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Magnetic resonance spectroscopy
Magnetic resonance spectroscopy (MRS) utilizes MRI special pulse sequences to identify atomic nuclei within molecules, enabling the detection of certain chemicals and metabolites and providing a non-invasive method to characterize biochemical processes in the body.

MRS of cord lesions
Magellan Healthcare has reviewed the use of MRS for intralesional spinal cord evaluation for cord pathology, such as tumors, multiple sclerosis and amyotrophic lateral sclerosis (ALS), as well as cervical myelopathy. While our current findings show that some technical issues need to be addressed, including respiratory and cardiac motion, and we expect that the number of studies requested for this indication will be limited, we will continue to monitor the MRS literature for evaluation of lesions inside the spinal cord for possible inclusion in our clinical guidelines.

References:


MRS for discogenic pain
MRS is currently being studied for discogenic pain. Although it is not ready for regular use and appears less promising than MRS for intralesional cord evaluation, it may be beneficial when performed in conjunction with conventional imaging. Our preliminary findings suggest that the MRS characteristics may explain a painful disc prior to surgery; however, this technique requires validation by larger studies.

Most studies performed to date have focused on the lumbar spine. Future studies of the cervical and thoracic regions are required to determine whether MRS for discogenic pain is technically feasible, since the size of the vertebral disc is much smaller.

MRS is typically requested by academic institutions in limited quantities. Magellan does not anticipate that MRS for discogenic pain will gain a foothold in busy private practices or smaller community hospitals anytime soon, if at all. We will continue to monitor the literature for future trends. At this stage, we do not recommend including this specific CPT code in clinical guidelines.

References:

Cone-beam breast computed tomography

Cone-beam computed tomography, a variant of computed tomography (CT) typically used in dental and extremity imaging, has recently found a new application in dedicated breast imaging. Unlike conventional CT, which uses a fan-shaped x-ray beam and one-dimensional detectors, cone-beam breast computed tomography (CBBCT) uses a cone-shaped x-ray beam and two-dimensional detectors.

CBBCT can be performed without contrast (i.e., non-contrast technique or NC-CBBCT) or after the intravenous administration of iodinated contrast media (i.e., contrast-enhanced CBBCT or CE-CBBCT). Administration of intravenous contrast has been shown to improve breast lesion detection compared to non-contrast exams. CBBCT yields a high average glandular dose, absorbing between 6–25 milligray of radiation to the breast.

Recent CE-CBBCT studies have focused on patients with dense breast tissue and/or patients with MRI contraindications. A few studies have reported superior diagnostic accuracy and sensitivity for 3D-CBBCT over ultrasound and mammography. A study of 41 patients with dense breast tissue (ACR type C or D breast density) demonstrated that the diagnostic accuracy of CE-CBBCT and MRI is superior to mammography and NC-CBBCT. Compared to MRI, CE-CBBCT has shown greater specificity, or ability to distinguish those with disease from those without, and lower sensitivity, or ability to identify true positive cases.

While accuracy was comparable in the diagnostic setting, further studies that directly compare CBBCT and breast MRI are warranted. Due to the small number of studies and patients reporting utilization of CBBCT, the ability of studies to fully detect differences in diagnostic performance are limited.

Magellan Healthcare does not recommend use of CBBCT at this time and will continue monitoring the literature.

References:


Positron emission tomography-magnetic resonance imaging

Positron emission tomography-magnetic resonance imaging (PET-MRI) is a relatively new imaging technique. Worldwide, the number of PET-MRI systems is gradually increasing, with most systems being installed in tertiary care centers. Although the scanning time with PET-MRI is typically longer than with PET-CT, they generally perform equally well, with PET-MRI having some advantages. PET-MRI reduces radiation exposure and has a higher soft-tissue resolution, often eliminating the need for additional dedicated MRI exams to evaluate the brain and/or liver.
One study found that PET-MRI caused management changes in eight percent of cancer patients who also underwent PET-CT. This change was primarily due to the superior performance of PET-MRI in detecting brain and liver metastases. However, PET-CT is superior in detecting lung lesions. This study also found that brain and liver metastases detected by the MRI component of PET-MRI caused management changes in 90% of patients. Additionally, lung lesions detected exclusively by PET-CT did not affect management in any patient.

Magellan will continue to monitor the literature for possible incorporation into upcoming guidelines.

References:


Breast-specific positron emission tomography imaging

Traditional positron emission tomography (PET) imaging using supine positioning is suboptimal for detecting isolated breast lesions. Recent studies suggest that prone positioning could be used to assist in identifying breast lesions. Dedicated PET scanning modalities for the breast are in development, including positron emission mammography (PEM) and PET.

PEM uses two planar or curved detectors that scan the breasts with mild compression. The detectors have significantly improved spatial resolution, allowing functional imaging of breast cancer earlier in the disease process than whole-body PET. PEM could play a future role in classifying suspicious calcifications detected in standard mammography, potentially improving accuracy to 95%. Acquisition geometry is currently a major limitation of PEM that can affect the clear imaging of structures at the edge of the camera near the chest wall. The addition of CT helps the PEM system to scan the breast uncompressed and the lesions three-dimensionally, capturing high-resolution breast images using multiple rotating planar detectors that help overcome the limitations of PEM. Currently, PEM has not been studied in large cohorts of patients or compared to conventional modalities, such as MRI, which does not cause radiation exposure.

In a small study, dedicated breast PET was unable to reliably characterize MRI indeterminate lesions as suspicious for malignancy or benign.

At this time, Magellan does not recommend the use of PEM or PET for detection of isolated breast lesions and will continue to monitor the development of this technology.
References:


Isotopes

**Copper Cu 64 dotatate**

Copper Cu 64 dotatate (Cu-64 dotatate), sold under the brand name Detectnet, is a radioactive diagnostic agent indicated for use with positron emission tomography (PET) for localization of somatostatin receptor positive neuroendocrine tumors (NETs).

Food and Drug Administration (FDA) approval in September 2020 was based on two trials. The first was a single-center trial that enrolled patients with known or suspected NETs and healthy volunteers. The second reanalyzed data from a published single-center trial that included 112 patients with histories of NETs and compared Cu-64 dotatate imaging with results from other imaging and biopsies.

Cu-64 dotate has a long half-life, which helps eliminate reliance on generators at imaging sites and provides a more flexible scanning window. Its physical half-life is 12.7 hours compared to Gallium-68 dotatate (Ga-68 dotatate), which has a physical half-life of 1.1 hours. Cu-64 dotatate has traditionally had a higher radiation exposure; however, recent studies indicate the exposure is comparable to Ga-68 dotatate.

When assessed per patient, Cu-64 dotatate and Ga-68 dotatate had the same 100% sensitivity, 90% specificity, 98% positive predictive value and 100% negative predictive value. However, on a per lesion basis, Cu-64 dotatate correctly identified more true-positive discordant lesions 83% of the time, compared to 17% of the time for Ga-68 dotatate. This was attributed to the physical properties of Cu-64 dotatate compared to Ga-68 dotatate. The shorter positron range of Cu-64 dotatate resulted in better spatial resolution, improved image quality and superior detection of smaller lesions.

Considering the recent FDA approval, Cu-64 dotatate is an advantageous alternative to Ga-68 dotatate and offers a long-term economic advantage, partly due to its higher half-life, which allows for a more flexible scanning window. Additionally, Cu-64 dotatate has a lower positron range than Ga-68 dotatate, resulting in better PET spatial resolution. Overall, the greater flexibility, availability and accuracy of Cu-64 dotatate, in addition to its financial advantages, result in it being preferable over Ga-68 dotatate in most instances.

This isotope has been included as an alternate to Ga-68 dotatate in Magellan’s upcoming 2022 PET guidelines.
**References:**


### Prostate-specific membrane antigen-targeted (PSMA) radiotracers

The effect of 18F-DCFPyL, a prostate-specific membrane antigen-targeted radiotracer, on patient care was assessed in the CONDOR trial and included 208 men with rising prostate-specific antigen levels after definitive treatment for prostate cancer and with negative or equivocal results on standard imaging, such as computed tomography, magnetic resonance imaging or bone scintigraphy. After the 18F-DCFPyL scan, 63.9% of patients had a management change. Of these, 21.0% had their care goal changed from noncurative systemic therapy to salvage local therapy, 28.3% had a change from salvage local therapy to systemic therapy, 23.9% switched from observation to initiating therapy and 4.4% went from planned treatment to observation.

Furthermore, other studies show superior detection rates for another prostate-specific antigen radiotracer, Ga68-PSMA-11 PET/CT, when compared with 18F-fluciclovine PET/CT in patients with recurrent prostate cancer after definitive treatment. Ga68-PSMA-11 has a higher sensitivity over 18F-fluciclovine with low prostate-specific antigen (PSA) levels, even below 0.5ng/ml.

When compared with current radiotracers, PSMA tracers are more sensitive with lower levels of PSA. Preliminary outcome data show that PSMA PET has resulted in modification of patient treatment plans.

Magellan has incorporated this prostate-specific membrane antigen-targeted radiotracer into its upcoming 2022 PET guidelines.

**References:**


Fluoroestradiol F-18

Fluoroestradiol F-18 (FES) is a new estrogen analog (16-[18F]-fluoro-17-estradiol) PET agent, which was approved by the FDA in May 2020. FES may be used in the detection of estrogen receptor positive lesions in patients with recurrent or metastatic breast cancer.

Some retrospective studies show that FES has higher sensitivity for diagnosing metastatic lesions when compared with F-18 fluorodeoxyglucose (FDG) (90.8% to 82.8%, respectively). FES has improved detection at axillary, cervical, mediastinal lymph nodes and bone sites when compared with FDG. Distinguishing inflammatory from malignant lesions can be difficult in FDG exams and in turn cause false-positive results. FES can potentially correct false-positive FDG findings due to its high specificity for ER-positive lesions. In a recent study, FES led to a treatment strategy change in 23.6% of patients. FES may also serve to predict response to endocrine therapy and assess tumor burden and heterogeneity.

A critical shortcoming of FES PET/CT is it cannot be reliably measured to detect liver metastases due to high background activity. Detection of lesions that are in close proximity to the bowel may also be difficult. FES is not specific for breast cancer and may occur in a variety of estrogen receptor positive tumors that are outside the breast, including those of uterine or ovarian origin. A negative scan does not exclude the possibility of ER-positive breast cancer.

To date, only a small number of comparative studies (FDG versus FES) have been performed. These studies document favorable metastatic disease detection rates of ER-positive malignancies; however, large prospective trials are needed.

Additionally, tissue biopsies must still be considered in recurrence of breast cancer and to verify ER status by pathology. FES is not useful for imaging other receptors, such as human epidermal growth factor receptor 2 and progesterone receptor.

While initial results appear promising, FES should be monitored closely as only small clinical trials have been conducted. Magellan Healthcare will continue to monitor the literature for large independent trials supporting use.

References:


Breast lymphatic mapping

Indocyanine green (ICG) dye is a fluorescent dye that can be detected using near infrared (NIR) cameras and has been used for more than 50 years with a favorable safety profile. This dye has been studied in mapping in gastrointestinal, melanoma, cervical, vulvar, anal, oropharyngeal, non-small cell lung and breast cancers.

Traditional sentinel lymph node (SLN) mapping in breast cancer uses a radiotracer labeled with technetium-99 (99mTc), visible blue dye (methylene blue or isosulfan blue) or a combination of both. Utilizing 99mTc has several limitations, including nuclear licensing and patient discomfort, as these injections typically occur before surgery. Blue-dye injections can be performed intraoperatively, but there are reported risks such as skin necrosis and anaphylaxis.

The advantages of ICG for SLN detection include the ability to inject intraoperatively, the ability of NIR to visualize the lymphatic anatomy and flow during the injection in real time, lower cost and no special training or certification is required to handle ICG (as with nuclear agents).

A prospective trial comparing ICG and 99mTc demonstrated no difference in the number of removed SLNs. The study suggests that the concentration of ICG injected and the smaller size of the ICG molecule allows it to travel faster than the 99mTc bound to albumin. Patients with a higher body mass index may have failed mapping as the NIR camera penetrates tissue to a maximum depth of two centimeters. This can be circumvented with an axillary image enhancer device that compresses the axillary tissue.

99mTc-labeled radiotracer alone is the more commonly used solo technique of SLN mapping with a detection rate of 97.5% accuracy. When blue dye is the primary mean of detection, it has a lower sensitivity of 91%. Lymph node detection rate using dual mapping with 99mTc and a blue dye is approximately 99%. Due to its high accuracy and low false-negative rates, 99mTc is advocated as the primary technique.

Overall, ICG NIR imaging is an efficient, convenient and equivalent intraoperative method of SLN detection compared with traditional 99mTc regarding the number of SLNs identified, rate of failed mapping and identification of pathologically positive SLNs with several recent studies supporting NIR-guided SLN biopsy for standard use. ICG offers the advantages of real-time imaging, ease of handling, low cost and rapid localization to the SLNs.

Magellan Healthcare will continue to monitor the literature, including the use of ICG in different facets of image-guided procedures, such as NIR angiography of blood vessels, skin flap perfusion for mastectomies, identification of the extrahepatic bile ducts and identification of oncologic tumor metastases.

References:


**Other upcoming advances**

**Prostate risk identification using micro-ultrasound (PRI-MUS™)**

Micro-ultrasound is a relatively new imaging platform that uses high-resolution ultrasound at 29 MHz compared to 9-12 MHz for conventional urological ultrasound. The higher resolution provides superior imaging, improving lesion targeting for biopsies.

PRI-MUS is the grading system for assessing prostatic lesions and their likelihood of being malignant. Unlike multiparametric magnetic resonance imaging (mpMRI), micro-ultrasound is performed in realtime during in-office biopsy procedures. It is therefore expected to maintain the cost-effectiveness of conventional ultrasound. Micro-ultrasound provides a sensitivity similar to mpMRI for clinically significant prostate cancer and can visualize all significant mpMRI targets that conventional ultrasound cannot.

A recent study by Claros et al. reaffirmed the role of micro-ultrasound visualization and the PRI-MUS score as reliable in the detection of clinically significant prostate cancer when compared to robotic ultrasound MRI fusion biopsies, but larger prospective studies are needed. A recent presentation by Dr. Lughezzani at the American Urological Association 2020 meeting compared mpMRI to micro-ultrasound. Micro-ultrasound has a greater sensitivity (95% vs. 89% for mpMRI) and negative predictive value (87% vs. 77% for mpMRI), but micro-ultrasound was less specific than mpMRI (21% and 23%, respectively). Both had similar positive predictive values (44% vs. 43% for mpMRI). The study also concluded that larger scale studies are needed to validate findings.

While this upcoming technology is a promising tool for detecting and targeting prostate cancer in active surveillance, larger multisite/multi-reader studies are needed. Currently, the American Urological Association guidelines do not support this modality. Magellan will continue to monitor the literature as new studies are reported.

**References:**


**Ultrasound carotid intima-media thickness**

Carotid intima-media thickness (CIMT) has been widely used to assess atherosclerosis and cardiovascular risk using B-mode ultrasonography. Previously, CIMT has been reported to be associated with risk of coronary artery disease and stroke. However, recent studies have found that its usefulness in predicting the risk of cardiovascular events may be limited and that measuring the carotid wall on MRI may have greater clinical benefit, as MRI measurements will also include the adventitia layer.

A previous cohort study found that routine use of CIMT in the general population to screen for cardiovascular disease above the Framingham risk score resulted in a small improvement. It was not recommended for routine use and did not result in a net reclassification of risk. Eighty-eight percent remained in the same risk category after addition of CIMT to the Framingham risk score. There are also inherent limitations, such as where the carotid artery is measured. CIMT is typically measured in the common carotid artery due to the technical ease of visualization. However, early carotid atherosclerosis occurs predominantly within or downstream from the carotid bulb, which may not be as easily visible. One study found that the presence of carotid plaque has significantly higher diagnostic accuracy for predicting future myocardial infarction than CIMT. More recent studies show that CIMT may be useful as a surrogate marker for cardiovascular events and as a marker for guiding new therapies.

Recently, MRI has emerged as a superior noninvasive modality for characterizing plaque features and imaging the arterial wall. Since MRI measurements include the adventitial layer, it has greater benefit than CIMT. This layer thickening results from vasa vasorum proliferation and may be a sign of early plaque development or plaque instability. Additionally, MRI can image the entire wall, may detect wall thickening earlier than CIMT, and identify plaque components such as fibrous cap and intraplaque hemorrhage, which are closely related to plaque vulnerability and cardiovascular risk. MRI has shown less operator variability compared with CIMT and more reader variability. Limitations with MRI include cost, motion and use in patients with foreign bodies.

CT is not a preferred study choice for measuring carotid wall or plaque due to limitations associated with dense calcifications, reduced contrast resolution between lipid and fibrotic components, and radiation exposure.

**References:**


**Machine learning and artificial intelligence**

Many artificial intelligence (AI) projects have received FDA approval, and more AI projects are pending. Computer-aided detection (CAD) is one of the products Magellan is currently watching. Presently, there are no CPT® codes for CAD outside of mammography. However, as the technology advances and studies are performed, this is likely to change.

**COVID and AI**

Since the outbreak of the pandemic, there have been over 500 submitted abstracts and over 200 articles on PubMed evaluating the effectiveness of AI and diagnosing COVID-19 on radiographs and or CT. AI software algorithms readily identified image findings in patients with COVID-19-associated pneumonia and distinguished non-COVID-related pneumonias with high specificity. One study found that AI was 10 times faster than radiologists. Further outcome studies will be required to determine if AI leads to changes in patient care, shortened hospitalizations and/or reduced morbidity and mortality.

**References:**


**Prostate**

Quantib® Prostate recently received FDA clearance for AI detection in prostate imaging. The release of Quantib’s prostate solution follows the PROMIS and Precision trials which indicated the added value of incorporating MRI into the prostate cancer workflow. This is one of several such AI systems available and approved by the FDA. Quantib’s prostate cancer software provides tools to improve diagnosis, including image-based calculation of prostate-specific antigen density that is incorporated into the final radiology report and a heat map that identifies suspicious areas to the radiologist. Quantib is currently used by only 10 facilities, and there are plans for later expansion. Initial literature shows promising results for AI algorithms and programs, but additional studies are needed to evaluate the clinical benefits. Magellan will continue to monitor the literature as new studies are published.

**Reference:**

**Functional MRI coils**

MRI is the gold standard for soft tissue injuries. NYU Langone Health has a prototype of coils that allow real-time, movable/functional scanning with an MRI glove to dynamically image the extremity via the National Institutes of Health. Potential applications include to all extremities where functional imaging and competency of ligaments and tendons would be needed to determine management.

*References:*

**Portable MRI units**

Typically, an MRI must be performed in specially engineered rooms with appropriate radiofrequency shielding. Recent FDA approval has allowed portable MRI imaging of the brain, neck and extremities. Hyperfine’s portable MRI machine will cost $50,000, which is 20 times cheaper than traditional systems, runs on 35 times less power and weighs 10 times less than normal 1.5T MRI machines. Currently this machine is 0.064T.

The FDA clearance includes head imaging for patients two years and older. This technology will probably be primarily used in the hospital/ICU setting, but has the potential to be incorporated into subspecialty offices such as neurology offices given the lack of special construction needed to house the units. Hyperfine is currently studying this for MSK exams as well.

*References:*


**Magnetic resonance imaging and Aduhelm™ (aducanumab) treatment for Alzheimer’s disease**

The anti-amyloid drug aducanumab, sold under the brand name Aduhelm, was recently approved by the FDA through its Accelerated Approval Program. It is the first novel therapy approved since 2003 for Alzheimer’s disease (AD) and the only one that targets the underlying pathophysiology of AD, the presence of amyloid beta plaques in the brain. Studies on patients treated with aducanumab have shown a reduction in the amount of amyloid plaques in the brain. However, the results of EMERGE and ENGAGE, recent Phase 3 clinical trials, have caused controversy. Uncertainty still exists about the clinical benefits of aducanumab.

The ENGAGE trial showed no benefit. The EMERGE trial, which used a higher dose of aducanumab, showed no initial benefit, but demonstrated significant positive benefit with prolonged follow-up. The current FDA approval is based on a surrogate clinical endpoint (reduction of amyloid plaque in the brain) rather than clinical outcomes and potential benefits versus risk. Reduction of amyloid plaque is expected to result in reduced clinical decline. However, there is little known correlation between the number and size of plaques and symptoms.

In both studies, participants included patients with early symptomatic AD who were positive for brain amyloid pathology as assessed by positron emission tomography (PET). Other inclusion criteria were baseline Mini-Mental State Exam score of 24 to 30 (inclusive) and a Clinical Dementia Rating global score of 0.5. The ε4 allele of apolipoprotein E (ApoE) is the strongest genetic risk factor for AD and associated with increased risk for both early- and late-onset AD. ApoE ε4 carriers and ApoE ε4 noncarriers were both enrolled. Exclusion criteria included comorbid medical condition, cerebrovascular disease, psychiatric illness, and unstable disease.
The FDA has approved aducanumab for the early stages of AD, mild cognitive impairment and mild dementia. The treatment is administered intravenously through infusion over a one-hour period every four weeks for an indefinite period of time. Monitoring using magnetic resonance imaging (MRI) is required by the FDA, including obtaining a brain MRI that was conducted within one year of treatment commencement, and prior to the seventh and twelfth infusions. When ten or more new incident microhemorrhages or > 2 focal areas of superficial siderosis (radiographic severe ARIA-H) are observed, treatment may be continued with caution only after a clinical evaluation and a follow-up MRI demonstrate radiographic stabilization. Repeat MRI is also indicated for changes in clinical status.

PET scan with amyloid disposition was an inclusion criterion in the Phase 3 studies. Current approval is based on a reduction in amyloid plaques on follow-up PET scans as a surrogate endpoint, as the clinical benefit is still unclear. The FDA prescribing information does not include PET as an inclusion criterion or as a required method of follow-up. Currently, the Society of Nuclear Medicine and Molecular Imaging plans to engage the Centers for Medicare and Medicaid Services to provide paid coverage of beta-amyloid PET imaging in prospective patients.

Although minimal evidence suggests that aducanumab has improved clinical endpoints in some patients who have mild dementia, it is appropriate for patients being administered the medication or those meeting medical necessity for this treatment, to receive the FDA-required initial brain MRI and MRIs after the seventh and twelfth infusions of the drug.

References:


While some literature suggests that aducanumab may be promising in patients who have amyloid deposition, the FDA requires an initial brain MRI and brain MRIs after the seventh and twelfth infusions of the drug. If a patient is being administered aducanumab or is a candidate for the medication, as deemed by the insurance company, the initial and follow-up brain MRIs required by the FDA would be appropriate.
Cardiology

AI in cardiology

AI is becoming increasingly useful in helping cardiologists through machine learning, both in medical imaging and at the point of care. Devices are available that provide automated calcium scoring software for cardiac CT scans, anatomic segments and optimal views for multiple cardiac studies. The benefits of AI in cardiology span multiple areas, including clinical practice, population health, and research and development of new products.

References:

Transcatheter pulmonary valve replacement

Approved by the FDA in March 2021, the Harmony™ Transcatheter Pulmonary Valve is the first minimally invasive alternative for patients with severe pulmonary regurgitation who have a native or surgically repaired right ventricular outflow tract and are clinically indicated for surgical pulmonary valve replacement. It is designed to delay the need for open heart surgery by restoring pulmonary valve function using a minimally invasive procedure and may also prove useful in the treating patients with Tetralogy of Fallot as they survive into adulthood.

Leadless Pacemakers

Leadless pacemakers were first introduced in the 1970s and approved by the FDA in 2016. This pacemaker system is introduced percutaneously via the femoral vein and affixed to the right ventricular myocardium via self-expanding nitinol tines or a screw-in helix mechanism. The delivery system is then released and removed, and the pacemaker remains embedded in the right ventricle. Insertion requires no chest incision or subcutaneous pocket.

The leadless pacemaker is 90% smaller than a conventional transvenous pacemaker and is about the size of a large vitamin capsule. Current devices are MRI-compatible. A leadless pacemaker’s battery life is 5-15 years, which is comparable to a transvenous pacemaker. At battery end of life, the device can be turned off and a new leadless pacemaker or standard transvenous pacemaker implanted. It does not need to be removed as it becomes endothelialized in the cardiac myocardium.

The main advantage of a leadless pacemaker is the elimination of adverse events associated with conventional transvenous pacemakers. Short- and long-term complications occur in approximately one in eight patients receiving a standard pacemaker. Early complications include hematomas and infections in the subcutaneous pocket, septicemia, pneumothorax, and venous thrombosis and occlusion. Long-term complications include lead fracture and insulation failure, lead-related infective endocarditis, tricuspid regurgitation, infection involving the pulse generator, and skin erosion over the generator. Complications with leadless pacemakers include femoral vascular trauma in 0.9% and cardiac perforation with subsequent pericardial effusion and cardiac tamponade in 1.5%.

Leadless pacemakers are best suited for patients with permanent atrial fibrillation (AF) and high-grade atroventricular (AV) block, resulting in bradycardia in which only ventricular pacing is indicated; patients with poor vascular access, such as patients with renal failure; and elderly patients with complete AV block who have limited physical activity. The device is not suitable for patients requiring dual-chamber pacing, including patients with advanced AV block or sinus node dysfunction.

References:
WATCHMAN is a quarter-sized, permanent implant, a minimally invasive, one-time procedure designed to reduce the risk of strokes originating in the left atrial appendage (LAA). It closes the LAA, preventing the escape of blood clots. It is considered an alternative to warfarin use for people with non-valvular AF.

Randomized control trial
The PROTECT AF study compared percutaneous closure of the left atrial appendage versus warfarin therapy for stroke prevention in patients with AF. A multicenter, randomized study was conducted at 59 hospitals with 707 patients with non-valvular AF and at least one additional stroke risk factor. Outcome variables include stroke, systemic embolism and cardiovascular/unexplained death.

Results
In the Watchman group, 8.4% met non-inferiority criteria compared to almost 14% in the warfarin group. Cardiovascular mortality was lower in the Watchman group (3.7% vs. warfarin group 9%) with an all-cause mortality of 12% in the Watchman group versus 18% in the warfarin group.

After 3.8 years of follow-up of patients with non-valvular AF and elevated risk for stroke, percutaneous LAA closure met criteria for both non-inferiority and superiority compared to warfarin for preventing the combined outcome of stroke, systemic embolism and cardiovascular death, as well as superiority for cardiovascular and all-cause mortality.

There is sufficient peer-reviewed evidence to classify the device as noninferior to warfarin for stroke prevention, systemic embolism, and bleeding.

References:


Interventional Pain Management

Most emerging trends in interventional pain management (IPM) have more to do with technological advances, such as better radiofrequency generators, better neurostimulators, etc., than procedural advances. At Magellan, however, the emerging trend is inclusion of more procedures. Currently, we only consider epidural injections, facet injections, facet denervations and sacroiliac joint injections.

**Sympathetic nerve blocks**

Sympathetic nerve blocks have been added to Magellan’s current list of procedures. Lumbar and cervical paravertebral sympathetic ganglia are most likely to be added to the list. Ganglion impar blocks and hypogastric plexus blocks are fairly likely to be included. Thoracic paravertebral sympathetic ganglia blocks, celiac plexus blocks, sphenopalatine ganglion blocks or other sympathetic nerve blocks are unlikely to be included. Guidelines are currently in development.

**Neurostimulation**

Neurostimulation has been identified for addition to Magellan’s list of procedures considered, including intraspinal procedures in all regions. We will consider trial procedures and permanent implants of all components, also including revisions and removals, as well as analysis and programming. Guidelines are currently in development. Also, selected peripheral nerve and cranial nerve stimulation procedures, including occipital nerve stimulation and fifth or seventh cranial nerve stimulation (extra cranial stimulation) are likely to be included. The 10th cranial nerve stimulation, commonly performed for seizure control, will not be included.

**Implantable infusion pumps**

Implantable infusion pumps are the third likely procedure to be considered for addition to the Magellan list. Trials are already considered, and permanent implants, revisions, removals, reprogramming and refills will be added. Draft guidelines currently exist.

**Other procedures**

Not currently prioritized, but within the scope of interventional pain management procedures, commonly performed are:

- Radiofrequency denervation of hips, knees, cervical cranial junction and other selected non-facet nerves
- Selected peripheral nerve blocks
- Kyphoplasty
Orthopedics

Subchondroplasty

Subchondroplasty is a relatively new procedure developed to treat bone marrow lesions (BML) of the knee by injecting a calcium phosphate bone substitute into the pathologic, subchondral area of the bone under fluoroscopic guidance. The advent of magnetic resonance imaging (MRI) has greatly facilitated the identification of these bone marrow lesions. BML are best visualized on fat-suppressed MRI sequences, such as T2, as a white hazy signal. Radiologists may refer to a BML as an osteochondral fracture, subchondral fracture, stress fracture, insufficiency fracture, micro-trabecular fracture or bone edema. Pathology studies have identified the white signal apparent on an MRI as the body’s response to a trabecular fracture, and research has consistently demonstrated that subchondral bone in the region of a chronic BML is significantly altered from healthy, normal subchondral bone.

The procedure is described as a minimally invasive technique, the goal of which is to improve the structural integrity of the subchondral bone to promote subchondral bone remodeling to relieve pain and associated symptoms as well as to potentially prevent or limit the progression of arthritis. It is frequently performed in addition to arthroscopic surgery that treats intraarticular pathology, such as meniscal tears or loose bodies, and confirms that none of the injected bone substitute material has become intraarticular.

Surgical technique

Preoperatively, the BML is identified on fat-suppressed MRI, using at least two planes:

The BML is targeted, using intraoperative fluoroscopy and a navigation guide to localize the bone defect relative to MRI findings:
The bone marrow lesion is accessed by insertion of a cannula system and wire driver:

The bone substitute material is injected into the defect:

**Conclusion**

Magellan has received numerous requests for subchondroplasty, usually in conjunction with a diagnostic arthroscopy, which is requested to inspect the intraarticular portion of the joint to confirm that none of the injected material leaked into the joint. However, the indications are not well-established, and no prospective, randomized clinical trials report on the efficacy of the procedure. Some articles state that subchondroplasty is an effective method for treating subchondral BML in the arthritic knee, resulting in improvement in symptoms and early return to activity. Others report that the procedure benefits patients with bone marrow lesions by reducing pain and improving function, along with a high level of satisfaction after the procedure. Still others state the low short-to-medium term conversion rate to arthroplasty indicates that subchondroplasty may play a role in delaying more invasive and more expensive procedures in patients with BML. However, long-term studies are required to evaluate if these benefits can last. Moreover, large-series or controlled studies have yet to show subchondroplasty is superior to established conservative approaches. Due to these concerns, NIA guidelines for arthroscopic knee surgery specifically state that this procedure is not managed by Magellan. Our position on this may change once long-term studies demonstrate its efficacy.

(The reimbursement and proper CPT® code for this procedure has not been established, and some providers have been instructed to submit the same code used for an ORIF of a tibial plateau fracture, a much larger and more invasive procedure.)

**References:**


Spine surgery

Outpatient surgery
One of the most significant trends in spine surgery is the migration of procedures to the outpatient setting. Advances in technology and surgical technique continue to create the opportunity for traditional inpatient procedures to be performed in the outpatient setting. This change will continue to be driven by patients, surgeons and payers, and fueled by improved experience, increased efficiency and lower costs into the foreseeable future.

Technology
Technology in the operating room is advancing at a record pace. Intraoperative CT guidance, robotics and augmented reality are all coalescing to allow surgeons to achieve surgical goals with less risk to the patient. Due to these technological advances, procedures that previously required multiple days in the hospital for recovery are now performed on an outpatient basis. Improvements in materials and design of disc replacement implants continue to advance the results of motion-preserving techniques. Three-dimensional printing of spinal implants enables more customized surgical planning, while creating new interbody cage designs that may give them osteoinductive properties and improve the overall rates of spinal fusion.

Promising new procedures
Five-year data on percutaneous sacroiliac joint fusion shows sustained positive outcomes for carefully selected patients. The Intracept® Procedure, a minimally invasive outpatient procedure targeted to ablate or destroy the basivertebral nerve, has shown promising results for improvement of chronic low back pain. Endoscopic spinal surgery is also showing promise for properly selected patients.
Physical therapy

Low-level laser therapy

Laser, or light amplification by stimulated emission of radiation, describes any device that produces monochromatic, collimated and coherent light. Low-level laser therapy (LLLT) is used by some physical therapists to treat various musculoskeletal conditions. LLLT is a non-invasive light source treatment that produces a single wavelength of light without emitting heat, sound or vibration. Wavelengths between 660-905 nm can penetrate the skin, and soft and hard tissues. The effects of LLLT can be beneficial in the initial stages of physical therapy treatment by reducing inflammation and pain as well as accelerated tissue regeneration. LLLT has been used to treat conditions such as low back pain, plantar fasciitis, subacromial impingement syndrome, temporal mandibular dysfunction, chronic pain and osteoarthritis, and to reduce volume and pain in patients with lymphedema. While the FDA cleared LLLT for treatment in 2019, low-level laser, like all modalities, should be part of a comprehensive treatment plan.

References:
Lamba D. To evaluate the efficacy of 780 nm low level laser therapy for the treatment of plantar fasciitis in South Western Ethiopia. Ind Jour of Physioth and Occupat Therapy - An Inter Jour. 2019;13(2):231.
**Telehealth/Telerehabilitation**

Telehealth is defined as the delivery of health-related services and information via telecommunications technologies. In 2010, President Barak Obama signed The Patient Protection and Affordable Care Act (Public Law 11-148) to address the use of telehealth as a means of delivering efficient and effective health care in the United States. In 2019, COVID-19 emerged, leading to many changes in physical therapy and the health care community. A 2019 survey found 66% of US consumers articulated interest in telehealth, yet only 8% have utilized it. Barriers to telehealth in 2019 remain, including reimbursement models, difficulties in obtaining multiple state licensures and overall lack of comfort with technology.

The advantages of telehealth include convenient access to high-quality care, patient/provider safety during the pandemic and reduced burden on patients requiring childcare and/or time off from work and travel to appointments. Overall, patient satisfaction with treatment via telehealth is comparable to in-person rehabilitation for treatment of cardiovascular, integumentary, neuromuscular and musculoskeletal conditions with little to no statistical difference. One study showed that patients who used telerehabilitation after total knee arthroplasty had similar outcomes to patients in a regular rehabilitation setting for measures such as range of motion, limb girth, pain level, Timed Up and Go score, quality of life and gait scores, and that patients showed significant clinical improvements over baseline standardized testing scores. The individual needs of the patient and the ability of the therapist to deliver skilled and quality care should be considered as well as the appropriate frequency and duration of care based on individual patient need and medical necessity prior to using telehealth/telerehabilitation.

While telehealth is a means of continuing therapy treatment during a global pandemic, more research is needed to evaluate costs, funding and copayment to determine the true benefits of care.

**References:**

Eannucci EF, Hazel K, Grundstein MJ, Nguyen JT, Gallegro J. Patient satisfaction for telehealth physical therapy services was comparable to that of in-person services during the COVID-19 pandemic. *HSS J.* Published online October 19, 2020:1-7.


Radiation oncology

Some of the key trends in radiation therapy include technologies that maximize radiotherapy accuracy. Also, additional data are showing equivalent outcomes using a shorter course of treatment (hypofractionation regimes) across multiple disease sites. These trends show promise for improving outcomes, increasing efficiency and lowering costs. In addition, CMS continues to evaluate a new radiation oncology payment model that aims to improve quality of care and lower costs using episode-based bundled payments.

Technologies maximizing radiotherapy accuracy

**Vysioneer**
- [www.vysioneer.com](http://www.vysioneer.com)
- First-ever tumor auto-contouring solution for radiation therapy
- Artificial intelligence
- Cloud-based software
- Brain tumors (brain metastasis, meningioma and acoustic neuroma)
- 12.2% higher sensitivity for lesion detection
- Decreases treatment planning time at a median of 30.8%
- Maximizes radiotherapy accuracy
- Speeds up crucial treatment time for patients (hours to minutes)

**Automated 3D dose-volume verification; RadCalc QA software**
- 3D dose verification increases likelihood of getting a better, more accurate picture of dose distribution inside the patient
- Higher degree of certainty that the planning treatment volume is being validated, while assisting in the evaluation of plan quality by comparing dose to adjacent critical structures and organs at risk
- Better targeting accuracy and dose distribution accuracy, and ultimately enhanced treatment outcomes
- Physicist exports a treatment plan via their DICOM RT and RadCalc automatically verifies the plan using either a Monte Carlo or collapsed-cone algorithm, generating results in minutes

**ExacTrac Dynamic: Patient positioning system**
- High-speed thermal surface tracking technology combined with an update of ExacTrac X-ray monitoring
- 4D thermal camera creates highly accurate and reliable hybrid thermal surface by correlating patient’s heat signature to their reconstructed 3D-surface structure
- 300,000 3D surface points acquired and matched to the heat signal generated by the thermal camera
RayPilot HypoCath

- www.micropos.se
- Removable electromagnetic tracking device that enables real-time localization of the prostate during radiotherapy

Hypofractionation

TARGIT-IORT: Single-dose radiotherapy for breast cancer

- www.nature.com/articles/s41416-021-01440-8
- Single-dose treatment replaces the need for extra hospital visits in eight out of ten cases
- Treatment lasts for around 20-30 minutes
- Delivered immediately after tumor removal (lumpectomy), and under the same anesthetic, via small ball-shaped device placed inside the breast
- Significant overall survival benefit with TARGIT-IORT in patients with grade 1 or 2 cancer
- Less likely to experience fatal cardiovascular disease, such as heart attacks, lung problems or other cancers
- Seems to lower the likelihood of death if patients develop cardiovascular disease
- May have an ‘abscopal’ (distant) effect, a beneficial immunological action
- Superior cosmetic outcome
- Clinical trial:
  - Started in March 2000
  - 2,298 women aged 45 or over with invasive breast cancer and a tumor up to 3.5 cm in diameter were randomly assigned to receive either TARGIT-IORT during lumpectomy or post-operative EBRT
  - Involved 32 hospitals and medical centers in ten countries: the U.K., France, Germany, Italy, Norway, Poland, Switzerland, the U.S., Canada and Australia
- To date, 45,000 patients in 260 centers in 38 countries have received TARGIT-IORT

Reference:
The Case for brachytherapy: Why it deserves a renaissance
• www.advancesradonc.org/article/S2452-1094(20)30308-0/fulltext

• Renewed call for shorter radiation courses based on data showing equivalent outcomes will likely establish hypofractionated radiation as the standard of care across multiple disease sites

• Attempts to replace brachytherapy with external beam treatment approaches have been unsuccessful

• A recent phase 2 study of patients with predominantly locally advanced cervical cancer examined the feasibility of using a SABR boost as an alternative option to brachytherapy
  – The study was closed early, owing to high toxicity rates, including death due to complications of therapy

• Advances in imaging technology, such as MRI, allow for adaptive image-guided brachytherapy with simultaneous dose escalation to tumor targets and sparing of organs at risk

• Partial-breast irradiation has demonstrated comparable treatment outcomes to whole-breast irradiation with regard to local tumor control, toxicity, and cosmetic outcomes

• Prostate brachytherapy results in excellent treatment and toxicity outcomes, has a short overall treatment time (OTT), and is more cost effective than other radiation treatment options

References:

CMS Radiation Oncology Model

CMS to Push Back Radiation Oncology Model After Industry Blowback

• CMS plans to solidify a July 2021 start date through upcoming rulemaking

• Bundled payment model, part of a final rule on specialty care models, is expected to save Medicare $230 million over five years

• New structure provides bundled payments for a 90-day episode of care and covers 16 cancer types

Reference:
## Glossary

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
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<tbody>
<tr>
<td>ACR</td>
<td>American College of Radiology</td>
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<tr>
<td>AF</td>
<td>Atrial fibrillation</td>
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<tr>
<td>AI</td>
<td>Artificial intelligence</td>
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<tr>
<td>ALS</td>
<td>Amyotrophic lateral sclerosis</td>
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<tr>
<td>ApoE</td>
<td>Apolipoprotein E</td>
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<tr>
<td>ARIA-H</td>
<td>Amyloid-related imaging abnormalities due to hemosiderin deposition</td>
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<tr>
<td>AV</td>
<td>Atrioventricular</td>
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<tr>
<td>BML</td>
<td>Bone marrow lesions</td>
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<tr>
<td>CAD</td>
<td>Computer-aided detection</td>
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<tr>
<td>CBBCT</td>
<td>Cone-beam breast computed tomography</td>
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<tr>
<td>CIMT</td>
<td>Carotid intima-media thickness</td>
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<tr>
<td>CMS</td>
<td>Centers for Medicare &amp; Medicaid Services</td>
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<tr>
<td>CE-CBBCT</td>
<td>Contrast-enhanced cone-beam breast computed tomography</td>
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<tr>
<td>CPT®</td>
<td>Current Procedural Terminology coding system of the American Medical Association</td>
</tr>
<tr>
<td>CT</td>
<td>Computed tomography</td>
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<tr>
<td>DICOM</td>
<td>Digital Imaging and Communications in Medicine</td>
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<tr>
<td>EBRT</td>
<td>External beam radiation therapy</td>
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<tr>
<td>ER</td>
<td>Estrogen receptor</td>
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<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
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<tr>
<td>FDG</td>
<td>Fluorodeoxyglucose</td>
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<tr>
<td>FES</td>
<td>Fluoroestradiol F-18</td>
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<tr>
<td>ICG</td>
<td>Indocyanine green</td>
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<tr>
<td>IORT</td>
<td>Intraoperative radiation therapy</td>
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<tr>
<td>IPM</td>
<td>Interventional pain management</td>
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<tr>
<td>LAA</td>
<td>Left atrial appendage</td>
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<tr>
<td>Abbreviation</td>
<td>Description</td>
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<td>--------------</td>
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<tr>
<td>LLLT</td>
<td>Low-level laser therapy</td>
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<tr>
<td>MBC</td>
<td>Metastatic breast cancer</td>
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<tr>
<td>MMSE</td>
<td>Mini-Mental State Exam</td>
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<tr>
<td>mpMRI</td>
<td>Multiparametric magnetic resonance imaging</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
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<tr>
<td>MRS</td>
<td>Magnetic resonance spectroscopy</td>
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<tr>
<td>MSK</td>
<td>Musculoskeletal</td>
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<tr>
<td>NC-CBBCT</td>
<td>Non-contrast-enhanced cone-beam breast computed tomography</td>
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<tr>
<td>NCCN</td>
<td>National Comprehensive Cancer Network</td>
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<tr>
<td>NET</td>
<td>Neuroendocrine tumor</td>
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<tr>
<td>NIR</td>
<td>Near infrared</td>
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<tr>
<td>NPV</td>
<td>Negative predictive value</td>
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<tr>
<td>ORIF</td>
<td>Open reduction internal fixation</td>
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<tr>
<td>OTT</td>
<td>Overall treatment time</td>
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<tr>
<td>PEM</td>
<td>Positron emission mammography</td>
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<tr>
<td>PET</td>
<td>Positron emission tomography</td>
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<tr>
<td>PPV</td>
<td>Positive predictive value</td>
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<tr>
<td>PRIMUS™</td>
<td>Prostate Risk Identification Using Micro-Ultrasound</td>
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<tr>
<td>PSA</td>
<td>Prostate-specific antigen</td>
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<tr>
<td>PSMA</td>
<td>Prostate-specific membrane antigen</td>
</tr>
<tr>
<td>RF</td>
<td>Radiofrequency</td>
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<tr>
<td>RO</td>
<td>Radiation oncology</td>
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<tr>
<td>RT</td>
<td>Radiation therapy</td>
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<tr>
<td>SABR</td>
<td>Stereotactic ablative radiotherapy</td>
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<tr>
<td>SI</td>
<td>Sacroiliac</td>
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<tr>
<td>SLN</td>
<td>Sentinel lymph node</td>
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<tr>
<td>SLNB</td>
<td>Sentinel lymph node biopsy</td>
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<tr>
<td>TARGITIORT</td>
<td>Targeted intraoperative radiotherapy</td>
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<tr>
<td>TUG</td>
<td>Timed Up and Go</td>
</tr>
<tr>
<td>US</td>
<td>Ultrasound</td>
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