Medical Policy Reference Manual
Medical Policy

6.01.034 Magnetic Resonance Spectroscopy

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Description

Magnetic resonance spectroscopy (MRS) is a noninvasive technique that can be used to measure the concentrations of different chemical components within tissues. MR spectroscopy, also known as nuclear or proton magnetic resonance spectroscopy, is a refinement of MRI. The technique is based on the same physical principles as magnetic resonance imaging (MRI), and the detection of energy exchange between external magnetic fields and specific nuclei within atoms. The major difference between MRI and MRS is that in MRI, the emitted radiofrequency is based on the spatial position of nuclei and gives information about the structure of the body (the distribution of water and fat), while MRS detects the chemical composition of the scanned tissue. The information produced by MRS is displayed graphically as a spectrum with peaks consistent with the various chemicals detected. MRS can be performed as an adjunct to MRI by attaching specialized hardware and software to standard existing MRI equipment. The MRI image is generated first and then the MRS spectra are developed at the site of interest, termed the voxel. While the MRI produces an anatomic or structural image, MRS provides a functional image related to underlying dynamic physiology. Combining MR spectroscopy with MRI data, especially in areas that may be difficult to biopsy, has the potential to yield significant clinical information about the biochemical and pathophysiologic composition of specific lesions. Limitations of MR spectroscopy technology include signal quality related to the size of tissue area under study, and signal sensitivity to tissue movement, blood flow, and fat or gas adjacent to the tissue study area.

MRS may be indicated for certain conditions (e.g., evidence or suspicion of primary or secondary neoplasm, grading of primary glial neoplasm, brain infection, traumatic brain injury etc.) when conventional imaging by magnetic resonance imaging (MRI) or computed tomography (CT) provides limited information regarding specific clinical questions. MRS has been studied most extensively in a variety of brain pathologies. *N*-acetylaspartate (NAA) is an amino acid that is generated by mitochondria and is present almost exclusively in neurons and axons in the adult central nervous system (CNS). NAA intensity is thought to be a marker of neuronal integrity and an elevated ratio of lactate to NAA can be an important indicator of central nervous system pathology. Decreases in the NAA signal are associated with neuronal loss, damage to neuronal structures, and/or reduced neural metabolism.

This spectrographic analysis of functional chemical processes within the body has been appealing to many different types of clinical specialists, but in the clinical setting there have been obstacles to its use, mainly having to do with suppression of signals generated by water and fats. Recent advances in the design of clinical MRS devices have contributed to greater reliability in MRS signals in a clinical setting. At the present time, it is possible to obtain reliable spectra from H-1 (hydrogen), P-31 (phosphorous), C-13 (carbon), F-19 (fluorine) and Na-23 (sodium). In the clinical setting this data can be used to detect spectra of entities such as those arising from N-acetylaspartate, choline-containing phospholipids, creatinine, lactate, and glutamine.

Policy

Magnetic Resonance Spectroscopy (MRS) may be considered **medically necessary** for the following indications:

- Brain neoplasm, and need for differentiation of recurrent or residual disease from post-therapy changes (e.g., radiation necrosis)
- Brain neoplasm and need for differentiation from non-neoplastic lesions.

Magnetic Resonance Spectroscopy (MRS) is considered **experimental / investigational** for all other indications as it does not meet TEC criteria # 2 - 5.

Policy Guidelines

Experimental/Investigational

The term "experimental/investigational" describes services or supplies that are in the developmental stage and are in the process of human or animal testing. Services or supplies that do not meet all 5 of the criteria listed below adopted by the BlueCross BlueShield Association (BCBSA) Medical Policy Services (MPS) Assessment Criteria (formerly known as the TEC Criteria or "Technology Evaluation Center" criteria are deemed to be experimental/investigational):

1. The technology* must have final approval from the appropriate U.S. government regulatory bodies; and
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes; and
3. The technology must improve the net health outcome; and
4. The technology must be as beneficial as any established alternatives; and
5. The improvement must be attainable outside the investigational settings.

* Technology includes drugs, devices, processes, systems, or techniques

Rationale:

1. The technology must have final approval from the appropriate U.S. government regulatory bodies:

Since 1994, multiple software packages for performing proton MRS have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. Single-voxel MRS is available, and most often the hardware is built into the modern MRI scanners. FDA product code: LNH.

2. The scientific evidence must permit conclusions concerning the effect on health outcomes:

Research is sufficient to show that Magnetic Resonance Spectroscopy (MRS) in brain neoplasm, can rule out radiation necrosis in patients with recurrence of anaplastic gliomas or glioblastomas. MRS has the ability to differentiate true tumor progression from treatment-related imaging changes and its highly sensitive imaging technique in conjunction with conventional MRI allows for characterizing and differentiating between neoplastic and non-neoplastic brain lesions. However, evidence is insufficient for other indications such cerebral ischemia, heart disease, liver disease, neonatal encephalopathy, prostate cancer, traumatic brain injury and multiple sclerosis. Data from meta-analysis, systematic reviews, case studies, and expert consensus failed to conclude that MRS is beneficial in diagnosing other conditions (MCG 25th edition, 2021). Studies have examined the use of MRS for localized prostate cancer for biopsy, for diagnosis, and for the monitoring of patients with prostate cancer. However, the cumulative evidence remains uncertain. Data comparing the diagnostic accuracy of MRS with alternative imaging strategies are limited and the clinical evidence is not sufficient to permit conclusions on the health outcome effects of magnetic resonance spectroscopy in the evaluation of prostate cancer. For heart disease MR spectroscopy may provide information on metabolic abnormalities related to valvular and ischemic heart disease, heart failure, cardiomyopathy, and cardiac transplant; however, MR spectroscopy is currently used primarily as a research tool because of its low spatial and temporal resolution and poor reproducibility. In addition, due to small sample size, clinical evidence was not sufficient to conclude that MRS improve patient outcomes when assessing liver diseases such as hepatic encephalopathy, liver steatosis, detecting fibrosis, staging cirrhosis, and response to hepatitis treatment. A study of MRS as a noninvasive alternative to liver biopsy indicated that dual-gradient echo MRI outperforms MRS. Data on the use of MRS in multiple sclerosis has indicated that the measure is not sufficiently reliable to predict the future disease course. According to Slanetz P.J.et al., (2022) breast MR spectroscopy is designed to detect choline and its derivatives, based on the observation that malignant tumors have elevated choline levels. Results showed that MR spectroscopy may have the potential to increase specificity and avoid benign biopsies in a substantial number of women as an adjunct to conventional breast MRI and MR spectroscopy is also promising for the evaluation of non-mass like suspicious findings on breast MRI. However, MR spectroscopy misses some breast cancers, because not all express choline. In a study of 16 invasive ductal tumors; 88 percent had detectable choline peaks. MR spectroscopy remains investigational, but it may have a future role in predicting outcome and monitoring response of therapy. Guo et al., (2016) stated, "MR spectroscopy is a complementary tool for the diagnosis of Hypoxic Ischemic Encephalopathy (HIE)." However, whether MR spectroscopy prior to conventional MR imaging should be used in the early diagnosis of neonate with HIE remains unknown. Recent studies by Shibasaki J, et al. (2018) showed that proton (1H) MR spectroscopy can noninvasively quantify the severity of HIE on the basis of disturbances in energy metabolism. However, changes in lactate, and glutamate and glutamine concentrations are often transient; therefore, caution needs to be exercised when MR spectroscopy is performed more than 1 week after hypoxic ischemic injury. According to an article by Wilkinson, D. (2010) article looking at the effects MR biomarkers had on determining whether to withdraw life support from newborn infants with hypoxic-ischemic encephalopathy. It

was determined that current evidence showed MR biomarkers alone are not sufficiently accurate to direct treatment-limitation decisions. Although there may be a role for using MRI or MR spectroscopy in combination with other prognostic markers to identify infants with very adverse outcome, it is not possible from meta-analysis to define this group clearly. Guidelines on central nervous system cancers from the National Comprehensive Cancer Network (NCCN, 2020) state that magnetic resonance spectroscopy may be useful in anaplastic gliomas and glioblastoma to determine if the changes seen on brain MRI are due to pseudo progression or RT-induced necrosis versus actual disease progression. However, NCCN fails to mention in its guidelines MRS for hypoxic ischemic encephalopathy. Moreover, The American College of Radiology (ACR) and American Society of Neuroradiology (ASNR) practice guidelines (revised 2019) lists hypoxic ischemic encephalopathy as one of 25 conditions that MRS might be indicated when conventional imaging by MRI or CT is inadequate for answering specific clinical questions, but states that these guidelines are not evidence-based and were developed through consensus and that there is an urgent need for improved prognostic research into HIE. Currently no studies have proven that MR spectroscopy findings have unequivocally led to improved detection or treatment outcomes and additional research is recommended.

3. The technology must improve the net health outcome:

According to (MCG 25th edition 2021) various MR spectroscopy-detected biochemical abnormalities have been characterized for central nervous system diseases, including neuropsychiatric systemic lupus erythematosus, brain abscess, acute disseminated encephalomyelitis, HIV/AIDS, progressive multifocal leukoencephalopathy, toxoplasmosis, Alzheimer disease, Parkinson disease, Huntington disease, spinocerebellar ataxia, schizophrenia, bipolar disorder and major depressive disorder, obsessive-compulsive disorder, posttraumatic stress disorder, first-episode psychosis, alcohol abuse and dependence, amyotrophic lateral sclerosis, primary lateral sclerosis, normal pressure hydrocephalus, neonatal encephalopathy, autism, and mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes (MELAS). However, no studies have proven that MR spectroscopy findings have led to improved detection or treatment outcomes. The evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. Zou et al., (2018) stated In addition to conventional MRI, magnetic resonance spectroscopy (MRS) can provide useful complimentary information regarding the nature and prognosis of brain injury underlying neonatal encephalopathy. Hypoxic-ischemic encephalopathy (HIE) is a major contributor to child mortality and morbidity. Reliable prognostication for HIE is of key importance. Proton MRS (1H-MRS) is a quantitative, non-invasive method that has been demonstrated to be a suitable complementary tool for prediction. However, the researchers stated that larger prospective multi-center studies with a standardized protocol for both measurement protocols and analysis methods are needed in future studies. NCCN (2022) clinical guidelines for Prostate Cancer lists MRS as an advanced imaging technique and states that it can provide useful complimentary information as an adjunct to conventional radiology, but the guidelines make no recommendations using MRS for detecting breast cancer. According to AIM 2017 and 2022 guidelines, MRS when performed usually accompanies an MRI exam. Although MR Spectroscopy is an evolving technology, its impact on health outcomes will continue to undergo review, as new evidence-based studies are published; however, at this point, medically necessary applications are limited.

4. The technology must be as effective as any established alternatives:

There is insufficient documentation as to the use of MRS as a diagnostic test related to how the results of that test may be used in treatment planning and patient management decisions. There are very few published articles that compare graphic representations obtained by MRS to other chemical methods of identifying disease processes such as tumor markers, enzyme studies, or immunology studies. Currently, magnetic resonance imaging (MRI) is the standard alternative for diagnosing conditions such as brain tumors, breast, and prostate cancer etc. Other forms of imaging include conventional radiology such as X-ray, ultrasound, CT, and PET scan and functional MRS may be as an adjunct to these established screening methods. However, the role of MRS in diagnosis and therapeutic planning has not been established by adequate clinical studies and there have been very few clinical trials demonstrating improved health outcomes compared to conventional imaging modalities.

5. The improvement must be attainable outside the investigational settings:

A net health outcomes improvement has not been demonstrated in the investigational settings. Therefore, it is not possible to determine whether an improvement outside of the investigational setting can be expected.

Update 2022:
A search of the peer-reviewed literature was performed from the period of December 2019 through September 2022. Changes to the Policy statement were made per Medical Director guidance. New Policy statement amended to "Magnetic Resonance Spectroscopy (MRS) may be considered medically necessary for the following indications:

Brain neoplasm and need for differentiation of recurrent or residual disease from post-therapy changes (e.g., radiation necrosis); Brain neoplasm and need for differentiation from non-neoplastic lesions. Magnetic Resonance Spectroscopy (MRS) is considered experimental / investigational for all other indications as it does not meet TEC criteria # 2 – 5".

Update 2020:
A search of the peer-reviewed literature was performed from the period of December 2017 through December 2019. Findings in the recent literature do not change the conclusion regarding the use of Magnetic Resonance Spectroscopy (MRS). Therefore, the policy statement remains unchanged.

Update 2017:
A search of the peer-reviewed literature for magnetic resonance spectroscopy was performed for the period of October 2015 through November 2017. Findings in the recent literature do not change the above conclusion. Therefore, the policy statement is unchanged.

Update 2015:
A search of the peer-reviewed literature for magnetic resonance spectroscopy was performed for the period of September 2013 through September 2015. Findings in the recent literature do not change the above conclusion. Therefore, the policy statement is unchanged.

Update 2013:
A search of the peer-reviewed literature for magnetic resonance spectroscopy was performed for the period of July 2011 through August 2013. Findings in the recent literature do not change the above conclusion. Therefore, the policy statement is unchanged.

Update 2011:
A search of the peer-reviewed literature for magnetic resonance spectroscopy was performed for the period of July 2009 through June 2011. Findings in the recent literature do not change the above conclusion. Therefore, the policy statement is unchanged.

Update 2009:
A search of the peer-reviewed literature for magnetic resonance spectroscopy was performed for the period of July 2007 through June 2009. Findings in the recent literature do not change the above conclusion. Therefore, the policy statement is unchanged.

Update 2007:
A recent search of the literature via MEDLINE indicates that MRS remains an active area of research into a wide variety of diseases, including malignant tumors of the brain, metabolic disorders, epilepsy, neurodegenerative diseases, traumatic brain injury, and psychiatric disorders. Published systematic literature reviews by authors within the specialty generally conclude that the use of MRS for characterizing brain tumors is promising, but that additional high-quality studies are needed. A number of authors have reported findings in such topics as tumor grading and differentiation, distinguishing tumor from tumor necrosis, identifying tumor versus cystic growths, and so on, but the studies generally have not been powered to determine what contribution MRS makes to improved medical decision making or patient outcomes.

A number of clinical trials are underway. One such trial is designed to evaluate MRS in staging brain tumors. Another is focused on the use of MRS in prostate cancer, to predict if disease is confined to the organ. Still another is aimed at improving the specificity of MRI of the breast through the use of concurrent MRS.

In January of 2004, CMS issued a decision memo reaffirming its national non-coverage determination. Medicare found that there was inadequate evidence to determine that MRS is reasonable and necessary for the diagnosis of brain tumors.

Benefit Applications
NOTE: For FEP business, check the member's contract for benefits.

Provider Guidelines
There are no Provider Guidelines for this Medical Policy.

Cross References to Related Policies and Procedures

There are no Related Policies for this Medical Policy.

References

The following were among the resources reviewed and considered in developing this policy. By reviewing and considering the resources, CareFirst does not in any way endorse the contents thereof nor assume any liability or responsibility in connection therewith. The opinions and conclusions of the authors of these resources are their own and may or may not be in agreement with those of CareFirst.

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