatment delivery, electrons, single treatment session	Proven for breast cancer; unproven for nonmelanoma skin cancer
77469	Intraoperative radiation treatment management	Proven for breast cancer; unproven for nonmelanoma skin cancer
84999	Unlisted chemistry procedure [when used to report VeriStrat]	Unproven
85547	Mechanical fragility, RBC	Unproven
86849	Unlisted immunology procedure	Unproven
88375	Optical endomicroscopic image(s), interpretation and report, real-time or referred, each endoscopic session	Unproven
92499	Multifocal electroretinography (mfERG) and Pattern Electroretinography (PERG)	Unproven
93668	Peripheral arterial disease (PAD) rehabilitation, per session	Unproven
93799	Unlisted cardiovascular service or procedure	Unproven
94011	Measurement of spirometric forced expiratory flows in an infant or child through 2 years of age	Unproven
94012	Measurement of spirometric forced expiratory flows, before and after bronchodilator, in an infant or child through 2 years of age	Unproven
94013	Measurement of lung volumes (ie, functional residual capacity [FRC], forced vital capacity [FVC], and expiratory reserve volume [ERV]) in an infant or child through 2 years of age	Unproven
94799	Unlisted pulmonary service or procedure	Unproven
96902	Microscopic examination of hairs plucked or clipped by the examiner (excluding hair collected by the patient) to determine telogen and anagen counts, or structural hair shaft abnormality	Unproven
97139	Unlisted therapeutic procedure (specify) [when used to report Kinesio Taping]	Unproven
99174	Instrument-based ocular screening (eg, photoscreening, automated-refraction), bilateral	Proven in certain circumstances
G0341	Percutaneous islet cell transplant, includes portal vein catheterization and infusion	Unproven
G0342	Laparoscopy for islet cell transplant, includes portal vein catheterization and infusion	Unproven
G0343	Laparotomy for islet cell transplant, includes portal vein catheterization and infusion	Unproven
L3999	Upper limb orthotic, not otherwise specified [when used to report MyoPro™]	Unproven
L8605	Injectable bulking agent, dextranomer/hyaluronic acid copolymer implant, anal canal	Unproven
P2031	Hair analysis (excluding arsenic)	Unproven

Code	Description	Conclusion
P2033	Thymol turbidity, blood	Unproven
P2038	Blood Mucoprotein	Unproven
Q2026	Injection Radiesse 0.1ML	Proven in certain circumstances
Q2028	Injection, Sculptra, 0.5 mg	Proven in certain circumstances
Q4115	AlloSkin, per sq cm	Unproven
Q4123	AlloSkin RT, per sq cm	Unproven
Q4131	Epifix, per square centimeter	Unproven
Q4132	Grafix core, per square centimeter	Unproven
Q4133	Grafix prime, per square centimeter	Unproven
Q4134	Hmatrix, per square centimeter	Unproven
Q4135	Mediskin, per square centimeter	Unproven
Q4136	Ez-derm, per square centimeter	Unproven
Q4137	Amnioexcel or biodexcel, per square centimeter	Unproven
Q4138	Biodfence dryflex, per square centimeter	Unproven
Q4139	Amniomatrix or biodmatrix, injectable, 1 cc	Unproven
Q4140	Biodfence, per square centimeter	Unproven
Q4141	Alloskin ac, per square centimeter	Unproven
Q4142	Xcm biologic tissue matrix, per square centimeter	Unproven
Q4143	Repriza, per square centimeter	Unproven
Q4145	Epifix, injectable, 1 mg	Unproven
Q4146	Tensix, per square centimeter	Unproven
Q4147	Architect extracellular matrix, per square centimeter	Unproven
Q4148	Neox 1k, per square centimeter	Unproven
Q4149	Excellagen, 0.1 cc	Unproven
S2102	Islet cell tissue transplant from pancreas; allogeneic	Unproven
S3902	Ballistocardiogram	Unproven
S9025	Omnicrodiogram/cardiointegram	Unproven

COVERAGE RATIONALE AND CLINICAL EVIDENCE

Code	Description
0054T	Computer-assisted musculoskeletal surgical navigational orthopedic procedure, with image-guidance based on fluoroscopic images (List separately in addition to code for primary procedure)
0055T	Computer-assisted musculoskeletal surgical navigational orthopedic procedure, with image-guidance based on CT/MRI images (List separately in addition to code for primary procedure)
20985	Computer-assisted surgical navigational procedure for musculoskeletal procedures, image-less

Computer-assisted musculoskeletal surgical navigational for orthopedic procedures (CAOS) is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Conventional fluoroscopic guidance provides imaging in only one plane. Standard surgical techniques for joint replacement currently utilize intramedullary or extramedullary guides; computer-assisted navigation is proposed as an adjunct to conventional arthroplasty or as an alternative to existing fluoroscopic image guidance.

Navigation involves 3 steps: data acquisition, registration, and tracking.

1. Data Acquisition

Data can be acquired in three different ways, i.e. fluoroscopic, CT or MRI guided, or imageless systems. This data is then used for registration and tracking.

2. Registration

Registration refers to the ability of relating images (i.e., x-rays, CT, MRI or patients' 3-D anatomy) to the anatomical position in the surgical field. Registration techniques may require the placement of pins or "fiducial markers" in the target bone. A surface-matching technique can be used in which the shapes of the bone surface model generated from preoperative images are matched to surface data points collected during surgery.

3. Tracking

Tracking refers to the sensors and measurement devices that can provide feedback during surgery regarding the orientation and relative position of tools to bone anatomy. For example, optical or electromagnetic trackers can be attached to regular surgical tools, which can then provide real time information of the position and orientation of the tools' alignment with respect to the bony anatomy of interest.

The published, peer-reviewed scientific literature reveals few clinical trials that have compared the outcomes of computer-assisted navigation to conventional surgery, and whether or not the accuracy of computer-assisted systems improves functional outcomes. Most of the evidence for computer-assisted orthopedic surgery is in the form of case series, consisting of small patient populations and lack of controls.

U.S. Food and Drug Administration (FDA): The FDA regulates computer-assisted navigation systems as Class II devices.

Ankle, Foot, Shoulder

There are limited studies in the literature that address the use of computer assisted surgery for these body areas.

Hip/Pelvis

The majority of studies within the literature are prospective studies, small in sample size, lack the long-term follow-up to determine the safety of applying CAOS and have produced conflicting data regarding the efficacy of these applications when compared to conventional techniques. Of the 4 studies reviewed (Najarian, 2008; Kalteis, 2006; Parratte, 2007; Hsieh, 2006), all concluded that the use of computer-assisted navigation is a feasible tool to provide real-time image guidance for hip/pelvis procedures; however, it offers little additional benefit when the surgery is done by an experienced surgeon and requires a learning curve in terms of accuracy of use.

A meta-analysis by Gandhi et al. (2009) found 3 relevant studies documenting the efficacy of computer assisted hip surgery however these all had small sample sizes. The authors found that while computer navigation appears promising for alignment of the acetabular cup, further studies are needed to evaluate the impact of this on clinical outcomes, survival and quality of life.

Knee

Yaffee and colleagues (2013) reported the results of a study that explored whether differences in clinical, functional, or radiographic outcomes existed at 5-year follow-up between subjects who underwent computer-assisted or manual TKA. At the five-year follow-up, 63 participants (34 from the manual group and 29 from the computer-assisted group) were evaluated. No statistically significant differences were found in the Knee Society knee, function score, range of motion pain score or UCLA activity score between the 2 groups.

In 2011, Barrett and colleagues, in a multicenter, prospectively randomized trial, compared the radiographic alignment of imageless computer-assisted surgery with conventional instrumentation in individuals undergoing TKA. A total of 208 subjects were enrolled in the study. The

preoperative surgical plan was compared to postoperative 2-dimensional radiographic alignment measured by a blinded reviewer. The authors found that the use of computer assisted surgery did not offer a clinically meaningful improvement in postoperative alignment, clinical, functional, or safety outcomes compared with conventional TKA.

Hayes (2006) conducted a search of the peer-reviewed medical literature to evaluate imageless computer-assisted surgical navigation for total knee replacement surgery. They concluded that results of some studies suggest computer-assisted navigation of knee surgery leads to statistically significant improvements in the placement and alignment of implanted components. However, these improvements were usually small, and only three studies assessed functional outcomes to determine if the improvements in accuracy of implantation provided improved clinical outcomes. Further studies with prolonged follow-up and measurement of functional outcomes are needed to determine if this navigation provides clinically significant benefits for patients.

The largest study, a meta analysis by Bauwens et al. (2007), of 33 studies (11 randomized trials) involving 3423 patients were reviewed comparing navigated and conventional knee arthroplasty and concluded that the navigated knee replacement provided few advantages over conventional surgery based on radiographic evidence; therefore, its clinical benefits are unclear and remain to be defined on a larger scale.

These findings were confirmed by Brin et al. (2011) in a meta-analysis of 23 papers. The authors found that while imageless navigation improves component orientation and postoperative limb alignment, further studies are needed to evaluate the clinical benefits.

Cheng et al. (2010) conducted a meta-analysis of 40 studies (29 quasi-randomized/ randomized controlled trials and 11 prospective studies) and found that imageless computer-assisted navigation systems improve lower limb axis and component orientation in the coronal and sagittal planes, but not the rotational alignment in total knee arthroplasty. Further multiple-center clinical trials with long-term follow-up are needed to determine differences in the clinical and functional outcomes of knee arthroplasties performed using computer-assisted techniques.

A study by Hasegawa et al. (2010) compared standard approach (jig-based) total knee arthroplasty (TKA) with computer-assisted navigation in 100 equally divided patients. The authors found no significant differences between the procedures in the frontal and sagittal planes as well as rotational alignment of the femoral or tibial components.

The American Association of Hip and Knee Surgeons (AAHKS) Position Statement (2008) states that longer and more comprehensive follow-up CAOS studies are needed to better understand the indications, limitations and complications of this surgical technology. Future studies will also determine if the short term improvements reported from CAOS can increase joint implant longevity and improve overall outcomes for patients undergoing total hip and knee replacement surgery.

Spine

There are limited studies in the literature that address the use of computer assisted surgery on the spine. Specific patient selection criteria have not been determined. While the literature suggests that the additional radiographic assistance may improve intra-operative realignment for the insertion of instrumentation or other surgical corrective measures, the long-term impact of utilizing these radiation enhanced techniques has not been determined in relation to clinical outcomes.

In summary, computer-assisted surgery is a complex process that is currently being introduced into the field of orthopedic surgery. Some of the proposed benefits of this emerging technology include intraoperative flexibility, accurate alignment of components and soft tissue balancing. Obstacles to computer-assisted surgery include increased operating time, additional exposure to ionizing radiation, and extensive training of the surgical team. At present, there is insufficient

evidence to allow strong scientific conclusions regarding the superiority or added value of computer assisted technologies for orthopedic surgery compared to conventional methods. Researchers have assessed only short-term outcomes; long-term effectiveness has not been demonstrated. Further studies are needed to determine if computer-assisted navigational systems for orthopedic procedures improve functional outcomes such as decreased pain and disability, and improve range of motion, joint function, and flexibility.

The clinical evidence was reviewed in May 2014 with no additional information identified that would change the conclusion.

Reference(s):

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Brin YS, Nikolaou VS, Joseph L, et al. Imageless computer assisted versus conventional total knee replacement. A Bayesian meta-analysis of 23 comparative studies. *Int Orthop*. 2011 Mar;35(3):331-9. Epub 2010 Apr 8.

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Kalteis T, Handel M, Balthis H, et al. Imageless navigation for insertion of the acetabular component in total hip arthroplasty: is it as accurate as CT-based navigation? *J Bone Joint Surg Br*. 2006 Feb;88(2):163-7.

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Parratte S, Argenson JN. Validation and usefulness of a computer-assisted cup-positioning system in total hip arthroplasty. A prospective, randomized, controlled study. *J Bone Joint Surg Am*. 2007 Mar;89(3):494-9.

Yaffe M, Chan P, Goyal N et al. Computer-assisted Versus Manual TKA: No Difference in Clinical or Functional Outcomes at 5-year Follow-up. *Orthopedics* 2013; 36(5):e627-632.

Code	Description
0085T	Breath test for heart transplant rejection

Breath testing for a measure of heart transplant rejection is unproven and not medically necessary. There is insufficient evidence in the peer-reviewed clinical literature to support the use of a breath test measuring methylated alkanes to predict organ rejection in heart transplant patients.

Clinical Evidence

In a manufacturer-sponsored, multicenter case-series study, Phillips et al. (2004) evaluated 1061 breath volatile organic compounds (VOC) samples collected from 539 heart transplant recipients before scheduled endomyocardial biopsy. The results of the breath methylated alkane contour (BMAC) tests were compared to the results of endomyocardial biopsies to calculate test

sensitivity and specificity. The study concluded that a breath test for markers of oxidative stress was more sensitive (sensitivity 78.6%) and less specific (specificity 62.4%) for grade three heart transplant rejections than a biopsy reading by a site pathologist. A screening breath test could potentially identify transplant recipients at low risk of Grade 3 rejection and reduce the number of endomyocardial biopsies.

The Centers for Medicare and Medicaid Services (CMS) issued a National Coverage Determination (NCD) for the Heartsbreath test (Menssana Research Inc.) concluding that the available clinical evidence did not demonstrate that the test, which is intended to predict heart transplant rejection, actually improved health outcomes in Medicare beneficiaries. CMS also found that the evidence failed to adequately define the technical characteristics of the test. Heartsbreath is a noninvasive test that was granted a Humanitarian Device Exemption (HDE) by the Food and Drug Administration (FDA) in 2004. The FDA approved the test for use as an adjunct to, and not as a substitute for, endomyocardial biopsy. Specifically, Heartsbreath is indicated to assist in the diagnosis of grade 3 heart transplant rejection in patients who have received a heart transplant within the preceding year and an endomyocardial biopsy within the prior month (CMS, 2008).

The Heartsbreath test received FDA approval under the Humanitarian Device Exemption (HDE) program on February 24, 2004 (H030004). Additional information is available at: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cftopic/pma/pma.cfm?num=H030004>. Accessed June 9, 2014.

No professional society guidelines addressing this technology were identified.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

Centers for Medicare and Medicaid Services (CMS). [Decision Memo for Heartsbreath Test for Heart Transplant Rejection](#) (CAG-00394N). December 8, 2008. Accessed June 9, 2014.

Phillips M, Boehmer JP, Cataneo RN, et al. Heart allograft rejection: detection with breath alkanes in low levels (the HARDBALL study). *J Heart Lung Transplant*. 2004 Jun;23 (6):701-8.

Code	Description
0100T	Placement of a subconjunctival retinal prosthesis receiver and pulse generator, and implantation of intra-ocular retinal electrode array, with vitrectomy

The use of retinal prosthetic devices is unproven and not medically necessary for the treatment of retinal disease due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

The Argus® II Retinal Prosthesis System (Second Sight Medical Products, Inc.) is a retinal implant that requires use of an external device to provide electrical stimulation to the retina to induce some visual perception in blind individuals with severe to profound retinitis pigmentosa (RP).

The Argus II Retinal Prosthesis System received a Humanitarian Device Exemption (HDE) from the U.S. Food and Drug Administration (FDA) in February 2013. According to FDA documentation, the device is indicated for use in individuals with severe to profound retinitis pigmentosa who meet the following criteria: age 25 or older; with bare light or no light perception in both eyes; a previous history of useful form vision; aphakic or pseudophakic eyes; and who are willing and able to receive the recommended postimplant clinical follow-up, device fitting, and

visual rehabilitation. Eligibility determination requires that patients with no residual light perception undergo testing for evidence of intact inner-layer retinal function. The procedure description indicates that patients with phakic eyes have their natural lens removed during the implant procedure. The device is intended for use in one eye—the worse-seeing eye. The HDE approval required the company to conduct 2 post-approval studies, including an extended (10-year) follow-up of patients receiving the implant and a 5-year, prospective, multicenter study of the visual function, device reliability, and adverse events in patients receiving the implant.

See the following Web sites for more information:

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cftopic/pma/pma.cfm?num=H110002>

Accessed May 2014.

In a systematic review, Chuang et al. (2014) compared selected retinal implant models by examining publications describing five representative retinal prostheses: Argus II, Boston Retinal Implant Project, Epi-Ret 3, Intelligent Medical Implants (IMI) and Alpha-IMS (Retina Implant AG). Publications were analyzed using three criteria for interim success: clinical availability, vision restoration potential and long-term biocompatibility. Clinical availability: Argus II is the only device with FDA approval. Argus II and Alpha-IMS have both received the European CE Marking. All others are in clinical trials, except the Boston Retinal Implant, which is in animal studies. Vision restoration: resolution theoretically correlates with electrode number. Among devices with external cameras, the Boston Retinal Implant leads with 100 electrodes, followed by Argus II with 60 electrodes and visual acuity of 20/1262. Instead of an external camera, Alpha-IMS uses a photodiode system dependent on natural eye movements and can deliver visual acuity up to 20/546. Long-term compatibility: IMI offers iterative learning; Epi-Ret 3 is a fully intraocular device; Alpha-IMS uses intraocular photosensitive elements. The authors concluded that based on the review of these three criteria, Alpha-IMS is the most likely to achieve long-term success decades later, beyond current clinical availability.

As part of a phase 1/2 feasibility study, Dorn et al. (2013) investigated the ability of blind patients implanted with the Argus II retinal prosthesis system to detect the direction of a moving object. Twenty-eight blind patients (bare light perception or worse in both eyes) with retinitis pigmentosa were included in the study. Patients were tested with the system on, system off, and with the system on but the spatial information scrambled. Fifteen patients experienced a significant improvement in their ability to detect the direction of motion with the system turned on, 2 subjects did worse, and 11 subjects remained the same. Of the 15 better-performing subjects, 11 were available for follow-up testing, and 10 of them had significantly better performance with normal rather than with scrambled spatial information. The authors concluded that this study demonstrates that blind subjects implanted with the Argus II retinal prosthesis were able to perform a motion detection task they could not do with their native vision, confirming that electrical stimulation of the retina provides spatial information from synchronized activation of multiple electrodes. While the results of this study are promising, more research is needed regarding adverse events and improvement of visual functions with this device.

Rizzo et al. (2014) studied the anatomical and functional outcomes of Argus II Retinal Prosthesis System implantation in retinitis pigmentosa patients in 6 patients with a visual acuity no better than light perception. Implantation of the Argus II Retinal Prosthesis System was safely performed in all patients. One patient experienced postoperative elevation in intraocular pressure, which was controlled medically. In one patient, moderate detachment of the choroid occurred postoperatively, which resolved spontaneously. One patient withdrew from the study. Wound dehiscence, endophthalmitis, or retinal detachment was not observed. All patients were able to locate a bright light on the ceiling and a dark line on the floor after the surgery. Performance in square localization tests improved in 4 patients, and direction of motion improved in 3 patients. One patient achieved grating visual acuity. Goldmann visual field test results improved in all patients. The authors concluded that the patients showed an improvement in visual tasks after the surgery, and the device was well tolerated and functional over a 1-year follow-up period. According to the authors, a rigorous patient selection process is necessary to maximize patient compliance with the rigorous follow-up testing schedule and lengthy, difficult rehabilitation

process. While the results of this study are promising, prospective randomized studies with long-term follow-up are needed to evaluate the safety and efficacy of retinal prosthetic devices.

da Cruz et al. (2013) conducted a prospective, internally controlled, multicenter trial of the Argus II system that included 28 subjects with light perception vision who received a retinal implant. Patients completed a force choice letter identification tests and an open-choice word identification test. Letters (L, T, E, J, F, H, I, U) were correctly identified 72.3 ±24.6% of the time with the system on and 17.7 ±(12.9)% of the time with the system off. Letters (K, R, G, X, B, Y, S, P) were correctly identified 51.7 ± 28.9% of the time with the system on and 15.3 (7.4) % of the time with the system off. Letters (A, Z, Q, V, N, W, O, C, D, M) were correctly identified 55 ±27.4% and 11.8 ±10.7% of the time with the system on and off, respectively. Average implant duration was 19.9 months. The authors concluded that multiple blind subjects fitted with the Argus II system consistently identified letters and words using the device, indicating reproducible spatial resolution. According to the authors, this, in combination with stable, long-term function, represents significant progress in the evolution of artificial sight. The authors stated that it is not immediately clear how the performance of the controlled tasks identified in this study will translate directly into useful function in daily life, and this is being studied further.

Published peer-reviewed medical literature is limited regarding the use of retinal prosthetic devices. While the results of available studies are promising, more research is needed regarding adverse events and improvement of visual functions with this device.

Clinical trials of artificial retinal devices are currently ongoing including a 3-year observational study of a larger group of patients implanted with the Argus II Retinal Prosthesis System than was available in the premarket approval study. This study will gather information on the nature and rate of adverse events and, secondarily, visual function. See the following Web site for more information: <http://www.clinicaltrials.gov/ct2/show/NCT01490827> Accessed May 2014.

Reference(s):

Chuang AT, Margo CE, Greenberg PB. Retinal implants: a systematic review. Br J Ophthalmol. 2014 Jan 8. doi: 10.1136/bjophthalmol-2013-303708.

da Cruz L, Coley BF, Dorn J, et al.; Argus II Study Group. The Argus II epiretinal prosthesis system allows letter and word reading and long-term function in patients with profound vision loss. Br J Ophthalmol. 2013 May;97(5):632-6.

Dorn JD, Ahuja AK, Caspi A, et al. Argus II Study Group. The Detection of Motion by Blind Subjects With the Epiretinal 60-Electrode (Argus II) Retinal Prosthesis. JAMA Ophthalmol. 2013 Feb;131(2):183-9.

ECRI Institute. Product Brief. Argus II Retinal Prosthesis System (Second Sight Medical Products, Inc.) for Restoring Some Functional Vision in Cases of Retinitis Pigmentosa. April 2013.

Rizzo S, Belting C, Cinelli L, et al. The Argus II Retinal Prosthesis: Twelve-Month Outcomes from a Single-Study Center. Am J Ophthalmol. 2014 Feb 19. pii: S0002-9394(14)00103-2.

Code	Description
0103T	Holotranscobalamin, quantitative

Testing for vitamin B-12 deficiency with a quantitative Holotranscobalamin testing is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Vitamin B12 (i.e., cobalamin) is an essential vitamin that is required for one-carbon metabolism and cell division. Cobalamin deficiency can result from nutritional and/or dietary deficiencies. Holotranscobalamin (HoloTC) is the sum total of cobalamin (Cbl), known as vitamin B12, bound to transcobalamin (TC), the plasma protein responsible for transporting vitamin B12 to all cells of the body. The diagnosis of cobalamin deficiency has traditionally been based on low total serum cobalamin levels, typically less than 200 pg/ml in conjunction with clinical evidence of disease.

However, this laboratory test has been found to be poorly sensitive and poorly specific. Therefore, attention has turned to measuring metabolites of cobalamin a surrogate marker. There are limited studies in the literature that address the use of Holotranscobalamin to diagnose vitamin B-12 deficiency. No evidence has demonstrated how this testing may be used to improve health outcomes.

A systematic review by Hoey et al. (2009) assessed the effectiveness of biomarkers (serum and plasma total vitamin B-12, methylmalonic acid and total homocysteine response) of vitamin B-12 status and found insufficient data were available to determine the effectiveness of plasma Holotranscobalamin, which was measured in only one randomized controlled trial. Future trials should include low-dose vitamin B-12 in adults across the entire age spectrum and measure the Holotranscobalamin response to supplementation.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

Hoey L, Strain JJ, McNulty H. Studies of biomarker responses to intervention with vitamin B-12: a systematic review of randomized controlled trials. *Am J Clin Nutr.* 2009 Jun;89(6):1981S-1996S. Epub 2009 Apr 29.

Code	Description
0174T	Computer-aided detection (CAD) (computer algorithm analysis of digital image data for lesion detection) with further physician review for interpretation and report, with or without digitization of film radiographic images, chest radiograph(s), performed concurrent with primary interpretation (List separately in addition to code for primary procedure)
0175T	Computer-aided detection (CAD) (computer algorithm analysis of digital image data for lesion detection) with further physician review for interpretation and report, with or without digitization of film radiographic images, chest radiograph(s), performed remote from primary interpretation

Computer aided detection (CAD) of chest x-rays is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Computer-aided detection (CAD) has become one of the principal research areas in medical imaging and diagnostic radiology. It can be defined as diagnoses rendered by radiologists who utilize the output from computerized algorithm analyses of medical images as a second opinion in detecting lesions and in making diagnostic decisions.

de Hoop et al. (2010) assessed how computer-aided detection (CAD) affects reader performance in detecting early lung cancer on chest radiographs. A total of 46 individuals with 49 computed tomographically (CT)-detected and histologically proved lung cancers and 65 patients without nodules at CT were retrospectively included in the study. Chest radiographs were obtained within 2 months after screening CT. Four radiology residents and two experienced radiologists were asked to identify and localize potential cancers on the chest radiographs, first without and subsequently with the use of CAD software. The investigators concluded that the sensitivity of CAD in identifying lung cancers depicted with CT screening was similar to that of experienced radiologists. However, CAD did not improve cancer detection because, especially for subtle lesions, observers were unable to sufficiently differentiate true-positive from false-positive annotations.

The diagnostic utility of using computer-aided detection (CAD) systems with chest radiographs has not been demonstrated in the published peer-reviewed scientific literature. Large, well-

designed, controlled clinical trials comparing radiograph CAD results to additional manual radiologist review (i.e., second opinion) results or computed tomography (CT) results (with and without CT CAD) are needed to determine whether the addition of CAD improves the interpretation of chest radiographs and ultimately, has an impact on meaningful health outcomes. Furthermore, additional studies are needed to determine if early detection of lung cancer, by CAD of chest radiographs in comparison with other methods of detection, will lead to an improvement in life expectancy.

American College of Radiology (ACR) appropriateness criteria for screening for pulmonary metastases states that computer-aided detection (CAD) for pulmonary metastatic disease has been adapted to chest CT from applications for mammography. Although these programs are in their developmental phases, it has been suggested that CAD can be used as a second look after the radiologist has completed reviewing the study. These programs require more development and currently can only be used when there is limited breathing artifact and stable lung expansion. CAD is still in the experimental phase and currently has limited use in evaluating patients with pulmonary metastatic disease (Mohammed et al., 2010).

The American College of Chest Physicians (ACCP) does not address the use of computer-aided detection of chest x-rays for detection of lung cancer and/or lung cancer screenings in their guidelines on the diagnosis and management of lung cancer (ACCP, 2013).

In summary, while CAD for chest radiographs may be potentially useful in screening lung cancer, its clinical value needs to be established by Randomized Controlled Trials.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

Diagnosis and management of lung cancer, 3rd edition. American College of Chest Physicians evidence-based clinical practice guidelines. 2013

de Hoop B, De Boo DW, Gietema HA, et al. Computer-aided detection of lung cancer on chest radiographs: effect on observer performance. *Radiology*. 2010 Nov;257(2):532-40.

Mohammed TL, Chowdhry A, Reddy GP, et al.; Expert Panel on Thoracic Imaging. ACR Appropriateness Criteria® screening for pulmonary metastases. *J Thorac Imaging*. 2011 Feb;26(1):W1-3.

National Cancer Institute. Lung Cancer Screening PDQ. Last updated March 29, 2012. Available at: <http://www.cancer.gov/cancertopics/pdq/screening/lung/healthprofessional/allpages/print>. Accessed June 11, 2014.

Code	Description
0182T	High dose rate electronic brachytherapy, per fraction
77424	Intraoperative radiation treatment delivery, x-ray, single treatment session
77425	Intraoperative radiation treatment delivery, electrons, single treatment session
77469	Intraoperative radiation treatment management

High dose rate electronic brachytherapy is proven and medically necessary for the treatment of breast cancer.

High dose rate electronic brachytherapy is unproven and not medically necessary for the treatment of nonmelanoma (i.e., basal cell or squamous cell carcinomas) skin cancer. Additional studies with larger numbers of patients and longer follow-up are needed to confirm preliminary results.

High dose rate electronic brachytherapy may be covered for the treatment of certain facial nonmelanoma skin cancers when location can impact treatment outcomes. Requests for these

exceptions will be evaluated by an independent radiation oncologist. UnitedHealthcare will make a coverage decision based on this review.

Clinical Evidence

Breast Cancer

Vaidya et al. (2010) completed a multi-centered, non-blinded, randomized control trial that included 2,232 patients ages 45 and older, with early invasive ductal breast carcinoma suitable for excision who were undergoing breast conserving surgery. Specific population characteristics include median age of 63 years, tumor sizes of <1 cm in 36%, 1-2cm. in 50% and 14% were >than 2 cm. Most tumors were grade 1 (34%) or grade 2 (50%) with 15% being grade 3. Nodes were not involved in 83% of the sample. Nearly half of the patients (1113) were randomly allocated to targeted intraoperative radiotherapy using the Intrabeam system and the other group (1119 patients) were randomly allocated to external beam radiotherapy. A total of 996 patients completed the intraoperative radiotherapy portion of the trial with 854 (86%) receiving targeted therapy alone and 142 (14%) had targeted radiotherapy plus external beam radiotherapy. No significant difference in adverse events, complications or local recurrence were noted between the two groups. Four year follow up noted that for 739 patients at risk, there was no local recurrence in either group. The authors concluded that the targeted intraoperative radiotherapy approach was non-inferior in terms of efficacy of control and "might be adequate for selected patients".

Accelerated partial breast irradiation (APBI) may be used to deliver radiation to the tumor bed post-lumpectomy in eligible patients with breast cancer. Dooley et al. (2011) describe a lumpectomy procedure and examine patient, tumor and surgical characteristics from a prospective, multicenter study of electronic brachytherapy. Forty-four patients were treated with APBI using the Axxent® electronic brachytherapy system following lumpectomy. The prescription dose of 34 Gy in 10 fractions over 5 days was delivered in 42 of 44 patients. The authors concluded that early stage breast cancer can be treated with breast conserving surgery and APBI using electronic brachytherapy. Treatment was well tolerated, and these early outcomes were similar to the early outcomes with iridium-based balloon brachytherapy.

Mehta et al. (2010) completed a phase IV prospective, non-randomized trial of 44 patients to evaluate the safety and device effectiveness of the Axxent electronic brachytherapy system. The study evaluated 44 patients. The subjects were over 50 years of age, had completely resected invasive ductal carcinoma or ductal carcinoma in situ and negative microscopic margins of equal to or greater than 1 mm. The treatment was completed with a balloon applicator with treatments twice per day for 5 days. Treatment was successfully completed in 42/44 patients. All 44 patients were followed up at one month, 43/44 followed up to 6 months and 36 of the 44 patients completed follow up at 1 year. No tumor recurrences were reported up to 1 year. The infection rate was 11%. Cosmetic evaluation was rated as good or excellent (minimal or no identifiable effects of radiation). The authors concluded that electronic brachytherapy system performed as expected with similar acute toxicity profiles to other high rate approaches in patients with resected, early breast cancer with no serious acute toxicities or serious adverse events. The evidence demonstrates benefits of the therapy given the lack of need for external beam radiation and lack of need for special loading precautions or procedures. Additional patient benefits include decreased toxicity to surrounding tissue.

Patient selection criteria include low risk of recurrence (e.g., women >45 years of age, sentinel node negative, clear surgical margins, mass of < 3 cm for diagnosis with invasive ductal carcinoma or ductal carcinoma in situ). (American Society of Breast Surgeons 2008; Smith et al., 2009; Arthur et al., 2010).

Skin Cancer Bhatnagar (2013) reported clinical outcomes at 1 year or more after high-dose-rate (HDR) electronic brachytherapy (EBT) using surface applicators for the treatment of nonmelanoma skin cancer (NMSC). A total of 122 patients with 171 NMSC lesions were treated with EBT to a dose of 40Gy in eight fractions, delivered twice weekly. At followup, patients were

assessed for acute and late toxicities, cosmesis and local control. No recurrences were reported with a mean follow-up of 10 months. Follow-up data at 1 year or more were available for 46 lesions in 42 patients. Hypopigmentation (all Grade 1) was present in 5 (10.9%) of 46 lesions at 1 year. Other late effects at 1 year included dry desquamation, alopecia and rash dermatitis, which occurred in 1 (2.2%), 1 (2.2%) and 3 (6.5%) of 46 lesions, respectively. Cosmesis was excellent for 39 (92.9%) and good for 3 (7.1%) of the 42 evaluable lesions. This study is limited by lack of randomization and control and short-term follow-up.

Bhatnagar and Loper (2010) reported their initial experience with high dose rate (HDR) brachytherapy for treating nonmelanoma skin cancers (NMSC). Thirty-seven patients with 44 cutaneous malignancies were treated. Lesion locations included the nose (16), ear (5), scalp (5), face (14) and an extremity (4). Median follow-up was 4.1 months. No severe toxicities occurred. Cosmesis ratings were good to excellent for 100% of the lesions at follow-up. This study is limited by its retrospective design, small patient numbers and short-term follow-up.

NCCN guidelines on basal cell and squamous cell skin cancers do not specifically address electronic brachytherapy but state that some institutions are using brachytherapy for anatomically challenging sites, such as the nose. Because this technique requires special equipment and expertise, it is not widely used (NCCN, 2014b).

Clinical trial [NCT01016899](#) is ongoing.

Reference(s):

American College of Radiology. ACR/ASTRO Practice guideline for the performance of high-dose-rate brachytherapy. Revised 2010. Available at: http://www.acr.org/~media/ACR/Documents/PGTS/guidelines/High_Dose_Rate_Brachy.pdf. Accessed January 21, 2014.

American Society of Breast Surgeons. Consensus statement for accelerated partial breast irradiation. Revised August 15, 2011. Available at: http://www.breastsurgeons.org/statements/PDF_Statements/APBI.pdf. Accessed January 21, 2014.

Arthur DW, Vicini FA, Kuske RR, et al; American Brachytherapy Society. Accelerated partial breast irradiation: an updated report from the American Brachytherapy Society. *Brachytherapy*. 2003;2(2):124-30.

Bhatnagar A. Nonmelanoma skin cancer treated with electronic brachytherapy: results at 1 year. *Brachytherapy*. 2013 Mar-Apr;12(2):134-40.

Bhatnagar A, Loper A. The initial experience of electronic brachytherapy for the treatment of non-melanoma skin cancer. *Radiat Oncol*. 2010 Sep 28;5:87.

Dooley WC, Algan O, Dowlatshahi K, et al. Surgical perspectives from a prospective, nonrandomized, multicenter study of breast conserving surgery and adjuvant electronic brachytherapy for the treatment of breast cancer. *World J Surg Oncol*. 2011 Mar 7;9:30.

ECRI Institute. Product Brief. Axxent electronic brachytherapy system (Xoft, Inc.) for adjuvant treatment of breast, vaginal and skin cancers. December 2012.

Mehta VK, Algan O, Griem KL, et al. Experience with an electronic brachytherapy technique for intracavitary accelerated partial breast irradiation. *Am J Clin Oncol*. 2010 Aug;33(4):327-35.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Breast cancer. V1.2014a.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Basal cell and squamous cell skin cancers. V1.2014b.

Smith BD, Arthur DW, Buchholz TA, et al. Accelerated partial breast irradiation consensus statement from the American Society for Radiation Oncology (ASTRO). *Int J Radiat Oncol Biol Phys* 2009; 74:987-1001. Available at: <https://www.astro.org/Clinical-Practice/Guidelines/Partial-breast-irradiation.aspx> Accessed June 24, 2014.

Vaidya JS, Joseph DJ, Tobias JS, et al. Targeted intraoperative radiotherapy versus whole breast radiotherapy for breast cancer (TARGIT-A trial): an international, prospective, randomised, non-inferiority phase 3 trial. *Lancet*. 2010 Jul 10;376(9735):91-102. Erratum in: *Lancet*. 2010 Jul 10;376(9735):90.

Code	Description
0205T	Intravascular catheter-based coronary vessel or graft spectroscopy (e.g., infrared) during diagnostic evaluation and/or therapeutic intervention including imaging supervision, interpretation, and report, each vessel (List separately in addition to code for primary procedure))

The use of intravascular catheter-based spectroscopy to assess coronary artery plaque vulnerability is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Waxman et al. (2009) reported on a diagnostic, nonrandomized, open label, uncontrolled trial designed to determine whether catheter-based near-infrared spectroscopy (NIRS) signals obtained with a catheter-based system from coronary arteries of living individuals are similar to those from autopsy specimens. The authors concluded that this intravascular NIRS system safely obtained spectral data in patients that were similar to those from autopsy specimens. These results demonstrate the feasibility of invasive detection of coronary LCP with this novel system yet does not establish the utility of testing.

Gardner et al. (2008) examined the ability of the NIRS system to detect lipid core containing plaques in human coronary artery autopsy specimens. The authors concluded that this novel catheter-based NIRS system accurately identified lipid core plaques through blood in a prospective study in coronary artery autopsy specimens. It is anticipated that this novel capability will be of assistance in the management of patients with coronary artery disease but further study is needed.

No professional society guidelines addressing this technology were identified.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

Gardner CM, Tan H, Hull EL, et al. Detection of lipid core coronary plaques in autopsy specimens with a novel catheter-based near-infrared spectroscopy system. JACC Cardiovasc Imaging. 2008 Sep;1(5):638-48.

Waxman S, Dixon SR, L'Allier P, et al. In vivo validation of a catheter-based near-infrared spectroscopy system for detection of lipid core coronary plaques: initial results of the SPECTACL study. JACC Cardiovasc Imaging. 2009 Jul;2(7):858-68.

Code	Description
0206T	Computerized database analysis of multiple cycles of digitized cardiac electrical data from two or more ECG leads, including transmission to a remote center, application of multiple nonlinear mathematical transformations, with coronary artery obstruction severity assessment.

The use of a two-lead, computerized, resting electrocardiography (ECG) analysis to diagnose heart disease is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Synonyms: MultiFunction Cardiogram (MCG), 3DMP, multiphase resting ECG analysis

The MCG uses a mathematical approach to diagnose heart disease. Practices using the technology provide an in-office test similar to a resting ECG and then send the information to an

MCG datacenter for analysis, which includes scoring the cardiac disease severity and listing differential diagnoses. The MCG system uses two leads (Premier Heart website).

Electrocardiogram (ECG) signal analysis technologies are enhanced versions of the standard resting or exercise ECG that utilize special software to analyze the ECG signals. The 3DMP™, mfEMT™ (sometimes referred to as mfEMT™) or Multifunction Cardiogram (MCG™) system (Premier Heart) rely on mathematical models derived from a very large clinical database. Only data from two of the standard 12 ECG leads are used. Evidence to date from several small studies shows this technology is sufficiently sensitive to have a possible role in ruling out coronary artery disease (CAD); specificity has been shown to be moderately high. However, no studies were designed to measure the effect on treatment plans or health outcomes. In addition, there has been no systematic attempt to determine whether these technologies are good alternatives to other noninvasive tests or how they might best be combined with other tests (Hayes, 2011; updated 2013).

An Agency for Healthcare Research and Quality (AHRQ) technology assessment concluded that the evidence regarding the clinical utility of ECG-based signal analysis technologies is insufficient. Further research is needed to better describe the performance characteristics of these devices to determine in what circumstances, if any, they would replace or add to the standard ECG in testing patients with CAD (Coeytaux et al., 2012).

Strobeck et al. (2009) conducted a meta-analysis of three published prospective trials performed in the US to assess sensitivity and specificity of a new computerized, multiphase, resting electrocardiogram analysis device (MultiFunction-CardioGram(sm) or MCG a.k.a. 3DMP) for the detection of relevant coronary stenosis. A total of 1076 patients were included in the analysis. The authors concluded that the new computerized, multiphase, resting ECG analysis device (MultiFunction-CardioGram(sm)) has been shown in this meta-analysis to safely and accurately identify patients with relevant coronary stenosis (>70%) with high sensitivity and specificity and high negative predictive value. The three trials used in the analysis were all authored by Joseph Shen, MD, founder and co-developer of the MCG technology.

No professional society guidelines addressing this technology were identified.

Reference(s):

Coeytaux R, Leisy P, Wagner G et al. Systematic review of ECG-based signal analysis technologies for evaluating patients with acute coronary syndrome. Agency for Healthcare Research and Quality Technology Assessment Report. Rockville, MD. June 2012.

Hayes, Inc. Hayes Medical Technology Directory. *Electrocardiogram signal-based analysis for diagnosis of coronary artery disease: multifunction cardiogram and signal-averaged electrocardiogram*. Lansdale, PA: Hayes, Inc.; December 2011; updated 2013.

Premier Heart website. Available at: <http://www.premierheart.com>. Accessed June 9, 2014.

Strobeck JE, et al. Comparison of a two-lead, computerized, resting ECG signal analysis device, the MultiFunction-CardioGram or MCG (a.k.a. 3DMP), to quantitative coronary angiography for the detection of relevant coronary artery stenosis (>70%) – a meta-analysis of all published trials performed and analyzed in the US. *Int J Med Sci*. 2009;6(4):143-55.

Code	Description
0207T	Evacuation of meibomian glands, automated, using heat and intermittent pressure, unilateral

The use of automated evacuation of meibomian glands using heat and intermittent pressure is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

In a prospective, randomized, crossover, observer-masked clinical trial, Finis et al. (2014) compared the effectiveness of a single LipiFlow treatment with combined lid warming and massage in patients with meibomian gland dysfunction (MGD). Study participants were randomized to receive either a single 12-min LipiFlow Thermal Pulsation (LTP) system treatment or to perform combined twice-daily lid warming and massage for 3 months. All subjects were examined before, and 1 and 3 months after initiation of treatments. A total of 31 subjects completed the 3-month follow-up. At 1 and 3 months, patients in the LipiFlow treatment group had a significant reduction in Ocular Surface Disease Index (OSDI) scores compared with those in the lid-margin hygiene group. Both treatments produced a significant improvement in expressible meibomian glands compared to the baseline parameters, but no significant difference was noted between the two groups. The other investigated objective parameters did not show a significant difference. The authors concluded that a single LipiFlow treatment is as least as effective as a 3-month, twice-daily lid margin hygiene regimen for MGD. According to the authors, a limitation of the present study was that it was observer-masked only, i.e., patients were aware of the fact that they received either an established or a new and modern treatment for MGD. Thus, a placebo effect may have confounded any improvements in subjective symptoms and other parameters in both groups. The authors also stated that additional studies using a sham LipiFlow treatment in a double-masked design with larger cohorts and longer follow-up times are warranted.

In a single-center, prospective, observational, open-label, 1-month registered clinical trial, Greiner (evaluated the 1-year post-treatment dry eye status of 18 patients with meibomian gland dysfunction (MGD) and dry eye symptoms after receiving a single LipiFlow® Thermal Pulsation System (LTPS) treatment. Both eyes of all patients were treated with a single 12-minute treatment using the LTPS that liquefies and expresses the secretory contents of the meibomian glands. Meibomian gland function, tear break-up time (TBUT) and dry eye symptoms were measured. Data were presented for pre-treatment (baseline), and 1-month and 1-year post-treatment. Significant improvement in meibomian gland secretion scores from baseline measurements to 1-month post-treatment was maintained at 1-year. Baseline TBUT was significantly increased at 1-month, however, this improvement was no longer evident at 1-year post-treatment. The significant improvement in symptom scores on Ocular Surface Disease Index (OSDI) and Standard Patient Evaluation for Eye Dryness (SPEED) questionnaires observed at 1-month was maintained at 1-year. The authors concluded that a single 12-minute treatment with the LTPS offers an effective treatment for evaporative dry eye and MGD resulting in significant and sustained improvement in signs and symptoms for up to 1 year. The limitations of this study include a lack of controls and a small sample size.

Lane et al. (2012) evaluated the safety and effectiveness of the LipiFlow System compared to the iHeat Warm Compress (WC) for adults with meibomian gland dysfunction (MGD) in a non-significant risk, prospective, open-label, randomized, crossover multicenter clinical trial. A total of 139 patients were randomized between LipiFlow (n=69) and WC control (n=70). Subjects in the LipiFlow group received a 12-minute LipiFlow treatment and were reexamined at 1 day, 2 weeks and 4 weeks. Control subjects received a 5-minute iHeat treatment with instructions to perform the same treatment daily for 2 weeks. At 2 weeks, they crossed over (LipiFlow Crossover) and received the LipiFlow treatment. LipiFlow resulted in significant improvement in meibomian gland secretion at 2 and 4 weeks and tear break-up time (TBUT) at 2 and 4 weeks. There was no significant change in meibomian gland secretion or TBUT in the control group. LipiFlow resulted in a greater significant reduction in dry eye symptoms than the iHeat WC. The crossover group demonstrated similar significant improvement 2 weeks post-treatment with the LipiFlow. There was no significant difference between groups in the incidence of non-serious, device-related adverse events. The authors concluded that the LipiFlow System was significantly more effective than iHeat WC. The significance of this study is limited by the short follow-up period.

In a prospective clinical trial, Greiner (2012) evaluated the effect of a single treatment with the LipiFlow Thermal Pulsation System on signs of meibomian gland dysfunction (MGD) and dry eye symptoms in 21 patients over a 9-month period. The LipiFlow device applies heat to the

conjunctival surfaces of the upper and lower inner eyelids while simultaneously applying pulsatile pressure to the outer eyelid surfaces to express the meibomian glands. Meibomian gland secretion scores improved significantly from baseline to 1-month post-treatment and this improvement was maintained with no significant regression at 9 months. Symptom scores on both Ocular Surface Disease Index (OSDI) and Standard Patient Evaluation for Eye Dryness (SPEED) questionnaires improved significantly at 1 month and this improvement was maintained at 9 months. The authors concluded that with such prolonged improvement in signs and symptoms of dry eye disease, the LipiFlow Thermal Pulsation System offers a technological advancement for the treatment of dry eye disease secondary to meibomian gland dysfunction. These findings require confirmation in a larger controlled trial.

Reference(s):

ECRI Institute. Hotline Response. Nonpharmacologic Options for Treating Dry Eye Syndrome. November 2013.

Finis D, Hayajneh J, König C, et al. Evaluation of an Automated Thermodynamic Treatment (LipiFlow®) System for Meibomian Gland Dysfunction: A Prospective, Randomized, Observer-Masked Trial. *Ocul Surf.* 2014 Apr;12(2):146-54.

Greiner JV. A Single LipiFlow® Thermal Pulsation System Treatment Improves Meibomian Gland Function and Reduces Dry Eye Symptoms for 9 Months. *Curr Eye Res.* 2012 Apr;37(4):272-8.

Greiner JV. Long-term (12-month) improvement in meibomian gland function and reduced dry eye symptoms with a single thermal pulsation treatment. *ClinExperiment Ophthalmol.* 2013 Aug;41(6):524-30. doi: 10.1111/ceo.12033.

Hayes, Inc. Search & Summary. LipiFlow® Thermal Pulsation System (TearScience) for Dry Eye. Lansdale, PA: Hayes, Inc.; August 2012. Archived September 2013.

Lane SS, DuBiner HB, Epstein RJ, et al. A new system, the LipiFlow, for the treatment of meibomian gland dysfunction. *Cornea.* 2012 Apr;31(4):396-404.

Code	Description
0223T	Acoustic cardiography, including automated analysis of combined acoustic and electrical intervals; single, with interpretation and report
0224T	Acoustic cardiography, including automated analysis of combined acoustic and electrical intervals; multiple, including serial trended analysis and limited reprogramming of device parameter - AV or VV delays only, with interpretation and report
0225T	Acoustic cardiography, including automated analysis of combined acoustic and electrical intervals; multiple, including serial trended analysis and limited reprogramming of device parameter - AV and VV delays, with interpretation and report

The use of computer-aided electronic auscultatory devices is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Acoustic cardiography devices simultaneously acquire, record and analyze the electrical and acoustic signals of the heart. A computer analyzes the recording to identify specific heart sounds that may be present, including S1, S2 and suspected murmurs according to processed algorithms. A graphic display then is shown on a monitor. These computer-aided electronic auscultatory devices are intended to provide support to the physician in the evaluation of heart sounds for the identification of suspected murmurs, a potential sign of heart disease.

There is insufficient evidence of the validity of computer-aided electronic auscultatory devices, or their impact on clinical outcomes in the peer-reviewed published medical literature. Clinical studies are necessary to determine the performance characteristics (sensitivity, specificity, and

predictive values) of computer-aided electronic auscultatory devices and their impact on clinical management and patient outcomes.

Wang et al. (2013) conducted a study to determine the diagnostic utility of acoustic cardiography in patients with heart failure (HF). Three cohorts of patients were studied (94 with hypertension, 109 with normal ejection fraction HF and 89 with reduced ejection fraction HF). All participants received acoustic cardiography and echocardiography examinations. Acoustic cardiographic parameters included S3 score, electromechanical activation time (EMAT) and systolic dysfunction index (SDI). EMAT significantly differentiated normal ejection fraction HF from hypertension, similar to echocardiography. SDI out-performed the other acoustic cardiographic parameters in differentiating reduced ejection fraction HF from normal ejection fraction HF. Echocardiography had a similar diagnostic performance. The authors concluded that this bedside technology may be helpful in identifying HF and its phenotypes, especially when echocardiography is not immediately available. Further studies with larger patient populations are needed.

Watrous et al. (2008) noted that a high percentage of asymptomatic children are referred for specialist evaluation or echocardiography because of a murmur but no heart disease. The researchers hypothesized that computer-assisted auscultation (CAA) might improve the sensitivity and specificity of referrals for evaluation of heart murmurs. However, while the sensitivity for detection of murmurs significantly increased with use of CAA from 76.6% to 89.1% ($p < 0.001$), the specificity remained unchanged (80.0 % versus 81.0%).

Maisel et al. (2010) evaluated if the strength of the S3 heart sound can provide diagnostic/prognostic information in problematic heart failure subgroups. In the 995 patients enrolled in the study, S3 strength was a significant prognosticator in univariate analysis for adverse events but not in a multivariable model. In patients with "gray zone" The use of S3 acoustic cardiography improved the diagnostic accuracy for those patients ($n=208$) with an intermediate BNP level (100-499 pg/ml) from 47 to 69%. Acoustic cardiography improved S3 detection sensitivity in obese patients when compared to auscultation. The implications of these findings for clinical practice need to be determined.

A Horizon Scanning Technology (2010) evaluated acoustic cardiography for the diagnosis of heart failure and concluded that although the good level of comparative evidence indicated that the adjunctive use of acoustic cardiography may be of benefit in the diagnosis of heart failure, the application of this technology in the acute setting was considered impractical.

In a scientific statement on acute heart failure, the American Heart Association states that electronic detection of third heart sounds (S3) using acoustic cardiography has been investigated as both a stand-alone and adjunct diagnostic measure, but appears to provide little benefit over existing approaches. (Weintraub et al., 2010)

The American College of Cardiology and American Heart Association joint guidelines on the management of heart failure identify acoustic cardiography as an option for the diagnostic evaluation of patients with suspected acutely decompensated heart failure but state that the test is not yet validated. (Yancy et al., 2013)

Reference(s):

Horizon Scanning Technology. Prioritising Summary. Acoustic cardiography for the diagnosis of heart failure. November 2010. Available at:

[http://www.horizonscanning.gov.au/internet/horizon/publishing.nsf/Content/C8A5BA60BD01A93ECA257757000A2015/\\$File/PS%20Acoustic%20cardiography%20for%20diagnosis%20of%20heart%20failure.pdf](http://www.horizonscanning.gov.au/internet/horizon/publishing.nsf/Content/C8A5BA60BD01A93ECA257757000A2015/$File/PS%20Acoustic%20cardiography%20for%20diagnosis%20of%20heart%20failure.pdf). Accessed June 16, 2014.

Maisel AS, Peacock WF, Shah KS, et al. Acoustic cardiography S3 detection use in problematic subgroups and B-type natriuretic peptide "gray zone": secondary results from the Heart failure and Audicor technology for Rapid Diagnosis and Initial Treatment Multinational Investigation. *Am J Emerg Med*. 2011 Oct;29(8):924-31.

Wang S, Lam YY, Liu M, et al. Acoustic cardiography helps to identify heart failure and its phenotypes. *Int J Cardiol*. 2013 Aug 10;167(3):681-6.

Watrous RL, Thompson WR, Ackerman SJ. The impact of computer-assisted auscultation on physician referrals of asymptomatic patients with heart murmurs. *Clin Cardiol.* 2008;31(2):79-83.

Weintraub NL, Collins SP, Pang PS, et al.; American Heart Association Council on Clinical Cardiology and Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. Acute heart failure syndromes: emergency department presentation, treatment, and disposition: current approaches and future aims: a scientific statement from the American Heart Association. *Circulation.* 2010 Nov 9;122(19):1975-96.

Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2013 Oct 15;62(16):e147-239.

Code	Description
0233T	Skin advanced glycation end products (AGE) measurement by multi-wavelength fluorescent spectroscopy

The use of advanced glycation end products as a diagnostic or predictive test is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Measurement of skin autofluorescence (AF) is safe, and the available studies provide evidence that elevated skin AF is associated with certain diabetes-related complications such as neuropathy, nephropathy, and foot ulcers. However, the available studies did not determine the diagnostic accuracy of skin AF in terms of its sensitivity and specificity for current or future complications. Furthermore, none of the available studies directly compared skin AF with current diagnostic tests such as urinalysis, retinal examination, monofilament testing, and ankle-brachial index for detection of diabetes-related complications. AF is not accurate in patients who have dark skin, including some dark-skinned Japanese patients. Also, skin AF measurement seems to be at a significant disadvantage relative to these other techniques in that although it may indicate the presence of certain complications, it does not appear to provide sufficient information to assess the severity of these complications. No studies examined the impact of AF measurement on patient management or health outcomes. Thus, it is not clear whether there is a clinical role for skin AF in the detection or prediction of diabetes-related complications and whether information obtained with this technique may improve patient management. (Hayes 2013)

Advanced glycation end products (AGEs) are long-lived tissue proteins that accumulate in diabetes. Skin AGEs measured in biopsy specimens strongly correlated with complications of diabetes. AGEs can also be measured noninvasively by the AGE Reader™. Bos et al. (2011) conducted a systematic review of studies on the association between skin autofluorescence (SAF), measured by the AGE Reader, and complications of diabetes. Seven articles met the inclusion criteria. The results showed an association of skin autofluorescence (SAF) with end-organ complications in diabetes, except retinopathy. However, studies were of large clinical heterogeneity, only three studies had a prospective design and five studies were from the same research group. More prospective studies, with a longer period of follow-up, larger group size and strict definitions of complications and end points, are needed to demonstrate the potential role and benefit in clinical management before the widespread use of the AGE Reader can be recommended.

Samborski et al. (2011) compared AGE accumulation in the skin of patients with type 1 diabetes and nondiabetic population to assess its association with disease duration and metabolic control. The study included 140 type 1 diabetes patients and 57 nondiabetic subjects. Mean autofluorescence (AF) in the diabetes group was 2.13 ± 0.55 and it was significantly higher than in controls. A significant positive correlation between AF and the age of patients was found for the whole study population. In diabetic subjects, a significant positive correlation was observed between AF and diabetes duration, and between AF and glycated hemoglobin (HbA1c). The investigators concluded that AF measurement is a simple and noninvasive method of assessing AGE accumulation in the skin. It may be useful as a secondary method of assessing metabolic

control, as it reflects glycemic control over a longer period of time than that reflected by HbA1c levels. Further research is needed to confirm these findings.

Advanced glycation end products (AGEs) are implicated in the complications of diabetes. Advanced glycation end products also accumulate in the skin and are sensitive biomarkers for the risk of developing diabetes and related complications. Noninvasive screening for diabetes has been evaluated in an 18-site study involving a cohort of 2793 subjects meeting American Diabetes Association-based screening criteria. Subjects were measured with a specialized skin fluorimeter and also received traditional blood glucose and glycosylated hemoglobin tests. Retrospective results indicated that the noninvasive technology measuring dermal fluorescence is more sensitive at detecting abnormal glucose tolerance than either fasting plasma glucose or glycosylated hemoglobin A1C. These results suggest that noninvasive measurement of dermal fluorescence may be an effective tool to identify individuals at risk for diabetes and its complications. The noninvasive technology yields immediate results, and since measuring dermal fluorescence requires no blood draws or patient fasting, the instrument may be well suited for opportunistic screening. The retrospective study design limits the applicability of the test and does not establish the utility of the test for screening or case management. (Ediger 2009)

There were no professional society guidelines identified addressing this technology.

Reference(s):

Bos DC, de Ranitz-Greven WL, de Valk HW. Advanced glycation end products, measured as skin autofluorescence and diabetes complications: a systematic review. *Diabetes Technol Ther.* 2011 Jul;13(7):773-9.

Ediger et al. Noninvasive Optical Screening for Diabetes *J Diabetes Sci Technol* 2009;3(4):776-780

Hayes, Inc. Directory. Skin autofluorescence to aid in assessment or prediction of diabetes-related complications. October 2013

Samborski P, Naskręć D, Araszkievicz A, et al. Assessment of skin autofluorescence as a marker of advanced glycation end product accumulation in type 1 diabetes. *Pol Arch Med Wewn.* 2011 Mar;121(3):67-72.

Code	Description
0239T	Bioimpedance Spectroscopy (SEAC SFB3, Impedimed)

The use of bioimpedance spectroscopy is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

An Agency for Healthcare Research and Quality (AHRQ) technology assessment states that there is too little evidence to draw conclusions about the reliability of bioimpedance for the diagnosis of secondary lymphedema. (AHRQ, 2010)

A prospective study by Berlit et al. (2012) evaluated resistance (R) and phase angle (Pa) determined by single-frequency whole-body bioelectrical impedance analysis (BIA) as predictors for the early onset of edema of the upper limb in 33 patients undergoing surgical treatment for breast cancer. Whole-body BIA was performed before surgery, as well as at two days, at one and three months after surgery. Four patients developed an edema of the upper limb within the first three months after surgery. Both analyzed parameters showed a fairly good performance in terms of sensitivity (R=75%, Pa=75%) and specificity (R=86%, Pa=83%). The positive predictive values of 43% (R) and 38% (Pa) were unsatisfactory, whereas the negative predictive values were 96% for both parameters. The authors concluded that Pa, as well as R, in whole-body BIA can be used to rule out a developing edema of the upper limb. This study is limited by lack of a control and small sample size.

Smoot et al. (2011) compared diagnostic accuracy of measures of breast cancer-related lymphedema (BCRL). Cross-sectional design comparing clinical measures with the criterion

standard of previous diagnosis of BCRL. Sensitivity, specificity, receiver operator characteristic curve and area under the curve (AUC) were used to evaluate accuracy. A total of 141 women were categorized as having (n=70) or not having (n=71) BCRL based on past diagnosis by a health care provider, which was used as the reference standard. Analyses of ROC curves for the continuous outcomes yielded AUC of .68 to .88; of the physical measures bioimpedance spectroscopy yielded the highest accuracy with an AUC of .88 for women whose dominant arm was the affected arm. The lowest accuracy was found using the 2-cm diagnostic cutoff score to identify previously diagnosed BCRL (AUC, .54-.65). The authors concluded that these findings support the use of bioimpedance spectroscopy in the assessment of existing BCRL; however, further investigation is warranted.

Bioelectrical impedance analysis is a noninvasive technique used to measure water content of the body or body part. It involves passing a small electrical current through the body and measuring the resistance or impedance to the flow. Both the Bioimpedance Spectroscopy and sum of arm circumferences methods gave similar prevalence estimates at most testing phases, despite including different women (demonstrated in later analyses). Self-reported arm swelling (including change in ability to perform certain functions) produced consistently higher prevalence when compared with the objective measures. Similarly, cumulative burden was substantially higher when based on personal perceptions of arm swelling. However, when participants were asked to self-report clinical diagnosis of lymphedema, cumulative burden was lower than for all other measures, at 19.4%. Long-term lymphedema, defined as measurable evidence of the condition for more than 3 months, was experienced by 40% of the sample according to the BIS method and 60% of the sample according to the other measurement methods. (Hayes et al., 2008)

In a position statement on the diagnosis and management of lymphedema, the National Lymphedema Network (NLN) reports that bioimpedance spectroscopy (BIS) has been shown to provide reliable data in the diagnosis of breast cancer-related lymphedema and that it can detect early changes associated with lymphedema. The organization further states that BIS may show promise for detecting smaller areas of localized lymphedema, but this application has not been subjected to adequate study to recommend it. BIS is not as accurate in advanced, fibrotic edema. As in measures of volume, BIS cannot differentiate lymphedema from other types of edema and does not determine when temporary post-operative arm edema becomes chronic lymphedema. (NLN, 2011)

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the unproven conclusion.

Reference(s):

ECRI Institute. Hotline Service. Bioimpedance spectroscopy for assessing lymphedema. January 2013.

Agency for Healthcare Research and Quality (AHRQ). Technology Assessment. Diagnosis and treatment of secondary lymphedema. May 2010.

Berlit S, Brade J, Tuschy B, et al. Comparing bioelectrical impedance values in assessing early upper limb lymphedema after breast cancer surgery. *In Vivo*. 2012 Sep-Oct;26(5):863-7.

Smoot BJ, Wong JF, Dodd MJ. Comparison of diagnostic accuracy of clinical measures of breast cancer-related lymphedema: area under the curve. *Arch Phys Med Rehabil*. 2011 Apr;92(4):603-10.

S. Hayes, M. Janda, B. Cornish, D. Battistutta, B. Newman. Lymphedema secondary to breast cancer: how choice of measure influences diagnosis, prevalence, and identifiable risk factors. *Lymphology* 41 (2008) 18-28

National Lymphedema Network (NLN) position statement. The diagnosis and treatment of lymphedema. February 2011. Available at: <http://www.lymphnet.org/pdfDocs/nlntreatment.pdf>. Accessed June 17, 2013.

Code	Description
0243T	Intermittent measurement of wheeze rate for bronchodilator or bronchial-challenge diagnostic evaluation(s), with interpretation and report
0244T	Continuous measurement of wheeze rate during treatment assessment or during sleep for documentation of nocturnal wheeze and cough for diagnostic evaluation 3 to 24 hours, with interpretation and report

The use of intermittent or continuous computerized wheeze detectors is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Gurung et al. (2011) performed a systematic review of studies implementing computerized lung sound analysis (CLSA) to aid in the detection of abnormal lung sounds for specific respiratory disorders. Following a qualitative review, the authors conducted a meta-analysis to estimate the sensitivity and specificity of CLSA for the detection of abnormal lung sounds. Eight studies were selected for review. Overall sensitivity for the detection of wheezes or crackles using CLSA was 80% and specificity was 85%. While quality data on CLSA are relatively limited, analysis of existing information suggests that CLSA can provide a relatively high specificity for detecting abnormal lung sounds. Further research and product development could promote the value of CLSA in research studies or its diagnostic utility in clinical settings.

Prodhan et al. (2008) studied wheeze detection in 11 pediatric patients in the ICU. Between the physician, RTs, and nurses there was agreement about the presence of wheeze in critically ill patients in the pediatric intensive care unit. Compared to the objective acoustic measurements from the PulmoTrack, auscultation by the intensive care unit staff was similar in their ability to detect the absence of wheeze.

Bentur et al. (2004) conducted a study to evaluate automatic computerized wheeze detection (CWD) in determining bronchial hyperreactivity (BHR) in young infants with prolonged cough, and its correlation with the subsequent development of wheezing in 20 infants <24 months. All patients underwent acoustic bronchial provocation tests (BPT) with the response determined by CWD and auscultation by a physician. The authors concluded that acoustic BPT is a technically feasible test for the detection of BHR in young infants and that CWD provides an earlier detection of wheeze than stethoscope auscultation. However, the clinical significance of this finding is unclear. Although the study showed promising indications for the technology, the non-controlled design and small sample size limits the generality of the results.

Beck et al. (2007) evaluated the use of the PulmoTrac in 25 infants with bronchiolitis. The authors concluded there was complete agreement between clinician and PulmoTrac results in all sound segments, in off-line auditory analysis of the data. No significant difference in wheezing and crackles by computerized lung was noted. Further studies are needed to clarify its potential role as a clinical tool for assessing and following infants with acute respiratory illnesses with wheezing as a component.

The additional clinical advantage, if any, of measuring wheeze rate in addition to auscultation and standard pulmonary function testing has not been determined.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the unproven conclusion.

Reference(s)

Gurung A, Scrafford CG, Tielsch JM, et al. Computerized lung sound analysis as diagnostic aid for the detection of abnormal lung sounds: a systematic review and meta-analysis. *Respir Med*. 2011 Sep;105(9):1396-403.

Prodhan P, Dela Rosa RS, Shubina M, et al. Wheeze detection in the pediatric intensive care unit: comparison

among physician, nurses, respiratory therapists, and a computerized respiratory sound monitor. *Respir Care*. 2008 Oct;53(10):1304-9.

Bentur L, Beck R, Berkowitz D, et al. Adenosine bronchial provocation with computerized wheeze detection in young infants with prolonged cough: correlation with long-term follow-up. *Chest*. 2004 Oct;126(4):1060-5.

Beck R, Nael E et al. Computerized lung sound analysis is feasible in young infants with RSV bronchiolitis. *BMC Pediatrics* 2007, 7:22doi:10.1186/1471-2431-7-22

Code	Description
0263T	Intramuscular autologous bone marrow cell therapy, with preparation of harvested cells, multiple injections, one leg, including ultrasound guidance, if performed; complete procedure including unilateral or bilateral bone marrow harvest
0264T	Intramuscular autologous bone marrow cell therapy, with preparation of harvested cells, multiple injections, one leg, including ultrasound guidance, if performed; complete procedure excluding bone marrow harvest
0265T	Intramuscular autologous bone marrow cell therapy, with preparation of harvested cells, multiple injections, one leg, including ultrasound guidance, if performed; unilateral or bilateral bone marrow harvest only for intramuscular autologous bone marrow cell therapy

Intramuscular autologous bone marrow cell therapy is unproven and not medically necessary for treating peripheral arterial disease.

Clinical Evidence

Peripheral arterial disease (PAD) is a narrowing of the blood vessels outside of the heart caused by a buildup of plaque (atherosclerosis). Standard treatment for severe cases of PAD is surgical or endovascular revascularization; however, not all patients are candidates for these procedures. Intramuscular autologous bone marrow cell therapy is being investigated as a potential new therapeutic option to induce angiogenesis. Early studies show promising results, but further large randomized controlled studies are needed to confirm these findings. Clinical trials are ongoing.

A European Society of Cardiology (ESC) guideline addresses novel therapies to stimulate neovascularization, known as therapeutic angiogenesis. These therapies promote revascularization and remodelling of collateral vessels to reduce the symptoms of peripheral vascular disease and prevent amputation. For autologous cell transplantation in humans, bone marrow and peripheral blood are rich sources of stem and progenitor cells. Bone marrow is currently the most frequent source of cells used for clinical repair trials, because it is easy to obtain and no complex purification steps are required. Another advantage is that it contains a variety of stem and progenitor cells. At present angiogenic gene and stem cell therapy are still being investigated, and it is too early to give firm recommendations. (Tendera et al., 2011)

Fadini et al. (2010) conducted a meta-analysis to determine whether autologous cell therapy is effective in the treatment of peripheral arterial disease (PAD). The authors included 37 controlled and non-controlled, randomized and non-randomized trials using autologous bone marrow or granulocyte colony stimulating factor (G-CSF) mobilized peripheral blood cells to treat PAD. Autologous cell therapy was effective in improving surrogate indexes of ischemia, subjective symptoms and hard endpoints (ulcer healing and amputation). G-CSF monotherapy was not associated with significant improvement in the same endpoints. Patients with thromboangiitis obliterans showed some larger benefits than patients with atherosclerotic PAD. The intramuscular route of administration and the use of bone marrow cells seemed somehow more effective than intraarterial administration and the use of mobilized peripheral blood cells. The authors concluded that intramuscular autologous bone marrow cell therapy is a feasible, relatively safe and potentially effective therapeutic strategy for PAD patients, who are not candidates for traditional

revascularization. Larger, placebo-controlled, randomized multicenter trials are needed to confirm these findings.

In the Therapeutic Angiogenesis using Cell Transplantation (TACT) Study, Tateishi-Yuyama et al. (2002) investigated efficacy and safety of autologous implantation of bone marrow mononuclear cells in patients with ischemic limbs because of peripheral arterial disease. In the initial pilot study, 25 patients (group A) with unilateral ischemia of the leg were injected with bone marrow mononuclear cells into the gastrocnemius of the ischemic limb and with saline into the less ischemic limb. The authors then recruited 22 patients (group B) with bilateral leg ischemia, who were randomly injected with bone marrow mononuclear cells in one leg and peripheral blood-mononuclear cells in the other as a control. Primary outcomes were safety and feasibility of treatment, based on ankle-brachial index (ABI) and rest pain. Two patients were excluded from group B after randomization. At 4 weeks in group B patients, ABI was significantly improved in legs injected with bone marrow mononuclear cells compared with those injected with peripheral blood mononuclear cells. Similar improvements were seen for transcutaneous oxygen pressure, rest pain and pain-free walking time. These improvements were sustained at 24 weeks. Similar improvements were seen in group A patients. Two patients in group A died after myocardial infarction unrelated to treatment. The authors concluded that autologous implantation of bone marrow mononuclear cells could be safe and effective for achievement of therapeutic angiogenesis, because of the natural ability of marrow cells to supply endothelial progenitor cells and to secrete various angiogenic factors or cytokines.

Matoba et al. (2008) reported 3-year follow-up results for the TACT trial. The study assessed the 3-year safety and clinical outcomes of angiogenic cell therapy by investigating the mortality and leg amputation-free interval as primary end points. The median follow-up time for surviving patients was 25.3 months (range, 0.8-69.0 months), and 3-year overall survival rates were 80% in patients with atherosclerotic peripheral arterial disease and 100% in 41 patients with thromboangiitis obliterans (TAO). Three-year amputation-free rate was 60% in PAD and 91% in patients with TAO. The multivariate analysis revealed that the severity of rest pain and repeated experience of bypass surgery were the prognostic factors negatively affecting amputation-free interval. The significant improvement in the leg pain scale, ulcer size and pain-free walking distance was maintained during at least 2 years after the therapy, although the ankle brachial index and transcutaneous oxygen pressure value did not significantly change. The authors concluded that angiogenic cell therapy using bone marrow mononuclear cells can induce a long-term improvement in limb ischemia, leading to extension of amputation-free interval. Larger, placebo-controlled, randomized multicenter trials are needed to confirm these findings.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the unproven conclusion.

Reference(s):

Tendera M, Aboyans V, Bartelink ML, et al. ESC Guidelines on the diagnosis and treatment of peripheral artery diseases: the Task Force on the Diagnosis and Treatment of Peripheral Artery Diseases of the European Society of Cardiology (ESC). *Eur Heart J.* 2011 Nov;32(22):2851-906. Available at: <http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/Guidelines-peripheral-AD-FT.pdf>. Accessed June 17, 2013.

Fadini GP, Agostini C, Avogaro A. Autologous stem cell therapy for peripheral arterial disease meta-analysis and systematic review of the literature. *Atherosclerosis.* 2010 Mar;209(1):10-7.

Tateishi-Yuyama E, Matsubara H, Murohara T, et al. Therapeutic angiogenesis for patients with limb ischaemia by autologous transplantation of bone-marrow cells: a pilot study and a randomized controlled trial. *Lancet.* 2002 Aug 10;360(9331):427-35.

Matoba S, Tatsumi T, Murohara T, et al. Long-term clinical outcome after intramuscular implantation of bone marrow mononuclear cells (Therapeutic Angiogenesis by Cell Transplantation [TACT] trial) in patients with chronic limb ischemia. *Am Heart J.* 2008 Nov;156(5):1010-8.

Code	Description
0266T	Implantation or replacement of carotid sinus baroreflex activation device; total system (includes generator placement, unilateral or bilateral lead placement, intra-operative interrogation, programming, and repositioning, when performed)
0267T	Implantation or replacement of carotid sinus baroreflex activation device; lead only, unilateral (includes intra-operative interrogation, programming, and repositioning, when performed)
0268T	Implantation or replacement of carotid sinus baroreflex activation device; pulse generator only (includes intra-operative interrogation, programming, and repositioning, when performed)
0269T	Revision or removal of carotid sinus baroreflex activation device; total system (includes generator placement, unilateral or bilateral lead placement, intra-operative interrogation, programming, and repositioning, when performed)
0270T	Revision or removal of carotid sinus baroreflex activation device; lead only, unilateral (includes intra-operative interrogation, programming, and repositioning, when performed)
0271T	Revision or removal of carotid sinus baroreflex activation device; pulse generator only (includes intra-operative interrogation, programming, and repositioning, when performed)
0272T	Interrogation device evaluation (in person), carotid sinus baroreflex activation system, including telemetric iterative communication with the implantable device to monitor device diagnostics and programmed therapy values, with interpretation and report (eg, battery status, lead impedance, pulse amplitude, pulse width, therapy frequency, pathway mode, burst mode, therapy start/stop times each day)
0273T	Interrogation device evaluation (in person), carotid sinus baroreflex activation system, including telemetric iterative communication with the implantable device to monitor device diagnostics and programmed therapy values, with interpretation and report (eg, battery status, lead impedance, pulse amplitude, pulse width, therapy frequency, pathway mode, burst mode, therapy start/stop times each day); with programming

Chronic baroreceptor stimulation of the carotid sinus is investigational, unproven and not medically necessary for treating hypertension, heart failure or other cardiovascular conditions due to lack of U.S. Food and Drug Administration (FDA) approval and insufficient clinical evidence of safety and/or efficacy in the published peer-reviewed medical literature.

The Barostim *neo*TM has not yet received U.S. Food and Drug Administration (FDA) approval and is limited to investigational use. Several large-scale randomized controlled clinical trials are ongoing to evaluate the long-term safety and efficacy of these devices.

Coverage for revision or removal of carotic sinus baroreflex activation devices may be addressed in the complication section of the benefit document. See the enrollee-specific benefit document.

Note: The Barostim *neo*TM is a second generation device that replaces the Rheos[®] System (CVRx website).

Clinical Evidence

Baroreflex activation therapy (BAT), or baroreflex stimulation, uses a pacemaker-like implantable pulse generator to deliver electrical signals to baroreceptors in the carotid arteries through electrodes placed in the carotid sinus. The baroreflex system is a network of natural blood

pressure sensors (baroreceptors) located throughout the arteries and veins that help regulate blood pressure. When pressure in the carotid arteries rises, carotid artery baroreceptors (located in the carotid sinus) are stimulated and transfer the pressure information to the brain through the carotid sinus nerve. The brain then signals other parts of the body to lower systemic blood pressure by dilating blood vessels, reducing heart rate and increasing fluid excretion through the kidneys. In chronic hypertension, the carotid baroreflex signal is often insufficient; therefore, investigators are evaluating carotid sinus baroreceptors as a potential nonpharmacotherapy for treatment-resistant hypertension (ECRI, 2013).

Hoppe et al. (2012) evaluated the Barostim neo™, a second-generation baroreflex activation therapy (BAT), in patients with resistant hypertension. Thirty patients with resting systolic blood pressure (SBP) ≥ 140 mm Hg despite treatment with ≥ 3 medications, including ≥ 1 diuretic, were included in the single-arm, open-label study. The authors reported results consistent with studies of the first-generation system and a safety profile comparable to a pacemaker. This study is limited by lack of randomization and control and small sample size.

The Rheos Pivotal Trial evaluated baroreflex activation therapy (BAT) for resistant hypertension in a double-blind, randomized, prospective, multicenter, placebo-controlled Phase III clinical trial. Two hundred and sixty five patients with resistant hypertension were implanted and subsequently randomized (2:1) 1 month after implantation. Subjects received either BAT (Group A) for the first 6 months or delayed BAT initiation following the 6-month visit (Group B). The 5 primary endpoints were: 1) acute systolic blood pressure (SBP) responder rate at 6 months; 2) sustained responder rate at 12 months; 3) procedure safety; 4) BAT safety; and 5) device safety. The trial showed significant benefit for the endpoints of sustained efficacy, BAT safety and device safety. However, it did not meet the endpoints for acute responders or procedural safety. The authors concluded that the weight of the overall evidence suggests that over the long-term, BAT can safely reduce SBP in patients with resistant hypertension. Future clinical trials will address the limitations of this study and further define the therapeutic benefit of BAT (Bisognano et al., 2011).

After completion of the randomized Rheos Pivotal Trial, Bakris et al. (2012) conducted an open-label, nonrandomized follow-up study to assess the long-term safety and efficacy of BAT. Clinically significant responder status was assessed according to FDA-mandated criteria. Of 322 patients implanted, 76% (n = 245) qualified as clinically significant responders. An additional 10% were indeterminate. Among long-term responders receiving BAT, the mean blood pressure drop was 35/16 mm Hg. Medication use was reduced by the end of the randomized phase and remained lower through the follow-up period. Among responders, 55% achieved targeted blood pressure reduction goals sustained through 22 to 53 months of follow-up.

Georgakopoulos et al. (2011) review the evidence suggesting that baroreflex activation therapy (BAT) may be a promising therapy for heart failure with preserved ejection fraction (HFpEF) and introduces the HOPE4HF trial (ClinicalTrials.gov NCT00957073), a randomized outcomes trial designed to evaluate the clinical safety and efficacy of BAT in the HFpEF population.

Scheffers et al. (2010) assessed the safety and efficacy of a novel implantable device therapy in resistant hypertension patients. The Rheos system (CVRx, Inc.) activates the carotid baroreflex. Forty-five patients with systolic blood pressure ≥ 160 mm Hg or diastolic ≥ 90 mm Hg despite at least 3 antihypertensive drugs were enrolled in a prospective, nonrandomized feasibility study to assess whether Rheos therapy could safely lower blood pressure. Subjects were followed up for as long as 2 years. After 3 months of device therapy, mean blood pressure was reduced by 21/12 mm Hg. This result was sustained in 17 subjects who completed 2 years of follow-up, with a mean reduction of 33/22 mm Hg. The device exhibited a favorable safety profile. This novel approach holds promise for patients with resistant hypertension and is currently under evaluation in a prospective, placebo-controlled clinical trial.

Heusser et al. (2010) studied the effects of electric field stimulation of carotid baroreceptors on blood pressure. Seven men and five women (ages 43 to 69 years) with treatment-resistant

arterial hypertension received an implantable bilateral electric baroreflex stimulator at the level of the carotid sinus (Rheos). Intra-arterial blood pressure was 193+/-9/94+/-5 mm Hg on medications. Acute electric baroreflex stimulation decreased systolic blood pressure by 32+/-10 mm Hg (range: +7 to -108 mm Hg; P=0.01). The authors concluded that electric field stimulation of carotid sinus baroreflex afferents acutely decreased arterial blood pressure in hypertensive patients, without negative effects on physiological baroreflex regulation.

The Food and Drug Administration-monitored phase II Rheos Feasibility Trial was performed to assess the response of patients with multidrug-resistant hypertension to electrical stimulation of the carotid sinus baroreflex system. The system consists of an implantable pulse generator with bilateral perivascular carotid sinus leads. Implantation is performed bilaterally. Ten patients with resistant hypertension (taking a median of six antihypertensive medications) underwent implantation. Results showed a significant acute decrease in blood pressure without significant side effects. (Illig, et al. 2006)

Reference(s):

Bakris GL, Nadim MK, Haller H, et al. Baroreflex activation therapy provides durable benefit in patients with resistant hypertension: results of long-term follow-up in the Rheos Pivotal Trial. *J Am Soc Hypertens.* 2012 Mar-Apr;6(2):152-8.

Bisognano JD, Bakris G, Nadim MK, et al. Baroreflex activation therapy lowers blood pressure in patients with resistant hypertension: results from the double-blind, randomized, placebo-controlled Rheos Pivotal Trial. *J Am Coll Cardiol.* 2011 Aug 9;58(7):765-73.

CVRx website. <http://www.cvr.com/> Accessed June 16, 2014.

ECRI Institute. Health Technology Forecast. Baroreflex activation therapy for severe drug-resistant hypertension. December 2013.

Georgakopoulos D, Little WC, Abraham WT, et al. Chronic baroreflex activation: a potential therapeutic approach to heart failure with preserved ejection fraction. *J Card Fail.* 2011 Feb;17(2):167-78.

Heusser K, Tank J, Engeli S, et al. Carotid baroreceptor stimulation, sympathetic activity, baroreflex function, and blood pressure in hypertensive patients. *Hypertension.* 2010 Mar;55(3):619-26.

Hoppe UC, Brandt MC, Wachter R, et al. Minimally invasive system for baroreflex activation therapy chronically lowers blood pressure with pacemaker-like safety profile: results from the Barostim neo trial. *J Am Soc Hypertens.* 2012 Jul-Aug;6(4):270-6.

Illig KA, Levy M, Sanchez L, et al. An implantable carotid sinus stimulator for drug-resistant hypertension: surgical technique and short-term outcome from the multicenter phase II Rheos feasibility trial. *J Vasc Surg.* 2006 Dec;44(6):1213-1218.

Scheffers IJ, Kroon AA, Schmidli J, et al. Novel baroreflex activation therapy in resistant hypertension: results of a European multi-center feasibility study. *J Am Coll Cardiol.* 2010 Oct 5;56(15):1254-8.

Code	Description
0281T	Percutaneous transcatheter closure of the left atrial appendage with implant, including fluoroscopy, transseptal puncture, catheter placement(s), left atrial angiography, left atrial appendage angiography, radiological supervision and interpretation

Cardiac devices for percutaneous closure (occlusion) of the left atrial appendage are investigational, unproven and not medically necessary due to lack of U.S. Food and Drug Administration (FDA) approval and insufficient clinical evidence of safety and/or efficacy in the published peer-reviewed medical literature. However, depending on the enrollee-specific benefit document, coverage may be available through participation in an eligible clinical trial.

Clinical Evidence

Evidence of low quality indicates that percutaneous left atrial appendage (LAA) closure is, at best, not inferior to oral anticoagulation therapy in reducing the risk of stroke in patients with atrial fibrillation (AF) and no contraindications to warfarin. In the absence of randomized controlled

trials directly comparing implantation of this device with available standard care for patients at high risk of stroke who are unable or unwilling to take anticoagulation therapy, data from four single-arm, prospective studies of percutaneous LAA closure reported a lower observed rate of stroke and transient ischemic attack (TIA) than predicted. This finding is not sufficient to recommend the use of these devices in this patient population. Percutaneous LAA closure devices were associated with a low frequency of serious adverse events, including cardiac tamponade, pericardial effusion, procedure-related ischemic stroke, and device embolization, but at least 3 patient deaths have been attributed to percutaneous implantation of an LAA device. There are no data to support the use of one currently available LAA closure device over another since none of the studies have directly compared their efficacy and safety. (Hayes, 2013)

Current evidence suggests that percutaneous occlusion of the LAA is efficacious in reducing the risk of thromboembolic complications associated with non-valvular atrial fibrillation (AF). With regard to safety, there is a risk of life-threatening complications from the procedure, but the incidence of these is low. Therefore, this procedure may be used provided that normal arrangements are in place for clinical governance, consent and audit. (NICE, 2010)

The PROTECT AF trial included 707 patients with nonvalvular AF who had at least 1 risk factor for stroke. Patients were randomized to chronic warfarin treatment (n=244) or percutaneous placement of the LAA device (n=463). The clinical endpoint of the study was a composite measure of stroke, cardiovascular death and embolism. The safety assessment included serious adverse events, including major bleeding, pericardial effusion and device embolization. After 1065 patient-years of follow-up, the efficacy event rate was 3.0 per 100 patient-years in the device group compared with 4.9 in the warfarin group - a relative reduction of 38%. However, serious safety events were more common in the device group (7.4 events per 100 patient-years) compared with the warfarin group (4.4). Most of these safety events were related to the procedural implant and pericardial effusion. Statistical analysis demonstrated that the LAA was 99.9% unlikely to be inferior to warfarin alone. At 2 years, both treatment groups had a similar intention-to-treat cumulative event rate. Since warfarin therapy is burdensome and carries risks of its own, closure of the LAA might provide an alternative strategy to chronic warfarin therapy for stroke prophylaxis in patients with nonvalvular AF. However, these data likely do not justify routine LAA occlusion in all patients with nonvalvular AF, primarily because the trial did not demonstrate prevention of embolism and stroke in high-risk patients. In addition, the short duration of follow-up does not offer enough information regarding long-term safety and efficacy. (Holmes et al., 2009)

Joint guidelines from the American Heart Association (AHA), American College of Cardiology (ACC) and Heart Rhythm Society (HRS) address percutaneous occlusion of the LAA but do not provide specific recommendations regarding the use of these devices. (January et al., 2014)

European Society of Cardiology guidelines for the management of atrial fibrillation state that although the concept of LAA closure seems reasonable, the evidence of efficacy and safety is currently insufficient to recommend these approaches for any patients other than those in whom long-term oral anticoagulation (OAC) therapy is contraindicated. However, in the absence of controlled clinical data this recommendation is based on expert consensus only. Additional, adequately powered, randomized studies in patients with high stroke risk and long-term follow-up, comparing interventional/percutaneous/surgical LAA closure with OAC therapy are needed for adequate assessment of such techniques. (Camm et al., 2012)

Additional product information

Amplatz® Cardiac Plug

PLAATO – this device is no longer on the market

Watchman®

References:

Camm AJ, Lip GY, De Caterina R, et al.; ESC Committee for Practice Guidelines (CPG). 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial

fibrillation. Developed with the special contribution of the European Heart Rhythm Association. Eur Heart J. 2012 Nov;33(21):2719-47. Erratum in: Eur Heart J. 2013 Mar;34(10):790. Eur Heart J. 2013 Sep;34(36):2850-1.

ECRI Institute. Health Technology Forecast. Transcatheter left atrial appendage occlusion for preventing stroke in patients with atrial fibrillation. May 2013. Updated March 2014.

Hayes, Inc. Hayes Medical Technology Directory. *Percutaneous left atrial appendage closure to reduce stroke risk in patients with atrial fibrillation*. Lansdale, PA: Hayes, Inc.; January 2013.

January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Circulation. 2014 Apr 10.

National Institute for Health and Care Excellence (NICE). IPG349. Percutaneous occlusion of the left atrial appendage in non-valvular atrial fibrillation for the prevention of thromboembolism. June 2010. Available at: <http://guidance.nice.org.uk/IPG349/Guidance/pdf/English>. Accessed June 14, 2014.

Holmes DR, Reddy VY, Turi ZG, et al; PROTECT AF Investigators. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. Lancet. 2009 Aug 15;374(9689):534-42.

Code	Description
0286T	Near-infrared spectroscopy studies of lower extremity wounds (e.g., for oxyhemoglobin measurement)

Near-infrared spectroscopy (NIRS) is unproven and not medically necessary for assessing tissue oxygenation in lower extremity wounds due to insufficient clinical evidence of safety and/or efficacy in the published peer-reviewed medical literature.

Clinical Evidence

The evidence is limited to one study.

Weingarten et al. (2010) conducted a pilot study to assess the efficacy of in vivo diffuse near-infrared spectroscopy (NIRS) in predicting wound healing in patients with diabetic foot ulcers. Sixteen chronic diabetic wounds were followed and assessed for subsurface oxyhemoglobin concentration using a NIR device. Weekly measurements were conducted until there was wound closure, limb amputation or 20 completed visits without healing. In the 16 patients followed, seven wounds healed, six limbs were amputated and three 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, the nonhealing wounds appeared to be improve clinically. The authors concluded that NIRS may determine wound healing earlier than that visibly assessed by current clinical approaches. Further studies with larger patient populations are necessary to determine the long-term safety and efficacy of this technology.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the unproven conclusion.

References:

Weingarten MS, Neidrauer M, Mateo A, et al. Prediction of wound healing in human diabetic foot ulcers by diffuse near-infrared spectroscopy: a pilot study. Wound Repair Regen. 2010 Mar-Apr;18(2):180-5.

Code	Description
0287T	Near-infrared guidance for vascular access requiring real-time digital visualization of subcutaneous vasculature for evaluation of potential access sites and vessel patency

Near-infrared vascular imaging systems (e.g., AccuVein® AV300 or VeinViewer™) are unproven and not medically necessary for guiding vascular access due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

In a randomized clinical trial van der Woude et al. (2013) evaluated the efficacy of near infrared imaging device to support intravenous cannulation in children with dark skin color. Poor vein visibility can make IV cannulation challenging in children with dark skin color. The trial was conducted to determine the effectiveness of a near-infrared vascular imaging device (VascuLuminator) to facilitate IV cannulation in children with dark skin color. In the operating room of a general hospital in Curacao, all consecutive children (0-15 years of age) requiring IV cannulation were included in a pragmatic cluster randomized clinical trial. The VascuLuminator was made available to anesthesiologists at the operating complex in randomized clusters of 1 week. Success at first attempt was 63% (27/43, 95% confidence interval [CI], 47%-77%) in the VascuLuminator group vs 51% (23 of 45 patients, 95% CI, 36%-66%) in the control group (P = 0.27). Median time to successful cannulation was 53 seconds (interquartile range: 34-154) in the VascuLuminator group and 68 seconds (interquartile range: 40-159) in the control group (P = 0.54), and hazard ratio was 1.12 (95% CI, 0.73-1.71). The author reported that VascuLuminator has limited value in improving success at first attempt of facilitating IV cannulation in children with dark skin color.

A Hayes report on the VeinViewer states that the quality of the evidence is low due to heterogeneity in the study populations, differences in procedures for which vein viewing was used, lack of blinded assessment of outcomes, and small sample sizes. While some evidence favored the VeinViewer, most of the studies showed no overall effect and may have lacked the power to detect small differences between the study groups and subgroups. The studies generally relied upon subjective assessment of the difficulty of needle insertion by nursing staff, which may vary according to the experience, training and confidence of the nurse. Differences in success rates for venous access between nursing staff at the different healthcare systems may have been due to differences in the extent of training with the device prior to use, and in pediatric nursing experience. The inconsistencies in the study results on the efficacy of the VeinViewer for guiding venous access procedures in children underlines the need for additional RCTs with larger study populations that use standardized measures of success for needle or catheter insertion and that control for diagnosis, comorbidities and staff experience in pediatric venous access procedures. (Hayes, 2012)

In a randomized, controlled trial, Kim et al. (2012) evaluated the efficacy of the VeinViewer for peripheral venous access in 111 hospitalized children between 1 month and 16 years of age. Children were randomized to peripheral vascular access by use of the VeinViewer (n=54) or by standard technique (n=57). The main outcome measures were first-attempt success rate and procedural time. Overall, the success rate at first attempt was similar in the VeinViewer and Control groups (72.2% versus 66.7%). The first-attempt success rate was 86.5% in patients with a low DIVA score (easier access) compared with 43.2% in patients with a DIVA score > 4. Among patients with a low DIVA score, there was no significant difference in the first-attempt success rate between the VeinViewer group and the Control group (83.3% versus 89.2%). Among patients with a high DIVA score, the first attempt success rate was significantly higher in the VeinViewer group than in the Control group (58.3% versus 25.0%). There was no significant difference in procedural times between groups either overall or among patients with low or high DIVA scores.

In a randomized, controlled trial, Phipps et al. (2012) evaluated the efficacy of the VeinViewer for placement of peripherally inserted central catheters (PICCs) in 115 neonates. Neonates were randomized to placement of a PICC by use of the VeinViewer (n=59) or by standard technique (n=56). The main outcome measures included first-attempt success rate and overall success. Use of the VeinViewer had no significant effect on the first-attempt success rate. Success at first attempt was 64% in the VeinViewer group and 59% in the Control group. Overall success was

86% in the VeinViewer group and 75% in the Control group, which was not a statistically significant difference. The authors reported that the most benefit was seen in infants of greater gestational age.

Perry et al. (2011) conducted a study to determine whether the use of a near-infrared light venipuncture aid (VeinViewer) would improve the rate of successful first-attempt placement of intravenous (IV) catheters in a high-volume pediatric emergency department (ED). Patients younger than 20 years with standard clinical indications for IV access were randomized to have IV placement using traditional methods (standard group) or with the aid of the near-infrared light source (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. A total of 123 patients (median age, 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 and device groups. Nurses placing IVs did report specific benefits to use of the device with specific patient groups, and future research should be conducted to demonstrate the role of the device in these patients.

Chapman et al. (2011) conducted a prospective, randomized study of children aged 0 to 17 who required nonemergent peripheral intravenous (PIV) catheter placement. Participants 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. A total of 323 patients completed the study: 174 boys and 149 girls. 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 aged 0 to 2 (n=107) did yield significant results for time to PIV placement (121 seconds (VV) vs. 167 seconds (SC)) and for nurses' perception of pain.

Cuper et al. (2011) conducted an observational feasibility study to evaluate a prototype of a near-infrared (NIR) vascular imaging system for venipuncture in children (0-6 years). The study gathered information during a period of 2 months without using the prototype (n = 80) then during a period of 1 month with a prototype NIR vascular imaging system (n = 45). Outcome measures were failure rate (i.e., more than 1 puncture) and time of needle manipulation. With the NIR vascular imaging system, failure rate decreased from 10/80 to 1/45 and time decreased from 2 seconds to 1 second.

References:

Chapman LL, Sullivan B, Pacheco AL, et al. VeinViewer-assisted Intravenous Catheter Placement in a Pediatric Emergency Department. *Acad Emerg Med*. 2011 Sep;18(9):966-71.

Cuper NJ, Verdaasdonk RM, de Roode R, et al. Visualizing veins with near-infrared light to facilitate blood withdrawal in children. *Clin Pediatr (Phila)*. 2011 Jun;50(6):508-12.

Hayes, Inc. Health Technology Brief. VeinViewer (Christie Digital Systems) for guiding venous access procedures in children. August 2012.

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Phipps K, Modic A, O'Riordan MA, Walsh M. A randomized trial of the Vein Viewer versus standard technique for placement of peripherally inserted central catheters (PICCs) in neonates. *J Perinatol*. 2012 Jul;32(7):498-501.

Perry AM, Caviness AC, Hsu DC. Efficacy of a near-infrared light device in pediatric intravenous cannulation: a randomized controlled trial. *Pediatr Emerg Care*. 2011 Jan;27(1):5-10.

van der Woude OC, Cuper NJ, Getrouw C. The effectiveness of a near-infrared vascular imaging device to support intravenous cannulation in children with dark skin color: a cluster randomized clinical trial. *Anesth Analg*. 2013 Jun;116(6):1266-71.

Code	Description
0288T	Anoscopy with delivery of thermal energy to the muscle of anal canal (e.g., for fecal incontinence)

Anoscopy with delivery of thermal energy such as radio-frequency energy is unproven and not medically necessary for treating fecal incontinence due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

The application of thermal energy to the anus muscles to produce scarring and improve anal closure has been proposed to treat fecal incontinence. The Secca procedure is an example of this type of treatment.

Although the results of the available studies suggest that the Secca procedure is reasonably safe, these studies do not provide sufficient evidence to assess the efficacy of this procedure. All of the reviewed studies found that the Secca procedure was associated with statistically significant improvements in fecal incontinence compared with pretreatment status; however, these studies were uncontrolled, and it is possible that the observed benefits were due to a placebo effect or bowel cleansing, which is believed to have a therapeutic effect in patients who have fecal incontinence. In addition to an absence of controls, all but one of the available studies enrolled fewer than 25 patients and the Secca procedure had limited benefits. While patients reported treatment-related improvements in fecal incontinence scores and quality-of-life scores, the changes were small, and their clinical relevance was inconclusive. Overall, low-quality evidence suggests that the Secca procedure may provide limited benefits for patients who have fecal incontinence. Controlled studies are needed to evaluate the effectiveness of the Secca procedure. (Hayes, December 2010, Updated November 2012)

The National Institute For Health And Care Excellence (NICE) clinical guidance report on endoscopic radiofrequency therapy of the anal sphincter for fecal incontinence states that the evidence on endoscopic radiofrequency therapy of the anal sphincter for fecal incontinence raises no major safety concerns. There is evidence of efficacy in the short-term, but in a limited number of patients. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research. The guideline also states that further research into endoscopic radiofrequency therapy of the anal sphincter for fecal incontinence should clearly define the patient groups being treated. (NICE 2011)

In a clinical guidance report on the management of fecal incontinence, the National Institute For Health And Care Excellence (NICE) states that the Secca procedure should be considered experimental. (NICE 2007)

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the unproven conclusion.

References:

Hayes Inc. Health Technology Brief. Secca® (Mederi Therapeutics Inc.) Procedure for Fecal Incontinence. December 2010 Updated November 2012.

National Institute For Health And Care Excellence (NICE). Endoscopic radiofrequency therapy of the anal sphincter for faecal incontinence. Interventional Procedure Guidance 393. May 2011. Available at: <http://www.nice.org.uk/nicemedia/live/13047/54501/54501.pdf>. Accessed June 2014.

National Institute For Health And Care Excellence (NICE). Faecal incontinence. The management of faecal incontinence in adults. Jun 27, 2007. Available at: <http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11012> Accessed June 2014.

Code	Description
0291T	Intravascular optical coherence tomography (coronary native vessel or graft) during diagnostic evaluation and/or therapeutic intervention, including imaging supervision, interpretation, and report; initial vessel (List separately in addition to primary procedure)
0292T	each additional vessel (List separately in addition to primary procedure)

Optical coherence tomography (OCT), using near-infrared light, is unproven and not medically necessary for evaluating coronary arteries due to insufficient clinical evidence of safety and/or efficacy in the published peer-reviewed medical literature.

Clinical Evidence

Optical coherence tomography (OCT) generates a highly detailed, magnified view of a thin layer of tissue using reflected infrared light. This technology has been adapted to percutaneous catheters and is used to examine features of intracoronary plaques or stents that may increase the risk of subsequent adverse events, such as clot formation or blockage of the affected coronary artery. (Hayes, 2011; updated 2013)

Although there are several studies comparing OCT to IVUS for assessing plaque characteristics and stent placement, these studies are limited by size and design. Larger, well-designed prospective studies are needed to determine the clinical utility of OCT compared to standard diagnostic methods.

An ECRI emerging technology report concluded that the quantity, quality and consistency of the evidence base for OCT is low. (ECRI, 2013)

A Hayes report concluded that available studies do not provide convincing evidence that assessment of intracoronary plaques and stents with optical coherence tomography (OCT) provides information that can be used to improve patient management. Studies did not involve sufficient follow-up to determine whether the potentially problematic plaque and stent characteristics observed with OCT were associated with significant increases in long-term adverse cardiac events. Additional studies are needed to determine whether OCT provides diagnostic information that can be used to benefit patients. (Hayes, 2011; updated 2013)

Joint guidelines developed by the American College of Cardiology, American Heart Association and Society for Cardiovascular Angiography and Interventions concluded that the appropriate role for optical coherence tomography in routine clinical decision making has not been established. (Levine et al., 2011)

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Additional product information

C7 Dragonfly™, C7 XR™ , Extreme Resolution™, Ilumien™ System, Terumo-OFDI system

References:

ECRI Institute. Emerging Technology Evidence Report. Optical coherence tomography during angiography to inform decision making for treating coronary artery disease. March 2013.

Hayes, Inc. Hayes Medical Technology Directory. *Optical coherence tomography for coronary artery plaque characterization and stent evaluation*. Lansdale, PA: Hayes, Inc.; December 2011. Updated November 2013.

Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *Circulation* 2011 Dec 6;124(23):e574-651.

Code	Description
0293T	Insertion of left atrial hemodynamic monitor; complete system, includes implanted communication module and pressure sensor lead in left atrium including transeptal access, radiological supervision and interpretation, and associated injection procedures, when performed
0294T	pressure sensor lead at time of insertion of pacing cardioverter-defibrillator pulse generator including radiological supervision and interpretation and associated injection procedures, when performed (List separately in addition to code for primary procedure)

Implantable devices for monitoring left atrial pressure are investigational, unproven and not medically necessary due to lack of U.S. Food and Drug Administration (FDA) approval and insufficient clinical evidence of safety and/or efficacy in the published peer-reviewed medical literature. However, depending on the enrollee-specific benefit document, coverage may be available through participation in an eligible clinical trial.

Clinical Evidence

The phase III Left Atrial Pressure Monitoring to Optimize Heart Failure Therapy (LAPTOP-HF) trial is underway. The purpose of this clinical study is to evaluate the safety and clinical effectiveness of the use of a physician-directed, patient self-management system, guided by left atrial pressure measurements, for use in patients with heart failure. The system allows patients to adjust heart failure (HF) medications daily based on a physician-directed prescription plan and current HF status, similar to the manner in which diabetes patients manage their insulin therapy. The goal of the LAPTOP-HF study is to demonstrate reductions in episodes of worsening HF and hospitalizations in patients who are managed with the left atrial pressure (LAP) management system (treatment group) versus those who receive only the current standard of care (control group). <http://www.clinicaltrials.gov/ct2/show/NCT01121107?term=laptop-hf&rank=1>

Ritzema et al. (2010) conducted the HOMEOSTASIS[®] trial, a feasibility study to evaluate the clinical results of a permanently implanted left atrial pressure (LAP) sensor linked to a physician directed patient self-management treatment paradigm. This small observational study assessed early safety and clinical outcomes with the goal of generating hypotheses for subsequent randomized trials.

Heart Failure Society of America guidelines (Lindenfeld et al., 2010) state that the routine use of invasive hemodynamic monitoring in patients with acute decompensated heart failure (ADHF) is not recommended. (Strength of Evidence = A; based on randomized, controlled trial(s))

Invasive hemodynamic monitoring should be considered in a patient:

- who is refractory to initial therapy,
- whose volume status and cardiac filling pressures are unclear,
- who has clinically significant hypotension (typically SBP !80 mm Hg) or worsening renal function during therapy, or
- who is being considered for cardiac transplant and needs assessment of degree and reversibility of pulmonary hypertension, or
- in whom documentation of an adequate hemodynamic response to the inotropic agent is necessary when chronic outpatient infusion is being considered. (Strength of Evidence = C; based on expert opinion)

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Additional product information

CardioMEMS[™] HF System

HeartPOD® System
Promote® LAP System

References:

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Ritzema J, Troughton R, Melton I, et al.; Hemodynamically Guided Home Self-Therapy in Severe Heart Failure Patients (HOMEOSTASIS) Study Group. Physician-directed patient self-management of left atrial pressure in advanced chronic heart failure. Circulation. 2010 Mar 9;121(9):1086-95.

Code	Description
0301T	Destruction/reduction of malignant breast tumor with externally applied focused microwave, including interstitial placement of disposable catheter with combined temperature monitoring probe and microwave focusing sensocatheter under ultrasound thermotherapy guidance

Focused microwave thermal ablation is unproven and not medically necessary for treating breast cancer due to insufficient clinical evidence of safety and/or efficacy in the published peer-reviewed medical literature.

Clinical Evidence

Zhao et al. (2010) reviewed studies evaluating minimally-invasive thermal ablation techniques for treating early-stage breast cancer. The analyzed studies were mostly feasibility or pilot studies using different energy sources, patients, tumor characteristics and ablation settings. Despite many methodological differences, complete tumor ablation could be achieved in 76-100% of breast cancer patients treated with radiofrequency ablation, 13-76% in laser ablation, 0-8% in microwave ablation, 36-83% in cryoablation and 20-100% in high-intensity focused ultrasound ablation. The authors concluded that minimally-invasive thermal ablation is a promising new tool for local destruction of small carcinomas of the breast. Large randomized control studies are required to assess the long-term advantages of minimally-invasive thermal ablation techniques compared to the current breast conserving therapies.

Externally applied wide-field adaptive phased-array FMT has been investigated both as a preoperative heat-alone ablation treatment and as a combination treatment with preoperative anthracycline-based chemotherapy for breast tumors ranging in size from 0.8 to 7.8 cm. Dooley et al. (2010) reviewed the results of four multi-institutional clinical studies of preoperative focused microwave thermotherapy (FMT) for treating invasive carcinomas in the intact breast. The authors found that wide-field adaptive phased-array FMT can be safely administered in a preoperative setting, and data from randomized studies suggest both a reduction in positive tumor margins as a heat-alone treatment for early-stage breast cancer and a reduction in tumor volume when used in combination with anthracycline-based chemotherapy for patients with large breast cancer tumors. Larger randomized studies are required to verify these conclusions.

Earlier studies concluded that focused microwave phased array thermotherapy was safe in treating breast carcinomas but acknowledge that further studies with larger patient populations were needed. (Vargas, 2004; Gardner, 2002)

National Comprehensive Cancer Network (NCCN) guidelines on the treatment of breast cancer do not address microwave thermal ablation as a treatment option. (NCCN, 2014)

The American Cancer Society (ACS) states that hyperthermia may be a promising way to improve cancer treatment; however, it is largely an experimental technique at this time. (ACS, 2013)

References:

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Gardner RA, Vargas HI, Block JB, Vogel CL, Fenn AJ, Kuehl GV, Doval M. Focused microwave phased array thermotherapy for primary breast cancer. *Ann Surg Oncol*. 2002 May;9(4):326-32.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Breast cancer. v3.2014.

Vargas HI, Dooley WC, Gardner RA, et al. Focused microwave phased array thermotherapy for ablation of early-stage breast cancer: results of thermal dose escalation. *Ann Surg Oncol*. 2004 Feb;11(2):139-46.

Zhao Z, Wu F. Minimally-invasive thermal ablation of early-stage breast cancer: a systemic review. *Eur J Surg Oncol*. 2010 Dec;36(12):1149-55.

Code	Description
0302T	Insertion or removal and replacement of intracardiac ischemia monitoring system including imaging supervision and interpretation when performed and intra-operative interrogation and programming when performed; complete system (includes device and electrode)
0303T	Insertion or removal and replacement of intracardiac ischemia monitoring system including imaging supervision and interpretation when performed and intra-operative interrogation and programming when performed; electrode only
0304T	Insertion or removal and replacement of intracardiac ischemia monitoring system including imaging supervision and interpretation when performed and intra-operative interrogation and programming when performed; device only
0305T	Programming device evaluation (in person) of intracardiac ischemia monitoring system with iterative adjustment of programmed values, with analysis, review, and report
0306T	Interrogation device evaluation (in person) of intracardiac ischemia monitoring system with analysis, review, and report
0307T	Removal of intracardiac ischemia monitoring device

Implantable devices that detect cardiac ischemia are investigational, unproven and not medically necessary due to lack of U.S. Food and Drug Administration (FDA) approval and insufficient clinical evidence of safety and/or efficacy in the published peer-reviewed medical literature. However, depending on the enrollee-specific benefit document, coverage may be available through participation in an eligible clinical trial.

Coverage for revision or removal of intracardiac ischemia monitoring devices may be addressed in the complication section of the benefit document. See the enrollee-specific benefit document.

Clinical Evidence

The AngelMed Guardian® system is an implantable cardiac device, designed to detect rapid ST segment changes that may signify major cardiac events, such as coronary artery occlusions or heart failure progression. Once an ST shift is detected, the system is designed to alert patients to seek immediate medical care, often before symptoms occur. (AngelMed website)

The AngelMed for Early Recognition and Treatment of STEMI (ALERTS) study is ongoing to evaluate the long-term safety and efficacy of these devices. The phase-III prospective,

randomized multicenter study is enrolling patients with a high-risk of having a heart attack due to acute coronary syndrome or bypass surgery. (ClinicalTrials.gov, [NCT00781118](https://clinicaltrials.gov/ct2/show/study/NCT00781118))

Fischell et al. (2010) reported the initial clinical results using intracardiac monitoring in 37 patients at high risk for acute coronary syndromes. During follow-up (median 1.52 years, range 126 to 974 days), 4 patients had ST-segment changes of ≥ 3 standard deviations (SDs) of their normal daily range, in the absence of an elevated heart rate. This in combination with immediate hospital monitoring led to angiogram and/or intravascular ultrasonography, which confirmed thrombotic coronary occlusion/ruptured plaque. The median alarm-to-door time was 19.5 min (6, 18, 21 and 60 min, respectively). Alerting for demand-related ischemia at elevated heart rates, reflective of flow-limiting coronary obstructions, occurred in 4 patients. There were 2 false-positive ischemia alarms related to arrhythmias, and 1 alarm due to a programming error that did not prompt cardiac catheterization. The authors concluded that shifts exceeding 3 SD from a patient's daily intracardiac ST-segment range may be a sensitive/specific marker for thrombotic coronary occlusion. Patient alerting was associated with a median alert-to-door time of 19.5 min for patients at high risk of recurrent coronary syndromes who typically present with 2- to 3-hour delays.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

References:

AngelMed website. <http://www.angel-med.com>. Accessed June 14, 2014

Fischell TA, Fischell DR, Avezum A, et al. Initial clinical results using intracardiac electrogram monitoring to detect and alert patients during coronary plaque rupture and ischemia. J Am Coll Cardiol. 2010 Sep 28;56(14):1089-98.

Code	Description
0319T	Insertion or replacement of subcutaneous implantable defibrillator system with subcutaneous electrode
0320T	Insertion of subcutaneous defibrillator electrode
0321T	Insertion of subcutaneous implantable defibrillator pulse generator only with existing subcutaneous electrode
0322T	Removal of subcutaneous implantable defibrillator pulse generator only
0323T	Removal of subcutaneous implantable defibrillator pulse generator with replacement of subcutaneous implantable defibrillator pulse generator only
0324T	Removal of subcutaneous defibrillator electrode
0325T	Repositioning of subcutaneous implantable defibrillator electrode and/or pulse generator
0326T	Electrophysiologic evaluation of subcutaneous implantable defibrillator (includes defibrillation threshold evaluation, induction of arrhythmia, evaluation of sensing for arrhythmia termination, and programming or reprogramming of sensing or therapeutic parameters)
0327T	Interrogation device evaluation (in person) with analysis, review and report, includes connection, recording and disconnection per patient encounter; implantable subcutaneous lead defibrillator system
0328T	Programming device evaluation (in person) with iterative adjustment of the implantable device to test the function of the device and select optimal permanent programmed values with analysis; implantable subcutaneous lead defibrillator system

Subcutaneous implantable cardioverter-defibrillators are unproven and not medically necessary for detecting and treating ventricular arrhythmias due to insufficient clinical evidence of safety and/or efficacy in the published peer-reviewed medical literature.

Clinical Evidence

Conventional implantable cardioverter-defibrillators (ICDs) require the placement of electrode leads through major veins and into the heart's ventricular chambers. Subcutaneous ICD leads are placed just beneath the skin. These devices cannot provide long-term pacing so are therefore not an alternative to transvenous ICDs when antibradycardia pacing is required.

A Hayes report concluded that while subcutaneous ICDs are a promising technology, the overall quality of the evidence is low due to a lack of randomized controlled trials and to methodological limitations of the existing studies. The studies were relatively small and lacked adequate follow-up times to determine the durability and long-term efficacy and safety of the device compared with conventional ICD therapy. Despite weak evidence, study results suggest that subcutaneous ICDs may be efficacious and have a safety profile that is comparable with that of conventional ICDs. However, there is insufficient evidence to draw definitive conclusions about the technology or to establish optimal patient selection criteria. Ongoing studies may address the remaining questions about this technology and help to establish its place in the algorithm for treatment of patients at high risk for sudden cardiac death. (Hayes, 2013)

Evidence suggests that subcutaneous ICDs work to restore normal cardiac rhythm and provide protection against sudden cardiac arrest in patients with life-threatening ventricular tachycardia (VT) who do not have symptomatic bradycardia, incessant VT or spontaneous, frequently recurring VT that is reliably terminated with antitachycardia pacing. Registry data suggests that subcutaneous ICDs produce fewer lead complications but more major infections than transvenous ICDs; however, no direct comparison studies have been completed. (ECRI, 2014)

Weiss et al. conducted a prospective, nonrandomized, multicenter trial evaluating the safety and efficacy of a subcutaneous ICD in 330 patients with an indication for an ICD but not for pacing. A total of 314 patients underwent successful implantation. The cohort was followed for a mean duration of 11 months. The study population was 74% male with a mean age of 52±16 years and mean left ventricular ejection fraction of 36±16%. A previous transvenous ICD had been implanted in 13%. The 180-day system complication-free rate was 99%, and sensitivity analysis of the acute ventricular fibrillation conversion rate was >90% in the entire cohort. There were 38 discrete spontaneous episodes of ventricular tachycardia/ventricular fibrillation recorded in 21 patients (6.7%), all of which successfully converted. Forty-one patients (13.1%) received an inappropriate shock. This study is limited by a lack of randomization and control.

Bardy et al. (2010) designed and tested an entirely subcutaneous ICD system (Cameron Health). The authors conducted two short-term clinical trials to identify a suitable device configuration and assess energy requirements. Four subcutaneous ICD configurations were evaluated in 78 patients with the best configuration tested in 49 additional patients. The goal was to determine the subcutaneous defibrillation threshold in comparison with that of the standard transvenous ICD. Next, the authors evaluated the long-term use of subcutaneous ICDs in a pilot study, involving 6 patients, followed by a trial of 55 patients. The best device configuration consisted of a parasternal electrode and a left lateral thoracic pulse generator. This configuration was as effective as a transvenous ICD for terminating induced ventricular fibrillation, albeit with a significantly higher mean energy requirement (36.6±19.8 J vs. 11.1±8.5 J). Among patients who received a permanent subcutaneous ICD, ventricular fibrillation was successfully detected in 100% of 137 induced episodes. Clinically significant adverse events included two pocket infections and four lead revisions. After a mean of 10±1 months, the device had successfully detected and treated all 12 episodes of spontaneous, sustained ventricular tachyarrhythmia. A potential for bias exists due to manufacturer sponsorship of the study. This study is limited by small sample size and lack of randomization and control. Further results from large, long-term,

randomized, prospective, multicenter trials are needed to determine if this technology is comparable to conventional ICDs in selected patients who do not require long-term pacing.

In a multicenter case-control study, Köbe et al. (2013) reported the results of patients with an entirely subcutaneous implantable-cardioverter defibrillator (ICD) system (S-ICD®) compared to a matched conventional transvenous ICD group. Sixty-nine patients (50 male, 19 female, mean age 45.7±15.7 years) received an S-ICD in three centers and were randomly assigned to 69 sex and age matched conventional ICD patients. Conversion rates of induced ventricular fibrillation were 89.5% for 65 Joules (15J safety-margin) and 95.5% including reversed shock polarity (15J safety-margin) in the study group. Termination of induced ventricular fibrillation was successful in 90.8% (10J safety-margin device dependant) of the control patients. Procedural complications were similar between the two groups. The mean follow-up is 217±138 days. During follow-up, three patients with S-ICD were appropriately treated for ventricular arrhythmias. Three inappropriate episodes occurred (5.2%) in three S-ICD patients due to T-wave oversensing, whereas atrial fibrillation with rapid conduction was the predominant reason for inappropriate therapy in conventional devices. The authors concluded that the S-ICD system could safely be implanted with similar perioperative adverse events compared to standard transvenous devices. This observational study is limited by its retrospective design, small sample size and lack of randomization. Further results from large, long-term, randomized, prospective, multicenter trials are needed to determine if this technology is comparable to conventional ICDs in selected patients who do not require long-term pacing.

Several retrospective studies assessed the safety and efficacy of subcutaneous ICDs. The studies generally support the efficacy of the technology, showing that the device delivers appropriate shocks to a high proportion of patients experiencing spontaneous ventricular tachycardias, achieving successful conversion of the arrhythmia to a normal cardiac rhythm. The rate of patients who received an appropriate shock ranged from 7% to 25%, with a successful conversion rate of 96% to 100%. The rates of patients receiving an inappropriate shock ranged from 5% to 25%. No major adverse events were observed perioperatively or during follow-up; however, the device is associated with a moderate rate of infectious complications. These studies are limited by retrospective design and lack of randomization and control. (Jarmon and Todd, 2013; Olde Nordkamp et al., 2012; Aydin et al., 2012; Dabiri Abkenari et al., 2011)

On September 28, 2012, the U.S. Food and Drug Administration (FDA) approved a premarket approval application (P110042) for the S-ICD™ device. The device is approved to provide defibrillation therapy for the treatment of life-threatening ventricular tachyarrhythmias in patients who do not have symptomatic bradycardia, incessant ventricular tachycardia or spontaneous, frequently recurring ventricular tachycardia that is reliably terminated with antitachycardia pacing. Available at: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=7216>. Accessed June 17, 2014.

A National Institute for Health and Care Excellence (NICE) report states that the current evidence on the efficacy of subcutaneous ICDs for the prevention of sudden cardiac death in the short and medium term is adequate. Evidence on its safety in the short term is adequate but there are uncertainties about long-term durability. Therefore this procedure should only be used with special arrangements for clinical governance, consent and audit or research. (NICE, 2013)

Several clinical trials are ongoing.

No professional society guidelines addressing this technology were identified.

References:

Aydin A, Hartel F, Schlüter M, et al. Shock efficacy of subcutaneous implantable cardioverter-defibrillator for prevention of sudden cardiac death: initial multicenter experience. *Circ Arrhythm Electrophysiol*. 2012 Oct;5(5):913-9.

Bardy GH, Smith WM, Hood MA, et al. An entirely subcutaneous implantable cardioverter-defibrillator. *N Engl J Med*. 2010 Jul 1;363(1):36-44.

Boston Scientific website. Available at: <http://www.bostonscientific.com/s-icd/index.html>. Accessed June 17, 2014.

Dabiri Abkenari L, Theuns DA, Valk SD, et al. Clinical experience with a novel subcutaneous implantable defibrillator system in a single center. *Clin Res Cardiol*. 2011 Sep;100(9):737-44.

ECRI Institute. Health Technology Forecast. Subcutaneous implantable cardioverter-defibrillator for preventing sudden cardiac arrest. November 2011. May 2013.

ECRI Institute. Product Brief. Subcutaneous implantable cardioverter-defibrillator (Boston Scientific Corp.) for preventing sudden cardiac arrest. March 2014.

Hayes, Inc. Hayes Health Technology Brief. *S-ICD (subcutaneous implantable cardioverter defibrillator; Boston Scientific Corp.) for prevention of sudden cardiac death*. Lansdale, PA: Hayes, Inc.; December 2013.

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Köbe J, Reinke F, Meyer C, et al. Implantation and follow-up of totally subcutaneous versus conventional implantable cardioverter-defibrillators: A multicenter case-control study. *Heart Rhythm*. 2013 Jan;10(1):29-36.

National Institute for Health and Care Excellence. IPG 454. Insertion of a subcutaneous implantable cardioverter defibrillator for prevention of cardiac death. April 2013. Available at: <http://www.nice.org.uk/nicemedia/live/13737/63667/63667.pdf>. Accessed June 17, 2014.

Olde Nordkamp LR, Dabiri Abkenari L, Boersma LV, et al. The entirely subcutaneous implantable cardioverter-defibrillator: initial clinical experience in a large Dutch cohort. *J Am Coll Cardiol*. 2012 Nov 6;60(19):1933-9.

Weiss R, Knight BP, Gold MR, et al. Safety and efficacy of a totally subcutaneous implantable-cardioverter defibrillator. *Circulation*. 2013 Aug 27;128(9):944-53.

Code	Description
0330T	Tear film imaging, unilateral or bilateral, with interpretation and report

Tear film imaging to monitor or assess tear film disorders is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Techniques that gather information from the tear film by processing reflected light or images from the tear are being investigated as representing the true state of the ocular surface. This includes techniques such as interferometry, meniscometry, high speed video topography, and optical coherence tomography (Dry Eye Workshop 2007). These tear film imaging techniques are being investigated to assist in better differentiating dry eye disorders and developing dry eye treatments.

In a prospective case-control study, Hosaka et al. (2011) compared tear film thickness between normal subjects and aqueous tear deficiency dry eye patients by tear interferometry. Central precorneal tear film thickness was measured noninvasively using an interference thin-film thickness measurement device (Quore MSPA1100; Mamiya-OP). Tear film thickness of 14 eyes from 14 normal subjects and of 28 eyes from 28 aqueous tear deficiency dry eye patients were compared along with noninvasively measured tear meniscus height, DR-1 (Kowa) dry eye severity grading, fluorescein and rose bengal staining scores, tear film break-up time, and Schirmer test results. Among dry eye patients, 13 eyes underwent punctal occlusion, and tear film thickness was compared before and after the surgery. Tear film was significantly thinner in dry eye patients than normal subjects. Tear film thickness showed good correlation with other dry eye examinations. After punctal occlusion, tear film thickness increased significantly from $1.7 \pm 1.5 \mu\text{m}$ to $4.9 \pm 2.8 \mu\text{m}$ with the improvement of tear meniscus height, fluorescein and rose bengal staining scores, tear film break-up time, and Schirmer test values. The authors concluded that interferometric tear film thickness measurement revealed impaired precorneal tear film formation in aqueous tear deficiency dry eyes and was useful for showing the reconstruction of tear film after punctal occlusion surgery. According to the authors, interferometry of precorneal tear film

may be helpful for the evaluation of aqueous tear deficiency in conjunction with other dry eye examinations. These findings require confirmation in a larger study.

In a retrospective analysis, Finis et al. (2013) evaluated the LipiView interferometer by assessing if there is a correlation between the tear-film lipid layer thickness (LLT) and other diagnostic criteria for meibomian gland dysfunction (MGD) in 110 patients (199 eyes). Subjective symptoms, break-up time (BUT), expressible Meibomian glands, and LLT were measured. There was a significant correlation between expressible Meibomian glands and LLT. Also, a possible trend of inverse correlation between subjective symptoms (standard patient evaluation of eye dryness) and the LLT was observed; however, this was not significant. Analysis of the whole study collective revealed no correlation between the BUT and the LLT. For a cut-off value of ≤ 75 -nm LLT, the authors found a sensitivity of 65.8% and a specificity of 63.4% for the detection of an MGD. For a cut-off value of ≤ 60 , the sensitivity was 47.9%, and the specificity was 90.2%. The authors concluded that the positive correlation between the LLT and expressible meibomian glands found in this study suggests a higher probability of MGD in patients with a low LLT. According to the authors, the LipiView interferometer might be a suitable screening test for detecting MGD. The authors stated that further prospective studies are needed to confirm these results and to identify potential confounders.

Szczesna et al. (2011) measured tear film surface quality in 34 patients with healthy or dry eyes using three noninvasive techniques of tear film quality assessment and evaluated the ability of these noninvasive techniques to predict dry eye. Three noninvasive techniques were applied for measurement of tear film surface quality: dynamic-area high-speed videokeratoscopy (HSV), wavefront sensing (DWS), and lateral shearing interferometry (LSI). To investigate the capability of each method to discriminate dry eye subjects from normal subjects, the receiver operating curve (ROC) was calculated and then the area under the curve (AUC) was extracted. The best result was obtained for the LSI technique, which was followed by HSV. The best result for DWS was an AUC of 0.64 obtained for changes in vertical coma in suppressed blinking conditions (SBC), whereas for natural blinking conditions (NBC), the results were poorer. The authors concluded that noninvasive techniques of tear film surface assessment can be used for predicting dry eye. In this study, LSI showed the best detection performance, closely followed by the dynamic-area HSV. The DWS technique was less powerful, particularly in NBC. The study did not confirm the utility of such findings in improving care and outcome of patients.

The American Academy of Ophthalmology Preferred Practice Pattern on dry eye syndrome does not address tear film imaging. See the following Web site for more information:
<http://one.aaopt.org/CE/PracticeGuidelines/PPP.aspx?sid=9955f101-a94b-4f8f-a3c9-15d014f613b9>
Accessed May 2014.

Reference(s):

Dry Eye WorkShop (DEWS). Methodologies to diagnose and monitor dry eye disease: report of the Diagnostic Methodology Subcommittee of the International Dry Eye WorkShop (2007). *Ocul Surf.* 2007c;5(2):108-152. Available at: <http://www.tearfilm.org/dewsreport/pdfs/Methodologies%20to%20Diagnose%20and%20Monitor%20Dry%20Eye%20Disease.pdf> . Accessed May 2014.

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Hosaka E, Kawamorita T, Ogasawara Y, et al. Interferometry in the evaluation of precorneal tear film thickness in dry eye. *Am J Ophthalmol.* 2011 Jan;151(1):18-23.e1.

Szczesna DH, Alonso-Caneiro D, Iskander DR, et al. Predicting dry eye using noninvasive techniques of tear film surface assessment. *Invest Ophthalmol Vis Sci.* 2011 Feb 9;52(2):751-6.

Code	Description
0331T	Myocardial sympathetic innervation imaging, planar qualitative and quantitative assessment
0332T	Myocardial sympathetic innervation imaging, planar qualitative and quantitative assessment; with tomographic SPECT (For myocardial infarct avid imaging, see 78466, 78468 and 78469)

Myocardial sympathetic innervation imaging is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Molecular imaging has several potential applications in the study of cardiovascular disease. Many of these approaches are aimed at detecting early stages of cardiovascular disease, determining the severity and stage of disease and aiding in preventing disease progression. Molecular imaging approaches are also being designed to detect and localize myocardial biomarkers specific for cellular changes associated with congestive heart failure (CHF). These new approaches may allow clinicians to determine disease severity, predict mortality, guide therapy and assess treatment success. CHF is characterized by an increase in norepinephrine (NE) release from sympathetic nerve terminals in the heart and a decrease in NE reuptake by the same nerve terminals. The uptake of the radiolabeled NE analog ¹²³I-metaiodobenzylguanidine (¹²³I-mIBG) may be a marker of CHF severity, as healthier hearts retain more of the NE analog than less healthy hearts. ¹²³I-mIBG uptake may also be able to identify patients at greater risk of sudden death from severe arrhythmia, which has been linked to overactive sympathetic activity in CHF. (ECRI, 2012)

The ADMIRE-HF (AdreView Myocardial Imaging for Risk Evaluation in Heart Failure) study validated the prognostic value of iodine-123 meta-iodobenzylguanidine (¹²³I-mIBG) imaging in assessing patients with heart failure (HF). A total of 961 subjects with New York Heart Association (NYHA) functional class II/III HF and left ventricular ejection fraction (LVEF) ≤35% were followed for up to 2 years. The results suggest that, in appropriately selected patients, ¹²³I-mIBG imaging could alert clinicians to the potential need for advanced therapies. ADMIRE-HF was not powered to evaluate the benefit of ¹²³I-mIBG imaging as a guide to clinical management. ClinicalTrials.gov NCT00126425 and NCT00126438 (Jacobson et al., 2010)

An American Society of Nuclear Cardiology (ASNC) review looks at cardiac autonomic innervation imaging with a radiotracer such as ¹²³I-meta-iodobenzylguanidine (¹²³I-mIBG). Cardiac ¹²³I-mIBG uptake can be assessed by planar and SPECT techniques. Cardiac ¹²³I-mIBG findings have consistently been shown to correlate strongly with heart failure severity, pre-disposition to cardiac arrhythmias and poor prognosis independent of conventional clinical, laboratory and image parameters. ¹²³I-mIBG imaging may help monitor a patient's clinical course and response to therapy. Autonomic imaging also appears to help diagnose ischemic heart disease and identify higher risk, as well as risk-stratify patients with diabetes. The review concludes that while cardiac ¹²³I-mIBG imaging shows promise as an emerging technique for recognizing and following potentially life-threatening conditions, prospective studies in larger study populations are needed to establish its clinical utility. (Travin, 2013)

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

References:

ECRI Institute. Hotline Service. Molecular imaging approaches for diagnosing severity of cardiovascular disease. August 2012.

Jacobson AF, Senior R, Cerqueira MD, et al. Myocardial iodine-123 meta-iodobenzylguanidine imaging and cardiac events in heart failure. Results of the prospective ADMIRE-HF (AdreView Myocardial Imaging for Risk Evaluation in Heart Failure) study. J Am Coll Cardiol. 2010 May 18;55(20):2212-21.

Travin MI. Cardiac autonomic imaging with SPECT tracers. J Nucl Cardiol. 2013 Feb;20(1):128-43; quiz 146.

Code	Description
0335T	Extra-osseous subtalar joint implant for talotarsal stabilization

The use of extra-osseous subtalar joint implant for talotarsal stabilization is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Flexible flatfoot is a common disorder, anatomically described as excessive pronation during weight bearing due to anterior and medial displacement of the talus. It may be congenital in nature, or it may be acquired in adulthood due to posterior tibial tendon dysfunction, which in turn may be caused by trauma, overuse, and inflammatory disorders, among others. Symptoms include dull, aching and throbbing cramping pain, which in children may be described as growing pains. Additional symptoms include refusal to participate in athletics or walking long distances. Conservative treatments include orthotics or shoe modifications. Surgical approaches for painful flatfoot deformities include tendon transfers, osteotomy, and arthrodesis. Arthroereisis with a variety of implant designs has also been investigated.

Subtalar arthroereisis is a surgical procedure designed to correct the excessive talar displacement and calcaneal eversion by placing an implant in the sinus tarsi, a canal located between the talus and the calcaneus.

The body of literature evaluating subtalar arthroereisis (SA) consists mainly of retrospective case series and case reports and presents low-quality, limited evidence regarding efficacy and safety. All of the studies consistently found positive effects for the majority of patients. SA consistently improved pain, functionality, and radiographic findings associated with flatfoot (FF) in children, and these effects were observed for 12 years following the procedure. However, all of these studies used a retrospective uncontrolled design, and biased results cannot be ruled out. The evidence regarding adults, while positive, is too limited in quantity to support conclusions regarding efficacy and safety. No randomized controlled studies are available to compare SA with other established surgical techniques for SA such as arthrodesis or osteotomy. The safety profile of the procedure appears to be favorable, with pain and sinus tarsi tenderness being the most frequent complications. These symptoms usually improve after removal of the implant. Based on the current published evidence, the following Hayes Ratings are assigned: C – For SA for the treatment of FF deformity, associated with pain or impairment of function and not responsive to conservative treatment, in children. This Rating is based on the results from six studies of poor quality consistently suggesting that SA improves pain, functionality, and radiographic findings associated with FF, and on the favorable safety profile of the procedure. D2 – For SA for the treatment of FF deformity, associated with pain or impairment of function and not responsive to conservative treatment, in adults. This Rating is based on the lack of sufficient evidence to evaluate the procedure for this population. (Hayes, 2012).

There is currently no published evidence from randomized controlled trials on subtalar arthroereisis. Numerous implant systems have received approval through the FDA's 510(k) process. A complete listing of subtalar implant devices that have received FDA approval are posted on the FDA's Center for Devices and Radiologic Health (CDRH) website (FDA, 2013).

The evidence in the published medical literature on subalar arthroereisis is inadequate to permit scientific conclusions. The main limitation is the lack of controlled studies comparing use of the

implants with other surgical procedures, alone or in combination .Another limitation of the published data is the lack of long-term outcomes

The American College of Foot and Ankle Surgeons (ACFAS) voted in 2012 to deactivate their clinical practice guidelines for adult and pediatric flatfoot stating that it has no longer met their current standards. While the documents will remain on the ACFAS web site, they are to be considered informational Clinical Consensus Statements. The published clinical consensus statement notes long-term results of arthroereisis has not been established.

The American Association of Orthopaedic Surgeons has not taken a formal position with regard to the use of surgically placed implants as a treatment option for adult (acquired) flatfoot, flexible flatfoot in children, or in combination with other comprehensive surgical procedures for ankle and foot conditions.

The evidence in the peer-reviewed published literature is insufficient to draw conclusions as to the safety and effectiveness of extraosseous subtalar implants for talotarsal stabilization and subtalar arthroereisis. Further research is required in the form of prospective controlled studies with long-term follow-up of functional improvement.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

American Academy of Orthopaedic Surgeons (AAOS). OrthoInfo. Diseases & Conditions. Available at: <http://orthoinfo.aaos.org/menus/diseases.cfm>. Accessed on June 10, 2014

Hayes, Inc. Directory. Subtalar Arthroereisis for the Treatment of Flatfoot: November 20, 2012.

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Code	Description
0338T	Transcatheter renal sympathetic denervation, percutaneous approach including arterial puncture, selective catheter placement(s) renal artery (ies), fluoroscopy, contrast injection(s), intraprocedural roadmapping and radiological supervision and interpretation, including pressure gradient measurements, flush aortogram and diagnostic renal angiography when performed; unilateral
0339T	Transcatheter renal sympathetic denervation, percutaneous approach including arterial puncture, selective catheter placement(s) renal artery (ies), fluoroscopy, contrast injection(s), intraprocedural roadmapping and radiological supervision and interpretation, including pressure gradient measurements, flush aortogram and diagnostic renal angiography when performed; bilateral

Transcatheter renal sympathetic denervation (unilateral or bilateral) for resistant hypertension is unproven due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Transcatheter renal sympathetic denervation for resistant hypertension is unproven due to the lack of high quality evidence regarding its safety and efficacy in the published medical literature. Although preliminary results, including results of a moderate quality RCT, are positive, the overall

evidence base in the peer-reviewed medical literature is small and of low quality. Additional well-designed studies are needed to confirm the safety and efficacy of this treatment approach. Symplicity HTN-2, a multicenter, randomized trial, demonstrated that catheter-based renal denervation produced significant blood pressure lowering in treatment-resistant patients at 6 months after the procedure compared with control, medication-only patients. Study authors reported longer-term follow-up, including 6-month crossover results. Eligible patients were on ≥ 3 antihypertensive drugs and had a baseline systolic blood pressure ≥ 160 mm Hg (≥ 150 mm Hg for type 2 diabetics). After the 6-month primary end point was met, renal denervation in control patients were permitted. At 12 months after the procedure, the mean fall in office systolic blood pressure in the initial renal denervation group (-28.1 mm Hg; 95% confidence interval, -35.4 to -20.7 ; $P < 0.001$) was similar to the 6-month fall (-31.7 mm Hg; 95% confidence interval, -38.3 to -25.0 ; $P = 0.16$ versus 6-month change). The mean systolic blood pressure of the crossover group 6 months after the procedure was significantly lowered (from 190.0 ± 19.6 to 166.3 ± 24.7 mm Hg; change, -23.7 ± 27.5 ; $P < 0.001$). In the crossover group, there was one case of renal artery dissection during guide catheter insertion, before denervation, corrected by renal artery stenting, and one incidence of hypotensive episode, which resolved with medication adjustment. Control patients who crossed over to renal denervation with the Symplicity system had a significant drop in blood pressure similar to that observed in patients receiving immediate denervation. Study authors posited that renal denervation provides safe and sustained reduction of blood pressure to 1 year.

Lambert et al. (2012) evaluated the effects of renal denervation on health-related quality of life (QOL) measures. Using the Medical Outcomes Study 36-Item Short-Form Health Survey and Beck Depression Inventory-II, (BDI-11) QOL was examined before and three months after renal denervation in patients with uncontrolled blood pressure. For baseline comparisons, matched data were extracted from the Australian Diabetes, Obesity, and Lifestyle database. Before renal denervation, patients with resistant hypertension ($n = 62$) scored significantly worse in 5 of the eight 36-Item Short-Form Health Survey domains and the Mental Component Summary score. Three months after denervation ($n = 40$), clinic BP was reduced (change in systolic and diastolic BP, -16 ± 4 and -6 ± 2 mm Hg, respectively; $P < 0.01$). The Mental Component Summary score improved (47.6 ± 1.1 versus 52 ± 1 ; $P = 0.001$) as a result of increases in the vitality, social function, role emotion, and mental health domains. The BDI scores were also improved, particularly with regard to symptoms of sadness ($P = 0.01$), tiredness ($P < 0.001$), and libido ($P < 0.01$). The magnitude of BP reduction or BP level achieved at 3 months bore no association to the change in QOL. Renal denervation did not have detrimental effect on any elements of the 36-Item Short-Form Health Survey. These results indicate that patients with severe hypertension resistant to therapy present with a marked reduction in subjective QOL. In this pre- and post-hypothesis generating study, several aspects of QOL were improved after renal denervation; however, this was not directly associated with the magnitude of BP reduction.

Kaltenbach et al. (2013) investigated the feasibility, safety, and effectiveness of renal sympathetic denervation in patients with recurrent mild hypertension despite treatment with ≥ 3 antihypertensive drugs. Consecutive patients with office systolic BPs of 140-160 mm Hg despite ≥ 3 antihypertensive medications treated with renal sympathetic denervation. Clinical evaluations were performed at baseline, 3, and 6 months to determine changes in office systolic blood pressure, 24-hr ambulatory blood pressure, and medication doses. Twenty patients treated with an average of 5.4 ± 1.5 antihypertensive drugs were treated with renal sympathetic denervation. The procedure was considered successful in all patients. There were no procedure- or device-related complications. The blood pressure reading at baseline was $148.4/83.0 \pm 6.6/11.0$ mm Hg and decreased by $5.7/0.6 \pm 20.0/8.3$ mm Hg ($P = 0.2$) and $13.1/5.0 \pm 13.6/8.3$ mm Hg ($P < 0.01$) at 3 and 6 months, respectively. Comparing baseline and 6-month follow-up, mean ambulatory 24 hr-BP was reduced by $11.3/4.1 \pm 8.6/7.3$ mm Hg ($P < 0.01$). Four patients were able to reduce antihypertensive medications prior to their 3-month visit.

Brandt et al. (2012) investigated the effect of catheter-based renal sympathetic denervation on left ventricular hypertrophy (LVH) and systolic and diastolic function in patients with resistant hypertension. Forty-six patients underwent bilateral RD, and 18 patients served as controls.

Transthoracic echocardiography was performed at baseline, and after 1 month and 6 months. Besides reduction of systolic and diastolic blood pressure (-22.5/-7.2 mm Hg at 1 month and -27.8/-8.8 mm Hg at 6 months, $p < 0.001$ at each time point), RD significantly reduced mean interventricular septum thickness from 14.1 ± 1.9 mm to 13.4 ± 2.1 mm and 12.5 ± 1.4 mm ($p = 0.007$), and LV mass index from 53.9 ± 15.6 g/m(2.7) (112.4 ± 33.9 g/m(2)) to 47.0 ± 14.2 g/m(2.7) (103.6 ± 30.5 g/m(2)) and 44.7 ± 14.9 g/m(2.7) (94.9 ± 29.8 g/m(2)) ($p < 0.001$) at 1 month and 6 months, respectively. The mitral valve lateral E/E' decreased after RD from 9.9 ± 4.0 to 7.9 ± 2.2 at 1 month and 7.4 ± 2.7 at 6 months ($p < 0.001$), indicating reduction of LV filling pressures. No significant changes were observed in control patients. Study authors suggest that RD significantly reduces LV mass and improves diastolic function, which might have important prognostic implications in patients with resistant hypertension at high cardiovascular risk.

References:

Brandt MC, Mahfoud F, Reda S et al. Renal sympathetic denervation reduces left ventricular hypertrophy and improves cardiac function in patients with resistant hypertension. *J Am Coll Cardiol.* 2012 Mar 6;59(10):901-909.

Esler MD, Krum H, Schlaich M, Schmieder RE et al. Renal sympathetic denervation for treatment of drug-resistant hypertension: one-year results from the Symplicity HTN-2 randomized, controlled trial. *Circulation.* 2012 Dec 18;126(25):2976-2982.

Kaltenbach B, Franke J, Bertog SC et al. Renal sympathetic denervation as second-line therapy in mild resistant hypertension: a pilot study. *Catheter Cardiovasc Interv.* 2013 Feb;81(2):335-339.

Lambert GW, Hering D, Esler MD et al. Health-related quality of life after renal denervation in patients with treatment-resistant hypertension. *Wien Klin Wochenschr.* 2012 Nov;124(21-22):789-98.

Code	Description
0340T	Ablation, pulmonary tumor(s), including pleura or chest wall when involved by tumor extension, percutaneous, cryoablation, unilateral, includes imaging guidance

Percutaneous cryoablation of pulmonary tumors, including the pleura or chest wall when involved by tumor extension, is unproven due to insufficient evidence of safety and/or efficacy in the published peer-reviewed medical literature.

Clinical Evidence

Percutaneous cryoablation of pulmonary tumors, including the pleura or chest wall when involved by tumor extension, is unproven due to the lack of high quality evidence regarding its safety and efficacy. With one exception, majority of the available evidence pertains primarily to early feasibility and safety evaluations. Although preliminary results are positive, the overall evidence base in the peer-reviewed medical literature is small and of low quality. Additional well-designed studies are needed to confirm the safety and efficacy of this treatment approach.

Niu et al. (2013) investigated the therapeutic effect of cryoablation treatment and palliative treatment in patients with stage IV lung cancer (n=54). Thirty-one patients received cryoablation treatment (including intra- and extrapulmonary tumors), and 23 patients had palliative treatment (no cryoablation). Both the safety of the procedure and overall survival (OS) for stage IV lung cancer were assessed during a 6.5year follow-up period. The OS of patients in both groups and the effects of treatment timing and frequency were compared. The OS in the cryoablation group was significantly longer than in the palliative group (median OS: 14months vs. 7months, $P=0.0009$). The OS of those who received delayed cryoablation treatment was longer than that observed for those who received timely treatment (median OS: 18.5months vs. 10months, $P=0.0485$), but this was not observed in those who received palliative treatment (median OS: 7months vs. 7.5months, $P=0.9814$). Multiple treatments played an important role in improving the OS of patients who received cryoablation treatment (median OS: 18months vs. 14months, $P=0.0376$). There was a significant difference between cryoablation and palliative treatment, in

terms of OS. In addition, multiple cryoablation treatments may have an advantage over single treatments.

In a prospective, before-and-after study, Zhang et al. (2012) evaluated the feasibility of computed tomography (CT)-guided cryoablation for patients with peripheral Non-Small Cell Lung Cancer (NSCLC) (n=43). CT was used to monitor the extent of cryoablation during the procedures. Results up to 24 months following the procedure were assessed using enhanced CT scans and/or PET-CT scans. The average tumor CT values were 32 ± 10 HU and -21 ± 8 HU before and after cryoablation, respectively. At 24 months, there were 36 cases of complete response (83.7%), 7 cases of partial response (16.3%), and no cases of stable disease or progressive disease. Three patients died due to multiple metastases.

Kawamura et al. (2006) conducted a nonrandomized uncontrolled study (n=20) to evaluate the safety and feasibility of cryoablation of pulmonary metastases in patients who are not appropriate for surgery. Complications included pneumothorax (n=11), hemoptysis (n=8), and phrenic nerve palsy (n=1). The mean hospital length of stay (HLOS) was 2.6 days. During a median follow-up of 21 months (range 9-28), the local recurrence was 20% in 7 patients (35%). One-year survival calculation using a Kaplan-Meier survival curve was approximately 89%.

In a nonrandomized uncontrolled feasibility study, Inoue et al. (2012) evaluated 117 consecutive patients with lung tumors. Pneumothorax, pleural effusion, and hemoptysis occurred after 119 (61.7%), 136 (70.5%), and 71 (36.8%) sessions, respectively. Phrenic nerve palsy, frostbite, and empyema occurred after one session each (0.52%). Proximal tumor implantation was observed in one of 471 punctures (0.20%). Of 119 sessions with pneumothorax, 21 (17.6%) required chest tube insertion and two (1.7%) required pleurodesis. Delayed and recurrent pneumothorax occurred in 15 of 193 sessions each (7.8%). A greater number of cryoprobes was a significant ($P = 0.001$) predictor of pneumothorax. Being male ($P = .047$) and no history of ipsilateral surgery ($P = .012$) were predictors for the need for chest tube insertion, and no history of ipsilateral surgery ($P = .021$) was a predictor for delayed or recurrent pneumothorax. Greater number of cryoprobes ($P = .001$) and no history of ipsilateral surgery ($P = .004$) were predictors for pleural effusion. Greater number of cryoprobes ($P < .001$) and younger age ($P = .034$) were predictors for hemoptysis. Study authors concluded that percutaneous cryoablation could be performed minimally invasively with acceptable rates of complications.

Another study evaluated risk factors for local tumor progression following percutaneous cryoablation of lung tumors. Seventy-one consecutive patients with 210 tumors were treated with 102 sessions of PCLT. Rates of local tumor progression and technique effectiveness were estimated by Kaplan-Meier method. The median follow-up period was 454 days (range, 79-2467). Local tumor progression occurred in 50 tumors (23.8%). Local progression-free survival rates were approximately 80%, (at one year), 69% (at two years) and 68% (at three years), respectively. Technique effectiveness rates 91%, 83%, and 83%, respectively. Existence of a thick vessel (diameter ≥ 3 mm) no more than 3 mm from the edge of the tumor was assessed as an independent factor [hazard ratio (HR), 3.84; 95% CI, 1.59-9.30; $P = .003$] associated with local progression by multivariate analysis.

Pusceddu et al. (2013) reported their initial experience with CT-guided thin cryoprobes for percutaneous cryoablation in patients with primary and secondary lung tumors. CT-guided cryoablation was performed on 34 lung masses in 32 consecutive patients. All cryoablation sessions were successfully completed. All primary and metastatic lung tumors were ablated. No procedure-related deaths occurred. Morbidity consisted of 21% (7 of 34) pneumothorax and 3% (1 of 34) cases asymptomatic small pulmonary hemorrhage, respectively, all of CTCAE grade 1 (Common Terminology Criteria for Adverse Events). Low density of entire lesion, central necrosis and solid mass appearance were identified in 21 (62%), 7 (21%) and 6 (17%) of cryoablated tumors, respectively. No lymphadenopathy developed in the region of treated lesions. Technical success (complete lack of enhancement) was achieved in 82%, 97% and 91% of treated lesions at 1-, 3- and 6-months CT follow-up scan, respectively ($p < .000$). Comparing the tumor longest

diameter between the baseline and at 6 month CT images, technical success was revealed in 92% cases (p<.000).

Bang et al. (2012) assessed the feasibility, complications, local tumor recurrences, overall survival (OS) for multisite cryoablation (MCA) of oligometastatic non-small-cell lung cancer (NSCLC). A total of 49 CT- and/or ultrasound-guided (US) percutaneous cryoablation procedures were performed on 60 tumors in 31 patients with oligometastatic NSCLC. Average patient age was 65 years. Tumor location was grouped according to common metastatic sites. Median OS was determined by Kaplan-Meier method. A mean of 1.6 procedures per patient were performed, with a median clinical follow-up of 11 months. Major complication and local recurrence rates were 8% (4/49) and 8% (5/60), respectively. Median OS was 1.33 years, with an estimated 1-year survival rate of approximately 53%.

References:

Bang HJ, Littrup PJ, Currier BP et al. Percutaneous cryoablation of metastatic lesions from non-small-cell lung carcinoma: initial survival, local control, and cost observations. *J Vasc Interv Radiol.* 2012 Jun;23(6):761-9.

Inoue M, Nakatsuka S, Yashiro H et al. Percutaneous cryoablation of lung tumors: feasibility and safety. *J Vasc Interv Radiol.* 2012 Mar;23(3):295-302.

Kawamura M, Izumi Y, Tsukada N, et al. Percutaneous cryoablation of small pulmonary malignant tumors under computed tomographic guidance with local anesthesia for nonsurgical candidates. *J Thorac Cardiovasc Surg.* 2006 May;131(5):1007-1013.

Niu L, Chen J, Yao F et al. Percutaneous cryoablation for stage IV lung cancer: A retrospective analysis. *Cryobiology.* 2013 Oct;67(2):151-5.

Pusceddu C, Sotgia B, Fele RM, Melis L. CT-guided thin needles percutaneous cryoablation (PCA) in patients with primary and secondary lung tumors: a preliminary experience. *Eur J Radiol.* 2013 May;82(5):e246-53.

Yashiro H, Nakatsuka S, Inoue M et al. Factors affecting local progression after percutaneous cryoablation of lung tumors. *J Vasc Interv Radiol.* 2013 Jun;24(6):813-821.

Zhang X, Tian J, Zhao L, et al. CT-guided conformal cryoablation for peripheral NSCLC: initial experience. *Eur J Radiol.* 2012 Nov;81(11):3354-62.

Code	Description
0341T	Quantitative pupillometry with interpretation and report, unilateral or bilateral

Pupillometry is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Pupillometry has been used in a research setting to evaluate the autonomic function, pain response, psychological processes, sleep disorders, and drug metabolism. Hayes classifies these tests as having no proven benefit (Hayes 2010, updated 2014).

Bremner and Smith (2006) employed light reflex pupillography (LRP) in 465 individuals, including 150 patients with generalized autonomic failure and symptoms of autonomic neuropathy and 315 age and sex-matched healthy controls. The patient group represented a variety of disorders (amyloidosis, multiple system atrophy, pure autonomic failure, diabetes mellitus, hereditary neuropathies, and paraneoplastic syndromes). The study characterized pupillary function for each of these disorders and analyzed data to identify correlations between pupillary dysfunction and systemic dysfunction. However, no significant correlations were found between the presence of sympathetic and/or parasympathetic pupillary dysfunction and systemic sympathetic and/or parasympathetic dysfunction.

In a cross-sectional cohort study, Kantor et al. (2014) studied the association between postoperative pain numerical rating scale (NRS) and pupillary diameter or pupillary light reflex amplitude (PLRA) using pupillometry in post-anesthesia care unit (PACU) patients after routine anesthetic care. One hundred and forty-five patients undergoing planned surgery under general anesthesia were included in the study. NRS, pupillary diameter and PLRA were measured on arrival in the PACU. When NRS was more than 4, intravenous morphine titration was started and a second measurement performed. Mean NRS was 4.7, and was more than 4 in 79 patients (55%). Twenty-seven patients (19%) received morphine titration with significant decreases in NRS, pupillary diameter and PLRA afterwards. No association was observed between NRS changes and pupillary diameter or PLRA changes. The authors concluded that acute postoperative pain is not associated with pupillary diameter or PLRA. Further research is required to develop tools to assess pain in the PACU.

In a double-blind, crossover design study, Noehr-Jensen et al. (2009) investigated the impact of cytochrome phenotypes on escitalopram metabolism and evaluated pupillometry as a serotonergic biomarker in 13 patients. Escitalopram treatment did not affect the maximum pupil size, but it did statistically significantly decrease the relative amplitude of the pupil light reflex compared to the placebo. According to the authors, the puzzling results from pupillometry could be due to interplay between a central and a local serotonergic effect. Based on these results, the authors concluded that pupillometry cannot be recommended as a serotonergic biomarker.

Other clinical trials have also assessed the usefulness of automated pupillometry (Rouche, 2013; Kardon, 2011; Ferrari, 2010; Guglielminotti et al. 2013; Isnardon et al. 2013); Suys, 2014). These studies were limited by small sample sizes or did not validate pupillometry findings with improved patient care.

An American Academy of Ophthalmology Summary Recommendations for Keratorefractive Laser Surgery (2013) states that the importance of pupillometry in the preoperative workup for keratorefractive laser surgery remains controversial. Measurement of pupil size is not required in the preoperative examination. See the following Web site for more information: <http://one.aao.org/guidelines-browse?filter=clinicalstatement> Accessed May 2014.

Reference(s):

Bremner F, Smith S. Pupil findings in a consecutive series of 150 patients with generalised autonomic neuropathy. *J Neurol Neurosurg Psychiatry*. 2006;77(10):1163-1168.

Ferrari GL, Marques JL, Gandhi RA, Heller SR, Schneider FK, Tesfaye S, Gamba HR. Using dynamic pupillometry as a simple screening tool to detect autonomic neuropathy in patients with diabetes: a pilot study. *Bomed Eng Online*. 2010 Jun 17;9:26.

Guglielminotti J, Mentré F, Gaillard J, et al. Assessment of pain during labor with pupillometry: a prospective observational study. *Anesth Analg*. 2013 May;116(5):1057-62.

Hayes, Inc. Directory. *Autonomic Nervous System Monitoring for Neuropathy*. Lansdale, PA: Hayes, Inc. January 2010. Update search February 2014.

Isnardon S, Vincilar M, Genty C, et al. Pupillometry to detect pain response during general anaesthesia following unilateral popliteal sciatic nerve block: a prospective, observational study. *Eur J Anaesthesiol*. 2013 Jul;30(7):429-34.

Kantor E, Montravers P, Longrois D, et al. Pain assessment in the postanesthesia care unit using pupillometry: A cross-sectional study after standard anaesthetic care. *Eur J Anaesthesiol*. 2014 Feb;31(2):91-7.

Kardon R, Anderson SC, Damarjian TG, Grace EM, Stone E, Kawasaki A. Chromatic pupillometry in patients with retinitis pigmentosa. *Ophthalmology*. 2011 Feb;118(2):376-81.

Noehr-Jensen L, Zwisler ST, Larsen F, et al. Impact of CYP2C19 phenotypes on escitalopram metabolism and an evaluation of pupillometry as a serotonergic biomarker. *Eur J Clin Pharmacol*. 2009 Sep;65(9):887-94.

Rouche O, Wolak-Thierry A, Destoop Q, et al. Evaluation of the depth of sedation in an intensive care unit based on the photo motor reflex variations measured by video pupillometry. *Ann Intensive Care*. 2013 Feb 22;3(1):5.

Suys T, Bouzat P, Marques-Vidal P, et al. Automated Quantitative Pupillometry for the Prognostication of Coma After Cardiac Arrest. *Neurocrit Care*. 2014 Apr 24.

Code	Description
0346T	Ultrasound, elastography (List separately in addition to code for primary procedure)

The use of ultrasound elastography is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Sonoelastography (SE) is a newly introduced ultrasound technique that evaluates tissue elasticity and thus provides additional information to that offered by conventional ultrasound images. In the musculoskeletal field, sonoelastography can help improve estimation of tendon stiffness. The technique employs external compression in order to induce strain inside the tissue that is scanned. Tissue compression produces strain or displacement within the tissue; therefore, the strain is smaller and harder in the malignant tissue than in the benign tissue. By measuring the tissue strain, tissue hardness can be estimated differentiating between malignant and benign masses.

Sonoelastography (SE): Evaluates reproducible differences in backscattered ultrasound signals that result from compression of tissues and uses color doppler to generate an image of tissue movement in response to the external vibrations,

Ultrasound elastography has been investigated in a variety of clinical applications, including, but not limited to, breast imaging, assessment of liver fibrosis, endoscopic, vascular and prostate imaging as well as thyroid, skin and brain tumors.

There was no information found in *MCG™*, ECRI or Hayes for this treatment.

Professional Organizations

The National Comprehensive Cancer Network (NCCN) practice guidelines for colon cancer, and lobular carcinoma in Situ, does not indicate elastography as a diagnostic modality in their clinical guidelines.

The evidence in the published medical literature for ultrasound elastography is inadequate to permit scientific conclusions. The main limitation is the lack of controlled studies as well as the lack of long-term outcomes.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

Cole JA, Emerton DP, Mackenzie A et al, Evidence Review: Ultrasound Elastograohy. February 2009.

J. Ophir, S. Alam, B. Garra, F. Kallel, E. Konofagou, T. Krouskop, and T. Varghese, "Elastography: Ultrasonic estimation and imaging of the elastic properties of tissues," *Annu. Rev. Biomed. Eng.*, vol. 213, pp. 203–233, Nov. 1999.

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National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Colon Cancer. (2012).

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Trombetti J. Sonoelastography and musculoskeletal imaging. <http://www.dotmed.com/news/story/7760/?lang=en>. Updated December 23, 2008. Accessed June 10, 2014.

Code	Description
0347T	Placement of interstitial device(s) in bone for radiostereometric analysis (RSA)
0348T	Radiologic examination, radiostereometric analysis (RSA); spine, (includes, cervical, thoracic and lumbosacral, when performed)
0349T	Radiologic examination, radiostereometric analysis (RSA); spine, (includes, cervical, thoracic and lumbosacral, when performed) upper extremity(ies), (includes shoulder, elbow and wrist, when performed)
0350T	Radiologic examination, radiostereometric analysis (RSA); spine, (includes, cervical, thoracic and lumbosacral, when performed) lower extremity(ies), (includes hip, proximal femur, knee and ankle, when performed)

The use of radiostereometric analysis in bone is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Radiostereometric analysis (RSA) is an imaging procedure intended to detect changes in implant position after orthopedic surgery. The process involves the insertion of spherical tantalum markers into the bone during surgery and then using a pair of x-rays of the surgical site with a RSA calibration cage to take simultaneous images from two different directions.

There are limited studies in the literature that address the use radiostereometric analysis of bone.

Bottner et al. (2005), conducted an analysis at Hospital for Special Surgery to evaluate the migration and wear of orthopaedic implants using radiostereometric analysis. The authors concluded after their analysis that RSA may have benefit of noting migration of implants before clinical failure is evident. More long-term randomized controlled studies are needed in the future.

There was no information found in *MCG™*, or Hayes for this treatment. No formal position statements issued by any societies at this time.

The evidence in the published medical literature for radiostereometric analysis in bone is inadequate to permit scientific conclusions. The main limitation is the lack of controlled studies, small sample size as well as the lack of long-term outcomes.

Reference(s):

Bostrom M, Su E, Wright, T. Hospital for Special Surgery. Radiostereometric analysis at HSS. January 2012

Bottner F, Su E, Nestor B, et al. Radiostereometric analysis: the hip. HSS J. 2005 Sep;1(1):94-9.

ECRI Institute. Product Brief. Radiostereometric Analysis (Halifax Biomedical, Inc.) for Assessing Orthopedic Implant Position. January 2013.

Orthopedic Innovation Centre. Radiostereometric analysis for the evaluation of medical devices. January 2012.

Code	Description
0351T	Optical coherence tomography of breast or axillary lymph node, excised tissue, each specimen; real time intraoperative
0352T	Optical coherence tomography of breast or axillary lymph node, excised tissue, each specimen; real time intraoperative interpretation and report, real time or referred

0353T	Optical coherence tomography of breast, surgical cavity; real time intraoperative
0354T	Optical coherence tomography of breast, surgical cavity; real time intraoperative interpretation and report, real time or referred

Optical coherence tomography (OCT) is unproven for the intraoperative assessment of lymph nodes or tumor margins in breast conserving surgery due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Microscopic examination of tissue is the gold standard for identifying metastatic involvement in malignant disease. OCT is a real-time, high-resolution imaging technique that is being evaluated for the intraoperative assessment of tissue.

Butler-Henderson et al. (2014) conducted a systematic review of current intraoperative methods for assessing tumor margin status. The final pathology status, statistical measures including accuracy of tumor margin assessment, average time impact on the procedure and second operation rate were used as criteria for comparison between studies. Although pathological methods, such as frozen section and imprint cytology performed well, they added on average 20-30 minutes to operation times. While ultrasound delivered results in a timely manner, it did not perform well where calcifications were present or in multifocal cancers. Further research, using larger samples, is required in other intraoperative tumor margin assessment techniques, such as mammography, radiofrequency spectroscopy and OCT.

In a prospective, observational study, Nguyen et al. (2009) reported a sensitivity of 100% and specificity of 82% for OCT as a real-time method for intraoperative margin assessment in breast-conserving surgeries. A total of 37 patients were enrolled in the study and split between the training (n=17) and study (n=20) groups. OCT images were acquired from surgical margins of lumpectomy samples. Of these samples, 11 were identified with a positive or close surgical margin and 9 were identified with a negative margin. Histologic findings identified nine true positives, nine true negatives, two false positives and no false negatives. Additional operation time and second operation rates were not reported. The authors concluded that OCT shows potential as a real-time method for intraoperative margin assessment in breast-conserving surgeries. This study is limited by lack of randomization and small sample size.

National Comprehensive Cancer Network (NCCN) clinical practice guidelines on breast cancer do not address OCT (NCCN, 2014).

Reference(s):

Butler-Henderson K, Lee AH, Price RI, Waring K. Intraoperative assessment of margins in breast conserving therapy: A systematic review. *Breast*. 2014 Apr;23(2):112-119.

Nguyen FT, Zysk AM, Chaney EJ, et al. Intraoperative evaluation of breast tumor margins with optical coherence tomography. *Cancer Res*. 2009 Nov 15;69(22):8790-6.

National Comprehensive Cancer Network (NCCN). *Clinical Practice Guidelines in Oncology. Breast Cancer*. v2.2014.

Code	Description
0356T	Insertion of drug-eluting implant (including punctal dilation and implant removal when performed) into lacrimal canaliculus, each

The use of drug eluting punctal plugs or implants into the lacrimal canaliculus is unproven due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

The use of drug-eluting plugs is a new approach to treating patients with various eye diseases including glaucoma, dry eye, and eye inflammation. The drug-eluting implant or plug is placed within the lacrimal canaliculus to deliver precise drug doses for a predetermined period.

There are few published studies addressing the use of drug eluting implants into the lacrimal canaliculus. Therefore, it is not possible to conclude whether these implants have a beneficial effect on health outcomes.

Chee (2012) assessed the safety and feasibility of a moxifloxacin-loaded punctum plug (MP) in 2 groups of cataract patients. Two prospective, single-arm, Phase I studies were conducted with 20 cataract patients (10 per study) at the Singapore National Eye Center. After cataract surgery, the MP was inserted into the punctum, and follow-up assessments were conducted at 1 h, 24 h, and on days 3, 7, 10, 20, and 30. Study endpoints included MP retention, ease of placement, and moxifloxacin concentrations in the tear fluid. After the course of therapy, the plug would resorb and be absent from the punctum by day 30. MP retention in the punctum was 95% (19/20) through day 10, and all plugs were absent at day 30. Average moxifloxacin concentrations in the tear film ranged from 155 to 785 ng/mL for Study 1 and 2,465 to 3,236 ng/mL for Study 2 through day 7. These values were above the target of 250 ng/mL for all time points except for day 1 of Study 1. The authors concluded that the MP delivered and maintained moxifloxacin tear fluid concentrations at therapeutic levels above the MIC(90) values for common susceptible conjunctivitis pathogens for 7 days (Study 2). The MP also exhibited a favorable safety and tolerability profile and, hence, may be a viable alternative to topical antibiotic drops for the treatment of bacterial conjunctivitis. Limitations of this study include non-randomization and a small sample size.

Reference(s):

Chee SP. Moxifloxacin punctum plug for sustained drug delivery. *J Ocul Pharmacol Ther.* 2012 Aug;28(4):340-9.

Code	Description
0358T	Bioelectrical impedance analysis whole body composition assessment, supine position, with interpretation and report

Bioelectrical impedance analysis whole body composition assessment is unproven due to insufficient clinical evidence of safety/ efficacy in published peer-reviewed medical literature.

Clinical Evidence

Bioelectrical impedance analysis (BIA) is a commonly used method for estimating body composition, and in particular body fat. Since the advent of the first commercially available devices in the mid-1980s the method has become popular owing to its ease of use, portability of the equipment and its relatively low cost compared to some of the other methods of body composition analysis. It is familiar in the consumer market as a simple instrument for estimating body fat. BIA actually determines the electrical impedance, or opposition to the flow of an electric current through body tissues which can then be used to calculate an estimate of total body water (TBW). TBW can be used to estimate fat-free body mass and, by difference with body weight, body fat. Research studies have shown that BIA was quite variable and that some users did not regard it as providing an accurate measure of body composition. In recent years technological improvements have made BIA a more reliable and therefore more acceptable way of measuring body composition.

Johnston et al. (2014) conducted this study utilizing three groups of six obese men to evaluate the accuracy of bioelectrical impedance spectroscopy (BIS) in measuring the following: fat mass (FM), total body water (TBW) and extracellular water (ECW) changes induced by different degrees of caloric deficit in obese men. Each group of men were instructed to participate in either (i) a total fast (for 6 days); (ii) a VLCD (2.5 MJ/day for 3 weeks); or (iii) LCD (5.2 MJ/day for 6 weeks). FM was measured using a 4-compartment (4-C) model. TBW and ECW were determined

by dilution methods. TBW, ECW and FM were also assessed with BIS. Body weight loss in the fasting group was 6.0 ± 1.3 kg over 6 days; the VLCD group lost 9.2 ± 1.2 kg over 21 days and the LCD group lost 12.6 ± 2.4 kg over 42 days. BIS underestimated FM changes (bias = -3.3 ± 3.8 kg) and overestimated changes in TBW and ECW by $+1.8 \pm 4.8$ kg and $+2.3 \pm 6.4$ kg, respectively. The measurement error was consistently larger in the fasting group and the magnitude of the bias is greater with greater weight loss.

In this study, Widen et al. (2014) was attempting to provide validation of bioelectric impedance analysis. The purpose of the study was to measure the total body water and percent body fat before and 12 months after bariatric surgery. The findings showed that the T0 to T12 median (IQR) change in deuterium TBW and 3C %fat was -6.4 L (6.4 L) and -14.8 % (13.4 %), respectively. There were no statistically significant differences between deuterium and BIA determined TBW [median (IQR) difference: T0 -0.1 L (7.1 L), $p = 0.75$; T12 0.2 L (5.7 L), $p = 0.35$; Δ 0.35 L(6.3 L), $p = 1.0$]. Compared with 3C, BIA underestimated %fat at T0 and T12 [T0 -3.3 (5.6), $p < 0.001$; T12 -1.7 (5.2), $p = 0.04$] but not change [0.7 (8.2), $p = 0.38$]. Except for %fat change, Bland-Altman plots indicated no proportional bias. However, 95 % limits of agreement were wide (TBW 15-22 L, %fat 19-20 %). According to the authors, BIA may be appropriate for evaluating group level response among severely obese adults. The authors state that clinically meaningful differences in the accuracy of BIA between individuals exist.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

Johnstone AM, Faber P, Gibney ER. Measurement of body composition changes during weight loss in obese men using multi-frequency bioelectrical impedance analysis and multi-compartment models. *Obes Res Clin Pract.* 2014 Jan-Feb;8(1):e46-54. doi: 10.1016/j.orcp.2012.07.006. PubMed PMID: 24548576.

Widen EM, Strain G, King WC. Bioelectrical Impedance Analysis for Measuring Changes in Body Water and Percent Fat After Bariatric Surgery. *Obes Surg.* 2014 Jan 24. [Epub ahead of print] PubMed PMID: 24464517.

Code	Description
28446	Open osteochondral autograft, talus (includes obtaining graft[s])

The use of osteochondral autograft of the talus is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Evidence evaluating the use of autograft for osteochondral defects of the talus is still elusive. The use of osteochondral autograft in ankles is limited to retrospective and prospective case series and few randomized controlled trials, nonrandomized controlled trials involving small patient populations and published reviews. Controlled trials with longer follow-up are needed to demonstrate that use of osteochondral autografts as a primary treatment results in improved clinical outcomes. The evidence base is not as robust when compared to that evaluating the knee, although reported clinical outcomes extend short-to intermediate-term; on average two to eight years post-operatively. In general, the clinical outcomes have been mixed regarding improvement in postoperative pain and function, with some authors reporting high failure rates and the need for further surgery. In 2004 Kolker et al. reported their concern as to the overall efficacy of the procedure when used in the treatment of full-thickness, advanced, osteochondral defects of the talar dome. Open bone grafting did not predictably improve symptoms and yielded poor results in the patient population studied. The authors have acknowledged further well-designed studies with larger sample size are needed to assess improved long-term outcomes (Balzer and Arnold, 2005; Scranton, et al., 2006).

Zengerink M, et. al. (2010), The aim of this study was to summarize all eligible studies to compare the effectiveness of treatment strategies for osteochondral defects (OCD) of the talus.

For each treatment strategy, study size weighted success rates were calculated. Fifty-two studies described the results of 65 treatment groups of treatment strategies for OCD of the talus. Nine of the studies were for osteochondral transplantation (OATS). OATS scored success rates of 87%, respectively. However, due to great diversity in the articles and variability in treatment results, no definitive conclusions can be drawn. Further sufficiently powered, randomized clinical trials with uniform methodology and validated outcome measures should be initiated to compare the outcome of surgical strategies for OCD of the talus.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

Baltzer AW, Arnold JP. Bone-cartilage transplantation from the ipsilateral knee for chondral lesions of the talus. *Arthroscopy*. 2005 Feb;21(2):159-66.

ECRI Institute. Hotline Response [database online] Plymouth Meeting (PA): ECRI Institute. 2009 October. Osteochondral autograft transplantation of the ankle. Available at URL address: <http://www.ecri.org>

Giannini S, Vannini F. Operative treatment of osteochondral lesions of the talar dome: current concepts review. *Foot Ankle Int*. 2004 Mar;25(3):

Gobbi A, Francisco RA, Lubowitz JH, Allegra F, Canata G. Osteochondral lesions of the talus: randomized controlled trial comparing chondroplasty, microfracture, and osteochondral autograft transplantation. *Arthroscopy*. 2006 Oct;22(10):1085-92.

Kolker D, Murray M, Wilson M. Osteochondral defects of the talus treated with autologous bone grafting. *J Bone Joint Surg Br*. 2004 May;86(4):521-6.

Kreuz PC, Steinwachs M, Erggelet C, Lahm A, Henle P, Niemeyer P. Mosaicplasty with autogenous talar autograft for osteochondral lesions of the talus after failed primary arthroscopic management: A prospective study with a 4-year follow-up. *Am J Sports Med*. 2005 Sep.

Scranton PE Jr, Frey CC, Feder KS. Outcome of osteochondral autograft transplantation for type-V cystic osteochondral lesions of the talus. *J Bone Joint Surg Br*. 2006 May;88(5):614-9.

Zengerink M, Struijs PA, Tol JL, van Dijk CN. Treatment of osteochondral lesions of the talus: a systematic review. *Knee Surg Sports Traumatol Arthrosc*. 2010 Feb;18(2):238-46. Epub 2009 Oct 27.

Code	Description
29799	Unlisted procedure, casting or strapping [when used to report Kinesio Taping]

See [97139](#) for additional information.

Code	Description
30999	Unlisted procedure, nose (Rhinophototherapy, intranasal application of ultraviolet and visible light, bilateral)

Rhinophototherapy for the treatment of allergies is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

In a prospective, randomized study, Tatar et al. (2013) investigated the effect of rhinophototherapy with medical therapy on quality of life in persistent allergic rhinitis. The study included 65 patients with dust mite allergies. The patients were divided into two groups. The first group (n=33) was given topical mometasone furoate 200 mcg/day and levocetirizine 5 mg/day for a month. Rhinophototherapy was applied with the same medical therapy to the second group (n=32), twice a week for three weeks continuously. The patients were evaluated before the treatment, at the first month and at the third month after treatment. Improvements of all variables

of the quality of life questionnaire, nasal symptom scores and visual analogue scale (VAS) were statistically significant in the second group both on the first and the third months when compared with the first group. The authors concluded that rhinophototherapy plus medical therapy was better than purely medical therapy in patients with persistent and moderate/severe allergic rhinitis with respect to quality of life and symptoms improvement. The study showed that the permanent effect of phototherapy at the third month decreased when compared with the first month. According to the authors, long-term assessments of rhinophototherapy are necessary to evaluate the impact of this treatment in patients with allergic rhinitis.

Albu and Baschir (2013) compared the efficacy of intranasal phototherapy with that of azelastine in patients with seasonal allergic rhinitis (SAR). Seventy seven patients were randomly assigned to the two treatment groups: Group A (phototherapy) and Group B (azelastine). The study demonstrated that both azelastine and intranasal phototherapy are able to significantly improve Total Nasal Symptom Score (TNSS), including individual nasal symptoms. Phototherapy reduced nasal obstruction better than azelastine. Both treatments were highly effective in improving Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) scores overall and in seven separate domains. The small study population limits the validity of the conclusion of this study. The authors state that phototherapy should be evaluated in future studies and clinical trials.

Leong (2011) reviewed the use of phototherapy in the treatment of allergic rhinitis with particular emphasis on clinical efficacy, scientific basis and safety. Fourteen full-text articles were included in the review. Most studies demonstrated symptomatic improvement and quality of life scores. No improvement in objective measures of nasal airflow was demonstrated. Beneficial effects of phototherapy on inflammatory markers remain equivocal. Phototherapy treatment results in DNA damage but does not appear to predispose to carcinogenesis. However, long-term prospective studies are required to verify this. According to the authors, the quality of published studies was variable and thus the current strength of recommending intranasal phototherapy is currently weak.

A randomized open study was conducted to compare the efficacy of intranasal phototherapy with that of the new generation antihistamine fexofenadine HCl in seasonal allergic rhinitis (SAR). Thirty-one patients were randomly assigned to receive either intranasal irradiation three times a week for 2 weeks or 180 mg fexofenadine HCl per day for 2 weeks. Each patient kept a diary of symptoms for nasal obstruction, nasal itching, rhinorrhea, sneezing and palate itching. In the rhinophototherapy group the individual scores significantly decreased compared with baseline for all of the parameters. In the fexofenadine HCl group none of the scores improved significantly at the end of the treatment except sneezing. TNS was significantly decreased in the rhinophototherapy group after 2 weeks of treatment. In conclusion, the investigators found that intranasal phototherapy is more efficient than fexofenadine HCl in reducing clinical symptoms for SAR (Garaczi et al. 2011). Conclusions from this study are limited because of an extremely small number of study participants. These findings require confirmation in a larger study.

Reference(s):

Albu S, Baschir S. Intranasal phototherapy versus azelastine in the treatment of seasonal allergic rhinitis. *Auris Nasus Larynx*. 2013 Oct;40(5):447-51.

Garaczi E, Boros-Gyevi M, Bella Z, Csoma Z, et al. Intranasal phototherapy is more effective than fexofenadine hydrochloride in the treatment of seasonal allergic rhinitis: results of a pilot study. *Photochem Photobiol*. 2011 Mar;87(2):474-7. doi: 10.1111/j.1751-1097.2010.00882.x.

Leong SC. Rhinophototherapy: gimmick or an emerging treatment option for allergic rhinitis? *Rhinology*. 2011 Dec;49(5):499-506.

Tatar EÇ, Korkmaz H, Sürenoğlu UA, et al. Effects of rhinophototherapy on quality of life in persistent allergic rhinitis. *Clin Exp Otorhinolaryngol*. 2013 Jun;6(2):73-7.

Code	Description
31634	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with balloon occlusion, with assessment of air leak, with administration of occlusive substance (eg, fibrin glue), if performed

Bronchoscopic treatment of bronchopleural fistulas with an occlusive substance, such as fibrin glue, is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

West et al. (2007) conducted a meta-analysis of six case series to address whether bronchoscopic or other minimal access approaches to the closure of bronchopleural fistulas were effective compared to a conventional re-thoracotomy. There was a 30% cure rate using a range of bronchoscopic techniques including cyanoacrylate or fibrin glue application, YAG laser therapy, injection of the vein sclerosant polidocanol and tracheo-bronchial stenting. The mortality was 40% in these patients reflecting the very high mortality with bronchopleural fistulas. Many patients required multiple bronchoscopic procedures and further drainage procedures. Bronchoscopic treatment has so far only been reported in small case series but may offer further treatment options in patients too unwell to undergo re-thoracotomy.

The diagnosis and management of bronchopleural fistulas remain a major therapeutic challenge and is associated with significant morbidity and mortality. While several case reports suggest the efficacy of balloon occlusion for bronchopleural fistulas in selected patients, there are no large-scale controlled trials evaluating the efficacy of this procedure (Sarkar, 2010).

Although rare, bronchopleural fistulas represent a challenging management problem and are associated with high morbidity and mortality. Treatment options include various surgical and medical procedures, including the use of bronchoscopy and different glues, coils and sealants. Therapeutic success has been variable, and the lack of consensus suggests that no optimal therapy is available. Further studies are required to establish the role of techniques and patient selection for endoscopic procedures, as well as which technique or combination will be most valuable (Lois 2005).

Although a minimally invasive technology to close bronchopleural fistulas is needed, further studies with larger study populations are necessary to determine patient selection criteria, safety and long-term efficacy of this technology.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

West D, Togo A, Kirk AJ. Are bronchoscopic approaches to post-pneumonectomy bronchopleural fistula an effective alternative to repeat thoracotomy? *Interact Cardiovasc Thorac Surg.* 2007 Aug;6(4):547-50.

Sarkar P, Chandak T, Shah R, Talwar A. Diagnosis and management bronchopleural fistula. *Indian J Chest Dis Allied Sci.* 2010 Apr-Jun;52(2):97-104.

Lois M, Noppen M. Bronchopleural fistulas: an overview of the problem with special focus on endoscopic management. *Chest.* 2005 Dec;128(6):3955-65.

Code	Description
31647	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with balloon occlusion, when performed, assessment of air leak, airway sizing, and insertion of bronchial valve(s), initial lobe
31648	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with removal of bronchial valve(s), initial lobe

Code	Description
31649	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with removal of bronchial valve(s), each additional lobe (List separately in addition to code for primary procedure)
31651	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with balloon occlusion, when performed, assessment of air leak, airway sizing, and insertion of bronchial valve(s), each additional lobe (List separately in addition to code for primary procedure[s])

The use of implantable bronchial valves, as an alternative to lung volume reduction surgery (LVRS) in patients with emphysema, is investigational, unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in the published peer-reviewed medical literature. Patient selection criteria to identify optimal candidates for the procedure are lacking. In addition, there is no long-term data on the durability of the treatment or long-term complications. However, benefit coverage for this less invasive alternative to LVRS may be available in the context of eligible clinical trials or for persons with life-threatening illness when certain conditions are met.

Clinical Evidence

This minimally invasive alternative to lung volume reduction surgery uses bronchoscopy to place small one-way valves into the airways of emphysema patients. These implantable valves close during inspiration to block air from reaching lung segments that have lost their elasticity, and open during expiration to permit usual escape of air and secretions. Two endobronchial valves are in development for the treatment of emphysema: the IBV[®] Valve System (Spiration, Inc.) and the Zephyr[®] Endobronchial Valve System EBV (Pulmonx Corporation).

The IBV device is in clinical trials under investigational device exemption (IDE) status from the U.S. Food and Drug Administration (FDA). In October 2008, the FDA approved a humanitarian device exemption (H060002) of the IBV Valve for use in patients who have undergone lung volume reduction surgery or partial or total removal of a lung lobe and who experience prolonged (longer than seven days) air leaks or significant air leaks that may become prolonged.

In October 2007, the FDA granted an expedited review of the premarket approval (PMA) application for the Zephyr EBV for the treatment of emphysema. However, on December 5, 2008, an FDA panel rejected the application. The advisory panel concluded that the clinical studies presented in support of the PMA did not demonstrate reasonable evidence of clinical effectiveness and that more long-term effectiveness data was necessary (Hayes, 2007; ECRI, 2010).

In a multicenter 91-patient pilot trial of the Spiration IBV Valve, Stermann et al. (2010) evaluated the safety and effectiveness of the IBV Valve for the treatment of severe emphysema. 609 bronchial valves were placed bilaterally into the upper lobes (UL). There were no procedure-related deaths and 30-day morbidity and mortality were 5.5 and 1.1%, respectively. Pneumothorax was the most frequent serious device-related complication and primarily occurred when all segments of a lobe, especially the left UL, were occluded. Highly significant health-related quality of life (HRQL) improvement was observed. HRQL improvement was associated with a decreased volume in the treated lobes without visible atelectasis. FEV(1), exercise tests, and total lung volume were not changed but there was a proportional shift, a redirection of inspired volume to the untreated lobes. Combined with perfusion scan changes, this suggests that there is improved ventilation and perfusion matching in non-UL lung parenchyma. Bronchial valve treatment of emphysema has multiple mechanisms of action and acceptable safety, and significantly improves quality of life for the majority of patients.

In the international Endobronchial Valve for Emphysema Palliation Trial (VENT), Sciruba et al. (2010) evaluated endobronchial valves in patients with pulmonary hyperinflation related to advanced emphysema. The randomized, controlled trial compared the safety and efficacy of

endobronchial valve therapy in patients with heterogeneous emphysema (n=220) versus standard medical care (n=101). Endobronchial valve treatment for advanced heterogeneous emphysema induced modest improvements in lung function, exercise tolerance and symptoms at the cost of more frequent exacerbations of COPD, pneumonia and hemoptysis after implantation.

National Institute for Health and Care Excellence (NICE) guidelines state that the current evidence on the efficacy and safety of endobronchial valves for persistent air leaks is limited in both quantity and quality. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research (NICE, 2013).

National Institute for Health and Care Excellence (NICE) guideline update (Nice, 2013) states current evidence on the efficacy of insertion of endobronchial valves for lung volume reduction in emphysema shows some clinical and quality-of-life benefits. However, this evidence includes data from patients who have and those who have not had assessment of collateral ventilation, which specialists now advise as fundamental to selection for treatment. Evidence of safety in the short term is adequate but the evidence of safety in the longer term is inadequate in quantity. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

Reference(s):

Hayes, Inc. News Service. Implantable Bronchial Valves. December 2007.

ECRI Institute. Hotline Service. IBV valve system (Spiration, Inc.) for controlling prolonged pulmonary air leaks. April 2012.

Serman DH, Mehta AC, Wood DE, et al; IBV Valve US Pilot Trial Research Team. A multicenter pilot study of a bronchial valve for the treatment of severe emphysema. *Respiration*. 2010;79(3):222-33.

Sciruba FC, Ernst A, Herth FJ, et al; VENT Study Research Group. A randomized study of endobronchial valves for advanced emphysema. *N Engl J Med*. 2010 Sep 23;363(13):1233-44.

National Institute for Health and Care Excellence (NICE). IPG448. Insertion of endobronchial valves for treatment of persistent air leaks. March 2013.

National Institute for Health and Care Excellence (NICE). Insertion of endobronchial valves for lung volume reduction in emphysema. September 2013

Code	Description
43206	Esophagoscopy, flexible, transoral; with optical endomicroscopy
43252	Esophagogastroduodenoscopy, flexible, transoral; with optical endomicroscopy
88375	Optical endomicroscopic image(s), interpretation and report, real-time or referred, each endoscopic session

Optical endomicroscopy is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Optical endomicroscopy also referred to as confocal endomicroscopy (CEM) or optical biopsy is a new endoscopic procedure that is being used to provide high-resolution images of the mucosal layer of the gastrointestinal (GI) tract. This technique can be performed with probe-based systems that pass through the accessory channel of an endoscope or with integrated endoscopic systems. Endomicroscopy can potentially expand the imaging capabilities of flexible endoscopy by obtaining optical biopsies (method that uses the interaction of light and tissue to make a diagnosis rather than using tissue excision). CEM has been used in patients suspected of colon cancer, gastric cancer, celiac disease, and Barrett’s esophagus and for the identification of *Helicobacter pylori* infection.

In a systematic review and meta-analysis, Su et al. (2013) assessed the effectiveness of confocal laser endomicroscopy (CLE) for discriminating colorectal neoplasms from non-neoplasms. The

secondary aim of the review was to compare the efficacy of endomicroscopy and chromoendoscopy for diagnosing colorectal neoplasms. Pooled sensitivity and specificity were compared using univariate regression analysis according to prespecified subgroups. Pooled relative risk was computed to compare the accuracy of endomicroscopy and chromoendoscopy. Fifteen studies (published between 2000 and 2012) involving 719 patients and 2290 specimens were included in the analysis. The pooled sensitivity of all studies was 0.94, and pooled specificity was 0.95. Real-time CLE yielded higher sensitivity and specificity than blinded CLE. For real-time CLE, endoscopy-based systems had better sensitivity and specificity than probe-based systems. CLE yielded equivalent accuracy compared with magnifying virtual chromoendoscopy and magnifying pigment chromoendoscopy. The authors concluded that CLE is comparable to colonoscopic histopathology in diagnosing colorectal neoplasms, and that CLE is better when used in conjunction with conventional endoscopy. According to the authors, this review was limited by the relatively high heterogeneity presented across the 15 enrolled studies. The authors stated that there is a need for prospective randomized studies to obtain unbiased results on the effectiveness and cost-effectiveness of CLE along with standardization of the procedure and a comparison between this strategy and conventional colonoscopy.

Sharma et al. (2011) compared the sensitivity and specificity of probe-based confocal laser endomicroscopy (pCLE) in addition to high-definition white-light endoscopy (HD-WLE) with HD-WLE alone for the detection of high-grade dysplasia (HGD) and early carcinoma (EC) in Barrett's esophagus (BE). The study was a prospective, multicenter, randomized, controlled trial that included 101 consecutive BE patients presenting for surveillance or endoscopic treatment of HGD/EC. All patients were examined by HD-WLE, narrow-band imaging (NBI), and pCLE, and the findings were recorded before biopsy samples were obtained. The order of HD-WLE and NBI was randomized and performed by 2 independent, blinded endoscopists. The sensitivity and specificity for HD-WLE were 34.2% and 92.7%, respectively, compared with 68.3% and 87.8%, respectively, for HD-WLE or pCLE. The sensitivity and specificity for HD-WLE or NBI were 45.0% and 88.2%, respectively, compared with 75.8% and 84.2%, respectively, for HD-WLE, NBI, or pCLE. The authors concluded that pCLE combined with HD-WLE significantly improved the ability to detect neoplasia in BE patients compared with HD-WLE. Additional large-scale randomized controlled trials comparing confocal laser endomicroscopy with standard endoscopy and biopsy in different patient subpopulations are warranted to confirm the findings in this study.

In a prospective, multicenter, randomized clinical trial, Wallace et al. (2012) assessed if use of probe-based confocal laser endomicroscopy (pCLE) in addition to high-definition white light (HDWL) could aid in determination of residual BE. After an initial attempt at ablation, patients were followed-up either with HDWL endoscopy or HDWL plus pCLE, with treatment of residual metaplasia or neoplasia based on endoscopic findings and pCLE used to avoid overtreatment. The study was closed after the interim analysis due to low conditional power resulting from lack of difference between groups as well as higher-than-expected residual Barrett's esophagus in both arms. After enrollment was halted, all patients who had been randomized were followed to study completion. Among the 119 patients with follow-up, there was no difference in the proportion of patients achieving optimal outcomes in the two groups. Other outcomes were similar in the two groups. The authors concluded that this study yields no evidence that the addition of pCLE to HDWL imaging for detection of residual Barrett's esophagus or neoplasia can provide improved treatment.

Yeung and Mortensen (2011) conducted a systematic review of the literature reporting on the use of new advances in endoscopic visualization including confocal laser endomicroscopy. The review focused on systematic reviews, national guidelines and randomized controlled trials. The authors concluded that although there is mounting evidence that these new technologies are superior to conventional endoscopy, current guidelines are limited and further large-scale randomized controlled trials comparing these modalities in different patient subpopulations are warranted.

According American Gastroenterological Association (AGA) Technical Review on the Management of Barrett's Esophagus, clinical trials describe some promising preliminary results for advanced imaging techniques such as confocal laser endomicroscopy in the detection of esophageal metaplasia and dysplasia. To date, however, these advanced techniques have not been shown to provide additional clinical information (beyond that available by high-resolution white light endoscopy) sufficient to warrant their routine application in clinical practice (AGA 2011).

Currently, there is insufficient evidence to demonstrate that confocal laser endomicroscopy improves clinical outcomes as compared with standard endoscopy and biopsy. The American Society of Gastroenterology (ASGE, 2009) states that “confocal laser endomicroscopy is being analyzed as a potentially valuable addition to conventional endoscopy as a means of in vivo optical biopsy enabling realtime histological examination of the superficial layer of the GI tract. How this will affect the practice of screening, surveillance, and early diagnosis of benign, premalignant, and malignant lesions of the GI tract requires further study.” According to the ASGE report, current confocal endomicroscopy devices have a very narrow field of view and allow only visualization of the superficial mucosal layer of the GI tract. Further technological developments are needed to enlarge the field of view, which will facilitate the use of confocal endomicroscopy for cancer screening and surveillance. The report also notes that confocal endomicroscopy is an examiner-dependent technology and interobserver and intraobserver variability of this technique has not been adequately studied.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

American Gastroenterological Association (AGA) Technical Review on the Management of Barrett's Esophagus. March 2011. Available at: <http://www.gastro.org/practice/medical-position-statements> Accessed June 2014

American Society of Gastrointestinal Endoscopy (ASGE). Confocal laser endomicroscopy. Report on emerging technology. *Gastrointestinal Endoscopy* 2009;70(2):197-200.

ECRI Institute. Hotline Response. Confocal Endomicroscopy for Diagnosis and Treatment of Gastrointestinal Disease. June 2011.

ECRI Institute. Product Brief. Cellvizio (Mauna Kea Technologies) for Aiding Diagnosis of Diseases of the Gastrointestinal Tract. December 2012.

Hayes Inc. Search & Summary. Confocal Laser Endomicroscopy for Diagnosis of Esophageal Disease. January 2013.

Sharma P, Meining AR, Coron E, et al. Real-time increased detection of neoplastic tissue in Barrett's esophagus with probe-based confocal laser endomicroscopy: final results of an international multicenter, prospective, randomized, controlled trial. *Gastrointest Endosc.* 2011 Sep;74(3):465-72.

Su P, Liu Y, Lin S, et al. Efficacy of confocal laser endomicroscopy for discriminating colorectal neoplasms from non-neoplasms: a systematic review and meta-analysis. *Colorectal Dis.* 2013 Jan;15(1):e1-12.

Yeung TM, Mortensen NJ. Advances in endoscopic visualization of colorectal polyps. *Colorectal Dis.* 2011 Apr;13(4):352-9. doi: 10.1111/j.1463-1318.2009.02142.x.

Wallace MB, Crook JE, Saunders M, et al. Multicenter, randomized, controlled trial of confocal laser endomicroscopy assessment of residual metaplasia after mucosal ablation or resection of GI neoplasia in Barrett's esophagus. *Gastrointest Endosc.* 2012 Sep;76(3):539-547.e1.

Code	Description
48160	Pancreatectomy, total or subtotal, with autologous transplantation of pancreas or pancreatic islet cells
48999	Unlisted procedure, pancreas
60659	Unlisted laparoscopy procedure, endocrine system

Code	Description
G0341	Percutaneous islet cell transplant, includes portal vein catheterization and infusion
G0342	Laparoscopy for islet cell transplant, includes portal vein catheterization and infusion
G0343	Laparotomy for islet cell transplant, includes portal vein catheterization and infusion
S2102	Islet cell tissue transplant from pancreas; allogeneic

Autologous pancreatic islet cell transplantation following total pancreatectomy for non-malignant conditions is proven and medically necessary per the UnitedHealth Group [Transplant Review Guidelines](#).

Allogeneic islet cell transplantation is unproven and not medically necessary for the treatment of diabetes due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature. Coverage may be reviewed when the treatment is

- Performed under a clinical trial; **and**
- A clinical trial benefit exists; **and**
- The trial conforms to the provisions of that benefit.

Generally, since diabetes does not meet the definition of a life-threatening illness found in most commercial benefit plans, allogeneic islet cell transplants will not be covered even in patients with a life-threatening clause in their benefit plan. The benefit plan must be checked carefully for the definition of life-threatening illness and other coverage provisions for investigational, experimental and “promising but unproven” treatments.

Clinical Evidence

At the present time, there is some very limited evidence to suggest that islet cell transplantation can provide at least several years of insulin independence and improvement in glycemic control for some patients with severe type 1 diabetes whose serum glucose level was uncontrolled despite intensive insulin therapy.

A Hayes report concluded that although the evidence is of low quality and very limited, total pancreatectomy and autologous islet cell transplantation (TP/AIT) is an appropriate therapy for highly selected patients with a poor quality of life due to severe, intractable pain from chronic pancreatitis that is unresponsive to standard medical and surgical therapies, who are fully informed about the risks and benefits of the procedure, and when it is performed at a center of excellence or as part of a well-designed and strictly monitored clinical trial (Hayes, 2010; updated 2012).

Bramis et al. (2012) performed a systematic review of the literature to evaluate the outcome of total pancreatectomy and islet autotransplantation for chronic pancreatitis. Five studies were included. TP/IAT was successful in reducing pain in patients with chronic pancreatitis. Comparing morphine requirements before and after the procedure, two studies recorded significant reductions. Concurrent IAT reduced the insulin requirement after TP. The impact on quality of life was poorly reported.

Pancreatic islet transplants hold significant potential advantages over whole-gland transplants. Recent strides have been made in improving the success rates of this procedure. However, at this time, islet transplantation is a rapidly evolving technology that also requires systemic immunosuppression and should be performed only within the setting of controlled research studies (Robertson, 2006).

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

Hayes, Inc. Health Technology Brief. Total pancreatectomy with autologous islet cell transplantation (TP/AIT) for chronic pancreatitis. December 2010. Updated December 2012.

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ECRI Institute. Hotline Service. Indications and contraindications for islet cell transplantation for treating type I diabetes. January 2013.

Robertson RP, Davis C, Larsen J, et al. Pancreas and islet transplantation in type 1 diabetes. Diabetes Care. 2006 Apr;29(4):935.

Code	Description
53855	Insertion of a temporary prostatic urethral stent, including urethral measurement

The insertion of a temporary prostatic urethral stent is unproven and not medically necessary. There is insufficient evidence to support the use of temporary prosthetic urethral stents. The evidence is conflicting regarding the safety and efficacy of these devices.

Clinical Evidence

Temporary urethral stents are either removable or absorbable. Temporary urethral stents include the Memokath™ and the Spanner™ Temporary Prostatic Stent.

Following transurethral microwave thermotherapy, 186 patients were randomized to receive a Spanner (n=100) or the standard of care (n=86). The stent group reported significantly superior improvement in symptoms at the one week follow-up visit. Thereafter, there was no significant difference between the stent and control groups. The investigators concluded that the Spanner is a safe, effective and well tolerated temporary stent for severe prostatic obstruction resulting from therapy induced edema after transurethral microwave thermotherapy (Dineen et al. 2008). Shore et al. published the same study in 2007. The study results are limited in demonstrating meaningful improvement in clinical outcomes in the group that received the temporary prostatic stent compared to the patients in the control group.

Jordan et al. (2013) investigated the ability of the Memokath™ 044TW stent to maintain urethral patency after dilation or internal urethrotomy for recurrent urethral stricture. A total of 92 patients with recurrent bulbar urethral strictures were treated with dilation or internal urethrotomy and randomized to short-term urethral catheter diversion (n=29) or insertion of a Memokath 044TW stent (n=63). The primary end point was urethral patency, as assessed by passage of a calibrated endoscope. Secondary end points included urinary symptoms and uroflowmetry parameters. Stents were scheduled to remain in situ for 12 months. The rate of successful stent insertion was 93.6%. In stented patients, patency was maintained significantly longer than controls (median 292 vs 84 days). Patency was reflected in significantly improved uroflowmetry and symptom scores. The stent was removed in 100% of patients. The most frequently noted side effects in stented patients were bacteriuria, hematuria and penile pain, which were usually mild and transient. Stent dislocation and occlusion were observed in 8 and 3 patients, respectively. The authors concluded that patients with recurrent bulbar urethral strictures treated with dilation or urethrotomy and a Memokath 044TW stent maintained urethral patency significantly longer than those treated with dilation or urethrotomy alone. Given the lack of FDA approval for the Memokath stent, these data are insufficient to draw conclusions regarding the use of this device.

Goh et al. (2013) assessed the ease of insertion and removal of a temporary prostatic stent (the Spanner) following the use of a prostatic urethral measuring device (the Surveyor™) in patients

with bladder outflow obstruction or urinary retention awaiting definitive surgery. 16 patients had the Spanner inserted following use of the Surveyor. All insertions were uncomplicated. No symptomatic infection was reported. The stents stayed in situ for a median of 10 days. 12 stents were removed prematurely due to severe symptoms or retention. A total of 12 stents had to be removed endoscopically. The authors concluded that the Spanner is easy to insert. Stent removal via the retrieval suture has been difficult necessitating the use of endoscopy in the majority of cases. Possible causes of stent failure include underestimation of the prostatic urethral length by the Surveyor leading to obstruction by apical prostatic tissue, excessive suture length between the stent and distal anchor permitting proximal migration or inadequate suture length leading to urinary incontinence. According to the authors, further design modifications are suggested.

Egilmez et al. (2006) evaluated the efficacy of intraurethral metal stents in preventing or eradicating urinary-tract infections (UTI) during the management of bladder outlet obstruction (BOO) by comparing the frequency and nature of the infections with indwelling-catheter-associated UTI. The SAS relative-risk test was used to compare the risks of UTI in 76 patients with temporary urethral stents, 60 patients with BOO who had never been catheterized nor stented, and 34 patients with a permanent indwelling urethral catheter (PIUC). Infection was assessed 1 month after placement of the devices. After insertion of the catheter, UTI developed in 79.4% of the patients who originally had sterile urine. However, after insertion of the stent, UTI developed in only 40.9% of the patients with sterile urine. In 21 (44.6%) of the catheterized patients who had infected urine, UTI was eradicated after stent insertion. The investigators concluded that urinary infection is a significant problem in patients with PIUC but is significantly less frequent and less severe in patients with urethral stents. These findings require confirmation in large controlled trials.

A series of 43 consecutive patients were stented with the Spanner temporary prostatic stent and reviewed retrospectively. Stents were removed and replaced every 3 months if tolerated. More than half of the patients (63%) had an unsatisfactory outcome, namely, immediate or delayed retention or elective removal because of unbearable symptoms. The remaining 37% of patients had a satisfactory outcome and either continued to have the stent in situ after a mean of five changes or are stent free after a successful voiding trial (Grimsley et al. 2007).

The American Urological Association's clinical guideline for the management of benign prostatic hyperplasia does not make a specific recommendation for or against temporary stents (AUA, 2010).

Reference(s):

American Urological Association (AUA). Clinical guideline for the management of benign prostatic hyperplasia. Updated 2010. Available at: <http://www.auanet.org/content/guidelines-and-quality-care/clinical-guidelines.cfm?sub=bph>. Accessed May 2014.

Dineen MK, Shore ND, Lumerman JH, Saslawsky MJ, et al. Use of a temporary prostatic stent after transurethral microwave thermotherapy reduced voiding symptoms and bother without exacerbating irritative symptoms. *Urology*. 2008 May;71(5):873-7.

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Grimsley SJ, Khan MH, Lennox E, Paterson PH. Experience with the spanner prostatic stent in patients unfit for surgery: an observational study. *J Endourol*. 2007 Sep;21(9):1093-6.

Jordan GH, Wessells H, Secrest C, et al. United States Study Group. Effect of a temporary thermo-expandable stent on urethral patency after dilation or internal urethrotomy for recurrent bulbar urethral stricture: results from a 1-year randomized trial. *J Urol*. 2013 Jul;190(1):130-6.

Shore ND, Dineen MK, Saslawsky MJ, et al. A temporary intraurethral prostatic stent relieves prostatic obstruction following transurethral microwave thermotherapy. *J Urol*. 2007 Mar;177(3):1040-6.

Code	Description
64999	Unlisted procedure, nervous system

Surgical treatment (that may include laminectomy and sacral reconstruction) of a Tarlov cyst from the sacrum is proven and medically necessary for patients who experience pain or neurologic symptoms attributed to the Tarlov cyst.

Information Pertaining to Medical Necessity Review (When Applicable)

Because most Tarlov cysts are asymptomatic, surgery is rarely required. Surgery for a Tarlov cyst is proven based on a correlation among symptoms, physical examination and radiographic findings.

- Where the cyst causes neurological symptoms
- Where pain is attributable to the cyst. In general, larger cysts (greater than 1.5 cm) with corresponding radicular symptoms are most likely to benefit from surgery.
- Where the patient has failed an appropriate course of non-operative treatment.

Clinical Evidence

Tarlov cysts are fluid-filled sacs that affect the nerve roots of the spine, especially near the base of the spine (sacral region). Individuals may be affected by multiple cysts of varying size.

Tarlov cysts are difficult to diagnose because of the limited knowledge about the condition, and because many of the symptoms can mimic other disorders. Most perineural cysts (Tarlov's cysts) are asymptomatic. They are usually diagnosed incidentally, and a specific treatment is not necessary. They should be operated on, only if they produce or have disabling symptoms clearly attributable to them.

There was no information found in *MCG™*, ECRI or Hayes for this diagnosis with this treatment.

Caspar et al. (2003): There is agreement that symptomatic perineural sacral cysts should be treated surgically. However, it is still debated whether the preference should be given to the curative option, consisting of excision of the cyst with duraplasty, or to drainage of the cyst to relieve symptoms. In this retrospective study the efficacy of microsurgical cyst resection with duraplasty is evaluated. In 15 patients presenting with pain and neurologic deficits, myelography and/or MRI detected sacral cysts. The clinical features suggested that the space-occupying lesions caused the disturbances. Microsurgical excision of the cyst along with duraplasty or plication of the cyst wall was performed in all the cases. Postoperative care included bed rest and CSF drainage for several days. In 13 out of 15 patients the preoperative radicular pain disappeared after surgery. The 2 patients with motor deficits and the 6 patients with bladder dysfunction recovered completely. In all except 1 of the 10 patients complaining of sensory disturbances a significant improvement was achieved. No complications were observed. Microsurgical excision of the cyst combined with duraplasty or plication of the cyst wall is an effective and safe treatment of symptomatic sacral cysts and, in the view of the authors, the method of choice. This was an uncontrolled retrospective study of extremely small sample size.

Guo et al. (2007) investigated the microsurgical results of symptomatic sacral perineural cysts of 11 patients and to discuss the treatment options of the past 10 years. Nine of the 11 patients (82%) experienced complete or substantial relief of their preoperative symptoms. One patient (Patient 4) experienced worsening of bladder dysfunction after surgery and recovered slowly to subnormal function during the subsequent 2 months. The symptoms of Patient 9 did not resolve, and magnetic resonance imaging showed that the cyst had reoccurred. The patient underwent reoperation 3 months later without any improvement. One patient (Patient 11) experience a cerebrospinal fluid leakage complication. This was an uncontrolled study of extremely small sample size.

Tanaka et al. (2006) investigated the surgical outcomes and indicators for surgical intervention. Twelve consecutive patients harboring symptomatic sacral perineural cysts were treated between 1995 and 2003. All patients were assessed for neurological deficits and pain by neurological examination. The researchers performed a release of the valve and imbrication of the sacral cysts with laminectomies in 8 cases or recapping laminectomies in 4 cases. After surgery, symptoms improved in 10 (83%) of 12 patients, with an average follow-up of 27 months. Ten patients had sacral perineural cysts with signs of positive filling defect. Two (17%) of 12 patients experienced no significant improvement. In one of these patients, the filling defect was negative. In conclusion, a positive filling defect may become an indicator of good treatment outcomes. This was an uncontrolled series of extremely small sample size.

National Institute of Neurological Disorders and Stroke:

Tarlov cysts are sacs filled with cerebrospinal fluid that most often affect nerve roots in the sacrum, the group of bones at the base of the spine. These cysts (also known as meningeal or perineural cysts) can compress nerve roots, causing lower back pain, sciatica (shock-like or burning pain in the lower back, buttocks, and down one leg to below the knee), urinary incontinence, headaches (due to changes in cerebrospinal fluid pressure), constipation, sexual dysfunction, and some loss of feeling or control of movement in the leg and/or foot. Pressure on the nerves next to the cysts can also cause pain and deterioration of surrounding bone.

Tarlov cysts may be drained and shunted to relieve pressure and pain, but relief is often only temporary and fluid build-up in the cysts will recur. Corticosteroid injections may also temporarily relieve pain. Other drugs may be prescribed to treat chronic pain and depression. Injecting the cysts with fibrin glue (a combination of naturally occurring substances based on the clotting factor in blood) may provide temporary relief of pain. Some scientists believe the herpes simplex virus, which thrives in an alkaline environment, can cause Tarlov cysts to become symptomatic. Making the body less alkaline, through diet or supplements, may lessen symptoms. Microsurgical removal of the cyst may be an option in selected individuals who do not respond to conservative treatments and who continue to experience pain or progressive neurological damage.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

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Tanaka M, et. al. Surgical results of sacral perineural (Tarlov) cysts. Department of Orthopaedic Surgery, Okayama University Hospital. [Acta Med Okayama](#). 2006 Feb;60(1):65-70.

Code	Description
76120	Cineradiography/videoradiography, except where specifically included
76125	Cineradiography/videoradiography to complement routine examination (List separately in addition to code for primary procedure)
76496	Unlisted fluoroscopic procedure (eg, diagnostic, interventional)
76499	Unlisted diagnostic radiographic procedure

The use of videofluoroscopy, cineradiography, Spinalyzer and similar technology and digital motion X-rays to diagnose spinal and skeletal dysfunction are unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Dynamic spinal visualization may involve different imaging techniques, including videofluoroscopy of the spine (also known as cineradiography) and digital motion X-ray. Videofluoroscopy of the spine is a specialized X-ray (fluoroscopy) that visualizes and records actual spinal movement. These technologies allow the simultaneous visualization of movement of internal body structures, such as the skeleton, intervertebral discs and ligaments, with corresponding external body movement. All of these methods use x-rays to create images either on film, on a video monitor, or on a computer screen. The Spinalyzer is used to visualize and measure the distortion of the spine and skeletal structure.

These imaging studies are used to assist with analysis of segment dysfunction. However, their inability to define structural changes such as impingement limits their utility. The lack of reference norms decreases the reliability of the test results.

The current literature evaluating the clinical utility of dynamic spinal visualization techniques, including but not limited to digital motion x-ray and cineradiography (videofluoroscopy), for the evaluation and assessment of the spine is limited to a few studies involving very small numbers of participants. While these studies do indicate that there may be some benefit from the use of these technologies, further evidence from large controlled trials is needed to demonstrate that the results have significant impact on clinical care and are superior to currently available alternatives.

A 2011 guideline from the American College of Occupational and Environmental Medicine states that for the assessment of acute, subacute, or chronic LBP, videofluoroscopy was “Not Recommended, Insufficient Evidence.”

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

ECRI Institute. Custom Hotline Response. Videofluoroscopy of the spine for diagnosing instability. April 16, 2008. Updated April 13, 2010.

ECRI Institute: .Dynamic Spinal Visualization for Diagnosing Spinal Disorders. February 13, 2013.

Lee SW, Wong KW, Chan MK, et. al. Development and validation of a new technique for assessing lumbar spine motion. Spine. 2002 Apr 15;27(8):E215-20.

National Guideline Clearinghouse Website. American College of Occupational and Environmental Medicine (ACOEM). Low back disorders (Updated 2011).

Teyhen DS, Flynn TW, Childs JD, et al. Fluoroscopic video to identify aberrant lumbar motion. Spine. 2007; 32(7):E220-229.

Zheng Y, Nixon MS, Allen R. Automated segmentation of lumbar vertebrae in digital videofluoroscopic images. IEEE Trans Med Imaging. 2004 Jan;23(1): 45-52.

Code	Description
84999	Unlisted chemistry procedure [when used to report VeriStrat]

Serum proteomic profiling, using mass spectrometry, is unproven as a prognostic tool in patients with advanced non-small cell lung cancer (NSCLC) due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

VeriStrat® serum test is intended to help identify patients with advanced NSCLC who are more likely to benefit from treatment with erlotinib, an epidermal growth factor receptor (EGFR) inhibitor. The test stratifies patients into two categories: those with significantly better (Good) and those with significantly worse (Poor) outcomes following treatment with EGFR inhibitor therapy. VeriStrat is not an EGFR mutation test (Biodesix website).

An ECRI product brief concluded that evidence from prognostic studies suggests that VeriStrat test findings (Good vs. Poor) successfully differentiated patients with NSCLC based on response to erlotinib treatment, progression-free survival and/or overall survival. However, the evidence is insufficient to determine whether VeriStrat performs better than alternative prognostic tests (e.g., EGFR mutation status) (ECRI, 2012).

A Hayes report concluded that evidence regarding the use of VeriStrat in NSCLC patients is too limited to draw meaningful conclusions about the value of this assay in guiding treatment selection. The evidence supporting the analytical and clinical validity of the VeriStrat test is limited. While most studies indicate that VeriStrat classification may have value as a predictive marker of EGFR treatment response, additional evidence supporting both analytical validity and clinical validity is needed. At this time, there is a lack of evidence regarding the clinical utility of the test. Noted limitations of the evidence include overlapping patient populations, potential bias due to proprietary analysis of data and retrospective study design (Hayes, 2012; updated 2014).

Taguchi et al. (2007) developed and evaluated the proteomic assay that is the basis for the VeriStrat test. Pretreatment serum mass spectrometry analysis of 139 NSCLC patients who were later treated with erlotinib or gefitinib was used to develop an algorithm to predict which patients might benefit from treatment with these agents. A predicted "good" outcome was associated with longer median time to progression and longer overall median survival, when compared with a predicted "poor" outcome. The authors reported that additional larger randomized trials are needed to confirm the findings.

Stinchcombe et al. (2013) performed a retrospective analysis of ninety-eight plasma or serum samples collected as part of a randomized phase II trial to investigate the ability of VeriStrat (VS) to predict treatment outcomes. In the original trial, patients were randomized into three treatment groups: gemcitabine (arm A), erlotinib (arm B) and gemcitabine and erlotinib (arm C). The majority of patients had stage IV disease (81%), adenocarcinoma histology (63%) and reported current or previous tobacco use (84%). Similar progression-free survival (PFS) and overall survival (OS) were observed in all arms. In arm A, patients with VS Good (n=20) compared with VS Poor status (n=8) had similar PFS. In arm B, patients with VS Good (n=26) compared with VS Poor (n=12) had a statistically significantly superior PFS. In arm C, patients with VS Good (n=17) compared with Poor (n=15) had a superior PFS and a trend toward superior OS. The authors noted that further results from larger, prospective trials are needed before using VS to direct treatment selection in routine clinical practice.

In a retrospective analysis, Akerley et al. (2013) assessed the impact of the VeriStrat test on physician treatment recommendations for patients with non-small-cell lung cancer (NSCLC). Pre- and post-test treatment recommendations were collected from ordering physicians on a voluntary basis. Only those tests that had both pre- and post-test treatment information were included in the analysis group. Over the duration of the study, 724 physicians ordered 2854 tests. The analysis group comprised the 226 physicians who provided pre- and post-test treatment information (n=403 tests). Following receipt of the test results, 90.3% of patients who tested as Good received erlotinib recommendations versus 9.6% of patients who tested as Poor. Ninety percent of post-test treatment recommendations positively correlated with test results, with 40% showing a change from pre-test considerations. The authors concluded that, among test orderers, serum-based proteomic mass spectrometry testing significantly influenced therapy recommendations in NSCLC. Usage patterns should be monitored as use expands. Limitations of the study include a retrospective design and reliance on voluntary submission of data. Lazzari et al. (2012) reported similar results in a separate retrospective study.

Carbone et al. (2012) investigated the predictive and prognostic effects of VeriStrat (VS) on response and survival in a subset of patients enrolled in a phase III trial of erlotinib versus placebo in previously treated advanced non-small-cell lung cancer patients. Pretreatment plasma samples were available for 441 of 731 enrolled patients. VS testing was successful in 436 samples (98.9%), with 61% classified as Good. VS was prognostic for overall survival in both erlotinib-treated patients and those on placebo. For VS Good patients, the median survival was 10.5 months on erlotinib versus 6.6 months for placebo. For VS Poor patients, the median survival was 4 months for patients receiving erlotinib, and 3.1 months for placebo. The authors reported that VS was able to predict response to erlotinib and was a prognostic biomarker in previously treated patients with advanced NSCLC. However, for both overall survival and progression-free survival, VS was not predictive of differential survival benefit versus placebo.

The clinical utility of the VeriStrat test as a prognostic tool in patients with advanced NSCLC has yet to be validated in a prospective clinical trial. Prospective studies evaluating the impact of VeriStrat test results on patient management or health outcomes are ongoing.

National Comprehensive Cancer Network (NCCN) guidelines do not address serum proteomic profiling as a prognostic tool in patients with advanced NSCLC.

References

Akerley WL, Nelson RE, Cowie RH, et al. The impact of a serum based proteomic mass spectrometry test on treatment recommendations in advanced non-small-cell lung cancer. *Curr Med Res Opin.* 2013 May;29(5):517-25.

Biodesix Inc. website. <http://www.veristratsupport.com/>. Accessed April 15, 2014.

Carbone DP, Ding K, Roder H, et al. Prognostic and predictive role of the VeriStrat plasma test in patients with advanced non-small-cell lung cancer treated with erlotinib or placebo in the NCIC Clinical Trials Group BR.21 trial. *J Thorac Oncol.* 2012 Nov;7(11):1653-60.

ECRI Institute. Product Brief. VeriStrat (Biodesix, Inc.) for determining relevancy of epidermal growth factor receptor inhibitor treatment in patients with advanced non-small cell lung cancer. December 2012.

Hayes, Inc. Hayes Genetic Test Evaluation Report. VeriStrat® test to predict response to epidermal growth factor receptor (EGFR) tyrosine kinase inhibitors (TKIs) in non-small cell lung cancer (NSCLC). Lansdale, PA: Hayes, Inc.; February 2012. Updated February 2014.

Lazzari C, Spreafico A, Bachi A, et al. Changes in plasma mass-spectral profile in course of treatment of non-small cell lung cancer patients with epidermal growth factor receptor tyrosine kinase inhibitors. *J Thorac Oncol.* 2012 Jan;7(1):40-8.

National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Non-small cell lung cancer. v3.2014. Available at: http://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed April 15, 2014.

Stinchcombe TE, Roder J, Peterman AH, et al. A retrospective analysis of VeriStrat status on outcome of a randomized phase II trial of first-line therapy with gemcitabine, erlotinib, or the combination in elderly patients (age 70 years or older) with stage IIIB/IV non-small-cell lung cancer. *J Thorac Oncol.* 2013 Apr;8(4):443-51.

Taguchi F, Solomon B, Gregorc V, et al. Mass spectrometry to classify non-small-cell lung cancer patients for clinical outcome after treatment with epidermal growth factor receptor tyrosine kinase inhibitors: a multicohort cross-institutional study. *J Natl Cancer Inst.* 2007 Jun 6;99(11):838-46.

Code	Description
85547	Mechanical fragility, RBC

The use of red blood cell mechanical fragility testing is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Mechanical fragility of red blood cells (RBCs) is a critical variable for the hemolysis testing of many important clinical devices, such as pumps, valves, cannulae and gas exchange devices.

Unfortunately, no standardized test for RBC mechanical fragility is currently well accepted. Although many test devices have been proposed for the study of mechanical fragility of RBCs, no one has ever shown that their results have any relevance to a blood pump (Gu et al., 2005).

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

Gu L, Smith WA, Chatzimavroudis GP. Mechanical fragility calibration of red blood cells. ASAIO J. 2005 May-Jun;51(3):194-201.

Code	Description
86849	Unlisted immunology procedure

The following information applies to the use of this unlisted code for antiprothrombin antibody testing.

Antiprothrombin antibody testing for antiphospholipid syndrome is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Anti-phospholipid syndrome (APS) is an autoimmune condition characterized by moderate-to-high levels of circulating anti-phospholipid antibodies. Antiphospholipid antibodies have been associated with a variety of medical problems, including arterial thrombosis, venous thrombosis, autoimmune thrombocytopenia and fetal loss. Research shows variable sensitivity and a lack of standardization with available tests.

In a practice bulletin, the American College of Obstetricians and Gynecologists (ACOG) makes the following recommendations based on limited or inconsistent scientific evidence:

- Obstetric indications for antiphospholipid antibody testing should be limited to a history of one fetal loss or three or more recurrent embryonic or fetal losses.
- Testing for antiphospholipid antibodies should be performed in women with a prior unexplained venous thromboembolism, a new venous thromboembolism during pregnancy or in those with a history of venous thromboembolism but not tested previously (ACOG, 2012).

Prothrombin (PT) is a target for antibodies with lupus anticoagulant (LA) activity, suggesting the possible application of anti-prothrombin antibody (aPT) assays in patients with antiphospholipid syndrome (APS). Different methods - both homemade and commercial - for the detection of aPT are available, but they seem to produce conflicting results. Tincani et al. (2007) compared the performance of different assays on a set of well-characterized serum samples. Sera were gathered from 4 Forum Interdisciplinare per la Ricerca nelle Malattie Autoimmuni (FIRMA) institutions, and distributed to 15 participating centers. Forty-five samples were from patients positive for LA and/or anticardiolipin antibodies (aCL) with or without APS, and 15 were from rheumatoid arthritis (RA) patients negative for antiphospholipid antibodies. The samples were evaluated for IgG and IgM antibodies using a homemade direct aPT assay (method 1), a homemade phosphatidylserine-dependent aPT assay (aPS/PT, method 2), and two different commercial kits (methods 3 and 4). In addition, a commercial kit for the detection of IgG-A-M aPT (method 5) was used. Inter-laboratory results for the 5 methods were not always comparable when different methods were used. Good inter-assay concordance was found for IgG antibodies evaluated using methods 1, 3, and 4 (Cohen $k > 0.4$), while the IgM results were discordant between assays. In patients with thrombosis and pregnancy losses, method 5 performed better than the others. While aPT and aPS/PT assays could be of interest from a clinical perspective,

their routine performance cannot yet be recommended because of problems connected with the reproducibility and interpretation of the results.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion

Reference(s):

American College of Obstetricians and Gynecologists. Practice Bulletin No. 132: Antiphospholipid syndrome. *Obstet Gynecol.* 2012 Dec;120(6):1514-21.

Tincani A, Morozzi G, Afeltra A, et al. Antiprothrombin antibodies: a comparative analysis of homemade and commercial methods. A collaborative study by the Forum Interdisciplinare per la Ricerca nelle Malattie Autoimmuni (FIRMA). *Clin Exp Rheumatol.* 2007 Mar-Apr;25(2):268-74.

Code	Description
92499	Unlisted ophthalmological service or procedure Multifocal Electroretinography (mfERG) and Pattern Electroretinography (PERG)

Multifocal electroretinogram is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Pattern electroretinogram (PERG) or pattern electroretinogram optimized for glaucoma screening (PERGLA) is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Multifocal electroretinogram (mfERG) is a noninvasive test used to detect the regional functional changes of the central retina by measuring the electrophysiological response. The available studies of multifocal electroretinography do not provide convincing evidence that multifocal electroretinography provide objective information regarding changes in retinal function. Pattern ERG (PERG) is being studied as a tool to diagnose glaucoma and retinal disorders and monitor success of surgical procedures. Pattern electroretinogram optimized for glaucoma screening (PERGLA) is a non-invasive, fully automatic version of the pattern ERG. Clinical evidence regarding the PERG test is limited. Well-designed controlled trials with larger patient populations are required to determine if these tests are effective for diagnosing retinal conditions.

A report by the American Academy of Ophthalmology reviewed the published literature to summarize and evaluate the effectiveness of visual function tests in diagnosing glaucoma and in monitoring progression. The report indicated that technologies, such as multifocal visual-evoked potential and electroretinography, which were designed as objective measures of visual function, provide testing free of patient input, but issues prevent their adoption for glaucoma management. The authors also state that objective visual field tests that do not depend on patient responses, such as multifocal electroretinography (mfERG), are under development. (Jampel et al. 2011).

In a prospective study, Kandel et al. (2012) evaluated the effects of ethambutol therapy in visual functions of both eyes in 44 patients. Parameters evaluated included multifocal electroretinography (ERG) with Roland-RETI scan. Based on the results of the study, the authors concluded that visual acuity, contrast sensitivity, and multifocal ERG are sensitive tests to detect ethambutol toxicity in subclinical stages and hence very useful tools for monitoring patients under ethambutol therapy for ocular toxicity. These findings require confirmation in a larger study.

Dale et al. (2010) compared the ability of the multifocal electroretinogram (mfERG) and frequency domain optical coherence tomography (fdOCT) to detect retinal abnormalities. A total of 198 eyes (100 patients) were included in the study to rule out a retinal etiology of visual impairment. All patients were evaluated with static automated perimetry (SAP), mfERG, and fdOCT. Local mfERG and fdOCT abnormalities were compared to local regions of visual field sensitivity loss

measured with SAP and categorized as normal/inconclusive or abnormal. 146 eyes were categorized as normal retina on both fdOCT and mfERG. The retina of 52 eyes (36 patients) was categorized as abnormal based upon mfERG and/or fdOCT. Of this group, 25 eyes (20 patients) were abnormal on both tests. However, 20 eyes (13 patients) were abnormal on mfERG, while the fdOCT was normal/inconclusive; and 7 eyes (7 patients) had normal or inconclusive mfERG, but abnormal fdOCT. According to the authors, considerable disagreement exists between these two methods for detection of retinal abnormalities. The authors stated that the mfERG tends to miss small local abnormalities that are detectable on the fdOCT. On the other hand, the fdOCT can appear normal in the face of clearly abnormal mfERG and SAP results. The authors indicated that while improved imaging and analysis may show fdOCT abnormalities in some cases, in others early damage may not appear on structural tests.

Tafreshi et al. (2010) compared the diagnostic accuracy of the pattern ERG to that of standard automated perimetry (SAP), short-wavelength automated perimetry (SWAP), and frequency-doubling technology (FDT) perimetry for discriminating between healthy and glaucomatous eyes in 83 eyes of 42 healthy recruits and 92 eyes of 54 glaucoma patients. The diagnostic accuracy of the pattern ERG amplitude was similar to that of SAP and SWAP, but somewhat worse than that of FDT. Agreement among the tests was characterized as fair to moderate.

Photopic negative response (PhNR) and pattern electroretinogram (PERG) are electrophysiological markers of retinal ganglion cell function; both are reduced in glaucoma. We compared PhNR and PERG in different stages of the disease.

Preiser et al. (2013) compared photopic negative response (PhNR) and pattern electroretinogram (PERG) in different stages of the disease. Eleven eyes with preperimetric glaucoma (glaucomatous optic disc with normal field); 18 with manifest glaucoma; and 26 normals were included in the study. Based on the results of the study, the authors concluded that both PhNR and PERG performed similarly to detect glaucoma; for both, ratios performed better than amplitudes. The authors stated that the PhNR has the advantage of not requiring clear optics and refractive correction; the PERG has the advantage of being recorded with natural pupils. This study is limited by a small study population.

Sehi et al. (2009) examined retinal ganglion cell function measured using pattern electroretinogram optimized for glaucoma screening (PERGLA) in 29 normal individuals, 28 glaucoma patients, and 37 glaucoma suspect volunteers. According to the authors, retinal ganglion cell function measured using pattern electroretinogram optimized for glaucoma screening (PERGLA) is reduced in glaucoma but only demonstrates modest correlations with central SAP sensitivity values and structural measures of optic nerve topography and retinal nerve fiber layer thickness.

Banitt et al. (2013) conducted a longitudinal cohort study that included 107 adults (201 eyes) at risk of glaucoma and compared pattern electroretinography (PERG) amplitudes and optical coherence tomography (OCT) imaging of retinal nerve fiber layer (RNFL) over a 4-year period in order to determine the time lag between loss of retinal ganglion cells (RGC) function and loss of RNFL thickness. RNFL thickness did not decrease until the PERG amplitude had lost at least 50% of its normal value for age, indicated by post hoc comparisons showing highly significant differences between RNFL thicknesses of eyes in the stratum with the most severely affected PERG amplitude ($\leq 50\%$ of normal) and the two strata with the least affected PERG amplitudes ($> 70\%$). The authors concluded from the results of the study that there was an approximate time lag of 8 years between a 10% loss in PERG amplitude and a 10% loss in RNFL thickness, which could be used as a window for intervention. The study did not confirm the utility of such findings in improving care and outcome of patients.

Jafarzadehpour et al. (2013) evaluated retinal ganglion cell (RGC) dysfunction in glaucoma suspects and patients with early primary open angle glaucoma (POAG) using pattern electroretinography (PERG). Transient PERG was recorded in response to 0.8° and 16° black

and white checkerboard stimuli. Amplitude and peak time (latency) of the P50 and N95 components of the PERG response, and the ratio of N95 amplitude in response to 0.8° and 16° checks were measured. Twenty glaucoma suspects, 15 early POAG and 16 normal controls were enrolled. N95 peak time (latency) was significantly increased in both early manifest POAG and glaucoma suspects as compared to normal controls. In early POAG, N95 amplitude in response to small (0.8°) checks and the small/large check ratio were reduced in comparison to normal eyes. However, in glaucoma suspects no significant N95 amplitude reduction was observed. No significant difference was observed among the study groups in terms of P50 amplitude or peak time. According to the authors, PERG may detect RGC dysfunction (increased latency) before cell death (decreased amplitude) occurs. The sample size in this study is too small to prove the usefulness of PERG as a diagnostic tool.

In another study of 71 patients, Bowd et al. (2009) reported that pattern electroretinograms recorded using the PERGLA paradigm can discriminate between healthy and glaucomatous eyes, although this technique performed no better than SAP at this task.

References:

Banitt MR, Ventura LM, Feuer WJ, et al. Progressive loss of retinal ganglion cell function precedes structural loss by several years in glaucoma suspects. *Invest Ophthalmol Vis Sci.* 2013 Mar 28;54(3):2346-52.

Bowd C, Vizzeri G, Tafreshi A, et al. Diagnostic accuracy of pattern electroretinogram optimized for glaucoma detection. *Ophthalmology.* 2009 Mar;116(3):437-43.

Dale EA, Hood DC, Greenstein VC, et al. A comparison of multifocal ERG and frequency domain OCT changes in patients with abnormalities of the retina. *Doc Ophthalmol.* 2010 Apr;120(2):175-86.

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Kandel H, Adhikari P, Shrestha GS, et al. Visual function in patients on ethambutol therapy for tuberculosis. *J Ocul Pharmacol Ther.* 2012 Apr;28(2):174-8.

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Sehi M, Pinzon-Plazas M, Feuer WJ, et al. Relationship between pattern electroretinogram, standard automated perimetry, and optic nerve structural assessments. *J Glaucoma.* 2009 Oct-Nov;18(8):608-17.

Tafreshi A, Racette L, Weinreb RN, et al. Pattern electroretinogram and psychophysical tests of visual function for discriminating between healthy and glaucoma eyes. *Am J Ophthalmol.* 2010 Mar;149(3):488-95.

Code	Description
93668	Peripheral arterial disease (PAD) rehabilitation, per session

Peripheral arterial disease rehabilitation is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Both physical activity and medications are used to treat peripheral arterial disease. Vascular specialists agree that long daily walks are the best treatment for people with intermittent claudication, thereby increasing the distance of pain-free walking through the development of collateral circulation. Regular exercise improves symptoms of PAD by a number of methods, including helping the body use oxygen more efficiently and promoting improved circulation. Exercise for intermittent claudication takes into account the fact that walking causes pain. Patients whose legs hurt during physical activity often find it hard to follow a walking program. For this reason, the rehabilitation departments of some hospitals have created supervised exercise

programs that offer support and encouragement. The usual duration of the program is 3 times a week for 12 weeks (36 visits). The goal of treatment is to improve endurance and decrease symptoms.

Niccoli et al. (2010) conducted a randomized controlled trial of 169 patients receiving supervised exercise therapy (SET) for intermittent claudication. The SET program consisted of at least two training sessions per week each lasting over 30 minutes, during the first 3 months of a 1-year program. No differences were found between program involving only walking and a combination of exercises, nor between individual and group training.

Another randomized controlled trial by Niccoli et al. (2010) compared exercise therapy in the form of "go home and walk" advice (WA) (n=102), SET (n=109), or SET with feedback (n=93). Walking distance was measured between baseline and 12 months. Walking distance for the WA group was 110 (0-300) meters, 310 (145-995) meters in the SET group, and 360 (173-697) meters in the SET with feedback group. While these results are promising, outcomes were subjective and walking distance was approximately ¼ mile which remains in a nonfunctional range.

A Cochrane systematic evidence review (Bendermacher et al, 2006) found that supervised exercise therapy has not been proven to be better than non-supervised exercise therapy in managing patients with intermittent claudication. Randomized and controlled clinical trials comparing supervised exercise programs with non-supervised exercise programs for people with intermittent claudication were selected. Two authors independently selected trials and extracted data. One author assessed trial quality and this was confirmed by a second author. For all continuous outcomes the authors extracted the number of participants, the mean differences, and the standard deviation. If data were available, the standardized mean difference was calculated using a fixed-effect model. These researchers identified 27 trials, of which 19 had to be excluded because the control group received no exercise therapy at all. The remaining 8 trials involved a total of 319 male and female participants with intermittent claudication. The follow-up ranged from 12 weeks to 12 months. In general, the supervised exercise regimens consisted of 3 exercise sessions per week. All trials used a treadmill walking test as one of the outcome measures. The overall quality of the included trials was good, though the trials were all small with respect to the number of participants, ranging from 20 to 59. Supervised exercise therapy showed statistically significant and clinically relevant differences in improvement of maximal treadmill walking distance compared with non-supervised exercise therapy regimens in the short-term, with an overall effect size of 0.58 at 3 months. This translated to a difference of approximately 150 meters increase in walking distance in favor of the supervised group. However, there is a high possibility of a training effect as the supervised exercise therapy groups were trained primarily on treadmills (and the home based were not) and the outcome measures were treadmill based. The authors concluded that supervised exercise therapy is suggested to have clinically relevant benefits compared with non-supervised regimens in the short-term, which is the main prescribed exercise therapy for people with intermittent claudication. However, the clinical relevance has not been demonstrated definitely and will require additional studies with a focus on durability of outcomes and improvements in quality of life (Bendermacher et al, 2006).

There is insufficient evidence in the medical literature demonstrating superior outcomes of such supervised exercise programs over exercise without supervision.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

Bendermacher BL, Willigendael EM, et al. Supervised exercise therapy for intermittent claudication in a community-based setting is as effective as clinic-based. *J Vasc Surg.* 2007;45(6):1192-1196.

Mayo Health at www.mayoclinic.com/health/peripheral-arterial-disease/DS00537/DSECTION=lifestyle-and-home

Nicolai SP, Hendriks EJ, Prins MH, et al. Optimizing supervised exercise therapy for patients with intermittent claudication. *J Vasc Surg.* 2010 Nov;52(5):1226-33. Epub 2010 Aug 8.

Code	Description
93799	Unlisted cardiovascular service or procedure [when used to report inert gas rebreathing]
94799	Unlisted pulmonary service or procedure [when used to report inert gas rebreathing]

The use of inert gas re-breathing for measuring cardiac output is unproven and not medically necessary due to insufficient evidence of safety and/or efficacy in published peer-reviewed clinical literature.

Clinical Evidence

When assessing the accuracy and precision of a new technique for cardiac output measurement, the commonly quoted criterion for acceptability of agreement with a reference standard is that the percentage error (95% limits of agreement/mean cardiac output) should be 30% or less. Peyton and Chong (2010) reviewed published data on four different minimally invasive methods adapted for use during surgery and critical care: pulse contour techniques, esophageal Doppler, partial carbon dioxide rebreathing and transthoracic bioimpedance. The authors assessed the bias, precision and percentage error in agreement with thermodilution. For each method a meta-analysis was done using studies in which the first measurement point for each patient could be identified. Forty-seven studies were included. None of the four methods achieved agreement with bolus thermodilution which meets the expected 30% limits.

Preliminary results suggest that cardiac output (CO) measurements using inert gas rebreathing (IGR) might be an eligible method to tailor atrioventricular (AV) and ventriculo-ventricular (VV) programming of cardiac resynchronization therapy (CRT) devices. Reinsch et al. (2010) evaluated whether an optimization of CRT can be obtained by noninvasive CO measurements and whether acute hemodynamic improvements obtained by this approach relate into increase in cardiac exercise capacity. In 24 patients on CRT, iterative VV- and AV-delay optimization was done using the IGR method. This blinded, randomized, crossover study compared the responses to optimization during two periods: a 4-week optimized and a 4-week standard programming. Exercise capacity after optimization was assessed after each period by New York Heart Association (NYHA) classification, a 6-minute walking test and quality of life (QoL) questionnaire. The NYHA class decreased by 17.8%, the mean distance walked in 6 minutes was 9.3% greater after optimization and the QoL improved by 14.5%. The portion of responders to CRT increased from 66.5% to 87.5%. The authors concluded that CRT optimization by iterative CO measurements leads to an increase in CO and an improvement of exercise capacity. These results suggest that this method might become an important additive tool to adjust CRT programming. However, additional studies are warranted to better define the role of this technology in the clinical management of cardiac disease.

In a prospective, observational study (n=42), Kotake et al (2009) investigated the accuracy of a noninvasive cardiac output (NICO) monitor equipped with newer software. Cardiac output was continuously monitored using both the NICO monitor and continuous cardiac output (CCO) measured by a pulmonary artery catheter. A NICO monitor equipped with ver. 4.2 software was used for the first 21 patients while a NICO monitor equipped with ver. 5.0 software was used for the rest of the patients. Cardiac output measured by bolus thermodilution (BCO) at 30 min intervals was used as a reference. The bias +/- precision of the NICO monitor was 0.18 +/- 0.88 l/min with ver. 4.2 software (n = 182) and 0.18 +/- 0.83 l/min with 5.0 software (n = 194). The accuracy of the NICO monitor is comparable to CCO, whose bias +/- precision against BCO is 0.19 +/- 0.81 l/min (n = 376). At the same level of CO(2) production and minute ventilation, PaCO(2) was lower in the patients monitored by NICO with ver. 5.0 software than patients with

ver. 4.2 software. This study demonstrated the improved performance of the NICO monitor with updated software. The performance of the NICO monitor with ver. 4.2 or later software is similar to CCO. However, the cardiac output measurement did not fulfill the criteria of interchangeability to the cardiac output measurement by bolus thermodilution.

Jakovljevic et al. (2008) compared cardiac output determined by different rebreathing methods at rest and at peak exercise. The aims of the study were threefold: first, to compare values for resting Q (T) produced by the equilibrium-CO(2), exponential-CO(2) and inert gas-N(2)O rebreathing methods and, second, to evaluate the reproducibility of these three methods at rest. The third aim was to assess the agreement between estimates of peak exercise Q (T) derived from the exponential and inert gas rebreathing methods. A total of 18 healthy subjects visited the exercise laboratory on different days. Two more exercise tests were used to measure Q (T) at peak exercise using the exponential and inert gas rebreathing methods. The exponential method produced significantly higher estimates at rest (averaging 10.9 l min⁻¹) compared with the equilibrium method (averaging 6.6 l min⁻¹) and the inert gas rebreathing method (averaging 5.1 l min⁻¹); P < 0.01). All methods were highly reproducible with the exponential method having the largest coefficient of variation (5.3%). At peak exercise, there were non-significant differences between the exponential and inert gas rebreathing methods (P = 0.14). The limits of agreement were -0.49 to 0.79 l min⁻¹). Due to the ability to evaluate the degree of gas mixing and to estimate intra-pulmonary shunt, we believe that the inert gas rebreathing method has the potential to measure Q (T) more precisely than either of the CO(2) rebreathing methods used in this study. At peak exercise, the exponential and inert gas rebreathing methods both showed acceptable limits of agreement.

Inert gas rebreathing using low-concentration soluble and insoluble inert gases can derive cardiac output (CO) by the Fick principle. In a case series, Lang et al. (2007) assessed the practicality of the Innocor rebreathing system in measuring CO and peak oxygen consumption (VO₂) during exercise in patients with heart failure (HF). Ninety-two consecutive exercise tests were prospectively performed in 88 patients with HF using the Innocor system. Eighty-six percent of the tests had successful measurement of metabolic and cardiac output data. Mean CO at rest was 3.5 +/- 1.1 L/min and increased to 7.2 +/- 2.7 L/min. Mean peak VO₂ was 12.6 +/- 4.7 ml/kg/min. A significant linear correlation was observed between peak VO₂ and peak CO (r = 0.64, p <0.0001). The authors concluded that the widespread clinical application of this technique in the evaluation of patients with HF remains to be determined by a large study with longer follow-up of clinical events to fully determine its prognostic value.

The American College of Cardiology and American Heart Association joint guidelines on the management of heart failure state that noninvasive cardiac output monitoring has not yet been validated for the diagnostic evaluation of patients with heart failure (Yancy et al., 2013).

Reference(s):

Jakovljevic DG, Nunan D, Donovan G, et al. Comparison of cardiac output determined by different rebreathing methods at rest and at peak exercise. *Eur J Appl Physiol.* 2008 Mar;102(5):593-9.

Kotake Y, Yamada T, Nagata H, et al. Improved accuracy of cardiac output estimation by the partial CO₂ rebreathing method. *J Clin Monit Comput.* 2009 Jun;23(3):149-55.

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Reinsch N, Konorza T, Woydowski D, et al. Iterative cardiac output measurement for optimizing cardiac resynchronization therapy: a randomized, blinded, crossover study. *Pacing Clin Electrophysiol.* 2010 Oct;33(10):1188-94.

Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA Guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2013 Oct 15;62(16):e147-239.

Code	Description
94011	Measurement of spirometric forced expiratory flows in an infant or child through 2 years of age
94012	Measurement of spirometric forced expiratory flows, before and after bronchodilator, in an infant or child through 2 years of age
94013	Measurement of lung volumes (ie, functional residual capacity [FRC], forced vital capacity [FVC], and expiratory reserve volume [ERV]) in an infant or child through 2 years of age

Spirometry and other pulmonary function tests are unproven and not medically necessary in children under the age of three due to insufficient evidence of safety and/or efficacy in published peer-reviewed clinical literature. Children in this age group are unable to perform the complex steps involved in these tests which require patient understanding and cooperation.

Clinical Evidence

In a 2009 guideline, published jointly with the European Respiratory Society, the American Thoracic Society addresses lung function tests in children 6 years of age and older. While they acknowledge that the use of such tests in children younger than 6 years of age was beyond the scope of their guideline, they state that with appropriate training, preschool children may be able to perform spirometry. Forced oscillation procedures and interrupter resistance (Rint) to measure airway resistance can be applied in children as young as 3 years of age (Reddel et al., 2009).

In a separate guideline, the ATS states that children aged 2 to 6 represent one of the major challenges in lung function assessment. These children are generally too old to sedate, as is done with infants, and measurement of lung function under anesthesia is neither ethically acceptable nor physiologically relevant to clinical management. Children in this age group are not able to perform many of the physiological maneuvers required for the pulmonary function tests used in older children and adults. They have a short attention span and are easily distracted (Beydon et al., 2007).

The 2009 Global Initiative for Asthma (GINA) guidelines specific to children 5 years and younger state that making a diagnosis of asthma in children 5 years and younger may be difficult because episodic respiratory symptoms such as wheezing and cough are also common in children who do not have asthma, particularly in those younger than 3 years. Furthermore, it is not possible to routinely assess airflow limitation and inflammation in this age group.

The 2012 GINA guidelines on asthma management and prevention address the challenges of diagnosing asthma in children 5 years and younger. The diagnosis of asthma in early childhood has to be based largely on clinical judgment and an assessment of symptoms and physical findings. Use of spirometry and other measures recommended for older children and adults is difficult and several require complex equipment making them unsuitable for routine use.

The National Asthma Education and Prevention Program (NAEPP) Expert Panel recommends that spirometry measurements before and after the patient inhales a short-acting bronchodilator should be undertaken for patients in whom the diagnosis of asthma is being considered, including children 5 years of age or older. For children 0-4 years of age, the panel recommends that the evaluation include the history, symptoms, physical examination and assessment of quality of life, as diagnosis can be difficult in this age group. A therapeutic trial with medications will also aid in the diagnosis (NHLBI, 2007).

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

Reddel HK, Taylor DR, Bateman ED, et al. An official American Thoracic Society/European Respiratory Society statement: asthma control and exacerbations: standardizing endpoints for clinical asthma trials and clinical practice. Am J Respir Crit Care Med. 2009 Jul 1;180(1):59-99.

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Global Initiative for Asthma (GINA). Global Strategy for the Diagnosis and Management of Asthma in Children 5 Years and Younger. May 2009. Available at: <http://www.ginasthma.org/Guidelines/guidelines-resources.html>. Accessed June 14, 2013.

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National Heart Lung and Blood Institute. National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. July 2007. Available at: <http://www.nhlbi.nih.gov/guidelines/asthma/>. Accessed June 14, 2013.

Code	Description
96902	Microscopic examination of hairs plucked or clipped by the examiner (excluding hair collected by the patient) to determine telogen and anagen counts, or structural hair shaft abnormality

Microscopic analysis of hair is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Trichograms are the microscopic examination of hair and identifies hair growth rate and anagen (hair growth) and/ telogen (hair resting phase) ratio. Alopecia is the most common indication for completing this test.

The Agency for Toxic Substance and Disease Registry reviewed the use of hair analysis. The primary consideration of the panel was to determine the utility of hair analysis in evaluating exposures to hazardous wastes. The panel concluded that there was insufficient evidence to support the use of microscopic testing of hair to predict exposure to toxic substances (ATSDR, 2001).

Microscopic analysis of hair for hair loss issues is not supported by the clinical evidence. The utility of hair analysis is limited by the inability to discern endogenous and exogenous reference(s). Interpretation is unreliable and there are no referenced norms to support the establishment that hair can be a consistent biological marker or that completion of such tests will change medical management (Chiang, 2001; Hryhorczuk and Eng, 2001).

The clinical evidence was reviewed in May 2014 with no additional information identified that would change the conclusion.

Reference(s):

Agency for Toxic Substances and Disease Registry (ATSDR). Hair Analysis Panel Discussion: exploring the state of the science. 2001 Jun 12-13 (reviewed 2011). Available at: http://www.atsdr.cdc.gov/hac/hair_analysis/table.html Accessed May 2014.

Chiang WK. Mercury: Laboratory Studies. In: Ford MD, Delaney KA, Ling LJ, Erickson T, editors: Clinical Toxicology. St. Louis: W.B. Saunders Company; 2001.

Hryhorczuk D, Eng J. Arsenic: Laboratory Studies. In: Ford MD, Delaney KA, Ling LJ, Erickson T, editors: Clinical Toxicology. St. Louis: W.B. Saunders Company; 2001.

Code	Description
97139	Unlisted therapeutic procedure (specify) [when used to report Kinesio Taping]

The use of Kinesio taping is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Kinesio taping is a method of taping utilizing a specialized type of tape. It differs from traditional white athletic tape in the sense that it is elastic and can be stretched to 140 % of its original length before being applied to the skin. It subsequently provides a constant pulling (shear) force to the skin over which it is applied unlike traditional white athletic tape. The fabric of this specialized tape is air permeable and water resistant and can be worn for repetitive days. Kinesio tape is being used immediately following injury and during the rehabilitation process. However, its effectiveness has yet to be established.

In a nonrandomized controlled trial, Kaya et al. (2011) compared the efficacy of the KTM versus standard physical therapy modalities in 55 patients with shoulder impingement syndrome. The first consecutive 25 patients were enrolled in the physical therapy group and the second consecutive 30 patients were enrolled in the KTM group. Baseline characteristics were similar for the two groups. Patients were treated with Kinesio Tape 3 times with intervals of 3 days, or with a daily program of local PT modalities for 2 weeks. Both groups followed a home exercise program. Response to treatment was evaluated with the Disability of Arm, Shoulder, and Hand (DASH) scale. The DASH Outcome Measure is a 30-item, self-report questionnaire designed to measure physical function and symptoms in patients with musculoskeletal disorders of the upper limb. A decrease in the score indicates improvement. Night pain, daily pain, and pain with motion were assessed with a 100-mm VAS. Outcome measures were assessed at baseline and at the first and second weeks of treatment although the DASH score was evaluated only before and after treatment. Kinesio Taping was more efficacious for relieving symptoms of shoulder impingement than the standard PT modalities during the first week but not completely efficacious during the second week since the VAS scores were similar between the two groups at that follow-up. Limitations of the study included a lack of randomization and inadequate follow-up.

Hayes (2011), Health technology report stated that additional randomized controlled studies are needed with larger sample sizes and long-term follow-up to determine if kinesio taping improves health outcomes alone or as an adjunct therapy in pain or disability rehabilitation protocols.

In a 2-part study, Paoloni et al. (2011) evaluated the immediate- and short-term efficacy of Kinesio Taping for treating chronic low back pain in 39 patients. The first part of the study used an intrasubject pretest/posttest procedure in which mean visual analog scale (VAS) scores for pain and FR values were obtained by sEMG as a measure of lumbar muscle function at baseline and after tape application. In the second part of the study, the patients were randomized into 3 groups: KTM Plus Exercise, KTM Alone, and Exercise Alone. Outcomes, which were assessed at 1 month after therapy by an investigator who was blinded to treatment assignment, included pain assessed by VAS, disability assessed by sEMG, and disability assessed by the Roland Morris Disability Questionnaire (RMDQ). In the first part of the study, after application of Kinesio Tape, the mean VAS decreased in the entire group from 7.4 at baseline to 5.7. The VAS response rate was 33.3% (13 of 39 patients), and normalized FR was observed in 17 (43.6%) patients. In the second part of the study, a significant reduction in mean VAS scores was observed in each of the 3 groups compared with baseline: KTM Plus Exercise (7.6 to 3.7), KTM Alone (7.1 to 3.1) and Exercise Alone (7.6 to 3.5). The mean RMDQ score decreased in each group compared with baseline but the difference was significant only for the Exercise Alone group. While the KTM appeared to be safe and possibly efficacious in the short term, there is insufficient evidence to determine its true effects on patient outcomes. The study is limited by its small sample size and short follow-up time.

A randomized controlled trial by González-Iglesias et al. (2009) examined the short-term effects of Kinesio taping applied to the cervical spine in patients with acute whiplash-associated disorder (WAD). Forty-one patients were randomly assigned to 1 of 2 groups: the experimental group received Kinesio taping to the cervical spine (applied with tension) and the placebo group

received a sham Kinesio taping application (applied without tension). Both neck pain (11-point numerical pain rating scale) and cervical range-of-motion data were collected at baseline, immediately after the Kinesio tape application, and at a 24-hour follow-up by an assessor blinded to the treatment allocation of the patients. Patients receiving Kinesio taping experienced a greater decrease in pain immediately post-application and at the 24-hour follow-up. However, patients in the experimental group obtained a greater improvement in range of motion than those in the control group. Improvements in pain and cervical range of motion were small, therefore, future studies are needed with longer follow-up times to evaluate whether Kinesio taping enhances outcomes.

In a prospective, randomized, double-blinded, clinical study using a repeated-measures design, Thelen et al (2008) determined the short-term clinical efficacy of Kinesio tape when applied to college students with shoulder pain, as compared to a sham tape application. A total of 42 subjects with clinically diagnosed rotator cuff tendonitis and/or impingement were randomly assigned to 1 of 2 groups: therapeutic Kinesio tape group or sham Kinesio tape group. Subjects wore the tape for 2 consecutive 3-day intervals. Self-reported pain and disability and pain-free active ranges of motion (ROM) were measured at multiple intervals to evaluate for differences between groups. While the therapeutic Kinesio tape group showed improvement in pain-free shoulder abduction ($p = 0.005$) after tape application, no other differences between groups regarding ROM, pain, or disability scores at any time interval were found.

Halseth et al (2004) examined if Kinesio taping the anterior and lateral portion of the ankle would enhance ankle proprioception compared to the untaped ankle. A total of 30 subjects (15 men, 15 women, age 18 to 30 years) participated in this study. Exclusion criteria: included ankle injury less than 6 months prior to testing, significant ligament laxity as determined through clinical evaluation, or any severe foot abnormality. Experiment utilized a single group, pre-test and post-test. Plantar flexion and inversion with 20° of plantar flexion reproduction of joint position sense (RJPS) was determined using an ankle RJPS apparatus. Subjects were bare-footed, blindfolded, and equipped with headphones playing white noise to eliminate auditory cues. They had 5 trials in both plantar flexion and inversion with 20° plantar flexion before and after application of the Kinesio tape to the anterior/lateral portion of the ankle. The treatment group (Kinesio taped subjects) showed no change in constant and absolute error for ankle RJPS in plantar flexion and 20° of plantar flexion with inversion when compared to the untaped results using the same motions. The application of Kinesio tape does not appear to enhance proprioception (in terms of RJPS) in healthy individuals as determined by measures of RJPS at the ankle in the motions of plantar flexion and 20° of plantar flexion with inversion.

In a pilot study, Yasukawa and colleagues (2006) described the use of the Kinesio taping method for the upper extremity in enhancing functional motor skills in children admitted into an acute rehabilitation program. A total of 15 children (10 females and 5 males; 4 to 16 years of age), who were receiving rehabilitation services at the Rehabilitation Institute of Chicago participated in this study. For 13 of the inpatients, this was the initial rehabilitation following an acquired disability, which included encephalitis, brain tumor, cerebral vascular accident, traumatic brain injury, and spinal cord injury. The Melbourne Assessment of Unilateral Upper Limb Function (Melbourne Assessment) was used to measure upper-limb functional change prior to use of Kinesio tape, immediately after application of the tape, and 3 days after wearing tape. Children's upper-limb function was compared over the three assessments using analysis of variance. The improvement from pre- to post-taping was statistically significant, $F(1, 14) = 18.9$; $p < 0.02$. The authors concluded that these results suggested that Kinesio tape may be associated with improvement in upper-extremity control and function in the acute pediatric rehabilitation setting. However, given the small sample size, further study is recommended to test the effectiveness of this method and to determine the lasting effects on motor skills and functional performance once the tape is removed.

In a pilot study, Fu and associates (2008) examined the possible immediate and delayed effects of Kinesio taping on muscle strength in quadriceps and hamstring when taping is applied to the

anterior thigh of healthy young athletes. A total of 14 healthy young athletes (7 males and 7 females) free of knee problems were enrolled in this study. Muscle strength of the subject was assessed by the isokinetic dynamometer under three conditions: (i) without taping; (ii) immediately after taping; (iii) 12 hours after taping with the tape remaining in situ. The result revealed no significant difference in muscle power among the three conditions. Kinesio taping on the anterior thigh neither decreased nor increased muscle strength in healthy non-injured young athletes.

The American College of Occupational and Environmental Medicine's practice guidelines on "Evaluation and management of common health problems and functional recovery in workers" did not recommend taping or kinesiotaping for acute, subacute, or chronic LBP, radicular pain syndromes or other back-related conditions. (Hegmann 2007).

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

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The American College of Occupational and Environmental Medicine's practice guidelines on "Evaluation and management of common health problems and functional recovery in workers" did not recommend taping or kinesiotaping for acute, subacute, or chronic LBP, radicular pain syndromes or other back-related conditions. " Halseth T, McChesney JW, DeBeliso M, et al. The Effects of Kinesio Taping on proprioception at the ankle. *J Sports Sci Med*. 2004;3:1-7.

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Code	Description
99174	Instrument-based ocular screening (eg, photoscreening, automated-refraction), bilateral

Instrument-based ocular screening using photoscreening is proven and medically necessary for vision screening for one of the following:

- As a mass screening instrument for children 1 year of age through 3 years of age
- Children older than 3 years of age who are developmentally delayed and are unable or unwilling to cooperate with routine visual acuity screening.

Instrument-based ocular screening using photoscreening is unproven and not medically necessary for all other patient populations including children younger than 1 year of age. More age-appropriate screening methods are available for these populations.

Clinical Evidence

Ocular photoscreening has been investigated as an alternative screening method to detect risk factors for amblyopia, which include strabismus, high refractive errors, anisometropia, and media opacities.

The U.S. Preventive Services Task Force (2011) recommends vision screening for all children at least once between the ages of 3 and 5 years, to detect the presence of amblyopia or its risk factors. The U.S. Preventive Services Task Force (USPSTF) concluded that the current evidence is insufficient to assess the balance of benefits and harms of vision screening for children less than 3 years of age. The USPSTF stated that various screening tests that are feasible in primary care are used to identify visual impairment among children. These tests include visual acuity tests, stereoacuity tests, the cover-uncover test, and the Hirschberg light reflex test (for ocular alignment/strabismus), as well as the use of photoscreeners (instruments that detect amblyogenic risk factors and refractive errors).

The National Institutes of Health–sponsored Vision in Preschoolers Study systematically evaluated instrument-based screening methods and compared them with visual acuity–based screening. Results of the study suggested that for detection of amblyopia at a similar specificity, photoscreening with Medical Technologies & Innovations (MTI) and iScreen devices was less sensitive than noncycloplegic retinoscopy (NCR), had essentially the same sensitivity as SureSight, Retinomax Autorefractor (RA), Lea Symbols visual acuity (VA), StereoSmile II, Power Refractor, and HOTV VA tests, and was more sensitive than Random Dot E and Cover-uncover tests. (Schmidt 2004).

Yanovitch et al. (2010) evaluated the sensitivity, specificity, and positive and negative predictive values of photoscreening in detecting treatable ocular conditions in children with Down syndrome (DS). Photoscreening and complete ophthalmologic evaluations were performed in 50 consecutive 3- to 10-year-old children with DS. Most children were able to complete photoscreening (94% with Medical Technology and Innovations [MTI] and 90% with Visiscreen OSS-C [VR]). Many children had an identified diagnosis on ophthalmologic examination (n = 46, 92%). Of these, approximately one-half (n = 27, 54%) had one or more condition(s) requiring treatment. Both the MTI and VR photoscreening devices had a sensitivity of 93% (95% confidence interval 0.76-0.99) for detecting treatable ocular conditions. The specificities for the MTI and VR photoscreening were 0.35 (0.18-0.57) and 0.55 (0.34-0.74), respectively. The authors concluded that photoscreening is sensitive but less specific at detecting treatable ocular conditions in children with DS. In specific instances, the use of photoscreening in the DS population has the potential to save time and expense related to routine eye examinations, particularly in children with a normal baseline comprehensive examination.

In a retrospective study, Longmuir et al. (2013) reported their experience with vision screening in children and compared the results of photoscreening in children younger than 3 years with those of children of preschool age and older. During the 11 years of the study, 210,695 photoscreens on children were performed at 13,750 sites. In the <3-year age group, the unreadable rate was 13.0%, the referral rate was 3.3%, and the overall positive-predictive value was 86.6%. In the 3- to 6-year-old children, the unreadable rate was 4.1%, the referral rate was 4.7%, and the overall positive-predictive value was 89.4%. The authors concluded that no statistically significant difference was found in screening children from 1 to 3 years old compared with screening children >3 years old. According to the authors, these results confirm that early screening, before amblyopia is more pronounced, can reliably detect amblyogenic risk factors in children younger than 3 years of age, and they recommend initiation of photoscreening in children aged 1 year and older.

Kirk et al. (2008) evaluated 21,367 rural and urban Alaskan children through grade 2 who underwent photoscreening. Of 411 positive screening photos from children younger than 4 years, 94 patients had more than 2 years follow-up. The 36 children photoscreened before age 2 years had a mean treated visual acuity of 0.17 logarithm of the minimum angle of resolution, which was significantly better than that of 58 children screened between ages 25 and 48 months. Despite similar levels of amblyogenic risk factors, the proportion of children failing to reach a visual acuity of 20/40 was significantly less among those screened before age 2 years (5%) than in those screened from ages older than 2.0 years and younger than 4.0 years (17%). The authors concluded that very early photoscreening yields better visual outcomes in amblyopia treatment compared with later photoscreening in preschool-aged children.

In a cross-sectional study, Longmuir et al. (2010) reported on a cohort of preschool children screened by a photoscreening program (using MTI PhotoScreener) over a 9-year period from a single, statewide vision screening effort. Children who failed the photoscreening were referred to local eye care professionals who performed a comprehensive eye evaluation. Over the 9 years of the continuously operating program, 147,809 children underwent photoscreens to detect amblyopic risk factors at 9746 sites. Because of abnormal photoscreen results, 6247 children (4.2%) were referred. The overall positive predictive value (PPV) of the MTI PhotoScreener was 94.2%.

In an Agency for Healthcare Research and Quality (AHRQ) Evidence Synthesis for Screening for Visual Impairment in Children, Chou, et al. (2011) identified 15 studies (13 fair-quality and two poor-quality) that evaluated the diagnostic accuracy of photoscreeners. According to the authors of this report, there is good evidence that commonly used visual acuity tests, stereoacuity tests, cover-uncover tests, autorefractors, and photoscreeners are useful for screening, though differences among studies in the populations evaluated, screening tests evaluated, screening thresholds applied, and target conditions sought make it difficult to reach strong conclusions about how they compare with one another. Screening tests were generally associated with a high rate of false-positives in low-prevalence populations which could result in unnecessary prescription of eyeglasses. The authors stated that evidence on when to initiate preschool screening remains limited. The authors concluded that direct evidence on effectiveness of preschool vision screening for improving visual acuity or other clinical outcomes remains very limited and does not adequately address the question of whether screening is more effective than no screening. However, good evidence on diagnostic accuracy and treatments suggest that preschool vision screening could lead to increased detection of visual impairment and greater improvement in visual outcomes than if children were never screened. According to the authors, additional studies are needed to better understand effects of screening compared with no screening, to clarify the risk for potential unintended harms from screening (such as use of unnecessary treatments), and to define optimal time at which to initiate screening during the preschool years.

According to the Bright Futures Handbook for performing preventative services, new vision screening technology (e.g., photoscreening, autorefraction) has been developed and is increasingly used in pediatric practice. The Bright Futures Handbook states that recommendations for the use of such technology will be made as evidence regarding their comparative effectiveness becomes available. According to the Handbook, assessing risk for ocular problems and vision impairment should begin in the newborn nursery and occur at all health supervision visits. Bright Futures recommends that all children have formal vision screening as part of their health supervision visit annually from 3 through 6 years of age, at 8 years of age, at 10 years of age, at 12 years of age, at 15 years of age, and at 18 years of age. Vision screening should be conducted at other health supervision visits based on risk assessment or any concern on the part of families or the child (Kemper and Delmonte, 2010).

Professional Societies

The American Academy of Ophthalmology (AAO) Preferred Practice Patterns for Pediatric Eye Evaluations (2012) state that after 6 months of age, an assessment of binocular alignment should

be performed because children should have aligned eyes at age 4 to 6 months. Instrument-based screening with photoscreening or autorefractive devices can be valuable in detecting amblyopia risk factors in this age group because the tests are rapid and noninvasive and minimal cooperation is required on the part of the child. The authors of the report state that instrument-based vision-screening techniques, such as photoscreening and autorefractive, are useful alternatives to visual acuity screening using eye charts for very young and developmentally delayed children and compare well with standard vision-testing techniques and cycloplegic refraction. They are not superior to quantitative visual acuity testing for children who are able to perform those tests. Most instrument-based vision-screening methods detect the presence of risk factors for amblyopia, including strabismus, high or asymmetric refractive errors, media opacities (e.g., cataract), retinal abnormalities (e.g., retinoblastoma), and ptosis.

A policy statement for instrument-based pediatric vision screening from the American Academy of Pediatrics Section on Ophthalmology, the Committee on Practice and Ambulatory Medicine, the American Academy of Ophthalmology, the American Association for Pediatric Ophthalmology and Strabismus, and the American Association of Certified Orthoptists states that photoscreening and handheld autorefractive may be electively performed in children 6 months to 3 years of age, allowing earlier detection of conditions that may lead to amblyopia, as well as in older children who are unable or unwilling to cooperate with routine acuity screening. The policy further states that photoscreening and handheld autorefractive are recommended as an alternative to visual acuity screening with vision charts from 3 through 5 years of age, after which visual acuity screening with vision charts becomes more efficient and less costly. The policy also states that alternatively, the use of vision charts and standard physical examination techniques to assess amblyopia in children 3 to 5 years of age in the medical home remains a viable practice at the present time. The writers of the policy advocate additional research of photoscreening and handheld autorefractive devices and other vision screening methods to elucidate the validity of results, and efficacy for identifying amblyogenic factors in different age groups and subgroups of children. The goal remains to eliminate preventable childhood visual impairment. The policy also states that alternatively, the use of vision charts and standard physical examination techniques to assess amblyopia in children 3 to 5 years of age in the medical home remains a viable practice at the present time. The authors of the policy advocate additional research of photoscreening and handheld autorefractive devices and other vision screening methods to elucidate the validity of results, efficacy, cost-effectiveness, and payment policies for identifying amblyogenic factors in different age groups and subgroups of children (Miller and Lessin, 2012).

According to the American Academy of Pediatrics policy statement, Use of Photoscreening for Children's Vision Screening (Committee on Practice and Ambulatory Medicine and Section on Ophthalmology, 2002, American Academy of Pediatrics, Pediatrics), photoscreening is a vision screening technique used to screen for amblyogenic factors, such as strabismus, media opacities, and significant refractive errors, in 1 or both eyes in children. Photoscreening does not represent a single technique or piece of equipment. Different optical systems can be used for photoscreening. Each photoscreening system may have its own advantages and disadvantages, and it appears that results published in the literature for one system are not necessarily valid for others. Studies performed by different investigators using the same photoscreening apparatus may yield a wide range of results in sensitivity, specificity, and predictive values when onsite interpretation is required. Likewise, it is not certain that data gathered about different groups of children or different settings can be extrapolated to other groups or settings.

The American Association for Pediatric Ophthalmology and Strabismus (AAPOS) Vision Screening recommendations indicate that an objective screening device such as photoscreening is recommended for children 12 months to 36 months of age. Visual acuity testing (preferred) or photoscreening is recommended for children 36 months to 5 years of age. See the following for more information: <http://www.aapos.org/terms/conditions/131> Accessed May 2014.

The clinical evidence was reviewed in May 2014 with no additional information identified that would change the conclusion.

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Code	Description
L3999	Upper limb orthotic, not otherwise specified [when used to report MyoPro™]

The use of the artificial limb known as the MyoPro™ is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

There is very limited information related to the use and ability of the device known as the Myopro. According to the manufactures website the MyoPro™ myoelectric limb orthosis is a powered brace that can reinitiate movement of a partially paralyzed arm to enhance function and quality of life. It is designed for individuals with stroke, MS, ALS, brain & spinal cord injury and other neuromuscular disorders. The procedure code within the Healthcare Common Procedure Coding System (HCPCS) to accurately describe the MyoPro Orthosis is code L3999. A recent coding clarification advisory article issued on 5/8/2012 was published by the Medicare Pricing, Data

Analysis, and Coding (PDAC) contractor Noridian Health Care Solutions: "The distinction in coding relates to the indicated use of the joint and the beneficiary's medical condition(s). The Concentric adjustable torsion-style joints used solely to provide an assistive function for joint motion must be coded L2999 or L3999." See the following Web sites for more information: <http://www.myopro.com/> Accessed April 2014.

A randomized controlled pilot trial was conducted by Page et al (2013). to compare the efficacy of a repetitive task-specific practice in a person with chronic, moderate upper extremity impairment. A total of 16 people were utilized (7 males; mean age 57.0 ± 11.02 years; mean time post stroke 75.0 ± 87.63 months; 5 left-sided strokes) all exhibiting chronic, stable, moderate upper extremity impairment. Each person was given a repetitive task-specific practice in which they participated in valued, functional tasks using their paretic upper extremities. Both groups were supervised by a therapist and were administered therapies targeting their paretic upper extremities that was 30 minutes in duration, occurring 3 days/week for eight weeks. One group participated in repetitive task-specific practice entirely while wearing the portable robotic, while the other performed the same activity regimen manually. Upon completion of the study itself each group showed the same Fugl-Meyer score increases of ≈2.1 points; the group using robotics exhibited larger score changes on all but one of the Canadian Occupational Performance Measure and Stroke Impact Scale subscales, including a 12.5-point increase on the Stroke Impact Scale recovery subscale. It was noted that the finding suggest that therapist supervised task- specific practice with an integrated robotic device could be as efficacious as manual practice in some subjects with moderate upper extremity impairment. Additional studies are needed as there is still insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

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Code	Description
L8605	Injectable bulking agent, dextranomer/hyaluronic acid copolymer implant, anal canal

The use of an injectable bulking agent such as Solesta® is unproven and not medically necessary to treat fecal incontinence due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Solesta is a sterile gel that is injected into the anal canal to treat the symptoms of fecal incontinence. It is composed of naturally-made materials, dextranomer and sodium hyaluronate. Solesta is classified as a medical device (injectable bulking agent for gastrourology use) and not a drug. Solesta Injectable Gel (Salix Pharmaceuticals Inc.) received U.S. Food and Drug Administration (FDA) premarket approval (PMA) on May 27, 2011 (P100014). See the following Web site for more information: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm?id=14770> Accessed June 2014

Graf et al. 2011 conducted a randomized double-blind, sham-controlled trial to assess the efficacy of injection of dextranomer in stabilized hyaluronic acid (NASHA Dx) for treatment of fecal incontinence. A total of 206 adults were randomized and assigned to receive NASHA Dx (n=136) or sham treatment (n=70). Of the NASHA Dx group, 132 were analyzed at six months, and 125 analyzed at 12 months. In the sham group, 65 were analyzed at six months. Seventy-one patients (52%) who received NASHA Dx had a 50% or more reduction in the number of incontinence episode, compared with 22 (31%) patients who received sham treatment. However, the median decrease in number of incontinence episodes was not significantly greater in the active treatment group than in the sham treatment group at both three months and six months. A

total of 128 treatment-related adverse events were recorded, of which two were serious (one rectal abscess and one prostatic abscess). Study limitations include small sample size and short term follow-up.

La Torre et al. (2013) evaluated the long-term efficacy and safety of dextranomer in stabilized hyaluronic acid (NASHA/Dx) assessed 24 months after treatment. Data on fecal incontinence (FI) episodes and quality of life measures were collected from diaries over the 28-day period immediately preceding the 24-month assessment. Eighty-three of 115 fifteen patients completed the 24-month follow-up assessment. At 24 months, 62.7% of patients were considered responders and experienced $\geq 50\%$ reduction in total number of FI episodes. The median number of FI episodes declined by 68.8%. Episodes of both solid and liquid stool incontinence decreased. The mean number of incontinence-free days increased from 14.6 at baseline to 21.7 at 24 months. Incontinence scores and FI quality of life scores also showed significant improvements. The most common adverse events (AEs) were proctalgia (13.3%) and pyrexia (9.6%). The majority of AEs were mild to moderate, self-limited, and resolved within 1 month of the injection. The authors concluded that NASHA/Dx is safe, effective, and durable over a 24-month period with a majority of patients experiencing significant improvement in multiple symptoms associated with FI. This study was nonrandomized and not case controlled.

Danielson et al. (2013) assessed the effects of NASHA Dx on continence and quality of life (QoL) and to evaluate the relationship between QoL and efficacy up to 2 years after treatment. Thirty-four patients (5 males, mean age 61) were injected with NASHA Dx in the submucosal layer. The patients were followed for 2 years with registration of incontinence episodes, bowel function and QoL questionnaires. Twenty-six patients reported sustained improvement after 24 months. The median number of incontinence episodes before treatment was 22 and decreased to 10 at 12 months and to 7 at 24 months. There was a clear correlation between the decrease in the number of leak episodes and the increase in the SF-36 Physical Function score but only patients with more than 75 % improvement in the number of incontinence episodes had a significant improvement in QoL at 24 months. The authors concluded that anorectal injection of NASHA Dx gel induces improvement of incontinence symptoms for at least 2 years. The authors stated that the treatment has a potential to improve QoL. According to the authors, a 75 % decrease in incontinence episodes may be a more accurate threshold to indicate a successful incontinence treatment than the more commonly used 50 %. Study limitations include the lack of controls and a small study population.

In an observational study, Dodi et al. (2010) evaluated 86 patients with fecal incontinence (FI) who received 4 injections of 1 mL NASHA/Dx gel. This study demonstrated a $\geq 50\%$ reduction from baseline in the number of FI episodes in 57% of patients at 6 months, and 64% at 12 months. A total of 7% of patients reported pyrexia that was assessed by the investigator as related to treatment. A total of 6 cases of anorectal abscess were reported in the study. All of these events resolved after treatment. According to the authors, NASHA/Dx gel is an efficacious in the treatment of FI. Lack of a comparison group limits the conclusions that can be reached from this study.

The overall quality of the evidence is low given the paucity of controlled studies and small study sizes. Larger, independent, randomized, sham-controlled studies are needed to further evaluate the efficacy, durability, and safety of this treatment, and to compare it with standard therapies and other alternatives. There is also a need to examine variables that predict which patients will derive the most clinical benefit from this therapy to better define patient selection criteria (Hayes, November 2012).

In a Cochrane review, Maeda et al. (2013) evaluated the effectiveness of perianal injection of bulking agents for the treatment of fecal incontinence in adults. Five eligible randomized trials with a total of 382 patients were included in the review. One of the five studies assessed dextranomer in stabilized hyaluronic acid (NASHA Dx). This study demonstrated that NASHA Dx was more effective than sham injection but with more adverse effects. Most trials reported a short

term benefit from injections regardless of the material used, including placebo saline injection. None of the studies reported patient evaluation of outcomes and thus it is difficult to gauge whether the improvement in incontinence scores matched practical symptom improvements that mattered to the patients. The authors concluded that one large randomized controlled trial has shown that this form of treatment using dextranomer in stabilized hyaluronic acid (NASHA Dx) improves continence for a little over half of patients in the short term. However, the number of identified trials was limited and most had methodological weaknesses.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

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Code	Description
P2031	Hair analysis (excluding arsenic)

Laboratory analysis of hair for content of environmental substances of concern for exposure assessment and health interpretation of the results is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Hair analysis has been proposed as an aid in the diagnosis of disorders such as mineral or protein deficiency or mineral toxicity. Hair analysis has not been proven to be effective in ascertaining mineral or metabolic imbalances or IgE-mediated allergic diseases. Hair analysis has also not been proven to be of use in either the diagnosis or treatment of conditions such as autism, schizophrenia, and mood disorders.

Wolowiec et al. (2013) conducted a systematic review on the relation between the mineral composition of hair and physical or mental disorders. Sixty-six studies were included in the review. Most of the authors reported that there exists a correlation between deficiency or excess of some elements in hair and occurrence of some diseases, such as: autism, cancer, hypertension, myocardial infarction, kidney disease and diabetes mellitus. However, not all results were consistent. The authors concluded that there is a need to standardize sample preparation procedures, in particular washing and mineralization methods.

While hair analysis is useful during a forensic exam, its use for hair loss issues is not supported by the clinical evidence. The utility of hair analysis is limited by the inability to discern endogenous and exogenous reference(s). Interpretation is unreliable and there are no referenced norms to support or establish that hair can be a consistent biological marker or that completion of

such tests will change medical management (Houck 2002, Chiang, 2001; Hryhorczuk and Eng, 2001).

Hirano et al. (2011) evaluated hair shaft abnormalities in 65 individuals with ectodermal dysplasia (ED) syndromes using light microscopy and compared findings with those in 41 unaffected controls. Light microscopy identified various pathologic hair shaft abnormalities in each type of ED, although none of the findings were statistically significantly different from those of the control group. According to the authors, light microscopy is a poor adjuvant tool in the diagnosis of ED syndromes. Most findings are nonspecific and not sufficiently sensitive.

The Agency for Toxic Substance and Disease Registry reviewed the use of hair analysis. The primary consideration of the panel was to determine the utility of hair analysis in evaluating exposures to hazardous wastes. The panel concluded that there was insufficient evidence to support the use of microscopic testing of hair to predict exposure to toxic substances (ATSDR, 2001).

According to Quackwatch, hair analysis is not useful for assessing the body's nutritional status or serving as a basis for dietary or supplement recommendations. Nor should these tests be routinely used to screen people for heavy metal toxicity.

A 2011 guideline for food allergy in children and young people from the National Institute for Health and Care Excellence (NICE) recommends against the use of hair analysis in the diagnosis of food allergy.

Three society guidelines provide a discussion of hair analysis, but none recommend its use (American Academy of Allergy, Asthma and Immunology, American College of Allergy, Asthma and Immunology 2008; American Academy of Neurology, Child Neurology Society 2002; American College of Allergy, Asthma, & Immunology 2006).

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Code	Description
P2033	Thymol turbidity, blood

Testing for Thymol turbidity is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

This test is considered obsolete by CMS and other lab references.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

U.S. Department of Health and Human Services, Center for Medicare & Medicaid Services (CMS). Obsolete or unreliable diagnostic tests. Medicare Coverage Issues Manual §50-34. Baltimore, MD: CMS; 2002.

Tietz NW. *Clinical Guide to Laboratory Tests*. 3rd ed. Philadelphia, PA: W.B. Saunders Co.; 1995.

Henry JB. *Clinical Diagnosis and Management by Laboratory Methods*. 19th ed. Philadelphia, PA: W.B. Saunders Co.; 1996.

Code	Description
P2038	Blood mucoprotein

Testing for blood mucoprotein is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

This test is considered obsolete by CMS and other lab references.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion

Reference(s):

U.S. Department of Health and Human Services, Center for Medicare & Medicaid Services (CMS). Obsolete or unreliable diagnostic tests. Medicare Coverage Issues Manual §50-34. Baltimore, MD: CMS; 2002.

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Code	Description
Q2026	Injection, Radiesse, 0.1ML
Q2028	Injection, Sculptra, 0.5 mg

Radiesse is proven and medically necessary and reconstructive for the following:

- treatment of facial defects due to facial lipidatrophy in persons with human immunodeficiency virus (HIV)
- treatment of vocal fold insufficiency

Sculptra is proven and medically necessary and reconstructive for treatment of facial defects due to facial lipidatrophy in persons with human immunodeficiency virus (HIV)

Other uses of these devices may be cosmetic.

Clinical Evidence

A U.S. Food and Drug Administration (FDA) search indicates that Radiesse or Sculptra injections are reviewed as devices. On December 22, 2006, the FDA approved Radiesse, an injectable (under the skin) implant to restore or correct signs of facial lipidatrophy, or fat loss, in people with human immunodeficiency virus (HIV) (FDA, 2006). Radiesse is a sterile, semi-solid cohesive implant consisting of synthetic calcium hydroxylapatite (CaHA) suspended in a gel carrier. Radiesse is also approved for use as a tissue marker, for treatment of vocal fold insufficiency, and to correct certain facial defects (FDA 2007).

On August 3, 2004, the FDA approved Sculptra, an injectable filler to correct facial fat loss in people with human immunodeficiency virus (HIV) (FDA, 2004). Sculptra is an injectable form of poly-L-lactic acid, a biodegradable, biocompatible synthetic polymer from the alpha-hydroxy-acid family.

In a multicenter prospective study, Rosen et al. (2007) evaluated the effectiveness of CaHA injection for patients with glottal incompetence. Voice-related outcome measures were collected for pre-injection and at one, three and six months. Sixty-eight patients were available for evaluation. Fifty percent of the injection procedures were done in the office setting. Fifty-seven percent were diagnosed with unilateral paralysis and 42% with glottal incompetence with mobile vocal folds. Patient satisfaction at six months post-procedure showed 56% had significantly improved voice, and 38% reported moderately improved voice. Information regarding the value and results of CaHA vocal fold augmentation beyond six months are presently not available but will be forthcoming with the 12- and 24-month reports from this prospective, open-label clinical trial.

Belafasky et al. (2004) prospectively evaluated 23 patients concerning indications, technique, functional outcome, and complications with CaHA. The authors concluded that initial experience with vocal fold augmentation using CaHA is promising.

In a preliminary report on vocal cord augmentation with injectable CaHA, Rosen et al. (2004) concluded that vocal fold injection of CaHA for UVCP improved voice quality and reduced mean airflow rates in this patient group with short-term results.

Individuals with HIV may experience facial lipidatrophy that may interfere with eating, speaking and swallowing. The safety and effectiveness of Radiesse for the treatment of facial lipoatrophy was evaluated in a prospective, open-label, multi-center study of 100 patients with human immunodeficiency virus and facial lipoatrophy. Patients received an initial treatment (initial injection and an additional injection at 1 month as needed). Six months later, all patients were assessed for the need for a touch up injection. Effectiveness was assessed at 3, 6 and 12 months from initial treatment by means of a Global Aesthetic Improvement Scale (GAIS) rating, cheek skin thickness measurements, and patient satisfaction assessment. Safety was assessed by the recording of adverse events through 12 months. Mean cheek thickness doubled in 6 months and was maintained over 12 months (Silvers et al. 2006).

The use of Sculptra or poly-L-lactic acid to treat facial lipoatrophy resulted in significant and prolonged improvement in HIV-infected patients in several clinical trials (Levy et al. 2008; Nelson and Stewart, 2012; Shuck, 2013; Bassichis, 2012).

The clinical evidence was reviewed in May 2014 with no additional information identified that would change the conclusion.

Reference(s):

Bassichis B, Blick G, Conant M, et al. Injectable poly-L-lactic acid for human immunodeficiency virus-associated facial lipoatrophy: cumulative year 2 interim analysis of an open-label study (FACES). *Dermatol Surg.* 2012 Jul;38(7 Pt 2):1193-205.

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Silvers SL, Eviatar JA, Echavez MI et al. Prospective, open-label, 18-month trial of calcium hydroxylapatite (Radiesse) for facial soft-tissue augmentation in patients with human immunodeficiency virus-associated lipoatrophy: one-year durability. *Plast Reconstr Surg.* 2006 Sep;118(3 Suppl):34S-45S.

Code	Description
Q4115	AlloSkin, per sq cm
Q4123	AlloSkin RT, per sq cm
Q4131	Epifix, per square centimeter
Q4132	Grafix core, per square centimeter
Q4133	Grafix prime, per square centimeter
Q4134	Hmatrix, per square centimeter
Q4135	Mediskin, per square centimeter
Q4136	Ez-derm, per square centimeter
Q4137	Amnioexcel or biodexcel, per square centimeter

Code	Description
Q4138	Biodfence dryflex, per square centimeter
Q4139	Amniomatrix or biodmatrix, injectable, 1 cc
Q4140	Biodfence, per square centimeter
Q4141	Alloskin ac, per square centimeter
Q4142	Xcm biologic tissue matrix, per square centimeter
Q4143	Repriza, per square centimeter
Q4145	Epifix, injectable, 1 mg
Q4146	Tensix, per square centimeter
Q4147	Architect extracellular matrix, per square centimeter
Q4148	Neox 1k, per square centimeter
Q4149	Excellagen, 0.1 cc

The following are unproven and not medically necessary for any indication due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature:

- Alloskin®
- Amnioexcel™ or Biodexcel™
- Amniomatrix™ or Biodmatrix™
- Architect Extracellular Matrix®
- Biodfence™ or Biodfence Dryflex™
- Epifix®
- Excellagen®
- Ez-derm®
- Grafix®
- Hmatrix®
- Mediskin™
- Neox®
- Repriza®
- Tensix®
- Xcm Biologic Tissue Matrix®

Clinical Evidence

AlloSkin

AlloSkin is a meshed human allograft skin for acute and chronic wound therapy. It is comprised of cadaveric epidermis and dermis. See the following Web site for more information:

<http://www.altrux.com/Products.aspx?e=33> Accessed May 2014.

There are few published studies addressing the use of Alloskin for wound treatment. Therefore, it is not possible to conclude whether Alloskin has a beneficial effect on health outcomes.

The clinical evidence was reviewed in May 2014 with no additional information identified that would change the conclusion.

Amnioexcel or Biodexcel

AmnioExCel (also marketed under trade name BioDExCel) is a dehydrated human amnion membrane allograft specifically processed for repair or replacement of lost or damaged dermal tissue. See the following Web site for more information:

<http://www.dermasciences.com/wp-content/themes/derma/images/AMNIOEXCEL-sell-sheet-2014.pdf> Accessed May 2014.

There are few published studies addressing the use of Amnioexcel or Biodexcel for wound treatment. Therefore, it is not possible to conclude whether Amnioexcel or Biodexcel has a beneficial effect on health outcomes.

The clinical evidence was reviewed in May 2014 with no additional information identified that would change the conclusion.

Amniomatrix or Biodmatrix

AmnioMatrix (also marketed under the trade name BioDMatrix) is a viable human placental allograft composed of morselized amniotic membrane and amniotic fluid components recovered from the same human donor. AmnioMatrix may be mixed with normal saline for application to surgical sites and open, complex or chronic wounds or mixed with the recipient's blood to fill soft tissue defects. See the following Web site for more information:

<https://www.netcells.co.za/membrane-products.php>

Accessed May 2014.

There are few published studies addressing the use of Amniomatrix or Biodmatrix for wound treatment. Therefore, it is not possible to conclude whether Amniomatrix or Biodmatrix has a beneficial effect on health outcomes.

The clinical evidence was reviewed in May 2014 with no additional information identified that would change the conclusion.

Architect Extracellular Matrix

The Harbor MedTech BriDGE Extracellular Collagen Matrix Wound Dressing is indicated for the local management of moderately to heavy exuding wounds, including:

- * Partial and full thickness wounds,
- * Draining wounds,
- * Pressure sores/ulcers,
- * Venous ulcers,
- * Chronic vascular ulcers,
- * Diabetic ulcers,
- * Trauma wounds (e.g., abrasions, lacerations, partial thickness burns, skin tears)
- * Surgical wounds (e.g., donor sites/grafts, post-laser surgery, post-Mohs surgery, podiatric wounds, dehisced surgical incisions). See the following Web site for more information:

<http://www.harbormedtech.com/products/wound-care> Accessed May 2014.

There are few published studies addressing the use of extracellular matrix for wound treatment. Therefore, it is not possible to conclude whether extracellular matrix has a beneficial effect on health outcomes.

The clinical evidence was reviewed in May 2014 with no additional information identified that would change the conclusion.

Biodfence or Biodfence Dryflex

BioDfence and BioDfence DryFlex are human placental-derived amniotic tissue based allografts composed of an epithelial layer and a stromal layer specifically processed for the repair and replacement of lost or damaged dermal tissue or the prohibition of adhesion formation. See the following Web sites for more information:

http://www.amediacorp.com/product_types/biologics/biodfence_trade_dryflex/

<http://www.biodlogics.com/index.php/products/biod-fence>

Accessed May 2104.

There are few published studies addressing the use of BioDfence or BioDfence DryFlex for wound treatment. Therefore, it is not possible to conclude whether BioDfence or BioDfence DryFlex has a beneficial effect on health outcomes.

The clinical evidence was reviewed in May 2014 with no additional information identified that would change the conclusion.

EpiFix

EpiFix is a dehydrated amniotic membrane extracellular collagen allograft comprised of an epithelial layer and two fibrous connective tissue layers. See the following Web site for more information: <http://www.mimedx.com/> Accessed June 2014.

In a prospective, randomized, single-center clinical trial, Zelen et al. (2013) compared healing characteristics of diabetic foot ulcers treated with dehydrated human amniotic membrane allografts (EpiFix®, MiMedx) versus standard of care. The study included patients with a diabetic foot ulcer of at least 4-week duration without infection having adequate arterial perfusion. Patients were randomized to receive standard care alone or standard care with the addition of EpiFix. Wound size reduction and rates of complete healing after 4 and 6 weeks were evaluated. In the standard care group (n = 12) and the EpiFix group (n = 13) wounds reduced in size by a mean of 32.0% ± 47.3% versus 97.1% ± 7.0% after 4 weeks, whereas at 6 weeks wounds were reduced by -1.8% ± 70.3% versus 98.4% ± 5.8%, standard care versus EpiFix, respectively. After 4 and 6 weeks of treatment the overall healing rate with application of EpiFix was shown to be 77% and 92%, respectively, whereas standard care healed 0% and 8% of the wounds, respectively. The authors concluded that patients treated with EpiFix achieved superior healing rates over standard treatment alone and that these results show that using EpiFix in addition to standard care is efficacious for wound healing. Limitations of this study include a small sample size. An additional limitation is that the comparative group in the study did not receive other advanced therapies to assess if the EpiFix allograft is as good as, or better, than other available advanced wound care products. According to the authors, additional comparative effectiveness studies are required to address this issue. It is also unknown how the EpiFix product performs in other patient populations and for other medical or surgical indications since the study was limited to patients with chronic diabetic foot ulcers.

In 2014, Zelen (2014a) published follow-up data from the Zelen et al., 2013 trial described above. Eighteen of 22 eligible patients returned for follow-up examination. At the 9–12 month follow-up visit, 17 of 18 (94.4%) wounds treated with dehydrated human amnion/chorion membrane (dHACM) remained fully healed. According to the authors, the limitations of this study include the retrospective study design and small sample size. The authors stated that larger studies are needed to confirm their findings.

Zelan et al. (2014b) assessed if weekly application of dehydrated human amnion/chorion membrane allograft reduces time to heal more effectively than biweekly application for treatment of diabetic foot ulcers. The study was an institutional review board-approved, registered, prospective, randomized, comparative, non-blinded, single-center clinical trial. Patients with non-infected ulcers of ≥ 4 weeks duration were included and randomized to receive weekly or biweekly application of allograft in addition to a non-adherent, moist dressing with compressive wrapping. The primary study outcome was mean time to healing. Overall, during the 12-week study period, 92.5% (37/40) ulcers completely healed. Mean time to complete healing was 4.1 ± 2.9 versus 2.4 ± 1.8 weeks in the biweekly versus weekly groups, respectively. According to the authors, these results validate previous studies showing that the allograft is an effective treatment for diabetic ulcers and show that wounds treated with weekly application heal more rapidly than with biweekly application. Limitations of this study include a small sample size. The lack of a standard care group not receiving dehydrated human amnion/chorion membrane (dHACM) can be perceived as a study weakness, although according to the authors the intent of the study was solely to examine rates of healing according to frequency of application and not compare with other treatment modalities. The authors state that their findings should be confirmed and expanded with subsequent multicentre clinical trials and long-term follow-up data to validate the durability of healed wounds.

Excellagen

Excellagen is a pharmaceutically formulated fibrillar Type I bovine collagen gel for wound care management. See the following Web site for more information: <http://www.excellagen.com/> Accessed May 2014

There are few published studies addressing the use of Excellagen for wound treatment. Therefore, it is not possible to conclude whether Excellagen has a beneficial effect on health outcomes.

The clinical evidence was reviewed in May 2014 with no additional information identified that would change the conclusion.

Ez-derm

Ez-Derm is a porcine-derived, biosynthetic xenograft. See the following Web site for more information: <http://www.woundsource.com/product/e-z-derm> Accessed May 2014.

In a retrospective review of medical records, Troy et al. (2013) evaluated the use of EZ Derm on partial-thickness burns in 157 patients. The average length of follow-up was 94.2 days. A total of 15.3% of patients (24/157) were lost to follow up. Eighteen complications were reported from 16 patients. Complications were attributed to positioning, infection, incomplete epithelialization at time of separation, need for additional excision and grafting, hypertrophic scarring, and cryptogenic. Clinically significant infections were seen in 22% (4/18) of complications and 3% of patients overall. The authors concluded that EZ Derm has proven to be a robust wound dressing that provides consistent durable wound coverage with minimal complications that resolve without long-term adverse sequelae. This study is limited by the retrospective nature of the data collection.

Grafix

Grafix is a living skin substitute allograft comprised of a biologic membrane with native mesenchymal stem cells. See the following Web site for more information: <http://www.osiris.com/grafix> Accessed May 2014.

There are few published studies addressing the use of Grafix for wound treatment. Therefore, it is not possible to conclude whether Grafix has a beneficial effect on health outcomes.

The clinical evidence was reviewed in May 2014 with no additional information identified that would change the conclusion.

Hmatrix

Hmatrix Acellular Dermis is an allograft derived from donated human skin. See the following Web site for more information: <http://bacterin.com/products/hmatrix-adm/> Accessed May 2014.

There are few published studies addressing the use of Hmatrix for wound treatment. Therefore, it is not possible to conclude whether Hmatrix has a beneficial effect on health outcomes.

The clinical evidence was reviewed in May 2014 with no additional information identified that would change the conclusion.

Mediskin

Mediskin is a porcine-derived decellularized fetal skin product. See the following Web site for more information: <http://www.woundsource.com/product/mediskin> Accessed May 2014.

There are few published studies addressing the use of Mediskin for wound treatment. Therefore, it is not possible to conclude whether Mediskin has a beneficial effect on health outcomes.

In a prospective randomized, 3-arm, clinical study, Karlsson et al. (2014) compared Aquacel, Allevyn, and Mediskin I in the treatment of split-thickness skin graft donor sites in 67 adults. Patients were randomly assigned to treatment with Aquacel, Allevyn, or Mediskin I. The donor site was assessed on postoperative days 3, 14, and 21 for healing, infection, pain, impact on everyday life, ease of use, and cost. The obtained results demonstrate significantly faster re-

epithelialization for patients treated with Aquacel or Mediskin I compared with Allevyn. Regarding infections, there were no significant differences between the groups. Patients wearing Aquacel experienced significantly less pain changing the dressing and less impact on everyday life than the patients wearing Allevyn. Aquacel was shown to be significantly easier for the caregiver to use than Allevyn and Mediskin I. The authors stated that their results support the use of Aquacel in the treatment of split-thickness skin graft donor sites.

Neox

Neox Wound Matrix is used as a wound covering for dermal ulcers and defects. It is made from cryopreserved human amniotic membrane. See the following Web site for more information: <http://www.amnioxmedical.com/NEOX-wound-matrix.html> Accessed May 2014.

There are few published studies addressing the use of Neox for wound treatment. Therefore, it is not possible to conclude whether Neox has a beneficial effect on health outcomes.

The clinical evidence was reviewed in May 2014 with no additional information identified that would change the conclusion.

Repriza

Repriza is an acellular dermal matrix prepared from human skin allograft. Repriza is intended for implantation for reconstructive surgery wherever an acellular dermal matrix may be used, as for example in breast reconstruction, abdominal wall reconstruction, and augmentation of soft tissue irregularities. See the following Web site for more information: http://www.ssp-inc.com/Repriza_ReadyToUse_ADM.aspx Accessed May 2014.

There are few published studies addressing the use of Repriza for wound treatment. Therefore, it is not possible to conclude whether Repriza has a beneficial effect on health outcomes.

The clinical evidence was reviewed in May 2014 with no additional information identified that would change the conclusion.

Tensix

TenSIX Acellular Dermal Matrix (ADM) is an allograft derived from voluntarily donated human tissue.

See the following Web site for more information: <http://evansmed.com/skin/> Accessed May 2014.

There are few published studies addressing the use of TenSIX for wound treatment. Therefore, it is not possible to conclude whether TenSIX has a beneficial effect on health outcomes.

The clinical evidence was reviewed in May 2014 with no additional information identified that would change the conclusion.

XCM Biologic

XCM Biologic is a sterile non-crosslinked 3-D matrix derived from porcine dermis.

See the following Web site for more information:

<http://www.synthes.com/sites/NA/Products/CMF/AcellularDermis/Pages/XCM-Biologic-Tissue-Matrix.aspx> Accessed May 2014.

There are few published studies addressing the use of XCM Biologic for wound treatment. Therefore, it is not possible to conclude whether XCM Biologic has a beneficial effect on health outcomes.

George et al. (2014) reported the first series of using XCM Biologic Tissue Matrix for chest wall reconstruction. It was used either alone or in conjunction with the Synthes titanium system to provide additional support. Since April 2010, 21 (12 females) patients received the device.

Average age at operation was 47 ± 17 years. Eleven (52%) patients had the patch inserted alone, while the remaining 10 received it in combination with another implantable medical device. The biological tissue matrix was used to reconstruct chest wall defects in cancer involving chest wall (n = 9), chest wall deformity (n = 6), chest wall hernia (n = 5) and chest wall repair following empyema drainage (n = 1). Complications occurred in 3 patients receiving the combined XCM and Synthes bar mechanisms; infection (n = 2) and bar displacement and infection (n = 1). The authors concluded that the XCM patch can be safely used to provide the strength required for chest wall reconstruction and to replace previously infected reconstructions. This is an uncontrolled study with a small sample size.

The National Institute For Health And Care Excellence (2011) did not recommend using dermal or skin substitutes in its guideline on inpatient management of diabetic foot problems; these products were to be used only in a clinical trial.

The Agency for Healthcare Research and Quality (AHRQ) Technology Assessment Report on Skin Substitutes for Treating Chronic Wounds states that applicability of the evidence base to address important questions about the effectiveness of skin substitutes in typical populations is limited. The overall applicability of the evidence base is limited to a small number of skin substitute products examining diabetic foot ulcers and venous and/or arterial leg ulcers and to patients in generally good health. According to the authors, the studies that are available are not generalizable to broader patient populations that are not as healthy as the patients in the reviewed studies. According to the AHRQ report, additional studies in this area of wound care would be helpful to provide treatment data for many of the other skin substitute products, to allow better comparisons between wound care products, and to provide better information on wound recurrence when using skin substitute products (AHRQ 2012).

Reference(s):

Agency for Healthcare Research and Quality (AHRQ). Skin Substitutes for Treating Chronic Wounds. Technology Assessment Report. December 18, 2012. Available at: http://www.ahrq.gov/research/findings/ta/skinsubs/HCPRO610_skinsubst-final.pdf Accessed May 2014.

ECRI, Inc. Product Brief. Graftix Cellular Repair Matrix (Osiris Therapeutics, Inc.) for Treating Chronic Wounds. November 2012.

ECRI, Inc. Hotline Response. Bioengineered Skin and Dermal Cell Replacement for Managing Chronic Diabetic and Venous Ulcers. March 2014.

George RS, Kostopanagiotou K, Papagiannopoulos K. The expanded role of extracellular matrix patch in malignant and non-malignant chest wall reconstruction in thoracic surgery. *Interact Cardiovasc Thorac Surg.* 2014 Mar;18(3):335-9.

Hayes, Inc. Search and Summary. Amniotic Tissue-Derived Allografts for Foot and Leg Ulcers. Lansdale, PA: Hayes, Inc.; Archived December 2013.

Hayes, Inc. Search and Summary. EpiFix (MiMedx Group) for Treatment of Nonhealing Wounds. Lansdale, PA: Hayes, Inc.; March 2014.

Hayes, Inc. Search and Summary. Mediskin (Molnlycke Health Care) for Postoperative Wound Care After Moh's Surgery. Lansdale, PA: Hayes, Inc.; October 2013.

Karlsson M, Lindgren M, Jarnhed-Andersson I, et al. Dressing the split-thickness skin graft donor site: a randomized clinical trial. *Adv Skin Wound Care.* 2014 Jan;27(1):20-5.

National Institute For Health And Care Excellence (NICE). Centre for Clinical Practice. Diabetic foot problems. Inpatient management of diabetic foot problems. London (UK): 2011 March. Summary.

Troy J, Karlnoski R, Downes K, et al. The Use of EZ Derm® in Partial-Thickness Burns: An Institutional Review of 157 Patients. *Eplasty.* 2013;13:e14.

Zelen CM, Serena TE, Denozieri G, et al. A prospective randomized comparative parallel study of amniotic membrane wound graft in the management of diabetic foot ulcers. *Int Wound J.* 2013 Oct;10(5):502-7.

Zelen CM, Serena TE, Fetterolf DE. Dehydrated human amnion/chorion membrane allografts in patients with chronic diabetic foot ulcers: A long-term follow-up study. *Wound Medicine.* 2014a; 4:1-4.

Zelen CM, Serena TE, Snyder RJ. A prospective, randomised comparative study of weekly versus biweekly application of dehydrated human amnion/chorion membrane allograft in the management of diabetic foot ulcers. *Int Wound J.* 2014b Apr;11(2):122-8.

Code	Description
S3902	Ballistocardiogram

Ballistocardiography is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Ballistocardiography refers to the recording of movements of the body caused by cardiac contractions and associated blood flow. It had been investigated for potential use in measuring cardiac output (CO) and other aspects of cardiac function.

Thermodilution is the preferred method of measuring CO, and has achieved universal acceptance in the clinical setting. The ballistocardiogram and other means of detecting CO, such as the impedance-cardiogram, have been developed and are being used clinically, but the development of the flow-directed thermodilution catheter has resulted in universal acceptance of the thermodilution method. Thermodilution techniques, when performed properly, are capable of obtaining accurate and reproducible results (Taylor and Sheffer, 1990).

McKay, et al. (1999) theorized a method to derive and analyze the long-axis ballistocardiogram that is less invasive than pulmonary artery thermodilution. The mathematical equation was tested on 39 patients. Of derived stroke volumes, 82 % were within 15 ml of pulmonary artery thermodilution-derived values. The authors concluded that sternal acceleration ballistocardiogram combined with hemodynamic and demographic data in a probabilistic model shows promise of providing a less invasive measure of CO than thermodilution.

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

McKay WP, Gregson PH, McKay BW, Militzer J. Sternal acceleration ballistocardiography and arterial pressure wave analysis to determine stroke volume. *Clin Invest Med.* 1999;22(1):4-14.

Taylor BC, Sheffer DB. Understanding techniques for measuring cardiac output. *Biomed Instrum Technol.* 1990;24(3):188-197

Code	Description
S9025	Omnicardiogram/cardiointegram

The use of omnicardiogram or cardiointegram is unproven and not medically necessary due to insufficient clinical evidence of safety and/or efficacy in published peer-reviewed medical literature.

Clinical Evidence

Omnicardiogram/Cardiointegram (CIG), a technique intended to detect abnormalities in the standard twelve-lead electrocardiogram that are beyond the standard, routine interpretation in patients at risk of cardiac ischemia. This additional technology consists of a microcomputer which receives output from a standard electrocardiogram (ECG) and transforms it to produce a graphic representation of heart electrophysiologic signals. This procedure is used primarily as a substitute for exercise tolerance testing with thallium imaging in patients for whom a resting ECG may be insufficient to identify changes compatible with coronary artery disease.

The results are based on a theoretical assumption that poor exercise tolerance is related to electrophysiologic signals, but this test does not consider the impact of other symptoms or blood flow.

In a joint clinical competence statement, the American College of Cardiology and the American Heart Association state that computer analysis cannot substitute for interpretation by experienced electrocardiographers and should not be used in making clinical decisions (Kadish et al., 2001).

The clinical evidence was reviewed in June 2014 with no additional information identified that would change the conclusion.

Reference(s):

Centers for Medicare and Medicaid Services (CMS). National Coverage Determination (20.27) for Cardiogram (CIG) as an Alternative to Stress Test or Thallium Stress Test. Available at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Accessed June 16, 2014.

Kadish AH, Buxton AE, Kennedy HL, et al. ACC/AHA clinical competence statement on electrocardiography and ambulatory electrocardiography: a report of the American College of Cardiology/American Heart Association/American College of Physicians-American Society of Internal Medicine Task Force on Clinical Competence (ACC/AHA Committee to Develop a Clinical Competence Statement on Electrocardiography and Ambulatory Electrocardiography); J Am Coll Cardiol 2001; 38: 2091-100.

POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
09/01/2014	<ul style="list-style-type: none"> • Revised coverage rationale: <ul style="list-style-type: none"> ○ Added language to indicate if service or device is “medically necessary” or “not medically necessary” to applicable proven/unproven statement ○ Changed coverage status for the following devices (Q4115, Q4123, Q4131, Q4132, Q4133, Q4134, Q4135, Q4136, Q4137, Q4138, Q4139, Q4140, Q4141, Q4142, Q4143, Q4145, Q4146, Q4147, Q4148, and Q4149) from “unproven for tissue repair or for treating wounds, burns or ulcers” to “unproven and not medically necessary for any indication”: <ul style="list-style-type: none"> ▪ Alloskin® ▪ Amnioexcel™ or Biodexcel™ ▪ Amniomatrix™ or Biodmatrix™ ▪ Architect Extracellular Matrix® ▪ Biodfence™ or Biodfence Dryflex™ ▪ Epifix® ▪ Excellagen® ▪ Ez-derm® ▪ Grafix® ▪ Hmatrix® ▪ Mediskin™ ▪ Neox® ▪ Repriza® ▪ Tensix® ▪ Xcm Biologic Tissue Matrix® • Updated supporting information to reflect the most current clinical evidence and references • Archived previous policy version 2014T0535Y