Cigna Medical Coverage Policy

Effective Date **9/15/2014**
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Coverage Policy Number **0504**

Subject **Omnibus Codes**

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INSTRUCTIONS FOR USE

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Coverage Policy

Capsule Endoscopy (CPT® Codes 91110, 91111)

Cigna covers small bowel capsule endoscopy (i.e., Pillcam® SB, Endo Capsule) as medically necessary in adults and children two years of age or older, when standard endoscopic and imaging evaluations (i.e., upper and lower endoscopy) are inconclusive and the individual has ONE of the following:

- obscure source of gastrointestinal bleeding
- suspected Crohn's disease
- suspected small bowel tumor
- celiac disease

Cigna does not cover small bowel capsule endoscopy for any other indication because it is considered experimental, investigational or unproven.

Cigna does not cover esophageal capsule endoscopy (Pillcam® ESO) for any indication because it is considered experimental, investigational or unproven.

Cigna does not cover colon capsule endoscopy (Pillcam® COLON) for any indication because it is considered experimental, investigational or unproven.

Cigna does not cover the patency capsule (Given AGILE™ Patency System) for any indication because it is considered experimental, investigational or unproven.

Transanal Endoscopic Microsurgery (TEMS) Approach for Excision of Rectal Tumor (CPT® Code 0184T)

Cigna covers transanal endoscopic microsurgery (TEMS) as medically necessary for EITHER of the following indications:

- Benign adenoma
- T1N0 rectal cancer when ALL of the following criteria are met:
  - tumor has a diameter of < 3cm
  - tumor is located within 8 cm of the anal verge
  - tumor is well to moderately differentiated
  - tumor is limited to < 30% of the rectal circumference
  - lesion is adequately identified in the rectum
  - no signs of systemic or metastatic disease

Cigna does not cover TEMS (CPT® code 0184T) for any other indication because it is experimental, investigational and unproven.

High Resolution Anoscopy (CPT® Codes 0226T, 0227T)

Cigna covers high resolution anoscopy (HRA) as medically necessary for diagnosis of EITHER of the following:

- suspicious anal lesion, including high-grade suspicious intraepithelial lesion (HSIL)
- anal dysplasia found in prior cytology/biopsy

Cigna does not cover HRA for any other indication because it is experimental, investigational and unproven.

Whole Body and Selective Head Hypothermia (CPT® Codes 99481, 99482)

Cigna covers whole body or selective head therapeutic hypothermia in a neonate ≤ 28 days of age for the treatment of moderate or severe hypoxic ischemic encephalopathy.

Cigna does not cover whole body or selective head therapeutic hypothermia in a neonate ≤ 28 days of age for any other indication because it is considered experimental, investigational or unproven.

Sublingual Immunotherapy (CPT® Code 95199)

Cigna does not cover sublingual-swallow immunotherapy because it is considered experimental, investigational or unproven.

Elastography (CPT® Codes 0346T, 92199)

Cigna covers transient elastography (TE) (e.g. Fibroscan) once every six months as medically necessary to assess the degree of liver fibrosis and cirrhosis in an individual with chronic liver disease, when a liver biopsy has not been performed within six months of TE.

Cigna does not cover TE for any other indication because it is experimental, investigational or unproven.

Cigna does not cover any other ultrasound elastographic technique for any indication because it is experimental, investigational or unproven.

Other Non-Covered Services

Cigna does not cover ANY of the following services for any indication because each is considered experimental, investigational or unproven:

CPT® Code	Description
34806	Transcatheter placement of wireless physiologic sensor in aneurysmal sac during endovascular repair, including radiological supervision and interpretation, instrument calibration, and collection of pressure data (List separately in addition to code for primary procedure)
34841	Endovascular repair of visceral aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) by deployment of a fenestrated visceral aortic endograft and all associated radiological supervision and interpretation, including target zone angioplasty, when performed; including one visceral artery endoprosthesis (superior mesenteric, celiac or renal artery) (Code effective 1/01/2014)
34842	Endovascular repair of visceral aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) by deployment of a fenestrated visceral aortic endograft and all associated radiological supervision and interpretation, including target zone angioplasty, when performed; including two visceral artery endoprostheses (superior mesenteric, celiac and/or renal artery[s]) (Code effective 1/01/2014)
34843	Endovascular repair of visceral aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) by deployment of a fenestrated visceral aortic endograft and all associated radiological supervision and interpretation, including target zone angioplasty, when performed; including three visceral artery endoprostheses (superior mesenteric, celiac and/or renal artery[s]) (Code effective 01/01/2014)
34844	Endovascular repair of visceral aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) by deployment of a fenestrated visceral aortic endograft and all associated radiological supervision and interpretation, including target zone angioplasty, when performed; including four or more visceral artery endoprostheses (superior mesenteric, celiac and/or renal artery[s]) (Code effective 01/01/2014)
34845	Endovascular repair of visceral aorta and infrarenal abdominal aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) with a fenestrated visceral aortic endograft and concomitant unibody or modular infrarenal aortic endograft and all associated radiological supervision and interpretation, including target zone angioplasty, when performed; including one visceral artery endoprosthesis (superior mesenteric, celiac or renal artery) (Code effective 1/01/2014)
34846	Endovascular repair of visceral aorta and infrarenal abdominal aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) with a fenestrated visceral aortic endograft and concomitant unibody or modular infrarenal aortic endograft and all associated radiological supervision and interpretation, including target zone angioplasty, when performed; including two visceral artery endoprostheses (superior mesenteric, celiac and/or renal artery[s]) (Code effective 1/01/2014)
34847	Endovascular repair of visceral aorta and infrarenal abdominal aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) with a fenestrated visceral aortic endograft and concomitant unibody or modular infrarenal aortic endograft and all associated radiological supervision and interpretation, including target zone angioplasty, when performed; including three visceral artery endoprostheses (superior mesenteric, celiac and/or renal artery[s]) (Code effective 01/01/2014)
34848	Endovascular repair of visceral aorta and infrarenal abdominal aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) with a fenestrated visceral aortic endograft and concomitant unibody or modular infrarenal aortic endograft and all associated radiological supervision and interpretation, including target zone angioplasty, when performed; including four or more visceral artery endoprostheses (superior mesenteric, celiac and/or renal artery[s]) (Code effective 01/01/2014)
83993	Calprotectin, fecal
91112	Gastrointestinal tract transit and pressure measurement, stomach through colon, wireless capsule, with interpretation and report
93982	Noninvasive physiologic study of implanted wireless pressure sensor in aneurysmal sac

	following endovascular repair, complete study including recording, analysis of pressure and waveform tracings, interpretation and report
0078T	Endovascular repair using prosthesis of abdominal aortic aneurysm, pseudoaneurysm or dissection, abdominal aorta involving visceral branches (superior mesenteric, celiac and/or renal artery(s)) (Code deleted 12/31/2013)
0079T	Placement of visceral extension prosthesis for endovascular repair of abdominal aortic aneurysm involving visceral vessels, each visceral branch (List separately in addition to code for primary procedure) (Code deleted 12/31/2013)
0080T	Endovascular repair using prosthesis of abdominal aortic aneurysm, pseudoaneurysm or dissection, abdominal aorta involving visceral vessels (superior mesenteric, celiac and/or renal artery[s]), radiological supervision and interpretation (Code deleted 12/31/2013)
0081T	Placement of visceral extension prosthesis for endovascular repair of abdominal aortic aneurysm involving visceral vessels, each visceral branch, radiological supervision and interpretation (List separately in addition to code for primary procedure) (Code deleted 12/31/2013)
0103T	Holotranscobalamin, quantitative
0106T	Quantitative sensory testing (QST), testing and interpretation per extremity; using touch pressure stimuli to assess large diameter sensation
0107T	Quantitative sensory testing (QST), testing and interpretation per extremity; using vibration stimuli to assess large diameter fiber sensation
0108T	Quantitative sensory testing (QST), testing and interpretation per extremity; using coding stimuli to assess small nerve fiber sensation and hyperalgesia
0109T	Quantitative sensory testing (QST), testing and interpretation per extremity; using heat-pain stimuli to assess small nerve fiber sensation and hyperalgesia
0110T	Quantitative sensory testing (QST), testing and interpretation per extremity; using other stimuli to assess sensation
0124T	Conjunctival incision with posterior extrascleral placement of pharmacological agent (does not include supply of medication) (Code deleted 12/31/2013)
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.
0185T	Multivariate analysis of patient specific findings with quantifiable computer probability assessment, including report (Code deleted 12/31/2013)
0186T	Suprachoroidal delivery of pharmacologic agent (does not include supply of medication) (Code deleted 12/31/2013)
0190T	Placement of intraocular radiation source applicator
0199T	Physiologic recording of tremor using accelerometer(s) and gyroscope(s), (including frequency and amplitude) including interpretation and report
0205T	Intravascular catheter-based coronary vessel or graft spectroscopy (eg, infrared) during diagnostic evaluation and/or therapeutic intervention including imaging supervision, interpretation, and report, each vessel
0207T	Evacuation of meibomian glands, automated, using heat and intermittent pressure, unilateral
0208T	Pure tone audiometry (threshold);automated; air only
0209T	Pure tone audiometry (threshold);automated; air and bone
0210T	Speech audiometry threshold, automated
0211T	Speech audiometry threshold, automated with speech recognition
0212T	Comprehensive audiometry threshold evaluation and speech recognition (0209T and 0211T combined), automated
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 trend analysis and limited reprogramming of device parameters, AV or VV delays only, with interpretation and report

0225T	Acoustic cardiography, including automated analysis of combined acoustic and electrical intervals; multiple, including serial trend analysis and limited reprogramming of device parameters, AV and VV delays, with interpretation and report
0233T	Skin advanced glycation endproducts (AGE) measurement by multi-wavelength fluorescent spectroscopy
0234T	Transluminal peripheral atherectomy, open or percutaneous, including radiological supervision and interpretation; renal artery
0235T	Transluminal peripheral atherectomy, open or percutaneous, including radiological supervision and interpretation; visceral artery (except renal), each vessel
0236T	Transluminal peripheral atherectomy, open or percutaneous, including radiological supervision and interpretation; abdominal aorta
0237T	Transluminal peripheral atherectomy, open or percutaneous, including radiological supervision and interpretation; brachiocephalic trunk and branches, each vessel
0238T	Transluminal peripheral atherectomy, open or percutaneous, including radiological supervision and interpretation; iliac artery, each vessel
0239T	Bioimpedance spectroscopy (BIS), measuring 100 frequencies or greater, direct measurement of extracellular fluid differences between the limbs
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
0254T	Endovascular repair of iliac artery bifurcation (eg, aneurysm, pseudoaneurysm, arteriovenous malformation, trauma) using bifurcated endoprosthesis from the common iliac artery into both the external and internal iliac artery, unilateral
0255T	Endovascular repair of iliac artery bifurcation (eg, aneurysm, pseudoaneurysm, arteriovenous malformation, trauma) using bifurcated endoprosthesis from the common iliac artery into both the external and internal iliac artery, unilateral; radiological supervision and interpretation
0266T	Implantation or replacement of carotid sinus baroreflex activation device; total system (includes generator placement, unilateral or bilateral lead placement, intraoperative 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
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
0282T	Percutaneous or open implantation of neurostimulator electrode array(s), subcutaneous (peripheral subcutaneous field stimulation), including imaging guidance, when performed,

	cervical, thoracic or lumbar, for trial, including removal at the conclusion of trial period
0283T	Percutaneous or open implantation of neurostimulator electrode array(s), subcutaneous (peripheral subcutaneous field stimulation), including imaging guidance, when performed, cervical, thoracic or lumbar; permanent, with implantation of a pulse generator
0284T	Revision or removal of pulse generator or electrodes, including imaging guidance, when performed, including addition of new electrodes, when performed
0285T	Electronic analysis of implanted peripheral subcutaneous field stimulation pulse generator, with reprogramming when performed
0286T	Near-infrared spectroscopy studies of lower extremity wounds (eg, for oxyhemoglobin measurement)
0287T	Near-infrared guidance for vascular access requiring real-time digital visualization of subcutaneous vasculature for evaluation of potential access sites and vessel patency
0288T	Anoscopy, with delivery of thermal energy to the muscle of the anal canal (eg, for fecal incontinence)
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
0292T	Intravascular optical coherence tomography (coronary native vessel or graft) during diagnostic evaluation and/or therapeutic intervention, including imaging supervision, interpretation, and report; each additional vessel
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,
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
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 electrodes)
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
0308T	Insertion of ocular telescope prosthesis including removal of crystalline lens
0311T	Non-invasive calculation and analysis of central arterial pressure waveforms with interpretation and report
0336T	Laparoscopy, surgical, ablation of uterine fibroid(s), including intraoperative ultrasound guidance and monitoring, radiofrequency (Code effective 1/01/2014)
0337T	Endothelial function assessment, using peripheral vascular response to reactive hyperemia, non-invasive (eg, brachial artery ultrasound, peripheral artery tonometry), unilateral or bilateral (Code effective 1/01/2014)
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(Code effective 01/01/2014)
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 (Code effective 01/01/2014)
0340T	Ablation, pulmonary tumor(s), including pleura or chest wall when involved by tumor extension, percutaneous, cryoablation, unilateral, includes imaging guidance (Code effective 1/01/2014)
0341T	Quantitative pupillometry with interpretation and report, unilateral or bilateral (Code effective 1/01/2014)
0342T	Therapeutic apheresis with selective HDL delipidation and plasma reinfusion (Code effective 1/01/2014)
0378T	Visual field assessment, with concurrent real time data analysis and accessible data storage with patient initiated data transmitted to a remote surveillance center for up to 30 days; review and interpretation with report by a physician or other qualified health care professional (Code effective 01/01/2015)
0379T	Visual field assessment, with concurrent real time data analysis and accessible data storage with patient initiated data transmitted to a remote surveillance center for up to 30 days; technical support and patient instructions, surveillance, analysis and transmission of daily and emergent data reports as prescribed by a physician or other qualified health care professional (Code effective 01/01/2015)
0380T	Computer-aided animation and analysis of time series retinal images for the monitoring of disease progression, unilateral or bilateral, with interpretation and report (Code effective 01/01/2015)
0381T	External heart rate and 3-axis accelerometer data recording up to 14 days to assess changes in heart rate and to monitor motion analysis for the purposes of diagnosing nocturnal epilepsy seizure events; includes report, scanning analysis with report, review and interpretation by a physician or other qualified health care professional (Code effective 01/01/2015)
0382T	External heart rate and 3-axis accelerometer data recording up to 14 days to assess changes in heart rate and to monitor motion analysis for the purposes of diagnosing nocturnal epilepsy seizure events; review and interpretation only (Code effective 01/01/2015)
0383T	External heart rate and 3-axis accelerometer data recording from 15 to 30 days to assess changes in heart rate to monitor motion analysis for the purposes of diagnosing nocturnal epilepsy seizure events; includes report, scanning analysis with report, review and interpretation by a physician or other qualified health care professional (Code effective 01/01/2015)
0384T	External heart rate and 3-axis accelerometer data recording from 15 to 30 days to assess changes in heart rate to monitor motion analysis for the purposes of diagnosing nocturnal epilepsy seizure events; review and interpretation only (Code effective 01/01/2015)
0385T	External heart rate and 3-axis accelerometer data recording more than 30 days to assess changes in heart rate to monitor motion analysis for the purposes of diagnosing nocturnal epilepsy seizure events; includes report, scanning analysis with report, review and interpretation by a physician or other qualified health care professional (Code effective 01/01/2015)
0386T	External heart rate and 3-axis accelerometer data recording more than 30 days to assess changes in heart rate to monitor motion analysis for the purposes of diagnosing nocturnal epilepsy seizure events; Review and interpretation (code effective 01/01/2015)
0387T	Transcatheter insertion or replacement of permanent leadless pacemaker, ventricular (Code effective 01/01/2015)
0388T	Transcatheter removal of permanent leadless pacemaker, ventricular (Code effective 01/01/2015)
0389T	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, review and report, leadless pacemaker system (Code effective 01/01/2015)
0390T	Peri-procedural device evaluation (in person) and programming of device system parameters before or after a surgery, procedure or test with analysis, review and report, leadless pacemaker system (Code effective 01/01/2015)
0391T	Interrogation device evaluation (in person) with analysis, review and report, includes connection, recording and disconnection per patient encounter, leadless pacemaker system (Code effective 01/01/2015)

HCPCS Code	Description
A4555	Electrode/transducer for use with electrical stimulation device used for cancer treatment, replacement only(Code effective 01/01/2014)
C9736	Laparoscopy, surgical, radiofrequency ablation of uterine fibroid(s), including intraoperative guidance and monitoring, when performed (Code deleted 01/01/2014)
E0766	Electrical stimulation device used for cancer treatment, includes all accessories, any type (Code effective 01/01/2014)
E2120	Pulse generator system for tympanic treatment of inner ear endolymphatic fluid
G0255	Current perception threshold/sensory nerve conduction test, (SNCT) per limb, any nerve
S2103	Adrenal tissue transplant to brain

General Background

This policy discusses the safety and effectiveness of certain technologies, services, and procedures, including those represented by some Category III CPT® codes. Category III codes are temporary codes that allow for data collection for these services/procedures.

Additionally, there are certain Category III codes that represent services which have not received Food and Drug Administration (FDA) approval:

CPT® Code	Description
0190T	Placement of intraocular radiation source applicator
0233T	Skin advanced glycation endproducts (AGE) measurement by multi-wavelength fluorescent spectroscopy
0254T	Endovascular repair of iliac artery bifurcation (eg, aneurysm, pseudoaneurysm, arteriovenous malformation, trauma) using bifurcated endoprosthesis from the common iliac artery into both the external and internal iliac artery, unilateral
0255T	Endovascular repair of iliac artery bifurcation (eg, aneurysm, pseudoaneurysm, arteriovenous malformation, trauma) using bifurcated endoprosthesis from the common iliac artery into both the external and internal iliac artery, unilateral; radiological supervision and interpretation
0266T	Implantation or replacement of carotid sinus baroreflex activation device; total system (includes generator placement, unilateral or bilateral lead placement, intraoperative 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

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
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,
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
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 electrodes)
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
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 (Code effective 01/01/2014)
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 (Code effective 01/01/2014)
0342T	Therapeutic apheresis with selective HDL delipidation and plasma reinfusion (Code effective 1/01/2014)
0387T	Transcatheter insertion or replacement of permanent leadless pacemaker, ventricular
0388T	Transcatheter removal of permanent leadless pacemaker, ventricular
0389T	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, review and report, leadless pacemaker system
0390T	Peri-procedural device evaluation (in person) and programming of device system parameters before or after a surgery, procedure or test with analysis, review and report, leadless pacemaker system
0391T	Interrogation device evaluation (in person) with analysis, review and report, includes connection, recording and disconnection per patient encounter, leadless pacemaker system

Fecal Calprotectin Testing (CPT© Code 83993)

This laboratory test measures the level of calprotectin in stool. Calprotectin is a calcium and zinc binding protein that is found predominantly in neutrophils. The concentration of calprotectin is higher in feces compared to plasma and can be measured by enzyme-linked immunosorbent assay (ELISA) using less than five grams of stool. Although the normal range has been defined for FC, an optimal cutoff point for distinguishing IDB from other diagnoses has not been defined (von Roon et al. 2007). It has been studied as a surrogate marker of intestinal inflammation in inflammatory bowel diseases (IBD) (e.g., Crohn's disease, ulcerative colitis), colorectal cancer, diverticular disease, and polyposis of the colon. It has also been studied as a marker to predict response to treatment and relapse of disease.

U.S. Food and Drug Administration (FDA)

PhiCal™ Fecal Calprotectin Immunoassay (Genova Diagnostics, Inc., Ashville, NC) received Class II device approval in 2006. The immunoassay is a lab test that measures the amount of fecal calprotectin in a patient's stool sample.

Literature Review
Randomized controlled clinical trial data are lacking regarding the clinical utility of fecal calprotectin testing to inform diagnosis, or predict relapse or response to treatment for IBD or any indication. Although patient numbers included in published studies are large, a number of study limitations have been identified by authors including uncontrolled and heterogeneous study design, and heterogeneous patient populations. Further, in some studies it is unknown whether FC samples were obtained before commencing treatment, which may be a major confounder in reports of diagnostic accuracy (Henderson, 2013). In the study by Henderson (2013) the authors note "The assessment of methodological quality determined that there were deficiencies in all the studies evaluated, but especially with regard to important aspects, such as the use of a representative spectrum of patients, an acceptable reference standard (upper and lower endoscopy), and the poor reporting of current treatment modalities in use during FC sampling."

Inflammatory Bowel Disease: Several meta-analyses of prospective and registry data have been performed to examine the predictive capacity of fecal calprotectin in individuals with IBD (e.g., Crohn's disease, ulcerative colitis). Reported results have been inconsistent with a wide variation in sensitivity and specificity of FC for included studies, ranging from 61-100% and 71-100%, respectively for diagnosis of IBD and other intestinal disorders. Sensitivity and specificity to predict relapse are 43-80% and 48-73%, respectively (Henderson, 2013; Kostakis, 2012; Mao, 2012; Jellema, 2011; Laharie, 2011; Garcia-Sanchez, 2010; van Rheenen, 2010; Gisbert, 2009; von Roon, 2007). In several studies (Henderson, 2013; van Rheenen, 2010), results regarding specificity of FC testing in children were significantly different compared with those for adults (96% and 68-97%, respectively).

Although several clinical trials reflect abnormal or elevated FC levels in individuals with inflammatory bowel disease compared with controls, the clinical utility of fecal calprotectin testing to impact management and improve overall health outcomes has not been demonstrated. Large randomized controlled trials are necessary to establish the role of FC testing when compared to available diagnostic tests.

Colorectal Cancer: Similar to IBD, RCT data are lacking in the published, peer-reviewed scientific literature to evaluate the clinical utility of FC testing for screening and diagnosis of colorectal cancer (CRC) in adults and children. Although levels of fecal calprotectin may be elevated in individuals with CRC compared with healthy control subjects, several meta-analyses of prospective and retrospective studies reflect inconsistent sensitivity and specificity with values of 36-75% and 64-84% respectively (von Roon, 2007; Shitrit, 2007; Kronberg, 2000). The role of FC testing as a means to diagnose CRC has not been established.

Other Intestinal Conditions: FC testing has also been proposed for other conditions such as colonic polyposis, diverticular disease, and diarrhea (Pezzilli, 2008, Tursi, 2014; Licata, 2012). Randomized controlled trial data are lacking in the published peer-reviewed scientific literature demonstrating the ability to impact care management or improve patient health outcomes with FC testing. Further, there is a lack of published literature reflecting that this is considered a standard of care option for these indications. At this time there is insufficient evidence to determine the role and clinical utility of such testing.

Professional Societies
American College of Gastroenterology (ACG): On behalf of the ACG, Lichenstein et al. (2009) published a guideline regarding the management Crohn's disease which notes the presence of fecal leukocytes as a way to confirm inflammation.

Use Outside of the US: World Gastroenterology Organisation (2009): The global guideline for irritable bowel syndrome (IBS), lists fecal inflammation marker (e.g., calprotectin) in the IBS Level I diagnostic cascade.

Summary
Although levels of calprotectin may be elevated in the stool of an individual with one or more of these indications there are insufficient published peer-reviewed clinical trial data to demonstrate that measurement of fecal calprotectin results in a change in clinical practice or improved patient outcomes. While prospective data is

available, controlled trial data are lacking and results regarding sensitivity and specificity are inconsistent between studies. At this time the role of fecal calprotectin testing has not been established for any indication.

Capsule Endoscopy (CPT® Codes 91110, 91111)

Wireless capsule endoscopy (WCE), or capsule endoscopy, is a noninvasive procedure in which an ingestible, multivitamin-sized capsule containing a miniaturized video camera, light, transmitter, and batteries, is swallowed. A video recording is taken as it moves through the gastrointestinal (GI) tract. The capsule was originally developed to reach inaccessible areas that standard endoscopic examination cannot reach due to significant length and distance from accessible orifices. Proponents currently support its use to view the entire gastrointestinal tract, esophagus to colon, for multiple conditions.

The most common indication for capsule endoscopy is the evaluation of obscure gastrointestinal bleeding (OGIB) after negative upper and lower endoscopy (esophagogastroduodenoscopy [EGD], push enteroscopy, colonoscopy, and small bowel radiography). Other proposed indications for capsule endoscopy include suspected Crohn's disease, diagnosing GI tumors or nonsteroidal anti-inflammatory drug (NSAID)-induced small bowel damage, abdominal pain, surveillance of polyposis syndromes, monitoring mucosal healing after various treatments (e.g., for Crohn's), assessing the extent of disease (e.g., Crohn's, celiac) and monitoring/surveillance of upper or lower GI damage (e.g., esophagitis, Barrett's, polyps) and most recently, as a replacement for colonoscopy. Some limitations to capsule endoscopy include: the device has no therapeutic capabilities; it cannot insufflate air to distend the bowel to enhance mucosal visualization; there is risk of impaction in a region of stricture; and it is difficult to discern the exact anatomic location of visualized lesions. Contraindications include: known or suspected obstruction or stricture; cardiac pacemakers; implanted defibrillators; implanted electromechanical devices; pregnancy; Zenker's diverticulum; intestinal pseudo-obstruction and motility disorders.

Two companies currently market a video capsule: Pillcam® (Given® Imaging, Ltd., Yoqneam, Israel); and the Olympus Capsule Endoscope System with Endo Capsule (Olympus Medical Systems Corporation, Tokyo, Japan). Both include the capsule that is swallowed, the data recorder (worn around patient's waist) and a computer workstation (with software and viewer/monitor).

The Given AGILE™ Patency System is an optional accessory to the PillCam video capsule and is intended to validate patency of the GI tract. The main capsule body contains a small inner radiofrequency identification (RFID) tag. The tag retransmits a radiofrequency signal once it is excited by an appropriate radiofrequency signal from the Patency Scanner. Following ingestion, detection of a radiofrequency signal by the Patency Scanner means that the capsule is still retained in the GI tract. Once the patient ingests the AGILE patency capsule, it is propelled through the GI tract by normal peristalsis. If the AGILE patency capsule is excreted structurally whole, then this indicates patency of the GI tract of the patient, and a PillCam capsule can be administered. The capsule is designed to dissolve starting 30 hours following ingestion, during a period of approximately 12 hours

U.S. Food and Drug Administration (FDA)

The FDA has classified Ingestible Telemetric Gastrointestinal Capsule Imaging System as class II devices; Product codes NEZ (System, Imaging, Gastrointestinal, Wireless, Capsule) and NSI (System, Imaging, Esophageal, Wireless, Capsule).

Small Bowel: In 2001, the PillCam® Small Bowel (SB) Capsule received clearance from the FDA for use as an adjunctive method of evaluating small bowel abnormalities in persons with unexplained or recurrent GI bleeding who have undergone conventional endoscopy and/or other diagnostic procedures that failed to locate the source of bleeding. It is intended "for visualization of the small bowel mucosa". It was originally approved as a tool in the detection of abnormalities of the small bowel in adults. In July 2003, the FDA approved the capsule endoscopy system as a first-line method for detecting small bowel abnormalities. In October 2003, the FDA approved the system for use in children ages 10–18 years.

In September 2009, FDA approved use of PillCam SB capsules to include use in children from two years of age. In May 2011, the FDA approved additional indications for use for the Given PillCam® Platform with RAPID 6.5 with PillCam® SB Capsule. The PilICam Platform with a PilICam SB capsule is intended for visualization of the small bowel mucosa. This capsule may be used in the visualization and monitoring of lesions that may indicate Crohn's disease not detected by upper and lower endoscopy. It may also be used in the visualization of lesions

that may be a source of obscure bleeding (either overt or occult) not detected by upper and lower endoscopy and in the visualization of lesions that may be potential causes of iron deficiency anemia (IDA) not detected by upper and lower endoscopy. Additionally the PillCam Platform with PillCam SB capsules may be used as a tool in the detection of abnormalities of the small bowel and is intended for use in adults and children from two years of age.

In June 2007, the FDA approved the Olympus Capsule Endoscope System Endo Capsule. The Olympus FDA-approved indications for use state it is to be used for visualization of the small intestine mucosa.

Esophageal In October 2004, FDA granted 510(k) marketing clearance for the system for visualization of the esophageal mucosa. Subsequently the FDA has granted additional clearances for device modifications, new accessories, and new or upgraded software. In May 2011, the Given PillCam® Platform with PillCam® ESO 3 Capsule received FDA approval. This system is intended for the visualization of esophageal mucosa in adults and children from 18 years of age.

Colon: In 2008, the FDA sent Given Imaging a "not substantially equivalent" (NSE) letter regarding its 510(k) application to market PillCam® COLON in the US. In 2009, Given Imaging made various upgrades, releasing PillCam® COLON 2 which has also received the CE Mark.

Other: In May 2006, the FDA granted marketing clearance for the Given AGILE™ Patency System. It is intended to verify adequate patency of the gastrointestinal tract prior to administration of the PillCam video capsule in patients with known or suspected strictures. In September 2009, FDA approved use of the AGILE Patency System to include use in children from two years of age. In June 2006, the FDA granted marketing clearance for RAPID® Access RT (real-time), a handheld device that enables real-time viewing during a PillCam endoscopy procedure and RAPID Access, the software installed on the device. RAPID Access also allows physicians to remotely initialize a Data Recorder to administer the PillCam video capsules to patients at satellite sites. Data can then be sent to a central location for processing and interpretation.

Literature Review
Evidence in published, peer-reviewed, scientific literature supports the use of capsule endoscopy in patients with obscure gastrointestinal bleeding (OGIB) with or without iron deficiency anemia (Milano, 2011; Laine, 2010; De Leusse, 2007; Apostolopoulos et al., 2007; Sturniolo et al., 2006; Qvigstad et al., 2006; Lai et al., 2006; Neu et al., 2005; Estevez et al., 2006; Hartmann et al., 2005), suspected Crohn's disease, suspected small bowel tumor and celiac disease, in which standard endoscopic and imaging evaluations are inconclusive and show no suspected obstruction or stricture. As long as contraindications are applied to patient selection, the small bowel capsule is considered safe. Small bowel capsule endoscopy (CE) can identify pathologies missed by standard endoscope; having a positive impact on clinical decision-making.

Studies evaluating the use of capsule endoscopy in suspected Crohn's disease (CD) have generally shown that capsule endoscopy detects early inflammatory lesions of the small bowel with a higher yield compared with alternative techniques (Park, et al., 2007; Fidder, et al., 2007; Girelli, et al., 2007; de Leusse, et al., 2007; Triester, et al., 2006; Sturniolo, et al., 2006; Qvigstad, et al., 2006; Hara, et al., 2006; Gay, et al., 2006; Dubcenco, et al., 2005; Eliakim, et al., 2004). Few studies are proposing capsule endoscopy for first line testing; the majority of studies, the American College of Gastroenterology (Lichtenstein, et al., 2009) and the American Society for Gastrointestinal Endoscopy (ASGE) (Leighton, et al., 2006) all support standard testing first.

Recurrence of symptoms has been predicted by the early endoscopic appearance of lesions following ileo-colonic resection for CD. There is insufficient evidence in the published peer-reviewed scientific literature to support the use of capsule endoscopy for the detection of postoperative recurrence of small bowel CD. The gold standard for assessing CD recurrence after ileo-colonic resection remains conventional ileocolonoscopy (Mergener, et. al., 2007; Pons Beltrán, et al., 2007; Biancone, et al., 2007).

Suspected Small Bowel Tumor: Small bowel tumors of all types have been a significant finding in most studies of capsule endoscopy (Mergener, et. al., 2007; Bailey, et. al., 2006; Urbain, et. al., 2006; Cobrin, et. al., 2006; Wong, et. al., 2006; van Tuyl, et. al., 2006). The studies support the use of capsule endoscopy in diagnoses such as hamartoma, cystic lymphangioma, polyps in familial adenomatous polyposis (FAP) and Peutz Jegher's syndromes, carcinoid or neuroendocrine tumor, adenocarcinoma, and gastrointestinal stromal tumor (GIST).

Celiac Disease: Celiac disease is recognized as being under-diagnosed, as many affected patients do not present with classical symptoms of malabsorption. Small retrospective and prospective studies support the use of capsule endoscopy in detecting the mucosal changes consistent with celiac disease (Atlas, et al., 2011; Ciaccio, et al., 2010; Rondonotti, et al., 2007; Hopper, et al., 2007; Culliford, et al., 2005; Petroniene, et al., 2005).

Esophageal Pathology: An esophageal capsule endoscopy procedure appears to be safe, providing contraindications are applied to patient selection. However, evidence in the peer-reviewed scientific literature demonstrates that the accuracy of the esophageal capsule is inferior to that of upper endoscopy in diagnosing esophageal pathologies, primarily varices, in a cirrhotic patient population. Evidence indicates sensitivity rates fall within the 60 – 80 percentile range. Overall accuracy rates were not provided in the studies. The majority of the studies are prospective, observational cohort studies comparing capsule endoscopy to standard upper endoscopy (EGD) which is utilized as the gold standard. In the majority of the studies, the procedures were performed on the same day. Limitations of these studies include small sample size and study populations with a high pretest probability of having pathology. This may give an overestimation of capsule endoscopy performance in detecting esophageal pathology. Additionally, the diagnostic utility esophageal capsule endoscopy can provide compared with upper endoscopy with biopsy, and in what specific population, remains unclear (Guturu et al., 2011; Chavalitdhamrong et al., 2011; Lapalus et al., 2009; Sharma et al., 2008; Heresbach et al., 2010; De Franchis et al., 2008; Galmiche et al., 2008; Lin et al., 2007; Eisen et al., 2006; Eliakim, et al., 2005). .

Guturu et al. (2011) conducted a meta-analysis of studies that compare diagnostic capabilities of esophageal capsule endoscopy (ECE) against conventional EGD in detecting esophageal varices. ECE and EGD were performed within 72 hours of each other. A total of nine studies with 619 patients were included. Compared with the gold standard of EGD, the pooled sensitivity and specificity of ECE for detecting esophageal varices were 83% and 85% respectively. The area under the curve (AUC) was 0.8961. ECE is not as accurate as EGD.

California Technology Assessment Forum (CTAF) evaluated PillCam capsule for the evaluation of esophageal disease (October, 2008) and concluded that most of the research to date has found that capsule endoscopy is a relatively safe technology and is significantly preferred by patients over EGD. EGD usually requires sedation and is rated as less pleasant and more inconvenient than capsule endoscopy. Some patients simply refuse to undergo EGD. However, since EGD is generally a safe and widely available procedure, capsule endoscopy cannot be recommended as an alternative until its performance is substantially equivalent to EGD.

Colon Pathology: There is insufficient evidence in the peer-reviewed scientific literature to support the safety or accuracy of colon capsule endoscopy. Additional larger trials are needed comparing capsule colonoscopy to conventional colonoscopy, barium radiography, and virtual (computed tomography or magnetic resonance) colonography.

Spada et al. (2011) conducted a multicenter, prospective trial to assess the accuracy of colon capsule endoscopy (CCE) in detecting patients with polyps ≥6 mm and≥10 mm or masses, using conventional colonoscopy as the reference standard. The study included 109 patients who were scheduled to undergo colonoscopy for either known or suspected colonic disease. Results are as follows: A) polyps ≥6 mm colonoscopy prevalence (number/%) 45/41%; CCE sensitivity 84%; CCE specificity 64%; B) polyps ≥10 mm colonoscopy prevalence (number/%) 32/29%; CCE sensitivity 88%; CCE specificity 95%. Positive and negative predictive values were not provided.

Pilz et al. (2010) prospectively compared capsule colonoscopy to conventional colonoscopy as the gold standard in 36 patients. Men and women above the age of 50 years without symptoms (indication for screening) or with lower gastrointestinal signs and symptoms and individuals younger than 50 years with positive family history for colorectal cancer, minimum 18 years were included in this study. The capsule was excreted within 10 hours after ingestion and within battery duration in 36 patients (64%). For polyps of any size, CCE showed a sensitivity of 79%, specificity 54%, PPV of 63% and NPV of 71%. Accuracy was not calculated.

Sacher-Huvelin et al. (2010) conducted a prospective study comparing colon capsule endoscopy to colonoscopy in patients at average or increased risk of colorectal cancer. Participants were either 1) healthy, asymptomatic individuals 50–74 years old who accept colonoscopy in the context of a screening program (average risk group),

or 2) asymptomatic patients with a personal or family history of CRC or polyps, but without colonoscopy during the preceding 3 years (increased risk group). Patients (n=545) underwent CCE on day one and colonoscopy (gold standard) on day two. CCE and colonoscopy were performed by independent endoscopists. For the 545 patients, the CCE accuracy of detection of polyps ≥6 mm or colorectal cancer was 39% for sensitivity, 88% for specificity, 47% for the positive predictive value (PPV) and 85% for the negative predictive value (NPV). Overall, colonoscopy detected more patients with polyps than did CCE with 311 (57%) patients having polyps of any size detected by colonoscopy compared with 249 seen at CCE (46%; p<0.0001, statistically significant). Regarding polyps ≥6 mm and ≥10 mm, the corresponding figures were 112 (21%) vs. 94 (17%) (p=0.097) and 43 (8%) vs. 29 (5%) (p=0.03, statistically significant), respectively.

Rokkas et al. (2010) reported results in a meta-analysis from four studies that contained data concerning polyps found (of any size). The pooled data (random effects analysis) showed colon capsule endoscopy sensitivity of 73% and specificity of 89%. The total number of patients included in the four studies is not reported.

Gay et al. (2010) prospectively compared colonoscopy and capsule endoscopy in a cohort of 128 patients in whom colonoscopy was scheduled. Colonoscopy was the gold standard and was performed the day after capsule endoscopy. The primary outcome of the study was the decision made by the capsule endoscopy reader to indicate a colonoscopy, compared with the final result of the colonoscopy. Secondary outcomes were the agreement between capsule endoscopy and colonoscopy for making a diagnosis of colorectal disease, as well as detection rate, number, and size of polyps. Two patients were excluded: one did not swallow the capsule and the other was diagnosed with a jejunal stenosis by the capsule. Results showed the sensitivity of capsule endoscopy to detect colonic findings was 87.5% and its specificity was 75.8 %. The sensitivity of capsule endoscopy for the detection of polyps of any size was 65.9 %. The authors reported that the PPV and NPV of capsule endoscopy to indicate a colonoscopy were 78.9% and 85.4 %, respectively. It should be noted that the accuracy of the capsule endoscopy to select patients who deserve a colonoscopy was assessed by calculating the PPV and NPV of the capsule endoscopy, according to a range of prevalence of colonic diseases obtained from data in literature and in the study.

Van Gossum et al. (2009) conducted a prospective, observational cohort study including 320 patients scheduled to undergo a colonoscopy because they were either known to have colonic disease or suspected of having colonic disease. There were 112 patients (35.0%) with known colonic disease (57 were ≥50 years of age) and 208 (65.0%) with suspected colonic disease (201 were ≥50 years of age). The purpose of the study was to determine the accuracy of capsule endoscopy in detecting colonic polyps, advanced adenomas, and carcinomas. Colonoscopy was the standard against which capsule endoscopy was compared, and it was performed after capsule endoscopy (after capsule excretion or at least ten hours after capsule ingestion, whichever came first), on either the same day as ingestion or the next morning. The sensitivity and specificity of capsule endoscopy for the detection of polyps was 72% and 78%. The sensitivity and specificity of capsule endoscopy for the detection of advanced adenoma was 85% and 50%. The sensitivity and specificity of capsule endoscopy for the detection of colorectal cancer was 74% and 74%. Overall accuracy was not calculated.

Eliakim et al. (2009) also conducted a prospective, observational cohort study to test the sensitivity of an updated (second-generation) capsule. Colonoscopy was performed after capsule endoscopy. A total of 98 patients scheduled to undergo a colonoscopy because they have known or suspected colonic disease, were included. The capsule sensitivity for the detection of patients with polyps' ≥6 mm was 89 % and for those with polyps' ≥10 mm it was 88 %, with specificities of 76 % and 89 %, respectively.

Eliakim et al. (2006) evaluated 84 patients referred for colonoscopy for colorectal cancer screening (43%), postpolypectomy surveillance (26 %), rectal bleeding (14%), iron deficiency anemia (8%) and "other" (9%). PillCam COLON endoscopy and conventional colonoscopy were performed the same day. Based upon the principal investigator's reading and compared with conventional colonoscopy in the detection of any polyp, the sensitivity, specificity, PPV and NPV of capsule endoscopy were 56%, 69%, 57%, and 67%, respectively. For the detection of significant polyps, the sensitivity, specificity, and positive and negative predictive values of capsule endoscopy were 50%, 83%, 40%, and 88%, respectively. For the detection of diverticulosis, the sensitivity, specificity, and positive and negative predictive values of capsule endoscopy were 78%, 76%, 47%, and 93%, respectively.

Schoofs et al. (2006) prospectively evaluated 36 patients referred for screening colonoscopy or there if was suspicion of polyps or colorectal cancer. Compared with conventional colonoscopy in the detection of any polyp,

the sensitivity, specificity, PPV and NPV of CE were 76%, 64%, 83%, and 54%, respectively. For the detection of three polyps or more, the sensitivity, specificity, PPV and NPV of capsule endoscopy were 63%, 68%, 36%, and 86%, respectively. The authors noted that results are encouraging, and that additional larger trials are needed. The future role of capsule colonoscopy in colon cancer screening and surveillance remains to be determined.

Other: There is a paucity of studies for other indications such as abdominal pain. Additional well-designed studies are needed.

Patency Capsule: Some small retrospective and prospective studies have evaluated the patency capsule. These studies do not demonstrate that the patency capsule can safely be used in lieu of conventional evaluations to rule out stricture or obstruction prior to capsule endoscopy; therefore, the medical necessity of the patency capsule is unclear (Herrerias, et al., 2008; Spada, et al., 2007; Signorelli, et al., 2006 ; Delvaux, et al., 2005).

Professional Societies/Organizations
American Gastroenterological Association (AGA): The AGA medical position statement on obscure gastrointestinal bleeding (Raju, et al., 2007) supports the use of capsule endoscopy once all the findings on standard examinations (EGD and colonoscopy) are negative.

American Society for Gastrointestinal Endoscopy (ASGE): The ASGE Report on Emerging Technology Capsule Endoscopy of the Colon (October, 2008), notes that colon capsule endoscopy is an emerging form of colon imaging that may be useful to improve compliance with colorectal cancer screening, but published experience with this device is extremely limited. Because the technology is currently only diagnostic, any positive findings require conventional colonoscopy for tissue sampling or polypectomy. Further, significant research on this topic is required, and many fundamental questions for this technology remain unaddressed.

The ASGE published Technology Status Evaluation Report: Wireless Capsule Endoscopy in April 2006 (Mishkin, et al., 2006). Mishkin noted that wireless capsule endoscopy is a relatively new technology for assessment of the digestive tract. Small intestinal applications are the most extensively studied, and it has quickly become a first-line test for visualizing the mucosa of the small intestine. Further research and experience are still necessary to better define its role. The esophageal capsule uses similar technology but clinical data on its use are limited.

Endoscopy in the Diagnosis and Treatment of Inflammatory Bowel Disease (Leighton, et al., 2006) notes that capsule endoscopy has been shown to be more sensitive than radiologic and endoscopic procedures for detecting small-bowel lesions (based upon observational studies).

American College of Gastroenterology (ACG): The ACG practice parameter for the management of Crohn's disease in adults (Lichtenstein, et al., 2009) supports the use of capsule endoscopy.

The ACG updated guidelines for the diagnosis, surveillance and therapy of Barrett's esophagus (Wang, et al., 2008) discusses capsule endoscopy under Screening. The ACG states that esophageal capsule endoscopy is a new technique that has the potential to provide a noninvasive diagnosis of suspected Barrett's esophagus, i.e. a columnar lined esophagus. The ACG noted “although intriguing, this technique cannot be recommended in the screening setting at this time.”

The ACG Practice Parameter Prevention and Management of Gastroesophageal Varices and Variceal Hemorrhage in Cirrhosis (Garcia-Tsao, et al., 2007) stated “capsule endoscopy may play a future role in screening for esophageal varices if additional larger studies support its use.”

ACG Practice Guidelines for the Management of Dyspepsia (Talley, et al., 2005) state that regarding additional diagnoses and testing in refractory cases, capsule endoscopy “does not yet have an established role here.”

Use Outside of the US: No relevant information.

Summary

The published, peer-reviewed scientific literature supports the safety and clinical utility of small bowel capsule endoscopy as an adjunctive diagnostic tool for patients with obscure gastrointestinal bleeding (OGIB), suspected Crohn's disease, and suspected small bowel tumor and celiac disease. Evidence indicates that the accuracy of esophageal capsule endoscopy is inferior to that of upper endoscopy in diagnosing suspected esophageal pathologies. Additionally, the role of capsule endoscopy in diagnosing suspected esophageal pathology has yet to be determined. The safety and diagnostic utility of capsule endoscopy for any other indication (e.g., any screening or surveillance, colon pathology) has not yet been established. Also, there is limited data on patient safety when using the patency capsule versus conventional evaluations to rule out stricture or obstruction prior to capsule endoscopy; therefore, conventional evaluations remain the gold standard for ruling out any known or suspected gastrointestinal obstruction, strictures, and fistulas prior to capsule endoscopy.

Wireless Gastrointestinal Motility Monitoring System (SmartPill®) (CPT® Code 91112)

The SmartPill Gastrointestinal (GI) Monitoring System® (The SmartPill Corporation, Buffalo, NY) has been proposed as an alternative testing method for the diagnosis of gastric conditions and intestinal motility disorders such as gastroparesis and chronic constipation. The system records pH and pressure measurements from the entire length of the gastrointestinal tract for use by physicians to aid in the evaluation of gastrointestinal motility diseases and conditions. Sensors on board an ingestible capsule measure pH and pressure as the capsule travels the length of the GI tract. Measurements are transmitted from the capsule within the GI tract via radiofrequency signal to a patient worn receiver and subsequently downloaded for analysis and review. Next, software performs data analyses providing the physician with a printable report containing regional gut transit times: gastric emptying or transit time (GET), small bowel transit time (SBTT), combined small and large bowel transit time (SLBTT), colonic transit time (CTT) and whole gut transit time (WGTT). The capsule is expelled naturally from the body.

U.S. Food and Drug Administration (FDA)

The SmartPill GI Monitoring System® was approved in 2006 by the U.S. by the Food and Drug Administration (FDA) under the 510(k) process. Indications for use state SmartPill is used in evaluating patients with suspected gastroparesis. In October 2009, the SmartPill was FDA-approved for the evaluation of colonic transit in patients with chronic constipation, to aid in differentiating slow and normal transit constipation. It is not indicated for use in children.

Literature Review

Published studies in the peer-reviewed scientific literature are observational or retrospectively conducted with small populations. Although well-established motility testing methods exist, studies are not designed to provide comparison of the accuracy—including sensitivity, specificity, positive and negative predictive values— of the SmartPill to conventional tests as the reference standard in same symptomatic patient population. As a result no strong conclusions can be made regarding the clinical utility of this technology (Kuo, 2011; Rao, 2011; Camilleri, 2010; Kloetzer, 2010; Sarsiek, 2010; Rao, 2009; Hasler, 2009; Kup, 2008).

Professional Societies/Organizations

American Neurogastroenterology and Motility Society (ANMS)/ Society of Nuclear Medicine (SNM): The ANMS/SNM Consensus Recommendations for Gastric Emptying Scintigraphy states that GES is the standard for the measurement of gastric motility in clinical practice (Abell, et al., 2008). The SNM Procedure Guideline for Adult Solid Meal Gastric Emptying Study (2009) states that radionuclide studies of gastric emptying and motility are the most comprehensive and physiologic studies available for studying gastric motor function. The study is noninvasive, uses a physiologic meal (solids with/without liquids), and is quantitative. Serial testing can determine the effectiveness of therapy. The SNM states that the standard measurement of gastric emptying is based on the percentage of gastric retention at specific times after meal ingestion (e.g., at 2, 3, and 4 hours).

American Gastroenterological Association (AGA): The AGA Medical Position Statement 'Diagnosis and Treatment of Gastroparesis' (Parkman, et al., 2004) states that GES of a radiolabeled solid meal is the best accepted method to test for delayed gastric emptying. The AGA Medical Position Statement Guidelines on Constipation (AGA, 2013) supports the use of special tests such as CTT, anorectal manometry, balloon-expulsion tests or defecography in refractory patients. Neither guideline addresses the use of SmartPill.

American Society of Colon and Rectal Surgeons (ASCRS): The ASCRS practice parameter for the evaluation and management of constipation notes that anorectal physiology and colon transit time investigations

may help to identify the underlying etiology and improve the outcome in patients with refractory constipation. The practice position notes the measurement of colon transit time using radio-opaque markers in patients with suspected slow-transit constipation is inexpensive, simple, and safe (Ternent, et al., 2007).

North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHN): The NASPGHN recommendations on evaluation and treatment of constipation in infants and children (2006) notes that an evaluation of colonic transit time with radiopaque markers may be helpful in children with a history of infrequent bowel movements who have no objective findings of constipation.

Use Outside of the US: No relevant information.

Summary
Evidence in the published, peer-reviewed scientific literature is insufficient to establish the accuracy or clinical utility of the SmartPill Gastrointestinal Monitoring System® for any indication. Large population well-designed, prospective, comparative trials are needed, comparing SmartPill with established gastrointestinal motility diagnostic tools in the same population.

Endovascular Repair of Aortic Aneurysm (CPT® Codes 34806, 34841, 34842, 34843, 34844, 34845, 34846, 34847, 34848, 93982, 0078T, 0079T, 0080T, 0081T)
The conventional treatment for AAA has been open surgical repair. Open surgical repair involves transabdominal surgery, exposure of the aneurysm, cross-clamping the aorta, resection of the aneurysm, and placement of graft prosthesis. Endovascular AAA repair developed as a minimally invasive alternative to open surgical repair in patients with suitable anatomy (ECRI, 2008). Endovascular repair of infrarenal abdominal or aortoiliac AAA has demonstrated reduced rates of perioperative mortality and morbidity compared to open surgical repair, with equivalent long-term aneurysm-related mortality, although this approach is associated with higher rates of reintervention, and requires long-term radiological monitoring. Endovascular repair may be a reasonable option for selected patients with suitable anatomy for whom the risk/benefit ratio favors endovascular repair.

The use of fenestrated grafts (e.g., Zenith® Fenestrated AAA Endovascular Graft) has been investigated for the treatment of patients with AAA involving the visceral arteries. These grafts include fenestrations, or scallops, in the graft material that allow the proximal edge of the material to be placed above the renal arteries while permitting blood flow to vessels accommodated by the fenestrations. Evidence published in the medical literature consists primarily of registry data, small feasibility studies, and case series with limited outcome data Additional evidence is needed to determine the safety, efficacy, and long-term outcomes of this procedure and to determine how this approach compares to surgical repair.

U.S. Food and Drug Administration (FDA)
A number of devices have received approval through the FDA Premarket Approval (PMA) process for endovascular treatment of AAA, including the following:

- AneuRx® Stent Graft System (Medtronic Vascular, Santa Rosa, CA)
- Zenith® AAA Endovascular Graft and H&L-B One-Shot™ Introduction System (Cook Incorpora32ed, Bloomington, IN)
- EXCLUDER™ Bifurcated Endoprosthesis (W.L. Gore & Associates, Inc., Flagstaff, AZ)
- Endologix PowerLink® System (Endologix, Inc., Irvine, CA).
- Talent™ Abdominal Stent Graft System (Medtronic Vascular, Santa Rosa, CA)
- Endurant Stent Graft System (Medtronic Vascular, Santa Rosa, CA)

The Zenith® Fenestrated AAA Endovascular Graft (with the adjunctive Zenith Alignment Stent) received FDA PMA approval on December 22, 2011. The Zenith graft is indicated for the endovascular treatment of patients with abdominal aortic or aortoiliac aneurysm having morphology suitable for endovascular repair, including:

- Adequate iliac/femoral access compatible with required introduction systems
- Nonaneurysmal infrarenal aortic segment (neck) proximal to the aneurysms with:
  - Length ≥ 4 mm and unsuitable for a non-fenestrated graft
  - Diameter ≤ 31 mm and ≥ 19 mm

  - Angle < 45 degrees relative to long axis of aneurysm
  - Angle < 45 degrees relative to axis of suprarenal aorta
- Ipsilateral iliac artery fixation site > 30 mm in length and between 9- 21 mm in diameter
- Contralateral iliac artery distal fixation site >30 mm in length and between 7 - 21 mm in diameter

The Zenith Alignment Stent is indicated for use as an adjunct to the Zenith Fenestrated AAA Endovascular Graft to secure positive alignment of fenestrations or scallops with the orifice of aortic branch vessels having diameters ranging from 3 to 8 mm. Unlike the standard Zenith AAA Endovascular Graft, the Zenith Fenestrated AAA graft has fenestrations or scallops in the graft material, which allow the proximal edge of graft material to be placed above the renal arteries while still permitting blood flow to vessels accommodated by the fenestrations or scallops. In order to account for anatomical variation, each proximal body graft is made to order for a specific patient. The Zenith fenestrated graft has been available outside the U.S. since 2002.

Literature Review
The British Society for the Endovascular Therapy and the Global Collaborators on Advanced Stent-Graft Repair (GLOBALSTAR) Registry published early results of endovascular repair of juxtarenal aortic aneurysms using the Zenith fenestrated graft in the United Kingdom. Data from 318 patients treated at 14 experienced centers (i.e., > 10 procedures) were retrospectively studied. The primary procedural success rate was 99% (316/318); perioperative mortality was 4.1%; and intraoperative target vessel loss was observed in 5 of 889 target vessels (0.6%). The early reintervention rate (i.e., < 30 days) was 7%. There were 11 deaths during the follow-up, but none were aneurysm-related. Freedom from target-vessel loss at one, two, and three years was 93%, 91%, and 85%, respectively, and freedom from late secondary intervention (> 30 days) was 90%, 86%, and 70% at one, two and three years, respectively. The authors stated that these results support continued use and evaluation of this technique for juxtarenal aneurysms, but illustrate the need for a more robust evidence base.

Amiot et al. (2010) conducted a retrospective analysis to evaluate the medium-term outcomes of aortic aneurysm repair using the Zenith fenestrated graft in 16 French academic centers (n=134). Patients were considered to be at high risk for open surgical repair. The median aneurysm size was 56 mm (range 45-91 mm), and the median patient age was 73 years (range 43-91 years). A total of 403 visceral vessels were treated, including 265 renal arteries. One early conversion to surgery was required. Angiography immediately following the procedure demonstrated patency in 398 of 403 target vessels. The 30-day mortality was 2%. Imaging prior to discharge revealed 16 (12%) endoleaks (3 type I, 12 type II, and 1 type III). Transient or permanent dialysis was required in 4 (3%) and two (1%) patients, respectively. During a median follow-up of 15 months (range 2-53 months), no aneurysms ruptured or required open conversion. Aneurysm sac size decreased by more than 5 mm in 52%, 65.6%, and 75% of patients at one, two and three years, respectively. Three patients had sac enlargement within the first year associated with persistent endoleaks. Four renal artery occlusions were detected during follow-up, and 12 procedures related to reintervention were performed in 12 patients, including six to correct endoleaks and five to correct threatened visceral vessels. Twelve of 131 patients died during follow-up; none of these were aneurysm related.

Greenberg et al. (2009) reported intermediate results of a multicenter prospective case series to assess the safety and efficacy of the Zenith fenestrated devices (n=30) in patients with juxtarenal AAA. Inclusion criteria consisted of aortic or aortoiliac aneurysms with diameter greater than five cm, or with aortic or aortoiliac aneurysms with a history of growth greater than 0.5 cm per year or clinical indication for AAA repair. Customized devices were designed for each patient based on calculations derived from computed tomography (CT) scan data. A total of 77 visceral vessels were accommodated by fenestrations within the sealing segment of the grafts. The most common design accommodated two renal arteries and the superior mesenteric artery (66.7%). Prostheses were successfully implanted in all patients. Of the 30 patients, 27 were available for follow up at 12 months, and 23 were available at 24 months. There were no aneurysm related deaths, aneurysm ruptures, or conversions during the follow-up period. There were no type I or type III endoleaks reported. Type II endoleaks were reported in six patients (26.1%) at 12 months, and in four (20.0%) at 24 months. None of the patients had aneurysm growth > 5 mm. Aneurysm size at 24 months decreased in 16 of 23 patients (69.6%) and was stable in the remaining patients. A renal event occurred in eight patients (4 renal artery stenoses, two renal artery occlusions, and two renal infarcts). Secondary interventions were performed in five patients. No patients experienced renal failure requiring dialysis. The authors concluded that the intermediate term results of this multicenter study are concordant with previous single-center studies and support the concept the placement of fenestrated endovascular grafts is safe and effective at centers with experience in endovascular repair and renal/mesenteric stent placement.

An Agency for Healthcare Research and Quality (AHRQ) evidence report/technology assessment (Wilt et al., 2006) compared endovascular and open surgical repairs for AAA. Randomized controlled trials of open surgical repair, endovascular repair, or active surveillance; systematic reviews; nonrandomized U.S. trials; and national registries were used to assess clinical outcomes. The assessment concluded that for AAA < 5.5 cm in diameter, active surveillance with delayed open surgical repair results in equivalent mortality, but less morbidity, due to fewer interventions, compared to immediate open surgical repair. Endovascular repair of aneurysms ≥ 5.5 cm has not been shown to improve long-term survival or health status compared to open surgical repair, although perioperative outcomes are improved. The assessment also stated that endovascular repair does not improve survival in patients who are medically unfit for open surgical repair. Endovascular repair is associated with more complications, need for reintervention, and monitoring compared to open surgical repair or no intervention. The AHRQ report recommended U.S. randomized controlled trials be conducted with approved endovascular repair devices to evaluate patient outcomes.

Implanted Wireless Pressure Sensor
The CardioMEMS EndoSure™ Wireless AAA Pressure Measurement System was approved for marketing through the 510(k) process on October 12, 2006 for the measurement of intrasac pressure during endovascular AAA repair and for use as an adjunctive tool in the detection of intraoperative leaks. In a subsequent approval on March 15, 2007, measurement of intrasac pressure during thoracic aortic aneurysm repair was added as an intended use.

According to the 510(k) summary, the sensor is implanted in the aneurysm sac during stent graft deployment and is left in place in the excluded portion of the aneurysm as a permanent implant. The main body of the sensor is composed of fused silica coated in silicone. Nitinol loops extend from and surround the sensor body. The sensor is interrogated using the antenna of the EndoSure Electronics System. Once the signal is acquired, a pressure waveform and numerical pressure data are displayed on the touch-screen, and a printout of the data and waveform is generated.

Published evidence on the use of the CardioMEMS system consists of several diagnostic cohort studies with short-term preliminary results (Hoppe et al., 2008, n=12; Silveira et al., 2008, n=25; Ohki et al., 2007, n=76). The safety and clinical utility of this technology in the intraoperative or long-term monitoring of patients following endovascular aortic aneurysm repair has not been established.

Use Outside of the US: No relevant information.

Summary
The use of fenestrated grafts (e.g., Zenith® Fenestrated AAA Endovascular Graft) has been investigated for the treatment of patients with AAA involving the visceral arteries. Evidence published in the medical literature to date consists primarily of registry data, small feasibility studies, and case series with limited outcome data Additional evidence is needed to determine the safety, efficacy, and long-term outcomes of this procedure and to determine how this approach compares to surgical repair. Implantable wireless pressure sensor monitoring (e.g., CardioMEMS EndoSure™ Wireless AAA Pressure Measurement System) has been proposed as a method to provide intraoperative and long-term monitoring of pressure within the aneurysm in conjunction with endovascular aneurysm repair. The safety and clinical utility of this technology have not been established.

Sublingual Immunotherapy (SLIT Therapy) (CPT® Codes 95199)
Standardized allergen extracts can be administered under the tongue to allow absorption through the sublingual mucosa. SLIT is used in Europe, and clinical experience with this technique is growing in both children and adults. SLIT has been studied as a therapy for patients with asthma and/or allergic rhinitis for treatment of a number of allergies. Because of mixed study results, the therapy is controversial. Questions remain about the optimal dosing, duration of treatment, and the use of multiple allergens. There are limited studies comparing sublingual immunotherapy to standard subcutaneous immunotherapy. Additionally, there is no U.S. Food and Drug Administration (FDA)-approved antigen preparation.

Lin et al. (2013) and colleagues reported results of a comparative effectiveness review of 60 studies comparing SLIT therapy to placebo or another intervention for the treatment of allergic rhinoconjunctivitis and/or asthma. Studies evaluated seasonal allergens, perennial allergens, or both. Sixty-eight percent of studies were considered to have a moderate risk of bias and 14% to have a high risk of bias, and there was heterogeneity

among studies regarding type of allergen extracts, sources of allergen extracts, doses, treatment duration, and outcome scoring systems. Eighty-five percent of studies evaluating sublingual immunotherapy had at least a medium risk of bias. Sixty-one percent of sublingual studies had industry support in the form of either funding and/or supplies. Regarding safety of sublingual immunotherapy the authors note the strength of evidence was insufficient for definitive statements, although few serious events were reported. Data were as also insufficient to describe the strength of evidence regarding efficacy or safety of sublingual immunotherapy for the elderly, pregnant women, racial and ethnic minorities, inner-city residents, rural residents, individuals with severe asthma, and children. Although overall the review concluded that there is high-grade evidence that SLIT improves asthma symptoms compared to placebo or another intervention and moderate-grade evidence that SLIT improves rhinitis/rhinoconjunctivitis symptoms compared to placebo or another intervention. There was moderate-grade evidence that SLIT improves other outcomes in this population, such as decreased medication use and increased quality of life. However, given the risk of bias and insufficient data regarding safety and effectiveness in multiple subpopulations additional high quality controlled trials are required before this therapy can be considered for routine use in clinical practice.

Calderon et al (2011) reported results of a Cochrane metaanalysis evaluating the effectiveness of SLIT compared with placebo for reductions in ocular symptoms, topical ocular medication requirements and conjunctival immediate allergen sensitivity in 42 studies involving 3958 patients (SLIT n= 2011, placebo 1947). Primary outcome was the total ocular symptom scores and secondary outcomes reported included individual ocular symptom scores, ocular medication scores, conjunctival immediate allergen sensitivity. Use of sublingual immunotherapy demonstrated a reduction in total ocular symptom scores, individual ocular symptom scores for red eyes, itchy eyes, and watery eyes ($p < 0.0001$ all symptoms) compared to placebo. No significant reduction was observed in ocular eye drops use ($p= 0.13$). The authors noted that the overall quality of the evidence was assessed to be low to moderate due in part to limitations with the description of allocation concealment in some studies, moderate statistical heterogeneity and possible publication bias. Further, large definitive trials are required as well as head-to-head comparative studies with currently available anti-allergic drugs. Whether SLIT may result in long-term benefits after discontinuation of therapy is an important question that warrants further evaluation. Further studies evaluating the mechanisms of SLIT are needed. There is a need to develop and validate standard instruments, such as questionnaires with adequate psychometrical properties, in this field of research, which would also make future studies more comparable and adequate for meta-analysis. There is need for further large rigorously designed studies that examine long-term effectiveness after discontinuation of treatment and establish the cost-effectiveness of SLIT.

De Bot et al. (2013) assessed the quality of systematic reviews and meta-analyses of sublingual immunotherapy (SLIT) for allergic rhinitis in children, published since 2000. Ten systematic reviews were included in the assessment. Of the 10 reviews, the six reviews with the highest overall score scored 5–8 points on the Assessment of Multiple Systematic Reviews (AMSTAR) quality evaluation tool, indicating moderate quality. The authors noted that SLIT for children could be promising, but methodological flaws in the reviews and individual studies preclude the ability to draw definite conclusions.

In a systematic review and meta-analysis, DiBona et al. (2010) assessed the effectiveness of SLIT with grass allergens in the reduction of symptoms and medication in patients with seasonal allergic rhinitis to grass pollen. Studies were included if they were double-blind randomized controlled trials (RCTs) comparing SLIT to placebo and if they included patients with history of allergy to grass pollen treated with natural grass pollen extracts. Nineteen RCTs with 2971 patients were analyzed. The outcomes assessed were symptom and medication scores. The authors reported that SLIT with grass allergens significantly reduces both symptoms (standardized mean difference, -0.32; 95% CI, -0.44 to -0.21) and medication use (standardized mean difference, -0.33; 95% CI, -0.50 to -0.16) compared with placebo. The treatment was more efficacious in adults than in children. Prolonging duration of preseasonal treatment for more than 12 weeks improves the treatment efficacy. The authors reported that SLIT with grass allergens is effective in patients with seasonal allergic rhinitis compared with placebo. The benefit is clinically modest, and criteria are needed to identify patients most likely to benefit from SLIT.

In a Cochrane study, Calamita et al. (2006) conducted a systematic review and meta-analysis of SLIT for the treatment of asthma. A total of 25 studies with 1706 patients were included in the meta-analysis. The authors concluded that their meta-analysis did not demonstrate a definitive result regarding the efficacy of SLIT for asthma treatment. The authors stated further studies are needed to investigate the optimal maintenance doses

and the length of treatment, identify whether there are subsets of patients that will respond better to treatment, and analyze the adherence to treatment.

In a Cochrane review, Wilson et al. (2004) conducted a systematic review and meta-analysis of SLIT for the treatment for allergic rhinitis. The authors identified 22 randomized controlled trials involving 979 patients. Only two of the studies compared injection therapy with SLIT. The studies reported similar improvements in symptoms and medication requirements. The authors found heterogeneity in the findings, due to varying methods used to administer SLIT and different clinical response scoring systems. Overall, SLIT therapy was followed by a significant reduction in mean symptom scores (p=0.002) and medication use (p=0.0003) when compared to placebo therapy. There were no significant variations in response to the use of different allergens in the SLIT studies. The total amount of allergen delivered may be a determinant of SLIT success, but the increasing time duration of SLIT did not clearly increase efficacy. SLIT did not appear to be effective in studies limited to allergic children; however, the numbers of children in such studies were too small to draw definitive conclusions. The subgroup analyses did not suggest a benefit for SLIT treatment in any particular patient or disease group. The content of this review was edited in 2011 with no change to the conclusions.

Professional Societies/Organizations
American Academy of Allergy, Asthma and Immunology/American College of Allergy, Asthma and Immunology/Joint Council of Allergy, Asthma and Immunology (2011): The Joint Task Force issued updated practice parameters for allergen immunotherapy. The guideline notes that RCTs of the use of SLIT for allergic rhinitis and asthma have demonstrated significant improvement in symptoms. However, the safety and efficacy of oral and sublingual immunotherapy for food hypersensitivity is currently investigational. The guideline further notes that oral and sublingual food immunotherapy is investigational. Further, the authors note that there are no FDA approved extract formulations for a non-injection route of immunotherapy.

American College of Allergy, Asthma, and Immunotherapy ([ACAAI], 2010): In its discussion of sublingual immunotherapy (SLIT) therapy for patients and the public the ACAAI notes SLIT is widely accepted and used in European, South American, and Asian countries as well as in Australia and is gaining interest from allergists in the United States. However, as neither the safety nor the efficacy of the procedure is as yet considered established by the FDA, SLIT is not approved in the United States and its usage is off-label. Trials for FDA registration are ongoing, with aspects of therapy including best dose and treatment duration, lasting effect and the exact way SLIT works are all under investigation.

Use Outside of the US: Singapore Ministry of Health (2010): The guideline regarding management of rhinosinusitis and allergic rhinitis notes that sublingual immunotherapy (SLIT) should be considered in children above age 5 years who have poor symptomatic control of allergic rhinitis despite maximal therapy or who cannot or will not take medication.

World Health Organization ([WHO], 2010): WHO published guidelines regarding allergic rhinitis and its impact on Asthma. The guideline panel suggests “Sublingual allergen specific immunotherapy in adults with rhinitis due to pollen (conditional recommendation | moderate quality evidence) or house dust mites (conditional recommendation | low quality evidence).” The guidelines also notes “In children with allergic rhinitis due to pollens, the guideline panel suggests sublingual allergen-specific immunotherapy (conditional recommendation | moderate quality evidence). In children with allergic rhinitis due to house dust mites, the guideline panel suggests that clinicians do not administer sublingual immunotherapy outside rigorously designed clinical trials (conditional recommendation | very low quality evidence).”

Holtranscobalamin Testing (CPT® Code 0103T)
Vitamin B12, also known as cobalamin is a water soluble vitamin important in normal neurologic functioning and the formation of red blood cells. Measurement of total serum cobalamin may be used to detect a deficiency state (i.e., <200pg/mL). Sensitivity and specificity of this test is poor in part because serum levels do not always correlate with body stores (Hogenauer, 2011). Only a portion of cobalamin is metabolically active (i.e., transcobalamin). Transcobalamin-cobalamin complex (i.e., holotranscobalamin or holo-TC) testing has been proposed as an alternative measurement of vitamin B12 deficiency. Testing may be by radio- or enzyme immunoassay.

U.S. Food and Drug Administration (FDA)

In January 2004, the HoloTC RIA device (Axis-Shield Biochemicals, ASA, San Diego, CA) was determined by the FDA to be substantially equivalent as an in-vitro diagnostic assay for quantitative measurement of cobalamin (vitamin B12) bound to the carrier protein transcobalamin in human serum or blood.

Literature Review
Randomized controlled trial (RCT) data are scarce in the published peer-reviewed scientific literature regarding the effectiveness of holotranscobalamin testing for the diagnosis of vitamin B12 deficiency or for use in monitoring response to therapy. Hoey et al (2009) reported results of a systematic review which assessed the effectiveness of biomarkers: vitamin B12, methylmalonic acid and total homocysteine in determining vitamin B12 status in eight RCTs. All studies measured serum and plasma total vitamin B12. All biomarkers were found to be effective measures of altered vitamin B-12 intake in populations with low and borderline baseline vitamin B-12 status (p<, 0.00001); however, in the case of total vitamin B-12, substantial heterogeneity that could not be fully explained by subgroup analysis was observed. Insufficient data were available to determine the effectiveness of plasma holotranscobalamin, which was measured in only one RCT.

Use Outside of the US: No relevant information

Summary
Data are lacking regarding the effectiveness of holotranscobalamin testing to determine vitamin B12 deficiency. At present the role of this testing has not been established.

Quantitative Sensory Testing (QST)(CPT® Codes 0106T, 0107T, 0108T, 0109T, 0110T, HCPCS Code G0255)
QST is a psychophysical test used to assess and quantify small and large-fiber sensory nerve function by the use of touch, thermal (i.e., hot and cold), pain, and/or vibratory sensations. QST, a noninvasive study, is proposed to be able to detect early, subtle changes in small and large sensory nerve fibers. It has been proposed as a complementary diagnostic and monitoring tool to be used with traditional testing (e.g., Semmes-Weinstein monofilaments, Rydel Seiffert graduated tuning fork) for the detection of sensory nerve abnormalities for conditions such as diabetic neuropathy, carpal tunnel syndrome, multiple sclerosis and vitamin B deficiencies. QST has also been proposed for multiple other indications including: identifying HIV-associated peripheral neuropathy, use before and after lumbar discectomy to analyze sensory nerve dysfunction in the lower-extremities, following greater saphenous vein stripping to evaluate postoperative sensory changes, and prior to and following spinal cord stimulation for patients with chronic neuropathic pain due to either failed back surgery syndrome or complex regional pain syndrome, evaluation of sexual dysfunction, peripheral nerve dysfunction, painful bladder syndrome, and radiculopathy.

Several limitations of QST have been documented including a potential for bias if the patient is cognitively impaired or desires an abnormal result. QST has no localizing value because it is reflective of the integrity of the entire sensory neuraxis from receptors to brain. Abnormal QST values may occur because of peripheral nerve or central nervous system dysfunction. The test may lack objectivity due to patient status (e.g., distraction, boredom, inattention, fatigue, drowsiness), which may be enhanced by the time it takes to complete the test (e.g., one to two hours). The inclusion of the patient's reaction time to a stimulus may distort the actual sensory threshold. Electrode size, site of stimulation, method and rate of change of the stimulation, method of obtaining patient's response, and variations in testing devices make reproducibility of the test results difficult. There is also a lack of standardization for testing procedures and reporting outcomes, therefore test execution may differ with different examiners. Due to these variables, it is proposed that quantitative sensory testing (QST) lacks the objectivity of conventional nerve conduction studies (Pavlaković and Petzke, 2010; Backonja, 2009; Siemionow, 2006; Chong and Cros, 2004; Freemen, 2003; Shy, 2003).

The various testing methods and devices used for QST to determine sensory abnormalities include:

- Electrical current testing such as current perception threshold (CPT) testing or sensory nerve conduction testing (sNCT) which assesses sensory function. Examples of these devices include the Medi-DX 7000 (Neuro-Diagnostic Associates, Laguna Beach, CA) and the Neurometer® CPT or s-NCT (Neurotron, Inc., Baltimore, MD).
- Pressure-specified sensory testing evaluates nerve function by detection of light, status, and moving touch. Devices include the NK Pressure-Specified Sensory Device™ (PSSD) (NK Biotechnical Engineering Co., Minneapolis, MN).

- Thermal testing is used to assess a distinction between predominantly C fiber and A-delta fiber activity by the application of cold and heat. Examples of thermal devices by Medoc Advanced Medical Systems LTD (Minneapolis, MN) include the Contact Heat-Evoked Potential Stimulator (CHEPS), GSA Genito, TSA-2001 Sensory Analyzer, and the TSA-2001 Sensory Analyzer.
- Vibration perception threshold testing, or vibratory testing, assesses large myelinated nerve fiber dysfunction and measures sensory thresholds. The VSA-3000 Vibratory Sensory Analyzer (Medoc Advanced Medical Systems, Eilat, Israel) and the Bio-thesiometer (Bio-Medical Instruments, Newbury, OH) are examples of these devices.
- Voltage-actuated sensory nerve conduction threshold (V-sNCT) testing is used to evaluate the sensitivity, specificity and predictive value of A-delta fibers to assess localize pain sources. These devices include the Neural-Scan (Neuro-Diagnostic Associates [NDA], Inc., Laguna Beach, CA).

U.S. Food and Drug Administration (FDA): QST systems and devices are approved by the FDA 510(k) process and are classified either as a Class II device or an unclassified device.

Literature Review
The clinical significance of QST has not been demonstrated in clinical trials (Atherton, 2007; Soomekh, 2006; Chong and Cros, 2004; Shy, 2003). Additionally, evidence in the published peer-reviewed scientific literature does not support the clinical utility of QST. Randomized controlled clinical trial data are scarce; studies are primarily in the form of nonrandomized comparative studies and case series with heterogeneous small patient populations, using a variety of different devices. QST has not been recommended as a stand alone test. Limitations of the studies include: weak study methodology; inability to verify data; lack of a control group; numbers of patients lost to follow-up; numbers of patients who did not complete all of the testing; lack of comparisons to conventional neurological tools; variations in testing parameters, equipment and protocol; and lack of randomization (Eisenberg, 2006; England, 2005; Gibbons, 2004; Centers for Medicare and Medicaid Services, 2003).

Brown et al. (2004) conducted a randomized controlled trial to “report the baseline and natural progression of diabetic peripheral neuropathy over 12 months in a large mild-to-moderate neuropathy population” using QST and NCS. The 1428 type 1 or type 2 diabetic patients included in the study, with mild distal symmetrical diabetic peripheral neuropathy (DPN) were randomized to one of three groups: placebo (n=472), zenarestat 600 mg/day (n=481) or zenarestat 1200 mg/day (n=475). The study was discontinued due to an increased serum creatinine in the zenarestat patients. However, data was available to report baseline and 12-month electrophysiologic, sensory and neuropathy outcomes. Diabetic peripheral neuropathy (DPN) was confirmed in the patients by nerve conduction studies (NCS) and qualitative sensory testing (QST). NCS and QST (vibration and cool thermal) were reported at baseline and at one year. In general, nerve conduction declined in all nerves tested, with the decline in sural sensory conduction velocity achieving statistical significance. Compared to baseline, qualitative sensory testing (QST) outcomes revealed a slight worsening in vibration and cooling thresholds, with the decline in cool thermal sensation being statistically significant (p=0.0005). Compared to baseline, nerve conduction study (NCS) results recorded an improvement or lack of progression in both treatment groups at 12 months. The cooling and vibratory quantitative sensory testing (QST) demonstrated significant worsening at the 12-month visit compared to baseline in the 1200 mg/day group. At 12 months, cool thermal threshold was worse in placebo patients, but a decrease in vibration perception was not statistically significant. The patients treated with zenarestat demonstrated slowing or improvement of neuropathy at 12 months on NCS, compared to significant worsening in all populations, including the placebo group, on the cool thermal testing.

Professional Societies/Organizations
American Academy of Orthopedic Surgeons (AAOS): In their guidelines on the diagnosis of carpal tunnel syndrome, AAOS (2007) noted that the physician should not routinely evaluate patients with suspected carpal tunnel syndrome with new technology such as pressure specified sensorimotor devices.

American Academy of Neurology (AAN): In a report on QST based on a review of 350 articles, the AAN (Shy, et al., 2003; reaffirmed 2008) noted QST is a potentially useful tool for measuring sensory impairment for clinical and research studies. However, QST results should not be the sole criteria used to diagnose pathology”. The AAN indicated that malingering and other nonorganic factors can affect the outcomes of the test results. They also noted that well-designed studies to compare the various types of QST devices and methodologies are indicated and should include patients with abnormalities detected solely by QST.

In a report on distal symmetric polyneuropathy (England, 2005; reaffirmed 2008), the American Academy of Neurology, the American Association of Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation stated that QST was not recommended as a diagnostic tool because the sensitivities and specificities varied widely among the studies, and the tests have inherent variability. QST is difficult to standardize, and reproducibility of results ranged from poor to excellent.

American Association of Electrodiagnostic Medicine (AAEM): The AAEM (Chong and Cros, 2004) conducted a review of the literature on QST to assess the "methodology, reliability, reproducibility, limitations, and potential clinical applications" of these studies. The authors noted the following conclusions:

- QST is a reliable psychophysical test of large- and small-fiber sensory modalities.
- QST tests the integrity of the entire sensory axis from receptors to brain. Abnormalities do not localize dysfunction to the central or peripheral nervous system, or any particular location along the peripheral nervous system.
- QST is highly dependent on the full cooperation of the patient and may be falsely abnormal if the patient is biased toward an abnormal result or is cognitively impaired. No algorithm can reliably distinguish between psychogenic and organic abnormality.
- QST has been shown to be reasonably reproducible over a period of days or weeks in normal subjects. Since longitudinal QST studies of patients in drug trials are usually done over a period of several months to a few years, reproducibility studies on the placebo-controlled group should be included.
- The reproducibility of thermal thresholds may not be as good as that of vibration threshold.
- For individual patients, more studies are needed to determine the maximum allowable difference between two QSTs that can be attributed to experimental error.
- Different commercially available QST instruments have different specifications (thermode size, stimulus characteristics), testing protocols, algorithms, and normal values. Only QST instruments and their corresponding methodologies that have been shown to be reproducible should be used for research and patient care.
- The results of QST can only be interpreted properly if machine calibration and testing protocol are strictly followed.
- The literature does not allow a conclusion to be made regarding whether any QST instrument is better than another.

Work Loss Data Institute (WLDI): In their guidelines for the diagnosis, evaluation, management and treatment of work-related acute and chronic carpal tunnel syndrome (2011a), acute and chronic lumbar and thoracic back pain (2011b), acute and chronic neck and upper back pain (2011c), and chronic pain (2011d), the WLDI stated that it considered but could not recommend the use of CPT testing.

Use Outside of the US: European Federation Of Neurological Societies (EFNS): In their 2009 guidelines on the assessment of neuropathic pain, EFNS stated that studies using qualitative sensory testing (QST) lack blinding, involve a broad spectrum of patients and controls, and only four of 50 new studies were prospective. The variability of methods, results, and patient populations (e.g., diabetic neuropathy, spinal cord injury, radiculopathy) prevent any conclusions from being drawn. The Society stated that qualitative sensory testing (QST) may be used to document the sensory profile, but the test "cannot be considered sufficient to separate differential diagnoses". "Quantitative sensory testing (QST) is helpful to quantify the effects of treatments on allodynia and hyperalgesia and may reveal a differential efficacy of treatments on different pain components". They "do not recommend the systematic measure of thermal stimuli except for pathophysiological research or treatment trials. A simple and sensitive tool to quantify pain induced by thermal stimuli in clinical practice is still lacking" (Cruccu, 2010).

International Association for the Study of Pain (IASP®): In guidelines on neuropathic pain assessment (Haanpää, 2011), the Special Interest Group on Neuropathic Pain of the IASP (NeuPSIG) explains that QST is biased towards thermal, including nociceptive, testing, which means that it excludes assessment of large fiber function. According to NeuPSIG, more studies with complete somatosensory profiles are needed. Results of available studies have been inconsistent and conflicting. Since QST abnormalities are found in non-neuropathic pains, these tests cannot be taken as a conclusive demonstration of neuropathic pain. Furthr, NeuPSIG notes QST can be used in clinic along with bedside testing, but it cannot allow for estimation of the level of the lesion

within the neuraxis. The relevance of QST to predict therapeutic outcome has yet to be established in prospective studies.

Summary
There is insufficient evidence in the published peer-reviewed literature to support quantitative sensory testing (QST). Studies have generally been poor in quality and design. The diagnostic utility of QST has not been established and its impact on health outcomes is unknown. Threshold standards and quantifiable outcomes have yet to be established and outcomes have varied from setting to setting, from device to device and from one patient group to another. Studies have been limited by sample size, lack of randomization, reproducibility of results and comparison of QST to conventional testing.

Conjunctival Incision with Posterior Extrascleral Placement of a Pharmacological Agent (CPT® Code 0124T, 68399)
Neovascular age-related macular degeneration (AMD) is associated with a rapid loss of vision due to an abnormal growth of blood vessels in the macula of the eye, leakage, and scarring (Geltzer, 2007). Treatment options for this disease are limited and there are a variety of therapies currently being investigated for neovascular AMD. Surgical implantation of steroids with antiangiogenic and anti-inflammatory properties has been proposed as a practical method of administering these agents into the eye (Geltzer, 2007). Extrascleral placement of steroids involves an incision into the orbit posterior to the limbus, through the conjunctiva. A cannula is inserted outside the sclera until the tip is near the macula, and the drug is administered. Advantages to this procedure may include a reduced risk for retinal detachment and endopththalmitis (Geltzer, 2007).

Literature Review
Randomized controlled trial (RCT) data are scarce regarding the safety and effectiveness of conjunctival incision with posterior juxtascleral placement of pharmacological agents. Geltzer et al. (2007) reported results of a systematic review which analyzed outcomes of three RCTs involving the administration of triamcinolone acetonide versus placebo, anecortave acetate versus placebo, and anecortave acetate versus photodynamic therapy for the treatment of age-related macular degeneration. One trial found posterior juxtrascleral depot of anecortave acetate may be effective in preventing severe vision loss. Overall the assessment noted weak evidence as to the benefits and harms of steroids with antiagiogentic properties for treating neovascular AMD by posterior juxtrascleral placement of drugs.

Use Outside of the US: No relevant information.

Summary
There is insufficient evidence to demonstrate the safety and effectiveness of conjunctival incision with juxtrascleral placement of pharmacologic agents for any indication. At this time the role of this therapy has not been established.

Computer-Aided Detection of Chest Radiographs (CPT® Codes 0174T, 0175T)
Computer-aided detection (CAD) systems for computed tomography or digital chest x-rays are software programs that subtract one lung from another to reveal subtle asymmetric opacities, and perform temporal subtraction of prior imaging from the current exam. The basic concept of computer-aided detection (CAD) is to provide computerized image recognition to assist and improve radiologist's interpretation. Through algorithms, CAD technology provides radiologists with regions of interest (ROI) for their interpretation. Although CAD is used most often in mammography, many different types of CAD technologies and/or devices are being developed for detection of various lesions in medical imaging, including conventional x-ray, computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound.

Proponents of computer-aided detection with chest x-ray state that diagnostic accuracy is improved with the use of a CAD program and that CAD can expedite screening of at-risk individuals at an earlier and more curable stage of lung cancer. Potential risks of using CAD with chest x-rays may include the generation of false-positive and false-negative results leading to over- and under-diagnosis. Abnormalities (e.g., scars from smoking, areas of inflammation, or other noncancerous conditions) can mimic lung cancer on x-ray. Subsequent additional testing may cause anxiety for the patient or may lead to unnecessary biopsy or surgery and increase medical costs. Also, the use of CAD programs in screening for lung cancer may detect small tumors that would never become life-threatening, putting a patient at risk for unnecessary treatments for cancer, such as chemotherapy or radiation.

U.S. Food and Drug Administration (FDA)
Deus Technologies received FDA premarket approval for its RapidScreen™ CAD system in July 2001. Its intended use is "to identify and mark regions of interest on digital or digitized frontal chest radiographs. It identifies features associated with solitary pulmonary nodules from 9–30 millimeters (mm) in size, which could represent early-stage lung cancer. The device is intended for use as an aid only after the physician has performed an initial interpretation of the radiograph. The device is of little value when used for patients who are not at high risk for lung cancer."

In 2007, Dues Technologies manufacturer Riverain Medical Group (Miamisburg, OH) received approval for a new trade name. The device, as modified, will be marketed under the trade name OnGuard™ and is indicated "to identify and mark ROIs on frontal chest radiographic films from adult males with an increased risk for lung cancer to bring ROI to the attention of the radiologist after the initial reading has been completed. Thus the system assists the radiologist in minimizing observational oversights by identifying areas on the original chest films that may warrant a second review." In March of 2012, Riverain's OnGuard software was renamed ClearRead Detect™. Currently, Riverain Medical's ClearRead Detect™ CAD System is the only FDA-approved CAD systems with a Product Device Description of "Analyzer, Medical Image" for chest x-rays (Product Code MYN). Other CAD systems (for example, mammography or lung computed tomography) are listed under this same device description.

The FDA approved EDDA Technology's (Princeton Junction, NJ) "IQQA® Chest Software Package" in October 2004 under the Product Device Description of Picture Archiving and Communications System (PACS). It uses a real-time interactive pulmonary nodule analysis system for chest digital radiographic image softcopy reading. Intended use states it is "used during the review of digital chest radiographic images. Combining image viewing, evaluation and reporting tools, the software is designed to support the physician in the identification of lung lesions (e.g. nodules), as well as the confirmation, evaluation and documentation of such physician-identified lesions. The IQQA-Chest software package supports a workflow based on automated segmentation for the visual identification of possible lesions. The tools also allow for regional analysis of possible lesions in terms of size, shape and position, thus aiding the physician in the characterization of physician-identified suspicious lesions." Philips Medical Systems (Hamburg, Germany) has licensed EDDA Technology's IQQA® Chest software and markets it under the name xLNA (x-ray lung node assessment) Enterprise.

Literature Review
There is insufficient evidence in the published, peer-reviewed scientific literature addressing the accuracy and clinical utility of CAD of chest x-rays. Well-designed clinical trials are lacking. Studies are primarily retrospective analyses of registry data and there is concern regarding unacceptable false-positive rates.. Retrospective registry studies address multiple variables that may impact accuracy such as the experience and training of radiologist using the CAD program, type of chest x-ray utilized (e.g., temporal subtraction, dual energy subtraction) and region of interest identification parameters in the algorithms themselves (e.g., nodules size, bone suppression, and nodule-in-center or nodule-in-circle criterion). Additionally, screening populations and timing for the use of CAD in the diagnostic work-up vary in studies. The clinical utility of CAD of chest x-rays for lung cancer screening is not established. The FDA wording regarding RapidScreen™ CAD systems states "the device is of little value when used for patients who are not at high risk for lung cancer" (Kligerman, et al., 2013; De Boo, et al., 2011; Meziane, et al., 2010; Szucs-Farkas, et al., 2010; Balkman, et al., 2010; Moore, et al., 2010; White, et al., 2009; Li, et al., 2008; Van Beek, et al., 2008; Bley, et al., 2008; Kakeda, et al., 2004).

Use Outside of the US: No relevant information.

Summary
The accuracy and clinical utility of using computer-aided detection (CAD) systems with chest radiographs have 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. Also, 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.

Transanal Endoscopic Microsurgical (TEMS) Approach for Excision of Rectal Tumor (CPT® Code 0184T)

A variety of surgical approaches are used to treat primary rectal cancer lesions, including transanal excision and transanal endoscopic microsurgery (TEMS, also referred to as TEM), depending on the location and extent of disease (National Comprehensive Cancer Network™ ([NCCN Guidelines™], 2013), According to the NCCN, transanal excision may be appropriate for selected T1N0 (i.e., American Joint Committee on Cancer TMN classification system) clinically staged cancers, that are <3 cm, well to moderately differentiated tumors, within 8 cm of the anal verge, limited to less than 30% of the rectal circumference, and no evidence of nodal involvement. Transanal endoscopic microsurgery (TEMS) may facilitate excision of small tumors through the anus when lesions can be adequately identified in the rectum.

TEMS is performed using laparoscopic instruments inserted through a rectoscope, which provides a seal through which tools such as scissors and forceps can be introduced while maintaining insufflation and improving visualization. This procedure may be used when lesions cannot be excised by colonoscopy or as an alternative to other surgeries such as conventional transanal excision or abdominal surgery (ECRI, 2012). Both transanal excision and TEMS involve a full thickness excision performed perpendicularly through the bowel wall into the perirectal fat. TEMS can facilitate excision of small tumors through the anus when lesions can be adequately identified in the rectum (NCCN, 2013).

U.S. Food and Drug Administration (FDA)
The Transanal Endoscopic Microsurgery (TEM) Combination System and Instrument Set (Richard Wolf Medical Instruments, Inc., Vernon Hills, IL) received FDA 50(k) approval in March 2001 as a substantially equivalent device. It is designed to provide access to the rectal cavity and accessible part of the lower sigmoid colon using a stereo and/or monocular endoscope under gas tight conditions for the excision of polyps and/or the removal of tumors that have previously been staged.

Literature Review
Evidence in the published peer-reviewed scientific literature includes one RCT performed in the U.S., several systematic reviews, and a number of prospective and retrospective clinical trials. Lezoche et al. (2008) reported results of a RCT involving 70 patients with stage T2N0M0 rectal cancer who underwent radiotherapy followed by chemotherapy. After chemotherapy the patients were randomized to either local excision by TEMS (Group A, n=35) or laparoscopic resection (Group B, n=35). Inclusion criteria for the TEMS group included a diameter of < 3cm, located within 6 cm of the anal verge, negative lymph nodes, no signs of systemic or metastatic disease, and a minimum follow-up of five years. The patients undergoing TEMS had significantly less operative time, blood loss, and hospital stay than the patients undergoing laparoscopic resection ($p<0.001$). For both approaches the 30-day mortality was zero. In group A, no intraoperative complications or conversion to other surgical procedures occurred. In group B, four procedures were converted to open surgery; in nine cases a laparoscopic abdominoperineal resection was performed. In the postoperative period, no significant differences in complication rates were observed between the two groups ($p = 0.111$). The median follow-up period was 84 months. The probability of local and distant failure at the end of the follow-up period was similar in both groups: 9% and 6% in the TEMS and laparoscopic groups, respectively. The probability of disease-free survival at the end of the follow-up period was 94% in both groups.

Doornebosch et al. (2009) reported outcomes of a systematic review involving four studies totaling 282 patients with T1 carcinoma comparing TEMS, local excision (LE) and/or radical surgery (RS). One study was a RCT; the other studies were retrospective. In the RCT patients were randomized to TEMS or RS. With median follow-up of more than 40 months, local recurrence rate after TEMS was 4.1%. In the RS group no local recurrence occurred. Five-year procedure specific survival rates were 96% for both groups. Two retrospective studies could be identified comparing TEMS to RS. Local recurrence rates are comparable (4% versus 3%, after TEMS and radical surgery, respectively) for low-risk (i.e., T1 cancer) carcinomas. Overall survival rates between both treatment groups were comparable (TEMS 79% versus RS 81%, respectively).

Middleton et al. (2005) conducted a systematic review of comparative studies and case series of TEMS. Three comparative studies, including one RCT (n=25 carcinomas, n=98 adenomas) and 55 case series were analyzed. The analysis suggests that TEMS appears to result in fewer recurrences than those with direct local excision in adenomas; it may be a useful procedure for several patient types (e.g., for large benign lesions of the middle to upper third of the rectum, for T1 low-risk rectal cancers, and for palliative, not curative, use in more advanced tumors). The authors note that the evidence regarding TEMS microsurgery is very limited, being largely based on a single relatively small randomized, controlled trial.

Professional Societies/Organizations
American College of Radiology (ACR, 2010): The ACR notes that transanal endoscopic microsurgery (TEM) allows locally complete excision of rectal neoplasms and has recently been evaluated for curative treatment of invasive cancer. Further, TEM has been shown to be as effective, and possibly better than, conventional transanal excision and safe to use following chemoradiation. In general, the best candidates for local excision include small (<4 cm), low-lying tumors confined to the muscularis propria.

American Society of Colon and Rectal Surgeons: Published practice parameters for the management of rectal cancer (2013) note that curative local excision is an appropriate treatment modality for carefully selected T1 rectal cancer without high-risk features. It can be performed with minimal morbidity and mortality either via transanal excision (Parks-type excision) or with a transanal endoscopic microsurgery approach.

National Comprehensive Cancer Network™ (NCCN™): The NCCN (2013) notes TEMS may be used when the lesion can be adequately identified in the rectum. TEMS for more proximal lesions may be technically feasible.

National Cancer Institute (NCI): The NCI (2013) notes the surgical approach to treatment varies according to the location, stage, and presence or absence of high-risk features (i.e., positive margins, lymphovascular invasion, perineural invasion, and poorly differentiated histology) and may include: transanal local excision (LE) and TEM for select clinically staged T1/T2 N0 rectal cancers. The primary treatment for patients with rectal cancer is surgical resection of the primary tumor. The NCI also notes that local excision of clinical T1 tumors is an acceptable surgical technique for appropriately selected patients.

Use Outside of the US: Canadian Agency for Drugs and Technologies in Health (CADTH) (2008): CADTH performed a technology assessment of transrectal endoscopic microsurgery. The review noted a number of limitations to the evaluated studies. No RCTs were identified on the topic of TEMS for rectal cancer; and observational studies do not control for potential selection bias; case series are a weak study design as there is no comparison group. Two studies did not provide carcinoma staging and the numbers of patients in each staging group was unknown. The evidence from the studies suggests that transanal endoscopic microsurgery (TEMS) is effective and safe in removing adenomas and T1 carcinomas when compared to local or radical resection. One study noted the local recurrence rate was higher for TEMS compared to resection, possibly because of lymphatic involvement; however, there was no difference in long term survival between the groups.

Summary
Randomized controlled clinical trial data are limited regarding the safety and effectiveness of transanal endoscopic microsurgery (TEMS) for the treatment of rectal tumors. However, there are a number of prospective and retrospective trials demonstrating similar long-term survival in TEMS compared to resection. Additionally this procedure has the support of several professional societies/organizations for the treatment of selected individuals with rectal cancer.

Multivariate Analysis of Patient Specific Findings with Quantifiable Computer Probability Assessment (CPT® Codes 0185T, 99199)
Quantitative pretest probability assessment or attribute matching matches an explicit clinical profile of a patient to a reference database to estimate the numeric value for the pretest probability of disease. It has been proposed that this assessment, which is available at the bedside, may aid the health care professional in making the decision to perform certain diagnostic tests.

According to Kline et al. (2010) attribute matching works by a selection process whereby a computer algorithm compares the results of a selected number of predictor variables obtained from the patient being evaluated to a library of research patients previously evaluated for a specific indication compiled from multiple hospitals. The algorithm returns from the library only the ‘‘matched’’ patients who share the same profile of predictor variables as the patient under consideration and reports the proportion of patients with disease in this matched sample.

The PREtestConsult ACS and PREtestConsult PE modules (BreathQuant Medical Systems, Inc., Charlotte, NC) are a software application that estimates the probability of acute coronary syndrome or pulmonary embolism in adult patients. According to information on the PREtestConsult website, clinical data are entered into the modules by means of a personal data assistant or computer.

Literature Review
Randomized controlled clinical data are limited to evaluate the effectiveness and clinical utility of quantifiable computerized probability assessment. Kline et al. (2008) reported the results of a randomized clinical trial involving 400 adult patients (control group, n=185; intervention group, n=184) who were evaluated for chest pain in a single medical center emergency department. Patients had neither obvious evidence for acute coronary syndrome nor other obvious reasons for admission. After an electrocardiogram was performed clinicians were asked to give their estimate of the percentage probability that the patient would have an acute coronary syndrome-defining event in the subsequent 45 days. Randomization was performed by way of a sealed, sequentially numbered envelope that contained assignment to either the control or intervention group. A member of the research team followed the patient to determine physical disposition status from the emergency department. Patients were contacted by telephone at seven and 45 days after enrollment by a research coordinator who was unaware of group assignment. The mean of the pretest probability estimates from the clinicians was 4 (5%) compared with 4 (6%) for the computerized device estimate. Safety and efficacy endpoints for controls versus intervention patients, respectively, were as follows: (1) delayed or missed diagnosis of acute coronary syndrome: 1 of 185 versus 0 of 184, (2) hospital admission with no significant cardiovascular diagnosis: 11% versus 5%, (3) thoracic imaging imparting greater than 5 mSv radiation with a negative result: 20% versus 9%, (4) median length of stay: 11.4 hours versus 9.2 hours, (5) reported feeling “very satisfied” with clinician explanation of problem on follow-up survey: 38% versus 49%, and (6) readmitted within 7: days: 11% versus 4%. Data suggest that use of a quantitative estimate of the pretest probability of acute coronary syndrome was associated with reduced resource use.

Use Outside of the US: No relevant information.

Summary
There is insufficient evidence in the published peer-reviewed scientific literature to demonstrate the effectiveness and clinical utility of quantifiable computerized probability assessment to improve health outcomes. The role of this technology has not yet been established.

Suprachoroidal Delivery of Pharmacological Agents (CPT® Codes 0186T, 67299)
The leading causes of blindness include those affecting the back of the eye: age-related macular degeneration, diabetic retinopathy, and uveitis. Although treatments are available, delivering drugs to the posterior regions of the eye is challenging because of architecture as well as natural barriers (Patel, 2011). Drug delivery techniques include intravitreal injections, periocular injections and intravitreal implants. Suprachoriodal drug delivery has been proposed as an alternative method to access the suprachoroid space.

U.S. Food and Drug Administration (FDA)
The iScience Surgical Opthalmic Microcannula (iScience Surgical Corporation, Redwood City, CA) is a flexible microcannula designed to allow atraumatic cannulation of spaces in the eye such as the anterior chamber and posterior segment (FDA, 2004). It received 510(k) approval on June 22, 2004 for the following indications: fluid infusion and aspiration, as well as illumination, during surgery.

Literature Review
Randomized control trial data are lacking to demonstrate the safety and effectiveness of suprachoroidal delivery of pharmacological agents for any indication. Studies are limited by uncontrolled design and small populations.

Professional Societies/Organizations
Guidelines of the American Academy of Ophthalmologists do not mention suprachoroid delivery as a method for delivering drugs to the posterior regions of the eye.

Use Outside of the US: No relevant information.

Summary
There is insufficient evidence in the published peer-reviewed scientific literature to demonstrate the safety and effectiveness of suprachoroid delivery of pharmacological agents. At this time the role of this therapy has not been established.

Physiologic Recording of Tremor Using Accelerometer/Gyroscope (CPT® Code 0199T)

Accelerometers and gyroscopes are devices that may be used to objectively record and monitor motion and electrical activity of muscles to measure tremor in individuals with movement disorders. Recent studies have examined the clinical utility of these devices as an adjunct in diagnosis and measurement of functional ability and recovery in individuals with dyskenetic disorders.

U.S. Food and Drug Administration (FDA)
The FDA approved the Kinesia™ device (Cleveland Medical Service, Cleveland, OH) in April 2007 for the monitoring and recording of motion and electrical activity of muscle to quantify kinematics of movement disorders such as tremor for research and diagnostic purposes. The Tremorometer® (FlexAble Systems, Inc., Fountain Hills, AZ) received substantial equivalency FDA 510 (k) approval in January 2001. It is a system designed to improve the measurement and quantification of tremor in human patients regardless of the etiology.

Literature Review
Controlled clinical trial data are lacking to inform the utility of these devices, including the translation of measurements into meaningful outcomes. Cheung et al. (2011) performed a systematic literature review; reviewing 54 studies that used accelerometers to classify human movement and to appraise their potential to determine the level of activity of older persons in hospital settings. Outcome measures criteria were comparisons of derived classifications of postural movements and mobility against those made by using observations. A number of limitations to the study were noted including the number and type of accelerometers used for measurement, varied age of study participants (varied from teenager to >60 yrs). Most studies were limited by small sample size; 54% had 10 subjects or less. Methods for validating data were also varied. Of the accelerometer studies included in this review, only 17 were conducted on patients and the remaining were conducted on healthy subjects (n=37 studies). The authors note that the literature review indicates that only a limited number of studies have applied accelerometry to measure activities in patients, of which six studies were of older patients. These studies were limited by smaller sample sizes and use of multiple accelerometer devices attached to different body positions. The activity classification algorithms validated in small sample size studies with <6 patients are insufficient for clinical use. A suitable algorithm for application in geriatric rehabilitation settings needs to be generic and accurate in older patients with different levels of mobility impairment.

Gebruers et al. (2010) reported results of a systematic review assessing the clinical applicability of different accelerometry based measurement techniques in persons with stroke, Twenty-five articles were selected for inclusion; there were 4 randomized controlled trials (RCT). The authors noted that although the available evidence may suggest that accelerometers yield valid and reliable data about individuals with stroke, data are young, limiting the ability to draw consistent conclusions. Further research is necessary to investigate predictive value and responsiveness.

Use Outside of the US: No relevant information.

Summary
A number of methods for measuring and monitoring movement are available; however, study limitations preclude application of results to the general population. There is insufficient evidence to demonstrate improved health outcomes as a result of the use of accelerometers and gyroscopes for any indication.

Intravascular Catheter-Based Coronary Vessel or Graft Spectroscopy (CPT® Code 0205T)
The leading cause of major morbidity and mortality is atherosclerotic cardiovascular disease, most commonly caused by thrombotic occlusion of a high-risk coronary plaque resulting in myocardial infarction or cardiac death, or embolization from a high-risk carotid plaque resulting in stroke (Alshiekh-Ali, 2010).

Near-infrared spectroscopy is proposed as a method to detect lipid and cholesterol deposits in coronary vessel walls. Ex vivo studies have demonstrated the feasibility of atherosclerotic lipid-rich plaque detection using near-infrared spectroscopy (NIRS). While near-infrared spectroscopy can collect data with rapid acquisition times, avoiding the need to obstruct blood flow it does not create an image of the vessel wall, which is a limitation of the device. Fibroatheromas that are thick capped or too small to be defined as lipid core plaques are major sources of false-positive readings (Alshiekh-Ali, 2010).

U.S. Food and Drug Administration (FDA)
The LipiScan Coronary Imaging System (InfraReDx, Inc., Burlington, MA) received FDA 510(k) approval in April 2008. The device is indicated for the near-infrared examination of coronary arteries.

Literature Review
Randomized controlled clinical trial data are lacking in the published peer-reviewed scientific literature. Waxman et al. (2009) reported initial results of the first-in-human uncontrolled validation study involving a catheter-based near-infrared spectroscopy system for the detection of lipid core coronary plaques (SPECTACL [SPECTroscopic Assessment of Coronary Lipid] trial). A total of 106 patients were enrolled in the study, spectroscopic data was obtained in 89 patients. Spectral similarity was demonstrated in 83% of available patients. The algorithm developed ex vivo identified the high-risk plaques in 60% of imaged segments in patients undergoing percutaneous coronary intervention. The authors note the feasibility of invasive detection of coronary lipid core plaques with this system.

Professional Societies/Organizations
The American Heart Association and the American College of Cardiology have not published guidance regarding use of intravascular catheter-based coronary vessel or graft spectroscopy to identify lipid core plaques or for any indication.

Use Outside of the US: No relevant information.

Summary
Controlled clinical trial data are lacking to demonstrate the safety and effectiveness of intravascular catheter-based coronary vessel or graft spectroscopy for any indication, including the detection of lipid core coronary plaques. Although results of the initial validation trial are promising; the role of this therapy has not yet been established.

Automated Evacuation of Meibomian Glands (CPT® Code 0207T)
The meibomian glands are located on the eyelids and are responsible for the production of sebum. Sebum prevents the tear film from evaporating too quickly from the eye's surface. Meibomian gland dysfunction leads to decreased secretion and abnormal composition of the tear film lipid layer, which in turn can lead to blockage of the glands, dry eye, and infection. Conventional treatment includes eyelid washing, use of preservative-free tears, omega-3 dietary supplementation, topical and oral antibiotics, corticosteroids, warm compresses and gentle eyelid massage. The use of an automated heated compression device has been proposed as a treatment of meibomian gland dysfunction.

U.S. Food and Drug Administration
The LipiFlow Thermal Pulsation System (TearScience, Morrisville, NC) received FDA 510(k) clearance in July, 2011. This system is intended to be used by a physician in an in-office procedure. The FDA approval indicates "The LipiFlow Thermal Pulsation System is intended for the application of localized heat and pressure therapy in adult patients with chronic cystic conditions of the eyelids, including meiboman gland dysfunction (MGD) also known as evaporative dry eye or lipid deficiency dry eye."

Literature Review
Lane et al. (2012) conducted a study examining the safety and effectiveness of the LipiFlow System compared with the iHeat Warm Compress (WC) for adults with meibomian gland dysfunction. This was a prospective open-label, randomized, crossover multicenter clinical trial. One hundred thirty-nine subjects 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 one day, two weeks and four weeks. Control subjects received a five-minute iHeat treatment with instructions to perform the same treatment daily for two weeks. At two weeks, they crossed over and received the LipiFlow treatment. LipiFlow resulted in significant improvement in meibomian gland secretion at two and four weeks ($p < 0.05$). There was no change in meibomian gland secretion in the control group. Limitations to the study were the small population size. Results replicated in larger RCTs are required to demonstrate the ability to apply outcomes to the general population.

Mitra et al. (2005) reported results of a prospective, controlled, observer masked, single intervention trial in which 24 normal subjects were randomized into three groups: Group 1: 10 minutes with the activated device, Group II: 10 minutes with the inactivated device, Group III: no intervention. The lipid layer thickness of each subject was measured prior and subsequent to the 10-minute period. A statistically significant increase in lipid layer thickness was seen in 87% of subjects in Group I ($p<0.001$, left eye, $p<0.003$, right eye.). Seventy-five percent of subjects experienced subjective improvement in ocular comfort. The authors note that meibomian

therapy using this novel device results in increased lipid layer thickness. A limitation of this study was the small study population.

Korb and Blackie (2011) reported on a study attempting to determine the pressure required to express the first non-liquid material from nonfunctional lower lid meibomian glands, the pressure required to evacuate all of the expressible material from the glands, and the level of pain associated with these actions. Custom instrumentation was applied to the lower lid, exerting pressures from 1.0 to 150.0 pounds per square inch (psi). pressure was monitored throughout the procedure as was pain level. The pressure required to obtain the first non-liquid material ranged between 5-40 pounds per square inch. Pain was the limiting factor for this treatment. Only 7% of the patients could tolerate the pressure necessary to administer complete expression of the non-liquid material.

Use Outside of the US: No relevant information.

Summary
At present there is insufficient evidence in the published peer-reviewed scientific literature to demonstrate the safety or effectiveness of automated devices for the treatment of meibomian gland dysfunction. Available studies are limited to small participant size which precludes application to the general population. The role of automated meibomian gland evacuation devices has not yet been established.

Automated Audiometry Devices (CPT® Codes 0208T, 0209T, 0210T, 0211T, 0212T)
Audiometers measure and characterize hearing loss by determining an individual's hearing threshold. Conventional tests utilized for assessment include the behavioral pure-tone audiogram (hearing sensitivity of single-frequency signals) and speech recognition (hearing sensitivity for spoken material). These tests require interaction between the trained technician or audiologist and the patient. Convention audiometry tests are performed manually and interpretation of the raw data is performed by the audiologist (ECRI, 2010).

The use of automated audiometry devices has been proposed as an alternative to manually operated devices. Automated units use conventional technology; however, the equipment is fully automated. Results are displayed as pass or fail/refer and do not require further interpretation by a technician or audiologist. A failure score may result in further referral to a health care professional.

U.S. Food and Drug Administration (FDA)
Several automated audiometric devices have received FDA 510 (k) approval. These include, but are not limited to: the AuDX Otoacoustic Emissions Measurement System with AuDX I/O Function (Natus Medical Incorporated, Mundelein, IL) received FDA 510(k) approval as an equivalent device in December 2011. The device is indicated for use when it is necessary for a trained health care professional to measure or determine cochlear function. The device can be used for patients of all ages, from newborn infants through adults to include geriatric patients. The otoacostic emissions test is especially indicated for use in testing individuals for whom behavioral results are deemed unreliable, such as infants, young children, and cognitively impaired adults. The Otogram™ Hearing Diagnostic System (Ototronix Diagnostics, Houston, TX, formerly marketed by Tympany, Inc., Salt Lake City, UT) received FDA 510(k) approval as an equivalent device in March 2007. The device is indicated for use by trained healthcare professionals on both adults and pediatric subjects for measurement of audiometric parameters to identify and supply to help diagnose hearing loss and ear disorders.

Literature Review
Although there are a number of cohort and case series reported in the published peer-reviewed scientific literature, randomized controlled trial, meta-analysis and systematic review data are lacking. In a nonrandomized comparison study by Lancaster et al. (2008) involving screening results of 32 children using on-site and tele-health screening methods the authors report identical otoscopic and immitance results. Pure-tone results were different between on-site and telehealth screening methods for five of 32 students. Using the on-site pure-tone screening protocol as the 'gold standard' the authors report that the tele-health pure-tone screening protocol yielded four false positive responses and one false negative response. This study was limited by uncontrolled study design and small study numbers.

Professional Societies/Organizations
American Academy of Pediatrics (AAP): On behalf of the AAP Harlor et al. (2009) published recommendations for hearing assessment in infants and children. These recommendations include discussion

of automated auditory brainstem response (ABR) test as an objective physiologic means of hearing screening. The guideline does not mention the automation of other tests.

Use Outside of the US: No relevant information.

Summary
There is insufficient evidence to demonstrate the effectiveness of automated audiometric devices. At present the role of these devices has not been established.

Acoustic Cardiography (CPT® Codes 0223T, 0224T, 0225T)
Acoustic cardiography, also referred to as correlated audioelectric cardiography is a noninvasive diagnostic tool designed to be used in the evaluation of cardiac conditions such as left ventricular hypertrophy (LVH), acute and age-undetermined myocardial infarction (MI), cardiac arrhythmias, and detection of S3 and S4 heart sounds. An S3 heart sound may be associated with heart failure in patients over age 40. Acoustic cardiography is intended to augment physician auscultation, since S3 and S4 heart sounds may be difficult to hear in some patients. The device acquires, displays, and analyzes 12-lead electrocardiogram (ECG) and heart sound data (Collins et al., 2006; Kobza et al., 2008; Wagner et al., 2002; Warner et al., 2002).

Traditional diagnostic methods include physical examination and auscultation, 12-lead ECG laboratory examinations, measurement of biomarkers of cardiac damage, and imaging.

U.S. Food and Drug Administration (FDA)
The Eli 200+ Audicor (Mortara Instrument, Inc., Milwaukee, WI) is an interpretive electrocardiograph device designed to acquire, record and store cardiac data. The device uses Audicor Correlated Audioelectric Cardiography (COR) technology (Inovise Medical, Inc., Newberg, OR) to simultaneously acquire both 12-lead electrocardiogram (ECG) and heart sound data. The Eli 200+ Audicor received U.S. Food and Drug Administration (FDA) clearance to market as a Class II device through the 510(k) process on July 25, 2003. The device was considered a technology evolution and substantially equivalent to the ELI 200, Inovise's Cardiovise Interpretive Software, and Hewlett Packard's 1514A ECG/Phono System.

The FDA 510(k) notification of clearance to market the Eli 200+ Audicor included the following indications for use:

- The device is indicated for use to acquire, analyze, display and print ECG and heart sound data (COR).
- The device is indicated for use to provide interpretation of the data for consideration by physicians.
- The device is indicated for use in a clinical setting by a physician or by trained personnel and is not intended as a sole means of diagnosis.
- The interpretations of ECG and heart sound data (COR) offered by the device are only significant when used in conjunction with physician over-read as well as consideration of all other relevant patient data.
- The device is intended for use on adult populations, typically symptomatic.
- The device is not intended to be used as a vital signs physiological monitor.
- The device is indicated for evaluation of cardiac conditions such as left ventricular hypertrophy (LVH), acute and age-undetermined myocardial infarction (MI), and detection of S3 and S4 heart sounds.

On October 31, 2003, the Audicor Upgrade System received FDA clearance as a Class II device through the 510(k) process. The Audicor Upgrade System is an add-on device used with Audicor Sensors in the V3 and V4 positions on the chest wall. The system consists of a pocket personal computer (PC) with proprietary software and can be used with several models of existing electrocardiographs to allow physicians access to the COR report, including graphical display of MI and LVH conditions, display of heart sound waveforms, and identification of S3 and S4 heart sounds.

The Zargis Acoustic Cardioscan (Zargis Medical Corporation, Princeton, NJ) received FDA approval through the 510(k) process on May 26, 2004. The system is an electronic auscultatory device intended to acquire, record, and analyze heart sounds. The system consists of an electronic stethoscope, notebook computer, software, printer and an isolation transformer. According to the FDA indications for use, the device acquires and records the acoustic signals of the heart and analyses these signals. The analysis procedure will identify specific heart sounds that may be present, including S1, S2, and suspected murmurs. The approval lists the Audicor system as a predicate device.

Literature Review
Published studies have evaluated the use of Cardiovise diagnostic software, a predicate device and component of the Audicor System, for the detection of acute and prior MI (Wagner, et al., 2002; Andresen, et al., 2002). Published studies involving the Audicor system or correlated audioelectric cardiography are limited.

Collins et al. (2009) conducted a multisite study to evaluate the effect of an S3 captured by acoustic cardiography on diagnostic accuracy and confidence in the diagnosis of acute decompensated heart failure in patients presenting to the emergency department (ED) with dyspnea (n=995). The study also evaluated the impact on patient prognosis. ED physicians who were initially blinded to all laboratory and acoustic cardiography results estimated the probability of acute decompensated heart failure on a scale of 0% to 100% on a visual analog scale. The visual analog scale was repeated after acoustic cardiography results were provided. Patients were followed for 90 days to determine the relationship of the S3 to adverse events. The initial sensitivity, specificity, and accuracy for acute decompensated heart failure as a possible diagnosis were 89.0%, 58.2%, and 71.0%, respectively. Sensitivity, specificity, and accuracy for acoustic cardiography were 40.2%, 88.5%, and 68%, respectively. The authors concluded that acoustic cardiography S3 was specific to acute decompensated heart failure, but did not improve diagnostic accuracy, primarily because of the low sensitivity. In addition, the acoustic cardiography S3 provided no significant independent prognostic information.

Maisel et al. (2011) conducted a secondary analysis of the Collins study (above) to determine if the strength of the S_3 can provide diagnostic prognostic information in problematic heart failure subgroups. The analysis included dyspneic ED patients older than age 40 who were not on dialysis. A gold standard acute heart failure diagnosis was determined by two cardiologists who were blinded to acoustic cardiography results. In the 995 enrolled patients, S3 strength was a significant prognosticator in univariate analysis for adverse events. When results were incorporated into the multivariable analysis in stepwise fashion, however, it was not as predictive as other variables, such as B-type natriuretic peptide (BNP) values and ST-depression on ECG. In the subgroup of patients with “gray zone” BNP levels, acoustic cardiography increased diagnostic accuracy of acute heart failure (AHF) from 47% to 69%. Acoustic cardiography also improved S_3 detection sensitivity in obese patients compared to auscultation. The authors stated that although acoustic cardiography appears to augment the use of BNP, particularly in problematic subgroups, there were limitations to the study, including the fact that the true diagnostic characteristics when used in real time are unknown, due to the retrospective nature of the study and limited data availability. In addition, cardiologists making the AHF diagnosis were not blinded to BNP results, which would have impacted the diagnosis.

Kobza et al. (2008) conducted a case series (n=57), to evaluate the use of acoustic cardiography using the Audicor device) during electrophysiological (EP) testing for known or suspected cardiac arrhythmias concluding that acoustic cardiography is useful for identifying VT and may facilitate the differential diagnosis of clinically important tachyarrhythmias, particularly when advanced techniques such as EP studies are not available.

Collins et al. (2006) evaluated the use of an S3 heart sound combined with B-type natriuretic peptide (BNP) levels in the diagnosis of emergency room patients with dyspnea (n=439). The author concluded that an S3 sound is highly specific for heart failure and is ideally suited for use in combination with BNP to improve diagnostic accuracy. The sensitivity, specificity , positive and negative predictive value, and diagnostic accuracy of the electronic S3 for primary heart failure were 34%, 93%, 66%, 7%, and 70%, respectively. The values obtained by physician auscultation were 16%, 97%, 84%, 3%, and 66%, respectively. The addition of an Audicor S3 to intermediate BNP levels improved the positive likelihood ratio from 1.3 to 2.9 and improved the positive predictive value from 53% to 80%. The overall ER misdiagnosis rate was 14%. Of the 48 cases, 44 were a failure to diagnose heart failure when it was present. If the Audicor had been used as the sole diagnostic tool among these 44 ultimately considered to have primary HF, 15 would have been correctly diagnosed. Similarly, if the Audicor tool had been used as the sole diagnostic tool, 14 of the 206 patients correctly diagnosed as nonprimary HF would have been incorrectly diagnosed as primary HF. Although the evaluation of S3 heart sounds in combination with BNP testing may improve diagnostic accuracy in patients with dyspnea of unclear etiology, this study does not demonstrate that the Audiocor system provides a benefit, when used alone or in combination with other tests, in terms of improved clinical outcomes.

Marcus et al. (2006) conducted a prospective study to determine the diagnostic test characteristics of the S3 and S4 heart sounds for prediction of left ventricular dysfunction using the Audicor system in patients undergoing elective left-sided heart catheterization (n=90). Patients underwent computerized heart sound

phonocardiographic analysis (Audicor system) for assessment of S3/S4 heart sounds, cardiac catheterization for assessment of left ventricular end-diastolic pressure (LVEDP), transthoracic echocardiography for evaluation of left ventricular ejection fraction (LVEF), and blood sampling for BNP. Mean LVEDP was significantly elevated; LVEF was reduced; and median BNP was elevated in those with an S3, S4, or both, compared to patients without a diastolic heart sound. The sensitivities of these heart sounds to detect an elevated LVEDP, reduced LVEF, or elevated BNP were 41%, 52%, 32% for an S3, and 46%, 43%, and 40% for an S4, respectively. The authors concluded that neither the phonocardiographic S3 nor the S4 is a sensitive marker of left ventricular dysfunction. The absence of an S3 or S4 using phonocardiographic testing (Audicor system) is therefore not sufficient to exclude ventricular dysfunction. If present, the phonocardiographic S3 and S4 are specific for an elevated LVEDP, depressed LVEF, and elevated BNP level.

Professional Societies/Organizations
American College of Cardiology/American Heart Association (ACC/AHA): ACC/AHA Guidelines for the Management of Patients with ST-Elevation Myocardial Infarction (Antman, et al., 2004) and the ACC/AHA Guideline Update for the Diagnosis and Management of Chronic Heart Failure in the Adult (Hunt, et al., 2005), make no mention of correlated audioelectric cardiography or acoustic heart sounds as a diagnostic tool. In addition, this technology is not mentioned in AHA/ACC Recommendations for the Standardization and Interpretation of the Electrocardiogram, Part I (Kligfield, et al., 2007) and II (Mason, et al., 2007).

American Heart Association (AHA): The AHA scientific statement, Acute Heart Failure Syndromes: Emergency Department Presentation, Treatment, and Disposition: Current Approaches and Future Aims, includes a discussion of focused areas for future investigation. The authors note that the search for additional tools to improve the diagnostic accuracy for patients with undifferentiated dyspnea and possible acute heart failure syndromes remains a high priority. Electronic detection of third heart sounds (S_3) using acoustic cardiography is included among several tools that have been investigated as both stand-alone and adjunct diagnostic measures, but appear to provide little benefit over existing approaches (Weintraub et al., 2010).

Use Outside of the US: No relevant information.

Summary
Acoustic cardiography, also referred to as correlated audioelectric cardiography has been proposed as a more accurate method for the detection of acute myocardial infarction (MI); the detection, sizing and location of prior MI; detection of left ventricular hypertrophy (LVH); cardiac arrhythmias, and identification of S3 and S4 heart sounds. There is insufficient evidence in the published medical literature to demonstrate that the diagnostic accuracy of acoustic cardiography is equal or superior to traditional diagnostic tools, including physical examination and auscultation, 12-lead electrocardiogram, laboratory examinations, measurement of biomarkers of cardiac damage, and imaging, or that the use of this technology as a stand-alone or adjunctive diagnostic measure results in improved clinical outcomes.

High Resolution Anoscopy (HRA) (CPT® Codes 0226T, 0227T)
During an anoscopy the perianal area and distal rectum are examined. High resolution anoscopy has been proposed as a method to identify anal lesions in high-risk populations, and for use in screening for anal cytology. High resolution anoscopy uses an anoscope as well as a colposcope or operating microscope for more detailed examination. After application of a 3% acetic acid solution and Lugol's iodine, the canal is inspected with the colposcope. Areas with acetowhitening are examined for abnormal patterns and targeted biopsies are performed on areas suspicious for high-grade squamous intraepithelial lesion (HSIL). Correlation of biopsy results with anal cytology results has been variable (Lee, 2010).

Literature Review
Randomized controlled clinical trial data are lacking to demonstrate improved health outcomes with the use of high-resolution anoscopy to detect anal cytology. However, there is support by a number of professional societies/organizations related to its use as diagnostic tool in individuals with a suspicious anal lesion, including high-grade suspicious intraepithelial lesion (HSIL) and anal dysplasia found in prior cytology/biopsy.

A case series by Chang (2002) reported on a prospective study of high resolution anoscopy directed surgery in 37 patients with high-grade squamous intraepithelial lesion. Twenty-nine patients tested positive for human immunodeficiency virus (HIV), eight patients tested negative. Mean follow-up was 32.3 months for HIV-positive patients and 28.6 months in HIV-negative patients. No HIV-negative patient developed recurrent high-grade

squamous intraepithelial lesions. Twenty-three of 29 HIV positive patients had persistent or recurrent high-grade squamous intraepithelial lesions (HSIL) (p<.003). Six patients underwent reoperation for HSIL; four recurred by six months. No patients developed incontinence, stenosis, postoperative infection, or significant bleeding after surgical treatment. Study limitations include small patient population and uncontrolled study design.

Professional Societies/Organizations
American Society of Colon and Rectal Surgeons (ACRS): On behalf of the ACRS, Steele et al. (2012) published a Practice Parameters for Anal Squamous Neoplasms. The Guideline notes that targeted destruction guided by high resolution anoscopy is effective to identify, biopsy, and destroy low grade anal intraepithelial neoplasm [LGAIN]/high grade anal epithelial neoplasm [HGAIN] without the morbidity associated with wide local excision. The Guidelines also note that a comprehensive approach with cytology, high resolution anoscopy, targeted biopsies, and directed therapy has reported clearance of high grade anal intraepithelial neoplasm [HGAIN] in up to 80%, with progression to higher-grade disease and invasive cancer in less than 5%. Therefore, expectant management with close follow-up may be considered in select cases depending on risk factors, comorbidities, and available resources. However, because of the high prevalence of concomitant cervical intraepithelial neoplasm, a referral to gynecology is recommended to complete the evaluation. Targeted destruction and close clinical long-term follow-up is appropriate therapy for LGAIN/HGAIN. (Grade of Recommendation: Strong recommendation based on low-quality evidence, 1C.)

Centers for Disease Control, National Institutes of Health, Human Immunodeficiency Virus Medicine Association of the Infectious Diseases Society of America: On behalf of these organizations, Kaplan et al. published Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents (2009). The Guidelines note anal cytology indicating atypical cells of undetermined significance (ASC-US), atypical squamous cells-cannot exclude high grade squamous intraepithelial lesion (ASC-H), low-grade intraepithelial lesion (LSIL), or high-grade intraepithelial lesion (HSIL) should be followed by high resolution anoscopy. No national recommendations exist for routine screening for anal cancer. Studies of screening and treatment programs for anal intraepithelial neoplasia (AIN) should be implemented before definitive recommendations for anal cytology screening can be made (Kaplan, 2009).

Use Outside of the US: Ontario Health Technology Assessment Series (OHTAS): OHTAS (2007) notes that high resolution anoscopy rather than routine anoscopy-guided biopsy is considered to be the diagnostic standard.

Summary
High resolution anoscopy is an appropriate tool as part of a comprehensive approach for detection of anal cytology. Although randomized controlled clinical trial data are lacking there is support for the use of high resolution anoscopy by several national professional societies/organizations as a standard of care.

Transluminal Peripheral Atherectomy (CPT® Codes 0234T, 0235T, 0236T, 0237T, 0238T)
The term peripheral artery disease (PAD) broadly encompasses the vascular diseases caused primarily by atherosclerosis and thromboembolic pathophysiologic processes that alter the normal structure and function of the aorta, its visceral arterial branches, and the arteries of the lower extremity (American College of Cardiology Foundation [ACCF]/American Heart Association [AHA], 2011). Obstructive atherosclerotic disease affecting the popliteal and infrapopliteal vessels is treated percutaneously or with medical therapy. Endovascular atherectomy of peripheral arteries (i.e., noncoronary) has been proposed as a method to allow the physical removal of atherosclerotic plaque material from a blood vessel, with a theoretical benefit of removing the obstructing plaque rather than merely displacing it, as with angioplasty and stenting (Silva, 2012).

Mahmud et al. (2007) notes “There is significant symptomatic improvement with the surgical approach; however the associated morbidity and mortality preclude its routine use. Although newer percutaneous treatment options are associated with lower procedural complications, the technical advances have outpaced the evaluation of these treatments in adequately designed clinical studies, and therapeutic options are available that may not have been rigorously investigated.” Atherectomy devices include those that cut and remove plaque from vessel walls, grind the plaque into small particles with distal embolization within the vessel, or capture plaque in the device for disposal.

U.S. Food and Drug Administration (FDA)

Several devices have received FDA 510 (k) approval for peripheral artery atherectomy. These include but are not limited to the Diamondback 360º Orbital Atherectomy System (August 2007, Cardiovascular Systems, Inc, St Paul, MN), SilverHawk™ Peripheral Plaque Excision System (ev3 Endovascular, Inc., Plymouth, MN, formerly marketed by Fox Hollow, Inc.), and the Pathway PV System (July 2008, Pathway Medical Technologies, Inc., Kirkland, Washington).

Literature Review
Although there are a number of prospective case series, registry analyses and retrospective reviews in the published peer reviewed scientific literature, randomized controlled clinical trial (RCT) data are limited. Shammas et al. (2011) reported results of an RCT comparing percutaneous transluminal angioplasty (n=29, 48 vessels) versus athrectomy of infrainguinal vessels (n=29, 36 vessels). There was no significant difference in the final acute angiographic success rates between the two approaches. There was no statistical difference between target revascularization rates between the two approaches (16.7% and 11.1% for angioplasty and atherectomy, respectively, P value not reported). The secondary endpoint of bailout stent implantation occurred in 18 of 29 patients (62%; 50% of vessels) in the angioplasty arm and eight of 29 patients (27.6%; 22.2% of vessels) in the atherectomy arm with adjunctive angioplasty (p<.017). Compared with PTA, atherectomy was associated with significant distal embolization (p<0.001). The authors note several study limitations: the patients were randomized only after the chronic occlusions were crossed with the wire which may have favored the outcome toward atherectomy. Another limitation is that embolic filter protection was not mandated by the protocol but was used more frequently in the atherectomy arm. Additionally bailout stents were used more frequently in the angioplasty arm which may have favored the angioplasty arm. The authors note that a type II error cannot be ruled out.

Garcia et al. (2009) notes that compared to conventional percutaneous transluminal angioplasty (PTA) and stent implantation for arterial occlusive diseases, atherectomy offers the theoretical advantages of eliminating stretch injury on arterial walls and reducing the, rate of restenosis. Historically, however, neither rotational nor directional atherectomy, whether used alone or with adjunctive PTA, has shown any significant long-term benefit over PTA alone in the coronary or peripheral arteries. Questions remaining for further research with this device include more accurate determination of an event rate for distal embolization, the appropriate use of distal protection, the value of and appropriate circumstances for adjunctive angioplasty, and definitive patency and clinical outcomes.

Professional Societies/Organizations
American College of Cardiology Foundation/American Heart Association ([ACCF/AHA], 2011): The ACCF/AHA published a guideline titled “Management of Patients with Peripheral Artery Disease (Lower Extremity, Renal, Mesenteric, and Abdominal Aortic) which is adapted from the 2005 ACCF/AHA Guideline and the 2011 ACCF/AHA focused update. Regarding endovascular treatment of claudication the Guideline notes:

- Class IIa, Level of Evidence C recommendation notes that stents (and other adjunctive techniques such as lasers, cutting balloons, atherectomy devices, and thermal devices) can be useful in the femoral, popliteal, and tibial arteries as salvage therapy for a suboptimal or failed result from balloon dilation (e.g., persistent translesional gradient, residual diameter stenosis >50%, or flow limiting dissection).
- Class IIb, Level of Evidence A recommendation notes that the effectiveness of stents, atherectomy, cutting balloons, thermal devices, and lasers for the treatment of femoral-popliteal arterial lesions (except to salvage a suboptimal result from balloon dilation) is not well established.
- Class IIb, level of evidence C recommendation notes that the effectiveness of uncoated/uncovered stents, atherectomy, cutting balloons, thermal devices, and lasers for the treatment of infrapopliteal lesions (except to salvage a suboptimal result from balloon dilation) is not well established.”

Definitions regarding class and level of evidence ratings are as follows: Class IIa, Level of Evidence: A: Benefit >>Risk. Additional studies with focused objectives needed. It is reasonable to perform procedure/administer treatment, recommendation in favor of treatment or procedure being useful/effective, some conflicting evidence from multiple randomized trials or meta-analyses; Class IIb, Level of Evidence: A: Benefit ≥ Risk. Additional studies with broad objectives needed; additional registry data would be helpful. Procedure/Treatment may be considered. Recommendation’s usefulness/efficacy less well established, greater conflicting evidence from multiple randomized trials or meta-analyses; Class IIb, level of Evidence: C: Benefit ≥ Risk. Additional studies with broad objectives needed; additional registry data would be helpful. Procedure/Treatment may be

considered. Recommendation's usefulness/efficacy less well established. Only diverging expert opinion, case studies, or standard of care.

Use Outside of the US: National Institute for Health and Care Excellence ([NICE], 2011): NICE published the following guidance regarding percutaneous atherectomy of femoropopliteal lesions with plaque excision devices:

- Current evidence on the efficacy of percutaneous atherectomy of femoropopliteal arterial lesions with plaque excision devices is inadequate in quality. Evidence on safety is inadequate, specifically with regard to the risk of distal embolisation. Therefore this procedure should only be used with special arrangements for clinical governance, consent and audit or research
- Further research into percutaneous atherectomy of femeropoliteal arterial lesions with plaque excision devices should take the form of well-conducted trials, which should define patient selection, treatment protocols and locations and types of arterial lesions treated, and report long-term patency outcomes.

Summary
Randomized controlled clinical trial data are limited in the published peer-reviewed scientific literature. Although results of prospective case studies and retrospective analyses are promising there is insufficient high-quality evidence to demonstrate safety and effectiveness of transluminal peripheral atherectomy.

Bioimpedance Spectroscopy to Measure Extracellular Fluid Differences Between Limbs (CPT® Code 0239T)
Bioelectrical impedance analysis is a noninvasive technique measures the body's response to electrical current. Current flows along the path of least resistance through the body and thus follows tissues with the highest water content, allowing measurement of edema (AHRQ, 2010). Bioimpedance spectroscopy has been proposed as a tool to detect early stage lymphedema.

Lymphedema is a pathological condition resulting from an accumulation of protein-rich fluid in the interstitial space because of congenital or acquired damage to the lymphatic system. Acquired or secondary lymphedema may be caused by disease, trauma, or an iatrogenic process such as surgery or radiation (Agency for Healthcare Research and Quality [AHRQ], 2010). Lymphedema is generally staged by observation of the individual's physical condition (i.e., stage 0-3) and is typically diagnosed by clinical history and physical examination. AHRQ notes that it is difficult to detect stage 0 or subclinical lymphedema with current methods. According to a technology assessment by AHRQ (2010) serial measurement of limb volume and or circumference are de facto gold standards for diagnosing secondary edema; however, no single method of assessment has emerged as the standard comparator for randomized clinical trials (AHRQ, 2010).

U.S. Food and Drug Administration (FDA)
Impedimed L-Dex U400 ExtraCellular Fluid analyzer received FDA 510(k) approval on October 3, 2008 with approval of an expansion of indications on November 4, 2011. According to the approval summary it is "indicated for use on adult human patients, utilizing impedance ratios that are displayed as an L-Dex ratio that supports the measurement of extracellular fluid volume between the limbs and is presented to the clinician as an aid to their clinical assessment of unilateral lymphedema of the arm and leg in woman and the leg in men. The device is only indicated for patients who will have or who have had lymph nodes from the axillary and pelvic regions either removed, damaged or irradiated. The device is not intended to diagnose or predict lymphedema of the extremity."

Literature Review
Controlled clinical trial data are lacking. Published studies are primarily limited to case series and validation studies. A technology review by AHRQ (2010) notes there is consistent evidence to indicate that lymphedema can be reliably measured using circumferential measurements or volume displacement. Additionally the assessment noted that there is insufficient evidence to draw conclusions about the reliability of other measures including tonometry, ultrasound, lymphoscintigraphy, or bioimpedance. The authors reviewed 41 studies related to diagnosis of lymphedema. In one study included in the technology assessment the test of interest involved differences in the sum of arm circumference between treated and untreated arms in persons with breast cancer. Circumferential differences to diagnose lymphedema were established at ≥5cm and ≥10cm. For differences of ≥5cm versus bioimpedance, sensitivity was 35% and specificity was 89%. For a difference of ≥10cm versus bioimpedance, sensitivity was 5% and specificity was 100%. For self-report compared to bioimpedance, sensitivity was 65%, specificity was 77%. In another included study bioimpedance was used diagnostically in

102 persons with breast cancer. The sensitivity of bioimpedance compared to limb volume was 10% and specificity was 98%. Two included studies involved bioimpedance alone. The first study found that mean and median bioimpedance measures were greater in the arms of women with lymphedema who survived breast cancer. In the other study single-frequency bioimpedance was highly correlated to bioimpendace spectroscopy (r=.99). The authors noted the tests did not drive the choice of treatment or outcome.

Use Outside of the US: No relevant information.

Summary
Randomized clinical trial data are lacking in the published peer-reviewed scientific literature. There is insufficient evidence to demonstrate the effectiveness or clinical utility of bioimpedance spectrometry as a tool to assess lymphedema. At this time the role of bioimpedance spectroscopy has not yet been established for this indication.

Intermittant and Continuous Measurement of Wheeze Rate for Bronchodilator or Bronchial Challenge (CPT® Codes 0243T, 0244T)
The American Thoracic Society Committee on Pulmonary Nomenclature defines wheezing as high-pitched (dominant frequency of ≥400 Hz) continuous adventitial lung sounds (i.e., >250msec) (Schraufnagel and Murray, 2010). The sound is generated by turbulence in larger airways that collapse with forced expiration (Boat and Green, 2011). Repeated examination may be required to verify a history of wheezing and should be directed toward assessing air movement, ventilatory adequacy, and evidence of chronic lung disease (Boat and Green, 2011). Computerized lung sound analysis involves recording the patient's lung sounds via an electronic device, followed by computer analysis and classification of lung sounds based on specific signal characteristics. Intermittant measurement of wheeze rate by pulmonary sound analysis has been proposed for use in bronchodilator or bronchial challenge diagnostic evaluation. Continuous measurement of wheeze rate by sound analysis has been proposed during treatment assessment such as bronchodilator or bronchial challenge evaluations, and during sleep for documentation of nocturnal wheeze and cough.

U.S. Food and Drug Administration (FDA)
Several devices have received FDA approval for the measurement of wheeze rate. The PulmoTrack™ 2020 System (iSonea, formerly KarmelSoniz, Binyamina, IS, US office:Alta Loma, CA) received 510(k) approval in March 2011. The approval summary notes "The PulmoTrack™ 2020 is intended for the analysis, interpretation and documentation of lung sounds. The PulmoTrack™ 2020 is indicated for use by or under the supervision of a physician while carrying out a provocation test, administering a bronchodilator or performing a physical examination in pulmonary function testing environment when there is a need for performing an acoustic pulmonary function measurement that quantifies the presence of wheezing. It is also indicated when there is a need to listen to amplified and filtered breath sounds. The PulmoTrack™ 2020 is indicated for patient population above two years old." The WIM-PC received 510(k) approval in November 2007. The FDA summary notes "The WIM-PC is intended for the analysis, interpretation and documentation of lung sounds."

Literature Review
Randomized controlled clinical trial data are scarce to inform the effectiveness and clinical utility of wheeze rate measurement. Gerung et al. (2011) performed a systematic review and meta-analysis to estimate the sensitivity and specificity of computerized lung sound analysis for the detection of lung sounds. Eight studies were selected for review. Overall sensitivity for the detection of wheezes or crackles was 88%, and specificity was 85%. The authors noted there is a lack of standardization across studies in the methods used for lung sound recording, computer algorithms for signal analysis and statistical methods for outcome analysis. Further research is needed to address the effectiveness of specific combinations of electronic devices and computing algorithms in clinical and community settings.

Beck et al. (2007) evaluated the use of computerized quantification of wheezing and crackles compared to a clinical score in assessing the effect of inhaled albuterol or inhaled epinephrine in infants with RSV bronchiolitis during a double blind, randomized, controlled nebulized treatment pilot study. Computerized quantification of wheezing and crackles (PulmoTrack) and a clinical score were performed prior to, 10 minutes post and 30 minutes post treatment. Breath segments containing at least five consecutive interference-free breaths were analyzed for a total of 20 breaths. Wheeze Rate (percent of time wheezing of total breath time) and crackle count (number of crackles per breath) were determined by the PulmoTrack® for each breath cycle, and averaged over the 20 breaths. Satisfactory lung sounds recording and analysis was achieved in all subjects. There was no

significant change in objective quantification of wheezes and crackles or in the total clinical scores either within the groups or between the groups. Although data suggest that automated wheeze rate measurement is feasible, the authors note that a larger study is necessary to assess the correlation between the computerized crackle and wheeze counts and the Clinical Score in response to treatment in RSV bronchiolitis.

Use Outside of the US: No relevant information.

Summary
There is insufficient evidence regarding the effectiveness and clinical utility of computerized pulmonary sound devices used to measure wheeze rate as an adjunct to auscultation and standard pulmonary testing. Although results are promising the role of these devices has not yet been established.

Total Body Systemic Hypothermia in the Neonate (CPT Codes 0260T, 0261T, 99481, 99482)
Hypoxic ischemic encephalopathy is characterized by the need for resuscitation at birth, neurologic depression, seizures, and electroencephalographic abnormalities. No specific clinical intervention has been shown to alter outcome. Total body and selective head hypothermia (e.g., a reduction in brain temperature of two-five degrees) in the neonatal population have been proposed as a therapeutic intervention to reduce death as well as neurodevelopmental disabilities.

According to Gluckman et al. (2005) the neuroprotective effects of experimental cooling are dependent on both a sufficient duration of cooling and on the timing of initiation of cooling. Extended cooling for 24–72 hours, started as late as six hours after injury, has been associated with persistent protection.

Literature Review
Gluckman et al. (2005) reported results of a randomized clinical trial investigating whether 72 hours of selective head cooling with mild systemic hypothermia, started within 6 h of birth, improved neurodevelopmental outcome at 18 months in infants with moderate or severe neonatal encephalopathy. Two hundred thirty-four term infants were randomly assigned to either head cooling for 72 hours, within six hours of birth, with rectal temperature maintained at 34–35°C (n=116), or conventional care (n=118). No difference was noted in the frequency of clinically important complications. Predefined subgroup analysis suggested that head cooling had no effect in infants with the most severe electroencephalogram (EEG) changes (n=46, p=0·51), but was beneficial in infants with less severe EEG changes (n= 172, p=0·009). The study was limited by small participant numbers. Data do not suggest a statistically significant difference with hypothermia; however, a sub-analysis of infants with less severe EEG changes suggests a potential benefit in complications with the use of hypothermia.

Shankaran et al (2005) reported results of a randomized controlled clinical trial of hypothermia in infants with a gestational age of at least 36 weeks who were admitted to the hospital at, or before six hours of age with either severe acidosis or peri-natal complications and resuscitation at birth. The infants had moderate or severe encephalopathy. Study participants were randomly assigned to standard care (control, n=106) or whole body cooling (i.e., esophageal temperature of 33.5 degrees Celsius for 72 hours, followed by slow re-warming, hypothermia group, n=102). Neurodevelopmental outcome was assessed at 18 to 22 months of age. The primary outcome was death or severe disability. Death or moderate or severe disability occurred in 44 % in the hypothermia group and 62 % of infants in the control group (p = 0.01). Twenty-four and 38 infants died in the hypothermia and control groups, respectively, p = 0.08).The rate of cerebral palsy was 19% and 30% in the hypothermia and control groups, respectively (p = 0.20). Data suggest that whole-body hypothermia reduces the risk of death or disability in this patient population.

In a follow-up to this study Shankaran et al. (2012) reported long-term outcomes of evaluable study participants. Of the 208 trial participants, primary outcome data were available for 190. Of the 97 children in the hypothermia group and the 93 children in the control group, death or an intelligence quotient (IQ) score below 70 occurred in 46 and 58, respectively (p=0.06). In these same groups, death occurred in 27 and 41, respectively, in the hypothermia and control groups (p=0.04). Death or severe disability occurred in 38 and 53, respectively, in the hypothermia and control groups (p=0.03). The rate of the combined end point of death or an IQ score of less than 70 at six to seven years of age was lower among children undergoing whole-body hypothermia than among those undergoing usual care. Outcomes were not statistically significant. Data suggest that hypothermia results in lower death rates; the rates of severe disability among survivors did not increase in the group undergoing hypothermia.

Azzopardi et al. (2009) performed a randomized controlled study of infants who were less than six hours of age and had a gestational age of at least 36 weeks and peri-natal encephalopathy. The study compared outcomes for infants receiving intensive care plus whole body hypothermia 33.5 degrees Celsius for 72 hours (n=163) with intensive care alone (n=162). The primary outcome was death or severe disability at 18 months of age.

In the group undergoing hypothermia 42 infants died; 32 infants survived but had severe neurodevelopmental disability. In the intensive care treatment arm 44 infants died and 42 had severe disability (p = 0.17). Infants in the cooled group had an increased survival without neurological abnormality (p = 0.003). Among survivors, cooling resulted in reduced risks of cerebral palsy (p = 0.03) and improved scores on the Mental Developmental and Psychomotor Developmental Indexes of the Bayley Scales of Infant Development II (p = 0.03 for each) and the Gross Motor Function Classification System (p = 0.01). Data suggest that moderate hypothermia for 72 hours did not significantly reduce the combined rate of death or severe disability but resulted in improved neurological outcomes in survivors who received hypothermia.

In a multi-center randomized controlled trial Zhou et al (2010) examined the safety and the effectiveness of selective head cooling (SHC) with mild systemic hypothermia (i.e., nasopharyngeal temperature of 34+/- 0.2 C and rectal temperature of 34.5-35.0 Celsius for 72 hours) in infants with hypoxic ischemic encephalopathy (HIE). Infants with were randomly assigned to the SHC or the control group. SHC was initiated within six hours after birth for infants in the hypothermia group. Rectal temperature was maintained at 36.0 to 37.5 degrees Celsius in the control group. Neurodevelopmental outcome was assessed at 18 months of age. The primary outcome was a combined end point of death and severe disability. The combined outcome of death and severe disability, mortality rate, and severe disability rates were significant (p = 0.01; p = 0.16; and p =0.01) for the SHC and control groups, respectively. Data suggest that SHC with mild systemic hypothermia may significantly decrease the combined outcome of severe disability and death, as well as severe disability.

Professional Societies/Organizations
American Heart Association (AHA): In a special report, the AHA published Neonatal Resuscitation: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Regarding therapeutic induced hypothermia the AHA recommendation notes that infants born at ≥ 36 weeks gestation with evolving moderate to severe hypoxic ischemic encephalopathy should be offered therapeutic hypothermia. The treatment should be implemented according to the studied protocols, which currently include commencement within six hours following birth, continuation for 72 hours, and slow rewarming over at least four hours. Further, therapeutic hypothermia should be administered under clearly defined protocols similar to those used in published clinical trials and in facilities with the capabilities for multidisciplinary care and longitudinal follow-up.

Use Outside of the US: No relevant information.

Summary
Randomized clinical trial data, meta-analyses and systematic reviews support the safety and effectiveness of therapeutic hypothermia (TH) in neonates for the treatment of hypoxic ischemic encephalopathy. The role of TH for other indications has not yet been established.

Percutaneous or Open Implantation of Neurostimulator Electrode Array (CPT® Codes 0282T, 0283T, 0284T, 0285T)
Percutaneous or open implantation of a neurostimulator electrode array is a technique being investigated for treatment of chronic pain where stimulation is delivered by a pulse generator and an electrode that is placed subcutaneously at the site of maximum pain rather than at the site of the nerve. This technique also referred to as subcutaneous target stimulation (STS) or peripheral nerve field stimulation (PNFS) involves a temporary trial period in which an electrode is placed subcutaneously by open or percutaneous approach, is secured in place with suture, and is then attached to a generator for approximately two to 14 days. A trial is considered successful if there is at least 50% pain reduction. Following a successful temporary trial the device is implanted permanently and connected to a pulse generator for management of chronic pain. PNFS treatment is being proposed as an alternative to other modalities of chronic pain management such as peripheral nerve stimulation where specific peripheral nerves are targeted rather than a field of pain.

U.S. Food and Drug Administration (FDA): FDA approval for specific PNFS devices was not found on the FDA site. However, PNFS can be carried out using leads and electrodes that are primarily designed for spinal cord stimulation and may be considered an off-label use of these devices.

Literature Review
Randomized controlled clinical trial data, and meta-analyses are lacking in the published, peer-reviewed scientific literature and there is insufficient evidence to determine safety and effectiveness of this therapy. Published peer-reviewed clinical trial data is primarily limited to case series and retrospective reviews.

The National Institute for Health and Care Excellence (UK, [NICE], 2012) prepared a draft interventional procedure consultation document evaluating peripheral field nerve stimulation for chronic low back pain. Although this is a draft document, NICE recommendations note that evidence on efficacy is very limited, in both quality and quantity. Likewise, evidence on safety is also limited and there is a risk of complications from any implanted device. Therefore this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

Use outside of the US: No relevant information.

Summary
There is insufficient evidence in the published peer-reviewed scientific literature to demonstrate the safety and effectiveness of peripheral subcutaneous field stimulation for management of chronic pain. Published evidence is limited to small sample populations, case series lacking control groups, and retrospective reviews and randomized controlled trial data supporting safety and efficacy are lacking. Clinical utility and impact on health outcomes cannot be determined at this time.

Near-Infrared Spectroscopy Studies of Lower Extremity Wounds (CPT® Code 0286T)
Foot ulceration remains a major health problem for diabetic patients. A standard method for determining the effectiveness of various treatment methods and quantifying wound healing has not been established. Measurements vary from observer to observer and rely on changes in length, width, and depth (Weingartner, 2010). Treatments can include moist wound healing protocols, offloading to reduce the pressure on the wound, active wound healing agents, and/or active therapies such as hyperbaric oxygen and/or negative pressure therapy. Near-infrared spectroscopy has been proposed as a noninvasive method of measuring the optical properties of tissue oxyhemoglobin content of lower extremity wounds beneath the skin surface to guide treatment.

Diffuse photon density wave (DPDW) methodology of near infrared spectroscopy (NIRS) can be used to measure the absolute concentrations of oxyhemoglobin and deoxyhemoglobin in tissue at depths of up to several centimeters. NIRS utilizes a detector and a dispersive element to allow the intensity at different wavelengths to be recorded. More data are needed to determine the threshold value that will distinguish healing from nonhealing wounds (Neidrauer, 2010).

In this procedure the wound is interrogated using a near-infrared spectroscopy device in up to 10 different locations. Data outputs are in the form of concentrations of oxygenated hemoglobin and total hemoglobin in the blood vessels in the wound. Comparing results on a weekly or biweekly basis, the clinician assesses wound healing progression to determine the need for changes in clinical approach.

Literature Review
Randomized controlled clinical trial data are lacking in the published peer-reviewed scientific literature regarding the safety and effectiveness of near-infrared spectroscopy for the measurement of lower extremity wound healing, including its use for the transcutaneous measurement of oxyhemoglobin.

Use Outside of the US: No relevant information.

Summary
There is insufficient evidence in the published peer-reviewed scientific literature to demonstrate the safety and effectiveness of near-infared spectroscopy for this indication. Randomized controlled clinical trial data with large patient populations are required to determine the role of this technology for the evaluation of lower extremity wound healing.

Near-Infrared Guidance for Vascular Access Requiring Real-Time Digital Visualization for Evaluation of Potential Access Sites and Vessel Patency (CPT® Code 0287T)

A peripheral venous catheter is most commonly used for venous access. Traditional techniques for determining the location of a peripheral vein includes palpating the skin, and unaided visualization of the skin in ambient light (Perry, 2011). Use of a near-infrared imaging system has been proposed as an alternative method to aid in visualization of the superficial vasculature. The imaging system provides a display of peripheral vasculature in real-time. It is purported to reduce the number of intravenous (IV) attempts, reduce the time it takes to initiate an IV and improve patient satisfaction (Christie Medical, 2013).

U.S. Food and Drug Administration (FDA): The VTS1000 Liquid Crystal Vein Locator (VueTek Scientific™, LLC, Gray, MN) received 510 (k) approval on Feb 18, 2011. The VTS1000 is a noninvasive electronic device to aid in the visualization of superficial vasculature. According to the 510(k) summary it is indicated for use during procedures requiring vascular or peripheral vascular access.

Literature Review

Chapman et al. (2011) reported results of 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 or PIV cannulation with the VeinViewer (Christie Medical Holdings, Cypress, CA, formerly Luminetx, Memphis, TN). 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. No differences in time to PIV placement, number of PIV attempts or pain scores was noted 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 ($p<0.047$), and for nurses' perception of pain ($p=0.01$). Data did not support improvement in outcomes for the total study group. Additional randomized controlled trials (RCT) should be conducted to determine the role of this device for evaluation of potential access sites.

Perry et al. (2011) conducted a prospective RCT to determine whether the use of a near-infrared light venipuncture aid (VeinViewer, Christie Medical Holdings, Cypress, CA, formerly Luminetx, Memphis, TN) would improve the rate of successful first-attempt placement of intravenous (IV) catheters in a high-volume pediatric emergency department (ED). One hundred twenty-three patients were randomized to use of the device (n=62) or the traditional technique of palpation of the overlying skin and unaided visualization of peripheral veins for IV access using only ambient room light (n=61). If a vein could not be cannulated after three 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 intravenous (IV) catheter placement. After completion of patient enrollment, a questionnaire was completed by study nurses as a qualitative assessment of the device. There was no significant difference in first-attempt success rate between the standard and device groups. Of the 19 study nurses, 14 completed the questionnaire. Seventy percent expressed neutral or unfavorable assessments of the device in nondehydrated patients. Ninety percent of nurses found the device a helpful tool for patients in whom IV access was difficult. Additional RCTs with large patient populations should be conducted to demonstrate the role of the device in these patients.

Use Outside of the US: No relevant information.

Summary

There is insufficient evidence in the published peer-reviewed scientific literature to demonstrate the safety and effectiveness of near-infrared devices to guide vascular access and to evaluate potential access sites. Randomized controlled trial data are lacking to inform on the clinical utility of near-infrared imaging systems in children and adults. The role of such devices has not yet been established.

Transanal Radiofrequency Therapy for Fecal Incontinence (e.g., SECCA Procedure) (CPT® Code 0288T)

Fecal incontinence is the inability to control the passage of gas, liquid and/or solid feces due to the loss of the coordinated function of the muscles and/or nerves of the rectum, anal canal, and pelvic floor. Treatment of minor incontinence (i.e., incontinence to flatus and occasional seepage of liquid stool) may be controlled by changes in diet and dietary habits, medication (e.g., bulking agents, antidiarrheal drugs), and bowel training (e.g., Kegel exercises, biofeedback). In the case of major incontinence (i.e., frequent loss of solid waste material) or incontinence unresponsive to conservative measures, surgical intervention may be indicated. In the event of an

isolated sphincter defect, the standard surgical treatment is sphincteroplasty. Other surgical procedures include repair of rectocele or rectal prolapse and, in severe cases, fecal diversion (i.e., colostomy) (Kim, et al., 2009; Lefebure, at al., 2008; Rao, 2004; Wexner and Sands, 2003; Takahashi, et al., 2002).

Transanal radiofrequency therapy (e.g., Secca® procedure) is a proposed alternative therapy for the treatment of fecal incontinence for patients who have not responded to medical therapy and are not good surgical candidates or have failed surgical intervention. The Secca procedure is noninvasive, typically takes 30–45 minutes, and is performed in an outpatient setting under local anesthesia and sedation. It is also proposed that there are fewer complications following the Secca procedure compared to invasive surgical procedures.

Radiofrequency therapy is based on the theory that "collagen deposition and subsequent scarring may increase one's ability to recognize and retain stool and permit improved continence" (Parisien and Corman, 2005). An anoscopic device uses four electrodes to deliver controlled radiofrequency energy to the sphincter muscles surrounding the anal canal. The energy creates precise, submucosal burn lesions, triggering collagen contraction. The lesions are subsequently resorbed, remodeling the tissue. The remodeling is proposed to improve barrier function of the anal sphincter (Efron, et al., 2003; Takahashi, et. al., 2002).

U.S. Food and Drug Administration (FDA)
The Secca® System (Curon Medical Inc., Sunnyvale, CA) was approved by the FDA as a 510(k) Class II device for general use for electrosurgical coagulation and "for use specifically in the treatment of fecal incontinence in those patients with incontinence to solid or liquid stool at least once per week and who have failed more conservative treatment" (FDA, 2002).

Literature Review
There is insufficient evidence in the published peer-reviewed scientific literature to support the effectiveness of transanal radiofrequency therapy (e.g., Secca procedure) for the treatment of fecal incontinence. Studies are primarily in the form of prospective case series with small patient populations (n=8–50). With the exception of one, five-year study (Tekashi, et al., 2008) follow-ups were short-term, ranging from 6–12 months. Various questionnaires (e.g., Fecal Incontinence Severity Index, Fecal Incontinence-related Quality of Life questionnaire, Vaizey scale) were utilized to measure quality of life (e.g., coping, depression, embarrassment) outcomes and results were inconsistent. Typically there were no significant improvements in physical component outcomes, such as anorectal manometry parameters, pudendal nerve motor latency, endoanal ultrasound results, and the thickness of internal anal sphincters. Some studies reported numerous complications while others reported no complications (Ruiz, et al., 2010; Kim, et al., 2009; Lefebure, et al., 2008; Takahashi-Monroy, et al., 2008; Felt-Bersma, et al., 2007; Efron, et al., 2003; Takahashi, et al., 2003). Studies comparing the use of transanal radiofrequency therapy to established medical and surgical treatment options are lacking.

Professional Societies/Organizations
American Society of Colon and Rectal Surgeons: In their practice parameters for the treatment of fecal incontinence, the American Society of Colon and Rectal Surgeons (Tjandra, et al., 2007) discussed the medical (e.g., fiber intake, antidiarrheal agents, enemas, laxatives, suppositories, anal plug) and surgical (e.g., sphincter repair, injectable therapy, sacral nerve stimulation, dynamic graciloplasty, artificial bowel sphincter, stoma) treatment options for this condition. Based on studies by Takahashi et al. (2003) (n=10) and Efron et al. (2003) (n=50), the ASCRS stated that the Secca procedure may be useful for selected patients with moderate fecal incontinence.

Use Outside of the US: National Institute for Health and Care Excellence (NICE): In an interventional procedure guidance document, NICE (2011) (United Kingdom) stated that endoscopic radiofrequency therapy of the anal sphincter for the treatment of fecal incontinence raised no major safety concerns, but the procedure should only be carried out in units specializing in the assessment and treatment of fecal incontinence. NICE noted that further research is needed to clearly define the appropriate patient group for this procedure. The guidance was based on three case series with small patient populations (n=19–50).

Summary
Evidence in the published peer-reviewed scientific literature does not support the efficacy of transanal radiofrequency therapy (e.g., Secca® procedure) for the treatment of fecal incontinence. Studies are primarily in the form of case series with small patient populations, short-term follow-ups and conflicting outcomes. Well-designed controlled trials comparing transanal radiofrequency therapy to standard medical and surgical

interventions are lacking. The role of this therapy in the management of individuals with fecal incontinence has not yet been established.

Intravascular Optical Coherence Tomography (OCT) (Coronary Native Vessel or Graft) (CPT® Codes 0291T, 0292T)

Invasive coronary angiography is considered the gold standard for evaluating patients with suspected myocardial ischemia. Intracoronary optical coherence tomography (OCT) is an intravascular imaging technique performed during cardiac catheterization that measures the echo time delay and intensity of backscattered light from tissue's internal microstructure. This diagnostic procedure creates high-resolution, cross-sectional images of the coronary arteries to permit quantification of lumen dimensions and the extent of lumen narrowing, visualization of atherosclerotic plaque, and characterization of the structure and extent of plaque (ECRI, 2011).

OCT systems comprise a fiberoptic imaging catheter attached to a patient interface unit, which connects to a system console. The console contains an optical engine (i.e., light source, beam splitter, reference arm, detectors, signal processor) and a computer that collects multiple light signals reflected from different tissue depths and combines them to make a three-dimensional image. Signal intensity is mapped to a color space that is displayed on a monitor (ECRI, 2011).

OCT is frequently compared to intravascular ultrasound (IVUS). Compared to IVUS, it is purported that OCT provides enhanced contrast between lumen and vessel walls, higher axial resolution of intracoronary plaque structures, and faster pullback. OCT catheters are smaller in diameter than IVUS catheters, allowing safer image acquisition from smaller-caliber vessels (St. Jude Medical, 2012).

The major limitation of OCT is its inability to consistently image the outer layer of the vessel wall and assess plaque burden due to limited tissue penetration (1.0 to 1.5 mm). Also, using OCT to measure large-diameter vessels at proximal target sites may be difficult, and the manufacturer has indicated that aorto-ostial lesions are not suitable for OCT imaging (ECRI, 2011).

U.S. Food and Drug Administration (FDA): Several intracoronary optical coherence tomography products made by St. Jude Medical, Inc., (St. Paul, MN), have received FDA 510 (k) approval. These include the C7 XR Imaging system (April 2010), C7 Dragonfly Intravascular Imaging catheter and disposable accessories (April, 2010) and the ILUMIEN System, (July 2011). The OCT Imaging system and catheter (Volcano Corporation (San Diego, CA) received 510(k) approval on Jan, 2010).

Literature Review

Although there are a number of prospective and retrospective studies and review articles in the published peer-reviewed scientific literature, randomized controlled trial data are lacking to inform health outcomes as a result of intracoronary optical coherence tomography. A number of clinical trials are ongoing.

In an emerging technology evidence report, ECRI (2011) found that a lack of data precludes the ability to draw conclusions regarding the clinical utility of intracoronary optical coherence tomography (OCT) to inform therapeutic decisions. No studies were identified that addressed the comparison of coronary angiography (CA) plus OCT to CA alone or CA plus other intravascular imaging techniques in terms of short- and/or long-term patient-oriented outcomes.

Professional Societies/Organizations

American College of Cardiology Foundation, American Heart Association, and Society for Cardiovascular Angiography and Interventions Association Task Force: These Societies published a joint practice guideline titled, Percutaneous Coronary Intervention (2011). The guideline notes that compared with IVUS, optical coherence tomography has greater resolution (10 to 20 micronmeter axially) but more limited depth of imaging (1 to 1.5 mm). Unlike IVUS, optical coherence tomography requires that the artery be perfused with saline solution or crystalloid during image acquisition and therefore does not permit imaging of ostial lesions. Clinical studies have shown low optical coherence tomography complication rates, similar to those of IVUS. The excellent resolution of optical coherence tomography permits detailed in vivo 2-dimensional imaging of plaque morphological characteristics (e.g., calcification, lipid, thrombus, fibrous cap thickness, and plaque ulceration or rupture) and evaluation of the arterial response to stent implantation (e.g., stent strut neointimal thickness and apposition) and may be of value in clinical research. The practice guideline notes the appropriate role for optical coherence tomography in routine clinical decision making has not been established.

Use Outside of the US: The Task Force on Myocardial Revascularization of the European Society of Cardiology and the European Association for Cardio-Thoracic Surgery: These Societies published joint Guidelines on Myocardial Revascularization in 2010. These guidelines note that OCT is a light-based modality of intravascular imaging with higher spatial resolution than intravascular ultrasound (15µm vs. 100µm). Its penetration is lower than intravascular ultrasound but it provides detailed imaging of the endoluminal borders. At present, OCT is a valuable research tool.

Summary
There is insufficient evidence to support the effectiveness and clinical utility of intravascular optical coherence tomography for intracoronary vessels in improving health outcomes. The role of this therapy has not yet been established.

Insertion of Ocular Telescope Prosthesis Including Crystalline Lens (CPT® Code 0308T)
The prosthetic intraocular telescope system is intended for the treatment of central vision loss (bilateral central scotomas) due to age-related macular degeneration (AMD). The device projects an image onto the part of the retina which is still healthy and can still see images. It does not cure AMD.

U.S. Food and Drug Administration (FDA): The Implantable Miniature Telescope™ (VisionCare Ophthalmic Technologies, Saratoga, CA) received FDA premarket approval in July 2010. According to the FDA, this device is an implantable device which, when combined with the optics of the cornea, constitutes a telephoto system for improvement of visual acuity in patients with severe to profound vision impairment due to bilateral, end-stage, age-related macular degeneration(AMD). The implantable miniature telescope (IMT) is surgically implanted in the capsular bag and is held in position by haptic loops. The intraocular telescope is available in two models: Wide Angle (WA) 2.2X and Wide Angle (WA) 2.7X. Both models are indicated for monocular implant. The implanted eye provides central vision, while the fellow eye continues to be used for peripheral vision is intended to improve vision in patients 75 years of age or older with stable, severe to profound vision impairment caused by end-stage age-related macular degeneration. It is indicated for patients with geographic atrophy or disciform scarring of the fovea, a visually significant cataract, and who achieve at least a 5-letter improvement on the visual acuity chart using a trial external telescope (FDA, 2010). Intraocular space for the telescope implant is created by removal of the lens to accommodate the placement of the telescope in the capsular bag.

As part of the approval the FDA requires extended follow-up of the premarket cohort population. According to the FDA, this continued follow-up of individuals in the long-term follow-up cohort (5 years postoperatively) will be conducted to provide additional long-term (up to eight years) safety data. The FDA also requires a multicenter, prospective, open label, single group assignment cohort study for safety. The study is required to consecutively will enroll 770 presurgical subjects aged 75 years and older with severe to profound vision impairment caused by end-stage age-related macular degeneration and a cataract. The subjects enrolled and undergoing implantation of the IMT will be followed for a total of five years with approximately six follow-up visits during the first year followed by annual visits thereafter for the next four years (FDA, 2010).

Literature Review
Randomized controlled clinical trial (RCT), meta-analyses and systematic review data are lacking in the published, peer-viewed scientific literature to inform the safety and effectiveness of the implantable miniature telescope. Prospective clinical trials are ongoing. Brown et al. (2011) reported findings of a comparative effectiveness review and the cost utility of the implantable miniature telescope. Data for this study was taken from previously published IMT2 Study Group clinical trial publications. A total of 115 eyes (56%) received the 2.2X device and 91 eyes (44%) received the 3X device. The authors note the following comparative effectiveness outcomes: Base Case Value Gain: the mean quality adjusted life year (QALY) gain over 12 years is 0.7577. This equates to a 12.5% human value (quality of life) gain daily for the average patient over the 12-year model. Fellow Eye Value gain: The cumulative QALY gain over 12 years is 0.0287. Fellow Eye with Cataract Surgery Value Gain: the vision gain corresponds to a utility gain of 0.0021, which represents a 0.35% improvement in quality of life. The authors concluded that data presented demonstrated that the 3X telescope prosthesis for end-stage AMD confers considerable improvement in quality of life compared with no therapy, all fellow eyes, and the fellow eyes that underwent cataract surgery during the two-year study period.

Use Outside of the US: No relevant information.

Summary
RCT data are lacking. There is insufficient evidence in the published peer-reviewed scientific literature to demonstrate the long-term safety and effectiveness of the implantable miniature telescope for individuals with central vision loss due to age-related macular degeneration, or for any indication. Although short-term results are promising, the role of the implantable miniature telescope has not yet been established.

Non-Invasive Calculation and Analysis of Central Arterial Pressure Waveforms (CPT® Code 0311T)
Blood pressure (BP) measurement is used routinely in clinical practice to manage cardiovascular disease. Since, BP determined at different sites can vary considerably and may be differently affected by antihypertensive drugs, new methods and technologies and devices are being researched to evaluate central blood pressure. It is theorized that the central BP may be more significant than peripheral BP in predicting target organ damage and cardiovascular outcomes. Noninvasive methods of measurement of central arterial pressure have been investigated with several methods including a method that utilized applanation tonometry to acquire an arterial pressure waveform which is then subject to calibration and/or calculation (Cheng, et al., 2012; McEniery, et al., 2008).

U.S. Food and Drug Administration (FDA): The SphygmoCoro® XCEL system (AtCor, West Ryde, Australia) received 501(k) approval. According to the 510(k) summary, the intended use of the device is to provide a derived ascending aortic blood pressure waveform and a range of central arterial indices. These measurements are provided non-invasively through the use of a brachial cuff. It is to be used on those patients where information related to ascending aortic blood pressure is desired but the risks of cardiac catheterization procedure or other invasive monitoring may outweigh the benefits. Additionally, the SphygmoCor XCEL System automatically measures systolic blood pressure and diastolic blood pressure. The SphygmoCoro XCEL Pulse Wave Velocity (PWV) option is intended to obtain PWV measurements. The PWV option is used on adult patients only.

Literature Review
Cheng et al. (2012) reported on a systematic review and meta-analysis that examined the measurement accuracy of non-invasively obtained central blood pressure by applanation tonometry. Studies were included if they had extractable data regarding measurements between estimated and measured central BP. The review included 22 studies for meta-analysis (857 subjects and 1167 measurements). The included studies were all conducted invasively in a catheterization laboratory or operating room and small in sample size (number range 12–100, mean 37.2). Ten studies performed the analysis by the software program and GTF from SphygmoCor. The authors concluded that the current tonometry-based central BP estimating methods are acceptable by using invasive calibration because they have small systematic and random errors. However, these errors were evident in the validation studies when cuff BP was used for noninvasive calibration. The authors noted that in order to utilize central BP concept in clinical practice, evidence of improved measurement accuracy of these noninvasive methods by either more accurate cuff BP or better calibration methods should be demonstrated. This study was a review of accuracy of central blood pressure measurement and did not examine the clinical utility of this measurement and did not compare to peripheral blood pressure measurement.

Use Outside of the US: No relevant information.

Summary
There is insufficient evidence in the published, peer-reviewed scientific literature that demonstrates the clinical utility of non-invasive calculation and analysis of central arterial pressure. Randomized controlled trial data on lacking on the clinical utility of this measurement. The role of this measurement in management of cardiovascular disease or other indications has not yet been established.

Radiofrequency Ablation (RFA) of Uterine Fibroids (CPT® Code 0336T, HCPCS Code C9736)
RFA has been proposed for the treatment of uterine fibroids of all sizes. In this minimally invasive procedure a laparoscopic ultrasound probe is used to determine the location and size of fibroids. An electrode array delivers alternating radiofrequency energy to drive a current through the tissue to be ablated, causing controlled, local heating, resulting in targeted tissue destruction.

U.S. Food and Drug Administration (FDA): The Acessa System (Halt Medical, Inc., Brentwood, CA) was given 510(k) approval in November 2012. According to the approval summary this system is indicated for use in percutaneous, laparoscopic coagulation and ablation of soft tissue, including treatment of symptomatic uterine

fibroids under laparoscopic ultrasound guidance. The FDA specifically notes the Acessa System must be used under laparoscopic ultrasound guidance. Laparoscopic ultrasound equipment is not included with the Acessa System.

Literature Review
Peer-reviewed published clinical trial data are limited to a small number of nonrandomized, uncontrolled prospective studies, with small participant numbers. Chudnoff et al. (2013), Guido et al. (2013) and Berman et al. (2014) report 12-, 24- and 36-month follow-up of a nonrandomized prospective interventional trial involving 135 women with symptomatic uterine fibroids. Several randomized controlled studies are ongoing.

Brucker et al. (2014) reported outcomes of a randomized, prospective single-center international clinical trial involving 51 women comparing radiofrequency volumetric thermal ablation (RFVTA) (n=26) and laparoscopic myomectomy (LM) (n=25) for symptomatic uterine fibroids. Primary outcomes were the mean hospital discharge times and perioperative outcomes. The predominant symptom reported by the patients in both groups was heavy menstrual bleeding followed by urinary frequency, pelvic discomfort and pain, backache, localized pain, dysmenorrhea, urinary retention, increased abdominal girth, dyspareunia, uterine pain, and sleep disturbance. There were no significant differences based on Fisher exact test between the two groups with regard to any of these symptoms, although the authors note this could be because of the relatively small number of patients in each group. Surgeons were blinded to the treatment until all fibroids were mapped by laparoscopic ultrasound. The mean hospitalization times were 10.0± 5.5 hours for the RFVTA group and 29.9 ± 14.2 hours for the LM group (p=.16). Intraoperative blood loss was 16 mL for the RFVTA procedures and 51 mL for the LM procedures. The percentage of fibroids imaged by laparoscopic ultrasound that were treated/excised was 98.6% for RFVTA and 80.3% for LM. Two complications were reported: vertigo (n=1; RFVTA) and port site hematoma (n=1; LM). The mean time between arrival in post-anesthesia recovery and discharge from the hospital was 8.2 hours for the RFVTA group and 28.0 hours for the LM group (p< 0.001). Mean hospitalization time was 10.0 hours and 29.9 hours for the RFVTA and LM groups, respectively, p<0.001. The authors note that short-term follow-up is a limitation to the study and plan five-year follow-up for pregnancy outcomes, symptom improvement, and overall treatment satisfaction as evaluated on the basis of participants' responses to validated questionnaires. Small study participant numbers is also a limitation to the study.

Chudnoff et al. (2013) reported one year results of a prospective, multicenter, interventional clinical trial (i.e., HALT trial) with primary outcome measures of change from baseline to 12 months and ongoing qualitative follow-up of women for three years in a cohort of 135 premenopausal symptomatic women with uterine myomas, uteri 14 weeks of gestation-sized or less with no single myoma exceeding 7 cm, and objectively confirmed heavy menstrual bleeding. Primary intervention was outpatient laparoscopic ultrasound-guided radiofrequency volumetric thermal ablation using the Acessa system (Halt Medical, Brentwood, CA). Bleeding outcomes and validated quality-of-life and patient satisfaction scales and objective measurements of uterine and myoma volume were conducted at 3, 6, and 12 months. Mean alkaline hematin and associated menstrual blood loss decreased from baseline levels by 31.8%, 40.7%, and 38.3%, respectively, at three-, six-, and 12-month intervals (p <.001 for all). Symptom severity and health-related quality of life improved (p<.001). There was one serious adverse event (0.7%) requiring readmission 5 weeks postprocedure and one surgical reintervention for persistent bleeding. Ninety-four percent of the women reported satisfaction with the treatment (p<.001).Although outcomes are promising the study was limited by uncontrolled design and short-term follow-up.

Guido et al. (2013) reported two-year outcomes of 124 subjects who participated in the HALT trial, of whom 112 were evaluable by questionaire. Outcome measures included: subject responses to validated questionnaires, treatment-emergent adverse events, and surgical re-intervention for fibroids at 24 months postprocedure. Significant changes from baseline were noted in symptom serverity (p< .001) and health-related quality of life scores (p< .001). There was a significant improvement in the mean health state score between baseline and 3 months after treatment (p < .001). Measurements at subsequent intervals showed no continued improvement. Six patients underwent surgical reintervention for fibroid-related bleeding between 12 and 24 months. The authors also reported on one patient who had an episode of bleeding post Cesarean section requiring receipt of six units of blood, which the study authors noted as possibly related to the RFA procedure. Limitations to the study include uncontrolled design, lack of comparator, short-term follow-up and small total patient numbers.

In a three-year follow-up of the HALT trial, Berman et al. (2014) reported subject responses to validated questionnaires and surgical repeat intervention to treat myomas outcomes for a cohort of 104 evaluable patients (104/135) who participated in the HALT trial. Change in mean symptom severity (p< .001) and Health-Related

Quality of Life questionnaire scores (p< .001) were improved from the baseline. Patient-reported Uterine Fibroid Symptom and Health-Related Quality of Life questionnaire subscores demonstrated statistically significant improvement from baseline to 36 months (p< .001) in all categories (i.e., Concern, Activities, Energy/Mood, Control, Self-consciousness, and Sexual Function). The cumulative repeat intervention rate was of 11% at 36 months. Although results are promising, study limitations include uncontrolled, nonrandomized design, lack of comparasion to other treatment methods, and small study participant numbers.

Robles et al. (2013) assessed outcomes of a prospective study assessing the laparoscopic radiofrequency volumetric thermal ablation (RFVTA) system among 114 screened women with symptomatic myomas. Thirty-five women completed the 12-month follow-up period. Uterine fibroid symptom and health-related quality-of-life (UFS-QOL) questionnaires were completed at zero, three-, six-, and 12-months. There was a significant reduction in average symptom severity score over the study period (p<0.001), and reductions in symptom severity scores from baseline to each of the follow-up visits, and from the 3-month visit to the 12-month follow-up visit were significant (p<0.001). There was a significant increase in average health-related quality of life (HRQL) scores from baseline to 12 months (p<0.001) and in the HRQL scores from baseline to each of the follow-up visits (p<0.001). After discharge, none of the participants was admitted to hospital for procedure-related complications. Within the study period, none of the participants required hysterectomy or any myoma treatment after RFVTA. No transfusions were required. Nine adverse events among eight women were reported as definitely not device- or procedure-related.Study limitations which limit the ability to routine clinical practice include lack of randomization and control, small study population and short-term follow-up.

Thirty-one women with symptomatic uterine fibroids underwent outpatient laparoscopic, ultrasound-guided, radiofrequency volumetric thermal ablation using the Halt 2000 System. Postoperative follow-up occurred at three, six, and 12 months. The primary outcome measures were patient safety, frequency of adverse events, repeat intervention rate, symptom severity and health-related quality-of-life scores from the validated Uterine Fibroid Symptom and Quality-of-Life Questionnaire. Secondary outcome measures were uterine volume changes over time. Mean symptom severity scores improved significantly compared with baseline at three, six, and 12 months. Mean health-related quality-of-life scores reached statistical significance over time. Mean uterine volume decreased at threem six, and 12 months. There were no procedure-related repeat hospitalizations, repeat treatments or procedures related to fibroid symptoms following treatment. The study is limited by lack of randomization and control, short-term follow-up and small sample size. Larger multicenter studies are needed to confirm these results (Garza, 2011).

Use Outside of the US: No relevant information.

Summary
There is insufficient evidence to demonstrate the effectiveness of radiofrequency ablation as a treatment of uterine fibroids. Although results are promising, published outcomes are primarily limited to one-, two- and three-year follow-up of a single trial involving 135 women with uterine fibroids, and a small randomized controlled trial comparing radiofrequency ablation and laparoscopic myomectomy. Additional well-designed randomized trials comparing this intervention with established treatment methodsare needed to demonstrate improvement in health outcomes. At this time the role of radiofrequency ablation for the treatment of uterine fibroids has not yet been established.

Endothelial Function Assessment (CPT® Code 0337T)
The endothelium helps to regulate regulate vascular tone, cellular adhesion, thromboresistance, smooth muscle cell proliferation, and vessel wall inflammation. Alteration in endothelial function precedes the development of morphological atherosclerotic changes and can also contribute to lesion development and later clinical complications (Deanfield, 2007). Noninvasive endothelial function assessment has been proposed as a means to predict the risk of atherosclerosis and cardiovascular disease.

One method involves measurement of the brachial diameter before and after an incease in shear stress induced by reactive hyperemia or flow-mediated dilation (FMD). Special probes that have pneumoelectrical tubing that connect to a computer are placed in an arm stabilizer and the index finger is placed in a probe. A sphygmomanometer cuff is placed on the forearm distal to the brachial artery, inflated and released for a timed period. This is repeated with higher pressures used to mimic occlusion. Finally the pressures are measured five minutes after the pressue is released. FMD occurs as a result of local endothelial release of nitrous oxide. The information is evaluated by proprietary software and a score indicating the endothelial health is generated.

Digital peripheral arterial tonometry (PAT) quantifies reactive hyperemia-induced changes in pulse volume amplitude (PVA) in the finger tip, and is an automated method to non-invasively assess endothelial function (Lee, 2012). According to the manufacturer, EndoPAT™ measures several vascular beds, composed of small vessels and microcirculation. The manufacturer also notes the EndoPAT™ corrects for systemic changes by a simultaneous measurement from the (un-occluded) contra-lateral arm.

U.S. Food and Drug Administration (FDA): The Endo PAT 2000 device (Itamar Medical, Inc., Framingham, MA) received 510(k) approval in November 2003. According to the approval summary it is a non-invasive device, intended for use as a diagnostic aid in the detection of coronary artery endothelialdysfunction (positive or negative) using a reactive hyperemia procedure.The summary also notes "The Endo PAT 2000 has been shown to be predictive of coronary artery endothelial dysfunction in the following patient population: patients with signs or symptoms of ischemic heart disease, who are indicated for coronary artery angiography, but who lack angiographic evidence of obstructive coronary artery disease. The device is intended to be used in a hospital or clinic environment by competent health professionals. The Endo PAT 2000 device is not intended for use as a screening test in the general patient population. It is intended to supplement, not substitute, the physician's decision-making process. It should be used in conjunction with knowledge of the patient's history and other clinical findings."

The CVProfilor® System, Cardiovascular Profiling System, original applicant Hypertension Diagnostics, Inc. Eagan, MN.) received 510(k) approval (K001948) from the FDA in November, 2000 as a Class II device for the noninvasive measurement of blood pressure and pulse rate. Accoding to the summary "It is classified as a noninvasive blood pressure measurement system providing a signal from which systolic, diastolic, mean, or any combination of the three pressures can be derived through the use of transducers placed on the surface of the body."

Literature Review
Randomized controlled clinical trial data are lacking to demonstrate the clinical utility and effectiveness of endothelial function assessment to predict cardiovascular risk. The majority of studies in the published peer-reviewed literature are prospective cohorts.

To asses whether endothelial dysfunction, as detected by peripheral artery tonometry , can predict late cardiovascular events, Rubenshtein et al. (2010) induced reactive hyperaemia (RH) following upper arm occlusion of systolic blood pressure in 270 outpatients. The natural logarithmic scaled RH index (L_RHI) was calculated from the ratio between the digital pulse volume during RH and at baseline. Follow-up was seven years. Seven-year adverse event rate was 48% in patients with L_RHI < 0.4 vs. 28% in those with L_RHI ≥ 0.4 (p=0.03). Univariate predictors of adverse events were LRHI, advancing age, and prior coronary bypass surgery. Multivariate analysis identified L_RHI < 0.4 as an independent predictor of AE (p=0.03). Study limitations include an uncontrolled study design,and dropout rate of 17%.

Hamburg et al. (2012) reported results of a correlational cohort study of 1957 Framingham Third generation Cohort participants. A fingertip peripheral arterial tonometry (PAT) device was used to measure digital pulse amplitude. Measurements were taken at baseline and in 30 second intervals for four minutes during reactive hyperemia induced by five minute forearm cuff occlusion. The relation of PAT ratio to cardiovascular risk factors was strongest in the 90-120 second postdeflation interval (overall model R2=0.159). To determine the relation between the hyperemic response over time following cuff deflation and clinical cardiovascular risk factors, stepwise regression models were performed for the PAT ratio for each 30 second interval with age and sex forced in, selecting from systolic blood pressure, diastolic blood pressure, heart rate, body mass index, total/HDL cholesterol, triglycerides, glucose, diabetes, current smoking, hormone replacement therapy, hypertension treatment, lipid-lowering treatment, and prevalent cardiovascular disease.The relation of PAT ratio to cardiovascular risk factors was strongest in the 90-120 second postdeflation interval (overall model R2=0.159). The authors note study findings support further investigations to define clinical utility and predictive value of digital pulse amplitude. The study was limited by uncontrolled design.

Professional Societies/Organizations
American College of Cardiology/American Hospital Association (ACC/AHA: On behalf of the ACC/AHA Greenland et al. published the 2010 Guideline for the Assessment of Cardiovascular Risk in Asymptomatic Adults.The guideline notes that it is unclear whether these measures of peripheral endothelial health provide incremental predictive information when controlling for traditional risk factors. The guideline further notes that

due to the limited data available, the writing committee concluded that it was premature to recommend serial FMD measurements to monitor treatment effects. In addition, due to the technical challenges of standardizing measurement of FMD and the relatively modest evidence of incremental change in risk assessment, measurement for risk assessment was not regarded as appropriate for risk assessment in the asymptomatic adult.

American Society of Echocardiography/Socienty for Vascular Medicine: On behalf of these Societies Roman et al. (2006) published a report regarding the clinical application of noninvasive vascular ultrasound in cardiovascular risk stratification. The report notes that the ability of flow-mediated endothelium-dependent brachial artery dilation to provide prognostic information in individuals at intermediate- or low-risk, independent of more standard risk-profiling approaches, remains to be identified.

Use Outside of the US: No relevant information.

Summary
There is insufficient evidence in the peer-reviewed scientific literature to demonstrate effectiveness and clinical utility of endothelial function assessment to establish the risk of cardiovascular disease. Additional well-designed high-level controlled clinical studies are needed before these tools can be applied to routine clinical practice. Further, concensus support in the way of practice guidelines are lacking. The role of endothelial function assessment has not yet been established.

Cryoablation of Lung Tumors (CPT® Code 0340T)
Pulmonary tumor cryoablation involves the destruction of tumor tissue using extreme cold. This is also known s cryoablation, cryosurgery, or cryotherapy. In this procedure a small thin wand-like needle, known as a cryoprobe, is inserted through the skin of the chest and between the ribs. Under computerized tomography (CT) guidance, the probe is advanced into the lesion of the lung and any tumor extensions to the pleura and/or chest wall. Compressed argon gas is passed through the probe and into the tumor, which freezes it and destroys the tissue. Treatment with the probe usually takes several minutes and may include repositioning the probe within the lesion so that overlapping ablations treat the entire tumor.

Literature Review
Randomized controlled clinical trial data are lacking in the published peer-reviewed scientific literature to demonstrate the safety and effectiveness of pulmonary tumor ablation by cryoablation. Studies are limited by uncontrolled design and small patient populations. Additional well-designed high quality studies are necessary to inform on health outcomes.Further, published professional consensus is necessary before this treatment can be translated into routine clinical practice.

Yashiro et al. (2013 reported results of a prospective study of 71 consecutive patients with 210 pulmonary tumors treated with 102 sessions of percutaneous cryoablation of lung tumors. A mean of 1.4 sessions was performed per case. A maximum of four cryoprobes was used on one lesion; the number and diameter of the probes were based on estimated tumor size. Every procedure was performed using a triple freeze/thaw protocol.High-pressure argon gas was used for freezing. There was no procedural mortality. Of 210 tumors, technical success was achieved for 167 (79.5%). At a median follow-up of 454 days, local progression occurred in 50 tumors (23.8%). One-, 2-, and 3-year local progression-free rates were 80.4%, 69.0%, and 67.7%, respectively, and technique effectiveness rates were 91.4%, 83.0%, and 83.0%, 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 (HR, 3.84; 95% CI, 1.59–9.30; P = .003) associated with local progression by multivariate analysis. Although results are promising, study limitations include uncontrolled design, and small patient numbers.

Kawamura et al. (2006) conducted a nonrandomized uncontrolled study to evaluate cryoablation of 35 pulmonary metastatic tumors in 20 patients who were not surgical candidates. In all cases cryoablation was performed percutaneously under CT guidance with local anesthesia. A total of 22 sessions of cryoablation were performed. Pneumothorax occurred in 11 of the 22 sessions, primarily after the completion of the ablation procedure. A chest tube was inserted in one case, transient needle aspiration was performed in three cases, and in seven cases no additional treatment was given. Phrenic nerve palsy occurred during one session. Mean hospital stay after treatment was 2.6 days, although for the initial five sessions, it was 5.4 days. There were no treatment-related deaths or conversion to surgical intervention. The follow-up period was 9 to 28 months. Local recurrence occurred in 7 (20%) of tumors. Five patients underwent repeat cryoablation without complications.

Study limitations which preclude the ability to apply results to other populations include uncontrolled randomized design and small study populations.

Use Outside of the US: No relevant information.

Summary
There is insufficient evidence in the published peer-reviewed scientific literature to demonstrate the safety and effectiveness of cryoablation for lung tumors. Data are very limited and of low quality; the majority of published studies report preliminary results or involve feasibility studies. At this time the role of cryoablation for pulmonary tumors has not been established.

Quantitative Pupillometry (CPT Code 0341T)
Pupil reactivity and sensitivity may indicate neurological issues or worsening of neurological status. The stimulation and subsequent measurement of pupil reactivity by a hand held infrared camera and use of a digital device and data processor to calculate measurements has been proposed for a number of indications including the evaluation of autonomic function, response to pain, drug metabolism, sleep disorders, and various psychological indications and has been use in the research setting. A pupillometer is made of three components: the light source to stimulate the pupil, an image capturing device capable of taking measurements of the pupil in real-time, and a data processor that performs the calculations using the measurements. The device is held in the patient's visual field, the data is interpreted, and a report is generated.

Literature Review
High level, randomized and controlled data are lacking regarding the effectiveness of this device in the published, peerviewed scientific literature.

Bremner and Smith (2006) reported results of a prospective study of involving the use of light reflex pupillography in 150 consecutive patients with symptomatic geralized autonomic failure. Inclusion criteria was heterogeneous with a variety of indications represented including amyloidosis, multiple system atrophy, pure autonomic failure, diabetes mellitus, hereditary neuropathies, and paraneoplastic syndromes. Infra-red video pupillography was used to measure resting pupil diameters in light and dark, the light reflex response, the miosis associated with an accommodative effort, and responses to topical administration of various pharmacological agents. No significant correlation between the type of pupil abnormality and the predominant type of systemic autonomic deficit was seen in most conditions. The authors note “Although there does appear to be some weak correspondence between our pupillographic findings and the results of autonomic function tests, a x2 test suggests that this association could have arisen by chance (p=0.072).”

Professional Societies/Organizations
American Academy of Ophthalmology ([AAO, 2013): The Guidelines for recommendations for keratorefractive laser surgery notes that measurement of pupil size is not required in the preoperative examination.

Use Outside of the US: No relevant information.

Summary
There is insufficient evidence in the published peer-reviewed scientific literature to demonstrate the effectiveness or clinical utility of quantitative pupillometry for any indication. Studies are limited by uncontrolled design; high-quality controlled clinical trial data are lacking. The role of pupillometry has not been established.

Elastography (CPT Code 0346T, 91299)
Elastography is a type of imaging technique that is proposed in concert with ultrasound to map the elastic properties of soft tissue, specifically to differentiate between normal or benign, and abnormal tissue. The elastographic image is taken while the ultrasound technician compresses the suspect area. This image is compared with an image that is taken when the area is not compressed. Elastography has been proposed for use with a number of clinical indications including estimation of tendon stiffness, breast cancer, liver fibrosis, prostate cancer, and tumors of the thyroid, brain, and skin.

Transient elastography (TE) has been proposed as a non-invasive technique to measure fibrosis and cirrhosis of the liver via shear wave speed measurement. At present, liver biopsy remains the gold standard for the

assessment of fibrosis and cirrhosis in liver disease; however, there are a number of limitations to biopsy. Limitations include its invasiveness, risk of complications, sampling error, variability in histopathologic interpretation, and the reluctance of patients to undergo repeated biopsies to monitor disease progression (Shaheen, 2007). TE uses ultrasound to track the shear wave and to measure its speed, which is correlated with the elasticity of the liver. The harder or more fibrotic the tissue, the faster the shear wave propagates. The final measurement of fibrosis severity is typically obtained as the median value of several measurements expressed in kilopascals (kPa) (Sandrin 2003).

U.S. Food and Drug Administration (FDA)
Several ultrasound devices have received FDA approval for use in the elastographic mode including the SonixTouch® Ultrasound Scanner (Ultrasonix Medical Corporation, Richmond, BC), October, 2008, SonoSite MaXXTM® Series Ultrasound System (SonoSite, Inc., Bothell, WA), August , 2008, GE LOGIQ E9 BT2010® Diagnostic Ultrasound System (GE Healthcare, Waukesha, WI), November, 2009, Diagnostic Ultrasound System Aplio MX® (Toshiba America Medical Systems, Inc., Tustin, CA), October, 2009, and the Aixplorer® (Supersonic Imagine, Inc., Bothell, WA), August, 2012.

Fibroscan® (Echosens SA, Paris, France, available in the US through Sandhill Scientific, Highlands Ranch, CO) received FDA 510(k) approval on April 5, 2013. Fibroscan is indicated for noninvasive measurement of shear wave speed at 50 Hz in the liver. The FibroScan® device uses transient elastography for the non-invasive measurement of liver shear wave speed. A mechanical vibrator produces low-amplitude elastic waves that travel through the skin and intercostal space into the liver. According to the FDA, the shear wave speed may be used as an aid to clinical management of patients with liver disease (2013).

Literature Review
A number of systematic reviews and meta-analyses have reported the diagnostic accuracy of transient elastography for assessment of fibrosis and cirrhosis in chronic liver disease (Abd El Rihim, 2013; Bota, 2013; Steadman, 2013; Adebajo, 2012; Tsochatzis, 2011; Poynard, 2010; Stebbing, 2010; Shaheen, 2007). When Fibrocan was used for mixed etiologies of liver disease, reported summary sensitivity and specificity for F2-3 (fibrosis) were 0.63-0.83 and 0.73-0.87, respectively; summary sensitivity and specificity for F4 (cirrhosis) were 0.67-0.98 and 0.84-0.94, respectively. Sensitivity and specificity for individuals with hepatitis C were reported as F≥2: 0.76, and 0.86, respectively, F≥3: 0.88 and 0.91, respectively, and F4: 0.85 and 0.91, respectively (Steadman, 2013). In the study by Tsochatzis, summary sensitivity and specificity was 0.78 and 0.80, respectively, for individuals with chronic hepatitis C (2011). Limitations noted in many of the meta-analyses include analysis of uncontrolled studies, risk of bias, lack of prospective validation of liver stiffness measure/index, and that a head-to-head comparison with liver biopsy was not published in a majority of studies.

Despite these limitations, there is published concensus support by professional societies/organizations for the use of TE for the assessment of chronic liver disease, including hepatitis C, as an evolving standard of care in clinical practice. These societies include the American Association for the Study of Liver Diseases ([AASLD], 2013), the World Health Organization ([WHO], 2014) National Institute for Health and Care Excellence, ([NICE], 2013) and the British HIV Association (2013). TE is an acceptable option for non-invasive assessment of liver fibrosis and cirrhosis in chronic liver disease.

Regarding the use of ultrasound elastography for other indications, several observational studies for measurement of soft tissue stiffness have been published in the peer-reviewed scientific literature (Lee et al. 2012; Lie et al., 2011; Siegmann et al. 2010; Bahn, 2009). Follow-up data regarding the impact on health outcomes and treatment decisions are unknown.

Sadigh et al. (2013) reported an individual patient data meta-analysis of the diagnostic performance of ultrasound elastography (USE) versus B-mode ultrasound (USB) across size ranges of breast masses. Five studies were analyzed involving 1,412 breast masses. Included studies were performed in Turkey, South Korea, Romania, Germany, and China. For breast masses <10 mm, the sensitivity/specificity of USE and USB were 76 %/93 % and 95 %/68 %, respectively. For masses 10–19 mm, sensitivity/specificity of USE and USB were 82 %/90 % and 95 %/67 %, respectively. For masses >19 mm, sensitivity/specificity of USE and USB were 74 %/94 % and 97 %/55 %, respectively. The authors noted that the sensitivity and specificity of each of these techniques for characterising breast masses were not significantly different among masses with sizes of less than 10 mm, 10–19 mm, and more than 19 mm. Subgroup analysis of masses more than 29 mm demonstrated similar result. The authors note none of the studies clearly stated whether the reference standard interpretation

was performed without the knowledge of index test (i.e., USE) results. Additionally, it was unclear in all studies whether relevant clinical data were available to radiologists when they interpreted the USE and USB images. An additional limitation is the inclusion of uncontrolled trial data for analysis.

Professional Societies/Organizations

American Association for the Study of Liver Diseases (AASLD)/Infectious Diseases Society of America (IDSA): The AASLD/IDSA published Recommendations for Testing, Managing, and Treating Hepatitis C which notes that vibration-controlled transient elastography is a noninvasive way to measure liver stiffness and correlates well with measurement of substantial fibrosis or cirrhosis in patients with chronic HCV infection; however, the measurement range does overlap between stages. Not limited to assessment by transient elastography, the AASLD notes that although an ideal interval for assessment has not been established, annual evaluation is appropriate to discuss modifiable risk factors and update testing for hepatic function and markers for disease progression. For all individuals with advanced fibrosis, liver cancer screening dictates a minimum of every six months evaluation (2014).

American College of Radiology (ACR, 2012): On behalf of the ACR, Newell et al. published ACR Appropriateness Criteria® for nonpalpable mammographic findings (excluding calcifications). The Guideline notes that elastography is being evaluated as a way to increase the specificity of ultrasound, especially regarding evaluation and management of solid masses.

Use Outside of the US: British HIV Association (2013): On behalf of this society, Wilkins et al. published "British HIV Association Guidelines for the Management of Hepatitis Viruses in Adults Infected with HIV." The Guidelines suggest that for the staging of liver disease in individuals with chronic hepatitis/HIV infection that transient elastography is a noninvasive investigative test of choice. The Guideline also suggests that repeated fibrosis assessment should be performed at least annually.

European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB): On behalf of the EFSUMB, Cosgrove et al. (2013) published "Guidelines and Recommendations on the Clinical Use of Ultrasound Elastography". In Part 2 Clinical Applications, Cosgrove notes that TE can be used to assess the severity of liver fibrosis in patients with chronic viral hepatitis provided that confounding factors are taken into account, and especially to distinguish patients with nil/mild fibrosis from those with significant fibrosis and to identify those with cirrhosis. Further, that TE is useful for assessment of liver fibrosis in patients with NAFLD, alcoholic liver diseases, and in patients co-infected with HIV and hepatitis C.

National Institute for Health and Care Excellence (NICE): The Guideline for the diagnosis and treatment of prostate cancer notes the optimal course of action in men who are still suspected of having prostate cancer following a negative initial TRUS biopsy is not well defined. The following may be considered review of initial biopsy, repeat TRUS biopsy, mpMRI, extended/saturation TRUS biopsy, 3D ultrasound plus biopsy, template biopsy, contrast enhanced ultrasound plus biopsy, and/or elastography plus biopsy. The guideline further notes that evidence about elastosonography rebiopsy is limited to a single small study published as an abstract only. In this study all men undergoing elastosonography had areas of increased texture and cancer was detected in 33%. There was very low quality clinical evidence for elastography and 3D ultrasound (2014).

Regarding use of TE for the diagnosis and management of chronic hepatitis B in children, young people and adults, NICE recommends that TE is offered as the initial test for liver disease in adults newly referred for assessment. Specific TE results are noted at which point a liver biopsy is recommended (2013).

Royal College of Radiologists: Regarding shear wave elastography, the Guideline on Screening and Symptomatic Breast Imaging notes it appears in early studies to show promise in improving either the sensitivity or specificity of breast ultrasound. Further UK-based multi-center studies are required before use in routine breast practice can be recommended.

World Health Organization (WHO): In "Guidelines for the Screening, Care, and Treatment of Persons with Hepatitis C Infection" (2014), WHO notes that Fibroscan, if available, can be used to assess liver stiffness.

Summary

Although data are not robust, a number of systematic reviews and meta-analyses of observational and retrospective studies have demonstrated acceptable diagnostic accuracy for the use of transient elastography to

assess fibrosis and cirrhosis in chronic liver disease, including hepatitis C. Further, there is professional society/organizational concensus support by way of published clinical guidelines, for its use as an evolving standard of care. There is insufficient evidence in the published, peer-reviewed scientific literature to support its use for other indications.

Although reported results are promising, there is insufficient high-quality data to demonstrate improvement in clinical outcomes with the use of ultrasound elastography for other indications. Consensus support in the form of published practice guidelines or positions is lacking.

Adrenal and Fetal Mesencephalic Transplantation for Parkinson Disease (HCPCS Code S2103)
There are scarce data in the published, peer-reviewed scientific literature regarding the current clinical use of adrenal-to-brain transplantation in humans for any indication. In a systematic review of the literature, the Agency for Healthcare Research and Quality ([AHRQ], 2003) noted that there is a lack of efficacy and substantial morbidity associated with the procedure for the treatment of Parkinson disease (PD). The AHRQ also concluded that adrenal medullary transplants are no longer performed to treat PD.

There is ongoing research in animal and human models relative to the use of fetal mesencephalic transplantation as a replacement source of dopamine-producing cells. In this procedure, fetal brain cells (i.e., neurons) that produce dopamine are implanted in the putamen or head of the caudate area of the brain, which is the area controlling movement. In theory, the transplanted neurons can replace the loss of normal dopamine-producing cells. These fetal cells may be human or xenogeneic (i.e., derived from a different species).

Clinical improvement was demonstrated in small numbers of individuals with PD undergoing transplantation of fetal tissue in several nonrandomized studies; however, results have not been replicated in double-blind sham-surgery controlled clinical trials (Olanow, 2003; Freed, 2001). Transplantation of fetal substantia nigra into the stratum has failed to show significant efficacy and has been associated with the side effect of transplant-induced off-medication dyskinesias. More recently, implanted dopamine neurons have been found to contain Lewy bodies, suggesting that they are dysfunctional and may have been affected by the PD pathological process (Olanow, 2009).

There are scarce data regarding the safety and effectiveness of xenogeneic fetal cells for any indication in humans. Schumacher et al. (2000) reported results of a case series study of 12 individuals with Parkinson disease who underwent unilateral implantation of embryonic porcine ventral mesencephalic tissue (Schumacher, 2000). In the medication-off state, total Unified Parkinson's Disease Rating Scale scores improved by 19% (p=.01). At the time of study publication there were no reported permanent complications. Limitations of the study include small size, uncontrolled study design, and short-term follow-up.

U.S. Food and Drug Administration (FDA)
The FDA Center for Biologics and Research regulates the transplantation of fetal/embryonic cells. Companies supplying cell and tissue-based products must register and list their products with the FDA.

Professional Societies/Organizations
Agency for Healthcare Research and Quality (AHRQ): The AHRQ (2003) published results of a systematic review of the literature regarding the diagnosis and treatment of Parkinson disease. The AHRQ noted an insufficient number of studies have been done to make more than tentative conclusions. They further noted "A recent randomized controlled trial comparing tissue transplant to sham surgery raised important questions regarding the long-term efficacy and safety of the procedure." "Due to the small number of studies within each meta-analysis, these findings are sensitive to possible publication bias in the literature."

American Academy of Neurology (AAN): On behalf of the AAN, Hallet and Litvan (1999) recommended that adrenal-to-brain transplantation not be performed because of unacceptable risk to the patient. They further noted that the procedure was no longer being studied. Regarding fetal mesencephalic transplantation the AAN (1999) notes that, while the procedure is promising, it remains experimental due to lack of controlled clinical trials. The authors determined that there were small, nonrandomized case studies which noted functional improvement in some patients; however, unacceptably high levels of morbidity and mortality were associated with the procedure. Review of pathologic reports found that few transplanted cells survived long term, suggesting that benefit of the procedure would be of short duration.

The authors also reviewed the documented studies of fetal mesencephalic transplantation (1999). Studies were small and nonrandomized. There was variation between the studies in the techniques utilized, the site of transplantation, the number of mesencephalons used, and the immuno-suppressive regimen provided. In all of the studies some of the patients demonstrated improvement in motor function.The summary notes that while the procedure is promising because it appears effective and has low morbidity and mortality, it is considered experimental because of the absence of controlled studies.

Use Outside of the US: No relevant information

Summary
The transplantation of tissues from the adrenal medulla (autograft) and human fetal mesencephalon (allograft) has been proposed as a replacement source of dopamine-generating neurons. Randomized, controlled trial data are lacking regarding the safety and effectiveness of human or xenogeneic adrenal medullary-to-brain or fetal mesencephalic transplantation for any indication and the role of these therapies has not been established. Although some short-term treatment effects have been noted in individuals with PD undergoing human or xenogeneic fetal mesencephalic transplantation, studies are limited by a lack of clear patient selection criteria, small patient populations, and short-term follow-up. Long-term safety and effectiveness has not been demonstrated.

Transtympanic Micropressure Device for Ménière's Disease (e.g., Meniett™ Device) (HCPCS Code E2120)
Ménière's disease (also called idiopathic endolymphatic hydrops) is a disorder of the inner ear. Although the cause is unknown, the disorder probably results from an abnormally large amount of fluid (called endolymph) collecting in the inner ear. The symptoms of Ménière's disease include episodic vertigo (i.e., a sensation of dizziness or spinning), hearing loss, tinnitus (i.e., ringing in the ears), and a sensation of fullness in the affected ear.

The use of a transtympanic micropressure device/low-pressure pulse generator (i.e., Meniett™) (Medtronic Xomed, Jacksonville, FL) has been proposed as an alternative to surgery. The device is prescribed by a physician and delivers low-frequency, low-amplitude pressure pulses within the range of 0–20 centimeter (cm) H_20 to the middle ear via a close-fitting ear cuff and tympanostomy tube. Its mode of action is thought to be transmission of the pulses to the inner ear, promoting the flow of endolymph out of the cochlea, alleviating the hydrops and relieving symptoms. The tympanostomy tube is inserted under local anesthetic in the office setting. The patient then uses the device at home three times per day for approximately three minutes per session. The patient discontinues use when symptoms remit.

U.S. Food and Drug Administration (FDA)
In December 1999, Pascal Medical AB (Sweden) received 510(k) approval from the FDA for the Meniett Low-Pressure Pulse Generator. In 2001, Medtronic Xomed, Inc. (Jacksonville, FL) purchased the device from Pascal Medical. The Meniett Low-Pressure Pulse Generator is classified as a Class II device and is indicated for the symptomatic treatment of Ménière's disease.

Literature Review
The Meniett device has been evaluated in several small clinical trials (Ashan et al., 2014; Shojaku, 2011; Dornhoffer, 2008, Mattox and Reichert, 2008; Gates, 2006; Stokroos et al, 2006; Boudewyns et al., 2005; Thomsen et al., 2005; Gates, 2004; Odvist et al., 2000), with the number of study participants ranging from 12-62 persons. Ashan et al. (2014) reported results of a systematic literature review (eight studies) and meta-analysis (18 studies). Eight studies reported hearing evaluation and improvement in in pure tone average after Meniett treatment (p=.0085). Data could not be combined for American Academy of Otolaryngology–Head and Neck Surgery functional score due to heterogeneity. Of six studies reporting frequency of vertigo, Meniett treatment significantly reduced frequency of vertigo (p< .0001). Limitations of the study include data derived from uncontrolled and retrospective studies, short follow-up of five months, and small numbers of study participants**.**

In the randomized controlled trial by Thomsen (2005), patients were evaluated for two months to obtain a baseline, after which tympanostomy tubes were placed, followed by two months without treatment to account for the effect of the tympanostomy tubes. Patients then received either the Meniett device for therapy or a sham device that was identical to the active device but did not give any pressure pulses except a slight pressure increase to 2 cm H20 for five seconds to maintain the leakage test. The authors state that the patients were

unable to detect whether they were using the active or placebo device, but the basis for this statement is not discussed. Patients were evaluated at two, four, and eight weeks of use. Outcomes demonstrated significant improvement in functional level and in patient perception of vertigo in those receiving therapy with the Meniett device compared to the control group. There was a nonstatistically significant trend, toward reduced frequency of vertigo in those using the Meniett device. Study limitations include small population, exclusion of a large number of participants, and the inability to determine whether the improvement is related to placement of the tympanostomy tube itself.

Limitations which limit the ability to transplate outcomes to routine use of this device include small study populations, lack of blinding and randomization in the majority of studies, and improvement in outcomes in individuals who were treated with the Meniett device as well as other interventions. Further large, randomized controlled trials are necessary to determine the effectiveness of this device to improve health outcomes.

Professional Societies/Organizations
The Equilibrium Committee of the American Academy of Otolaryngology-Head and Neck Surgery published a Policy Statement on Micropressure Therapy for Ménière's disease (2008, updated 2012) noted that there is there is convincing and well-controlled medical evidence to support the use of micropressure therapy (such as the Meniett device) as a second level therapy when medical treatment has failed. The Committee noted that the device represents a largely non-surgical therapy that should be available as one of the many treatments for Ménière's disease.

Use Outside of the US: No relevant information.

Summary
Studies supporting the use of a transtympanic micropressure device/low-pressure pulse generator for any condition including but not limited to the treatment of Meniérè's disease are limited by methodological flaws, including the inability to distinguish treatment effect from that of the natural course of disease, and the inability to discern whether any improvement in symptoms is related to placement of the tympanostomy tube itself. The effectivenss of the device has not been proven through well-designed trials. Prospective randomized controlled trials with sufficient sample sizes and long-term follow-up comparing transtympanic micropressure treatment to an alternative treatment, application of a sham device or to the natural course of Ménière's disease, are necessary to definitively determine the benefits of this technology in treating this condition.

Visual Field Assessment with Concurrent Real Time Data Analysis (CPT Codes 0378T, 0379T)
There is insufficient evidence in the published, peer-reviewed scientific literature to establish improved health outcomes. At this time the role of this service has not been established.

Computer-Aided Animation and Analysis of Time Series Retinal Images for the Monitoring of Disease Progression (CPT Code 0380T)
There is insufficient evidence in the published, peer-reviewed scientific literature to establish improved health outcomes using this technology. At this time the role of computer-aided animation and analysis of time series retinal images to monitor disease progression has not been established.

External Heart Rate and 3-Axis Accelerometer Monitoring to Diagnose Nocturnal Epilepsy (CPT Code 0381T, 0382T, 0383T, 0384T, 0385T, 0386T)
Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures (Abou-Khalil, 2012). Standard evaluation and diagnosis of seizures and epilepsy includes an in-depth clinical history; an electroencephalogram and other brain imaging may be used to supplement the history, help classify the type of seizure and determine underlying pathology. A number of epileptic seizure syndromes exist including several which are characterized by the occurrence of seizures at night, while the individual is sleeping and unattended. Nocturnal seizures often occur in children.

Use of external heart rate and 3-axis accelerometer monitoring has been proposed as a method to detect/diagnose nocturnal epilepsy. Three-axial accelerometer measures the movement (acceleration) in three orthogonal directions fixed to a sensor by way of soft bands generally affixed to the wrists and/or ankles.

Literature Review

Published, peer-reviewed data are limited regarding the effectiveness of accelerometer monitoring to diagnose epilepsy, including nocturnal epilepsy (Beniczky, 2013; Van de Vel, 2013). Studies are limited by uncontrolled design, small participant numbers and shortterm follow-up.

Beniczky et al. (2013) reported outcomes of a prospective study designed to assess the clinical reliability of a wrist-worn, wireless accelerometer sensor for detecting generalized tonic–clonic seizures in 73 consecutive patients. The wireless wrist accelerometer correctly detected 35 seizures (89.7%). The mean sensitivity per patient (with seizure) was 91%. Twenty-eight seizures occurred during sleep and eleven seizures occurred when the patient was awake. The device had a similar accuracy for detecting nocturnal and daytime seizures. One hundred forty-nine seizures other than generalized tonic-clonic seizures were recorded (simple partial, 37; complex partial/psychomotor,31; focal tonic, 6; hypermotor, 6; absence, 1; myoclonus,60; psychogenic nonepileptic seizure, 8). Study limitations include uncontrolled design, small study numbers and shortterm follow-up**.**

Use Outside of the US: No relevant information.

Summary
There is insufficient evidence in the published, peer-review scientific literature to demonstrate the effectiveness of 3-axis accelerometry to diagnose any type of seizure. Large, controlled clinical trials comparing accelerometry with established diagnostic methods are needed before it can be applied to routine clinical practice.

Tumor Treatment Fields Therapy (e.g., NovoTTF 100A) (HCPCS Codes A4555, E0766)
Electric tumor treatment fields (TTFields) therapy has been proposed for the treatment of recurrent glioblastoma multiforme (GBM). Inferred mechanism of action is disruption of the rapid cell division exhibited by cancer cells by alternating electrical currents applied to the brain through electrically insulated surface transducer arrays which are placed on the patient's shaved scalp. The fields alter the tumor cell polarity at an intermediate frequency. The frequency used for a particular treatment is specific to the cell type being treated (NovoCure, 2014).

At this time, the NovoTTF-100A System is the only TTFields device that has received FDA approval electric tumor fields therapy. This system is a wearable, non-invasive, portable battery or power-supply operated device designed for continuous use throughout the day or night. It produces continuous TTFields treatment at 100-200kH. TTFields are applied to two pairs of insulated electrode arrays in an alternating fashion. The electrodes are placed on the scalp over a layer of adhesive hydrogel which is held in place by adhesive strips. The scalp must be re-shaved to maintain optimal contact between the electrode and the skin. Gel under the electrodes requires replacement every three-four days. The treatment period is for a minimum of four weeks.

U.S. Food and Drug Administration (FDA)
The NovoTTF-100A System (Portsmouth, NH) was approved by the FDA in April, 2011. This device is indicated for treatment of adult patients who are 22 years of age or older who have histologically-confirmed glioblastoma multiforme (GBM), following histologically-or radiologically confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted The pre-market approval requires a post market nonrandomized, unblended, concurrent control study to be undertaken using the NovoTTF-100A system in patients with recurrent GBM (FDA, 2011).

Literature Review
Data regarding the safety and effectiveness for TTF are limited in the published, peer-reviewed scientific literature and consist of several prospective studies and a randomized clinical trial (RCT) involving a total of 273 patients (Stupp, 2012; Kirson, 2009; Salzberg, 2008; Kirson, 2007). In the prospective phase III RCT, Stupp et al. (2012) reported results of 237 individuals with recurrent GBM. Participants were randomized to TTF (n=120) versus physician's choice of chemotherapy (n=117). The study failed to reach its primary end-point of improved survival compared to active chemotherapy. Neither overall survival nor progression-free survival were significantly improved at six months in the group randomized to TTF versus chemotherapy (p=0.23 and 0.13, respectively). The authors noted that responses were more frequent in the group treated with TTF but this was not significant (p=0.19). Quality of life measurement favored TTF over chemotherapy for emotional and cognitive functioning; no significant difference was noted for global health and social functioning. Physical functioning favored the chemotherapy arm. TTF-related adverse events were mild (14%) to moderate (2%), usually

involving skin rash beneath the transducer arrays. Severe adverse events occurred in 6% and 16% (p = 0.022) of patients treated with TTF and chemotherapy, respectively. Results do not demonstrate improved OS or PFS with TTF compared to active chemotherapy. Although data suggest a decrease in serious adverse events, small study participant numbers limit the ability to translate use of this device into routine clinical practice**.**

Professional Societies/Organizations
National Comprehensive Cancer Network™ (NCCN™): The NCCN guideline for cancer of the central nervous system notes for treatment of recurrent disease, the option to consider alternating electric field therapy was changed from a category 2B recommendation to a category 3 recommendation. The NCCN describes a category 3 recommendation as based on any level of evidence, with major NCCN disagreement that the intervention is appropriate (NCCN, 2014).

Use Outside of the US: The NovoTTS-100A system has been studied in the European Union, Switzerland, and Australia.

Summary
Data are limited regarding the effectiveness of electric tumor treatment fields (TTF) for the treatment of recurrent glioblastoma or any indication. Evidence in the published, peer-reviewed scientific literature consists of several small case studies and a single randomized controlled trial (RCT). Results from the RCT did not demonstrate improved PFS or OS with this intervention compared with chemotherapy, although improvement in some quality of life domains was reported. Small trial participant numbers limit the ability to translate these results into routine clinical practice. Consensus support in the form of published guidelines is limited for this intervention. Several clinical trials are ongoing; however, at this time the role of TTF has not been established for any indication.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.
3) ICD-10-CM Diagnosis Codes are for informational purposes only and are not effective until 10/01/2015

Capsule Endoscopy Small Bowel

Covered when medically necessary:

CPT®* Codes	Description
91110	Gastrointestinal tract imaging, intraluminal (eg, capsule endoscopy), esophagus through ileum, with interpretation and report

Capsule Endoscopy Esophagus

Experimental/Investigational/Unproven/Not Covered:

CPT®* Codes	Description
91111	Gastrointestinal tract imaging, intraluminal (e.g.capsule endoscopy), esophagus, with physician interpretation and report

ICD-9-CM Diagnosis Codes	Description
	All codes

ICD-10-CM	Description

Diagnosis Codes (Effective 10/01/2015)	
	All codes

Transanal Endoscopic Microsurgical Approach (TEMS)

Covered when medically necessary:

CPT®* Codes	Description
0184T	Excision of rectal tumor, transanal endoscopic microsurgical approach (ie, TEMS), including muscularis propria (ie, full thickness)

Anoscopy, High Resolution (HRA)

Covered when medically necessary:

CPT®* Codes	Description
0226T	Anoscopy, high resolution (HRA) (with magnification and chemical agent enhancement); diagnostic, including collection of specimen(s) by brushing or washing when performed
0227T	Anoscopy, high resolution (HRA) (with magnification and chemical agent enhancement); with biopsy(ies)

Whole Body or Selective Head Therapeutic Hypothermia

Covered when medically necessary:

CPT®* Codes	Description
99481	Total body systemic hypothermia in a critically ill neonate per day (List separately in addition to code for primary procedure) (Code effective 01/01/2014)
99482	Selective head hypothermia in a critically ill neonate per day (List separately in addition to code for primary procedure)(Code effective 01/01/2014)
0260T	Total body systemic hypothermia, per day, in the neonate 28 days of age or younger (Code deleted 12/31/2013)
0261T	Selective head hypothermia, per day, in the neonate 28 days or younger (Code deleted 12/31/2013)

Sublingual Immunotherapy

Experimental/Unproven/Not Covered when used to report sublingual immunotherapy:

95199	Unlisted allergy/clinical immunologic service or procedure

Transient Elastography (e.g., Fibroscan)

Covered when medically necessary

0346T	Ultrasound, elastography
91299	Unlisted diagnostic gastroenterology procedure

Suprachoroidal and Extrascleral Placement of Pharmacologic Agent

Experimental/Investigational/Unproven/Not Covered when used to report suprachoroidal delivery of pharmacologic agent.or conjunctival incision with posterior extrascleral placement of pharmacologic agent.

67299	Unlisted procedure, posterior segment
68399	Unlisted procedure, conjunctiva

Additional Services Considered Experimental/Investigational/Unproven/Not Covered:

CPT®* Codes	Description
34806	Transcatheter placement of wireless physiologic sensor in aneurysmal sac during endovascular repair, including radiological supervision and interpretation, instrument calibration, and collection of pressure data (List separately in addition to code for primary procedure)
34841	Endovascular repair of visceral aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) by deployment of a fenestrated visceral aortic endograft and all associated radiological supervision and interpretation, including target zone angioplasty, when performed; including one visceral artery endoprosthesis (superior mesenteric, celiac or renal artery) (Code effective 01/01/2014)
34842	Endovascular repair of visceral aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) by deployment of a fenestrated visceral aortic endograft and all associated radiological supervision and interpretation, including target zone angioplasty, when performed; including two visceral artery endoprostheses (superior mesenteric, celiac and/or renal artery[s]) (Code effective 01/01/2014)
34843	Endovascular repair of visceral aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) by deployment of a fenestrated visceral aortic endograft and all associated radiological supervision and interpretation, including target zone angioplasty, when performed; including three visceral artery endoprostheses (superior mesenteric, celiac and/or renal artery[s]) (Code effective 01/01/2014)
34844	Endovascular repair of visceral aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) by deployment of a fenestrated visceral aortic endograft and all associated radiological supervision and interpretation, including target zone angioplasty, when performed; including four or more visceral artery endoprostheses (superior mesenteric, celiac and/or renal artery[s]) (Code effective 01/01/2014)
34845	Endovascular repair of visceral aorta and infrarenal abdominal aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) with a fenestrated visceral aortic endograft and concomitant unibody or modular infrarenal aortic endograft and all associated radiological supervision and interpretation, including target zone angioplasty, when performed; including one visceral artery endoprosthesis (superior mesenteric, celiac or renal artery) (Code effective 01/01/2014)
34846	Endovascular repair of visceral aorta and infrarenal abdominal aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) with a fenestrated visceral aortic endograft and concomitant unibody or modular infrarenal aortic endograft and all associated radiological supervision and interpretation, including target zone angioplasty, when performed; including two visceral artery endoprostheses (superior mesenteric, celiac and/or renal artery[s]) (Code effective 01/01/2014)
34847	Endovascular repair of visceral aorta and infrarenal abdominal aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) with a fenestrated visceral aortic endograft and concomitant unibody or modular infrarenal aortic endograft and all

	associated radiological supervision and interpretation, including target zone angioplasty, when performed; including three visceral artery endoprostheses (superior mesenteric, celiac and/or renal artery[s]) (code effective 01/01/2014)
34848	Endovascular repair of visceral aorta and infrarenal abdominal aorta (eg, aneurysm, pseudoaneurysm, dissection, penetrating ulcer, intramural hematoma, or traumatic disruption) with a fenestrated visceral aortic endograft and concomitant unibody or modular infrarenal aortic endograft and all associated radiological supervision and interpretation, including target zone angioplasty, when performed; including four or more visceral artery endoprostheses (superior mesenteric, celiac and/or renal artery[s]) (Code effective 01/01/2014)
83993	Calprotectin, fecal
91112	Gastrointestinal tract transit and pressure measurement, stomach through colon, wireless capsule, with interpretation and report
93982	Noninvasive physiologic study of implanted wireless pressure sensor in aneurysmal sac following endovascular repair, complete study including recording, analysis of pressure and waveform tracings, interpretation and report
99199†	Unlisted special service, procedure or report
0078T	Endovascular repair using prosthesis of abdominal aortic aneurysm, pseudoaneurysm or dissection, abdominal aorta involving visceral branches (superior mesenteric, celiac and/or renal artery(s)) (Code deleted 12/31/2013)
0079T	Placement of visceral extension prosthesis for endovascular repair of abdominal aortic aneurysm involving visceral vessels, each visceral branch (List separately in addition to code for primary procedure) (Code deleted 12/31/2013)
0080T	Endovascular repair using prosthesis of abdominal aortic aneurysm, pseudoaneurysm or dissection, abdominal aorta involving visceral vessels (superior mesenteric, celiac and/or renal artery[s]), radiological supervision and interpretation (Code deleted 12/31/2013)
0081T	Placement of visceral extension prosthesis for endovascular repair of abdominal aortic aneurysm involving visceral vessels, each visceral branch, radiological supervision and interpretation (List separately in addition to code for primary procedure) (Code deleted 12/31/2013)
0103T	Holotranscobalamin, quantitative
0106T	Quantitative sensory testing (QST), testing and interpretation per extremity; using touch pressure stimuli to assess large diameter sensation
0107T	Quantitative sensory testing (QST), testing and interpretation per extremity; using vibration stimuli to assess large diameter fiber sensation
0108T	Quantitative sensory testing (QST), testing and interpretation per extremity; using coding stimuli to assess small nerve fiber sensation and hyperalgesia
0109T	Quantitative sensory testing (QST), testing and interpretation per extremity; using heat-pain stimuli to assess small nerve fiber sensation and hyperalgesia
0110T	Quantitative sensory testing (QST), testing and interpretation per extremity; using other stimuli to assess sensation
0124T	Conjunctival incision with posterior extrascleral placement of pharmacological agent (does not include supply of medication) (Code deleted 12/31/2013)
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.
0185T	Multivariate analysis of patient specific findings with quantifiable computer probability assessment, including report (Code deleted 12/31/2013)
0186T	Suprachoroidal delivery of pharmacologic agent (does not include supply of

	medication) (Code deleted 12/31/2013)
0190T	Placement of intraocular radiation source applicator
0199T	Physiologic recording of tremor using accelerometer(s) and gyroscope(s), (including frequency and amplitude) including interpretation and report
0205T	Intravascular catheter-based coronary vessel or graft spectroscopy (eg, infrared) during diagnostic evaluation and/or therapeutic intervention including imaging supervision, interpretation, and report, each vessel
0207T	Evacuation of meibomian glands, automated, using heat and intermittent pressure, unilateral
0208T	Pure tone audiometry (threshold);automated; air only
0209T	Pure tone audiometry (threshold);automated; air and bone
0210T	Speech audiometry threshold, automated
0211T	Speech audiometry threshold, automated with speech recognition
0212T	Comprehensive audiometry threshold evaluation and speech recognition (0209T and 0211T combined), automated
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 trend analysis and limited reprogramming of device parameters, AV or VV delays only, with interpretation and report
0225T	Acoustic cardiography, including automated analysis of combined acoustic and electrical intervals; multiple, including serial trend analysis and limited reprogramming of device parameters, AV and VV delays, with interpretation and report
0233T	Skin advanced glycation endproducts (AGE) measurement by multi-wavelength fluorescent spectroscopy
0234T	Transluminal peripheral atherectomy, open or percutaneous, including radiological supervision and interpretation; renal artery
0235T	Transluminal peripheral atherectomy, open or percutaneous, including radiological supervision and interpretation; visceral artery (except renal), each vessel
0236T	Transluminal peripheral atherectomy, open or percutaneous, including radiological supervision and interpretation; abdominal aorta
0237T	Transluminal peripheral atherectomy, open or percutaneous, including radiological supervision and interpretation; brachiocephalic trunk and branches, each vessel
0238T	Transluminal peripheral atherectomy, open or percutaneous, including radiological supervision and interpretation; iliac artery, each vessel
0239T	Bioimpedance spectroscopy (BIS), measuring 100 frequencies or greater, direct measurement of extracellular fluid differences between the limbs
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
0254T	Endovascular repair of iliac artery bifurcation (eg, aneurysm, pseudoaneurysm, arteriovenous malformation, trauma) using bifurcated endoprosthesis from the common iliac artery into both the external and internal iliac artery, unilateral;
0255T	Endovascular repair of iliac artery bifurcation (eg, aneurysm, pseudoaneurysm, arteriovenous malformation, trauma) using bifurcated endoprosthesis from the common iliac artery into both the external and internal iliac artery, unilateral; radiological supervision and interpretation
0266T	Implantation or replacement of carotid sinus baroreflex activation device, total system (includes generator placement, unilateral or bilateral lead placement, intraoperative 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
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
0282T	Percutaneous or open implantation of neurostimulator electrode array(s), subcutaneous (peripheral subcutaneous field stimulation), including imaging guidance, when performed, cervical, thoracic or lumbar; for trial, including removal at the conclusion of trial period
0283T	Percutaneous or open implantation of neurostimulator electrode array(s), subcutaneous (peripheral subcutaneous field stimulation), including imaging guidance, when performed, cervical, thoracic or lumbar; permanent, with implantation of a pulse generator
0284T	Revision or removal of pulse generator or electrodes, including imaging guidance, when performed, including addition of new electrodes, when performed
0285T	Electronic analysis of implanted peripheral subcutaneous field stimulation pulse generator, with reprogramming when performed
0286T	Near-infrared spectroscopy studies of lower extremity wounds (eg, for oxyhemoglobin measurement)
0287T	Near-infrared guidance for vascular access requiring real-time digital visualization of subcutaneous vasculature for evaluation of potential access sites and vessel patency
0288T	Anoscopy, with delivery of thermal energy to the muscle of the anal canal (eg, for fecal incontinence)
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	Intravascular optical coherence tomography (coronary native vessel or graft) during diagnostic evaluation and/or therapeutic intervention, including imaging supervision, interpretation, and report; each additional vessel (List separately in addition to primary procedure)

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
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)
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 electrodes
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
0308T	Insertion of ocular telescope prosthesis including removal of crystalline lens
0311T	Non-invasive calculation and analysis of central arterial pressure waveforms with interpretation and report
0336T	Laparoscopy, surgical, ablation of uterine fibroid(s), including intraoperative ultrasound guidance and monitoring, radiofrequency (Code effective 1/01/2014)
0337T	Endothelial function assessment, using peripheral vascular response to reactive hyperemia, non-invasive (eg, brachial artery ultrasound, peripheral artery tonometry), unilateral or bilateral (Code effective 1/01/2014)
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(Code effective 01/01/2014)
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 (Code effective 01/01/2014)
0340T	Ablation, pulmonary tumor(s), including pleura or chest wall when involved by tumor extension, percutaneous, cryoablation, unilateral, includes imaging guidance (Code effective 1/01/2014)
0341T	Quantitative pupillometry with interpretation and report, unilateral or bilateral (Code effective 1/01/2014)
0342T	Therapeutic apheresis with selective HDL delipidation and plasma reinfusion (Code effective 1/01/2014)
0378T	Visual field assessment, with concurrent real time data analysis and accessible data storage with patient initiated data transmitted to a remote surveillance center for up to 30 days; review and interpretation with report by a physician or other qualified health care professional (Code effective 01/01/2015)
0379T	Visual field assessment, with concurrent real time data analysis and accessible data storage with patient initiated data transmitted to a remote surveillance

	center for up to 30 days; technical support and patient instructions, surveillance, analysis and transmission of daily and emergent data reports as prescribed by a physician or other qualified health care professional (Code effective 01/01/2015)
0380T	Computer-aided animation and analysis of time series retinal images for the monitoring of disease progression, unilateral or bilateral, with interpretation and report (Code effective 01/01/2015)
0381T	External heart rate and 3-axis accelerometer data recording up to 14 days to assess changes in heart rate and to monitor motion analysis for the purposes of diagnosing nocturnal epilepsy seizure events; includes report, scanning analysis with report, review and interpretation by a physician or other qualified health care professional (Code effective 01/01/2015)
0382T	External heart rate and 3-axis accelerometer data recording up to 14 days to assess changes in heart rate and to monitor motion analysis for the purposes of diagnosing nocturnal epilepsy seizure events; review and interpretation only (Code effective 01/01/2015)
0383T	External heart rate and 3-axis accelerometer data recording from 15 to 30 days to assess changes in heart rate to monitor motion analysis for the purposes of diagnosing nocturnal epilepsy seizure events; includes report, scanning analysis with report, review and interpretation by a physician or other qualified health care professional (Code effective 01/01/2015)
0384T	External heart rate and 3-axis accelerometer data recording from 15 to 30 days to assess changes in heart rate to monitor motion analysis for the purposes of diagnosing nocturnal epilepsy seizure events; review and interpretation only (Code effective 01/01/2015)
0385T	External heart rate and 3-axis accelerometer data recording more than 30 days to assess changes in heart rate to monitor motion analysis for the purposes of diagnosing nocturnal epilepsy seizure events; includes report, scanning analysis with report, review and interpretation by a physician or other qualified health care professional (Code effective 01/01/2015)
0386T	External heart rate and 3-axis accelerometer data recording more than 30 days to assess changes in heart rate to monitor motion analysis for the purposes of diagnosing nocturnal epilepsy seizure events; Review and interpretation (code effective 01/01/2015)
0387T	Transcatheter insertion or replacement of permanent leadless pacemaker, ventricular (Code effective 01/01/2015)
0388T	Transcatheter removal of permanent leadless pacemaker, ventricular
0389T	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, review and report, leadless pacemaker system (Code effective 01/01/2015)
0390T	Peri-procedural device evaluation (in person) and programming of device system parameters before or after a surgery, procedure or test with analysis, review and report, leadless pacemaker system (Code effective 01/01/2015)
0391T	Interrogation device evaluation (in person) with analysis, review and report, includes connection, recording and disconnection per patient encounter, leadless pacemaker system

†**Note: Experimental/Investigational/Unproven/Not Covered when used to report multivariate analysis of patient specific findings with quantifiable computer probability assessment.**

HCPCS Codes	Description
A4555	Electrode/transducer for use with electrical stimulation device used for cancer treatment, replacement only (Code effective 01/01/2014)
C9736	Laparoscopy, surgical, radiofrequency ablation of uterine fibroid(s), including intraoperative guidance and monitoring, when performed (Code deleted 01/01/14)

E0766	Electrical stimulation device used for cancer treatment, includes all accessories, any type (Code effective 01/01/2014)
E2120	Pulse generator system for tympanic treatment of inner ear endolymphatic fluid
G0255	Current perception threshold/sensory nerve conduction test, (SNCT) per limb, any nerve
S2103	Adrenal tissue transplant to brain

ICD-9-CM Diagnosis Codes	Description
	All codes

ICD-10-CM Diagnosis Codes (Effective 10/01/2015)	Description
	All codes

***Current Procedural Terminology (CPT®) ©2013 American Medical Association: Chicago, IL.**

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