

Corporate Medical Policy

Magnetic Resonance Spectroscopy

File Name:	magnetic_resonance_spectroscopy
Origination:	12/1997
Last CAP Review:	5/2019
Next CAP Review:	5/2020
Last Review:	5/2019

Description of Procedure or Service

Magnetic resonance spectroscopy (MRS) is a noninvasive technique that can be used to measure the concentrations of different chemical components within tissues. 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.

With MRI, this energy exchange, measured as a radiofrequency signal, is then translated into the familiar anatomic image by assigning different gray values according to the strength of the emitted signal. The principal difference between MRI and MRS is that in MRI the emitted radiofrequency is based on the spatial position of nuclei, 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 may be performed as an adjunct to MRI. An MRI image is first generated, and then MRS spectra are developed at the site of interest, at the level of the voxel (3 dimensional volume X pixel). The voxel of interest (VOI) is typically a cube or rectangular prism with a dimensional pixel with a volume of 1 to 8 cm. While an MRI provides an anatomic image of the brain, MRS provides a functional image related to underlying dynamic physiology. MRS can be performed with existing MRI equipment, modified with additional software and hardware which is provided on all new MRI scanners. Imaging time in the scanner is increased by 15 to 30 minutes.

MRS has been studied most extensively in a variety of brain pathologies. In the brain, both 1-H (i.e., proton) and 31-P are present in concentrations high enough to detect and thus have been used extensively to study brain chemistry. Proton MRS of the brain reveals 6 principal spectra:

- Arising from N-acetyl groups, especially n-acetylaspartate (NAA). 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 is the most important proton signal in studying central nervous system (CNS) pathology. Decreases in the NAA signal are associated with neuronal loss, damage to neuronal structures, and/or reduced neural metabolism.

- Arising from choline-containing compounds (Cho) such as membrane phospholipids (e.g., phosphocholine and glycerophosphocholine). An increase in Cho is considered a marker of pathological proliferation/degradation of cell membranes and demyelination. Choline levels increase in acute demyelinating disease, but an increase in Cho levels is most commonly associated with neoplasms. Cho levels can also be affected by diet and medication.
- Arising from creatine and phosphocreatine

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In the brain, creatine is a relatively constant element of cellular energetic metabolism and thus is sometimes used as an internal standard.

- Arising from Myo-Inositol (ml) is a polyalcohol that is present at high concentration in glial cells. An increase in the ratio of ml to NAA suggests gliosis and regional neuronal damage.
- Arising from lipid
- Arising from lactate: Normally this spectrum is barely visible, but lactate may increase to detectable levels when anaerobic metabolism is present. Lactate may accumulate in necrotic areas, in inflammatory infiltrates, and in brain tumors.

Different patterns of the above spectra and others, such as myoinositol and glutamate/glutamine, in the healthy and diseased brain are the basis of clinical applications of MRS. The MRS findings characteristically associated with non-necrotic brain tumors include elevated choline (Cho) levels and reduced N-acetylaspartate (NAA) levels. The International Network for Pattern Recognition using Magnetic Resonance (<http://azizu.uab.es/INTERPRET/index.html>) has developed a user-friendly computer program for spectral classification and a database of 300 tumor spectra with histologically validated diagnoses to aid radiologists in MRS diagnosis.

One of the limitations of MRS is that it provides the metabolic composition of a given voxel, which may include more than 1 type of tissue. For some applications, the voxels are relatively large (eg, >1 cm³), although they may be somewhat smaller using a 3T MRI machine versus a 1.5T magnet. High field strength increases the signal to noise ratio and spectral resolution. The 3T technique creates greater inhomogeneities, however, which require better shimming techniques.² There are 2 types of MRS data acquisition: single voxel or simultaneous multivoxel, also called chemical shift imaging. Reliable results are more difficult to obtain from some areas, eg, close to the brain surface or in children with smaller brains because of the lipid signal from the skull. Some techniques are used to deal with these issues; various MRS techniques continue to be explored as well. A combination of MRS is often used with other MRI techniques, including diffusion-tensor imaging, susceptibility-weighted imaging, etc., and possibly other types of imaging such as positron emission tomography.

Peripheral applications of MRS include the study of myocardial ischemia, peripheral vascular disease, and skeletal muscle. Applications in non-CNS oncologic evaluation have also been explored. Nomograms for prostate cancer are being developed that incorporate MRI and MRS results.

Multiple software packages for performing proton MRS have received clearance by the U.S. Food and Drug Administration (FDA) through the 510(k) process since 1993. Single voxel MRS is available on all modern MR scanners.

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

Magnetic Resonance Spectroscopy is considered investigational. BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit

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design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Magnetic Resonance Spectroscopy is covered

Not applicable.

When Magnetic Resonance Spectroscopy is not covered

The use of Magnetic Resonance Spectroscopy is considered investigational for all applications.

Policy Guidelines

The evidence for MRS in patients who have brain tumors includes a number of small studies and systematic reviews. Relevant outcomes are test accuracy, change in disease status, morbid events, and functional outcomes. Small studies have evaluated detection, characterization, grading, prognosis, and differentiation of tumor recurrence versus necrosis. Most studies included in the meta-analyses were small, retrospective, and used various ratios of MRS spectra. The largest prospective studies found that combining MRS with MRI resulted in a greater percentage of correct diagnoses of pediatric brain tumor type. These reports had limited information on the specific MRS spectra associated with the different tumor types. Additional study is needed to better define the spectra associated with tumor characteristics, to evaluate the diagnostic accuracy, and to determine the effect on health outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have breast cancer, prostate cancer, dementia, liver disease, or multiple sclerosis who receive MRS, the evidence includes prospective studies on diagnostic accuracy and systematic reviews. Relevant outcomes are test accuracy, change in disease status, morbid events, and functional outcomes. A number of studies have examined the use of MRS for localizing prostate cancer for biopsy and for monitoring of patients with prostate cancer. However, the cumulative evidence remains uncertain. Data comparing the diagnostic accuracy of MRS with alternative imaging strategies is limited. A systematic review of MRS to identify dementia concluded that to effectively characterize Alzheimer disease–associated neurochemical changes, future approaches need to interactively analyze multiple quantifiable metabolites from different brain regions. A study of MRS as a noninvasive alternative to liver biopsy indicates that dual-gradient echo MRI outperforms MRS. Data on use of MRS in multiple sclerosis indicates that the measure is not sufficiently reliable to predict the future disease course. The evidence is insufficient to determine the effects of the technology on health outcomes.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 76390

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

MEDLINE search January 1996 through December 1997

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MRI Clinics of North America, Volume 6, Number 1, February 1998; "*MR Spectroscopy in the Evaluation of Epilepsy*", pps. 21-29; Jill E. Thompson, M.D., Mauricio Castillo, M.D., and Lester Kwock, PhD.

Neuroimaging Clinics of North America, Volume 8, Number 4, November 1998; "*Proton MR Spectroscopy in Inflammatory and Infectious Brain Disorders*", pps. 863-880; Kim M. Cecil, PhD., Robert E. Lenkinski, PhD.

Neuroimaging Clinics of North America, Volume 8, Number 4, November 1998; "*Proton MR Spectroscopy in Ischemic Stroke and Other Vascular Disorders*", pps. 881-900; Peter E. Ricci, Jr., M.D.

Independent Consultant Review 8/99

Medical Policy Advisory Group - 12/99

BCBSA Medical Policy Reference Manual - 4/30/2000; 6.01.24

Specialty Matched Consultant Advisory Panel - 9/2000

Medical Policy Advisory Group - 10/2000

Specialty Matched Consultant Advisory Panel - 8/2002

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.24, 4/29/03

Wartenberg KE, Patsalides A, Yepes MS. (April 2004). Is magnetic resonance spectroscopy superior to conventional diagnostic tools in hypoxic-ischemic encephalopathy. *J Neuroimaging*, 14(2), 180-6. Retrieved on May 10, 2004 from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15095566.

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Rock JP, Scarpace L, Hearshen D, Gutierrez J, Fisher JL, Rosenblum M, et al. (May 2004). Associations among magnetic resonance spectroscopy apparent diffusion coefficients, and image-guided histopathology with special attention to radiation necrosis. Retrieved on May 10, 2004 from http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=15113465.

Specialty Matched Consultant Advisory Panel - 7/2004

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Centers for Medicare & Medicaid Services. Decision Memo for Magnetic Resonance Spectroscopy for Brain Tumors (CAG-00141N). January 29, 2004. Retrieved 1/20/06 from <http://www.cms.hhs.gov/mcd/viewdecisionmemo.asp?id=52>

Centers for Medicare & Medicaid Services. National Coverage Determination for Magnetic Resonance Spectroscopy (220.2.1). September 2004. Retrieved 1/20/06 from <http://www.cms.hhs.gov>

Ontario Ministry of Health, Medical Advisory Secretariat (MAS). Ontario Health Technology Advisory Committee (OHTAC). Recommendation Functional Brain Imaging. Toronto, ON: MAS; January 25, 2007. Retrieved 2/19/08 from http://www.health.gov.on.ca/english/providers/program/ohtac/tech/reviews/pdf/rev_fbi_012507.pdf

BCBSA Medical Policy Reference Manual [Electronic Version] 6.01.24, 5/08/08

BCBSA Medical Policy Reference Manual [Electronic Version] 6.01.24, 7/09/09

BCBSA Medical Policy Reference Manual [Electronic Version] 6.01.24, 11/11/10

BCBSA Medical Policy Reference Manual [Electronic Version] 6.01.24, 12/8/11

BCBSA Medical Policy Reference Manual [Electronic Version] 6.01.24, 12/13/12

Specialty Matched Consultant Advisory Panel 7/2013

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BCBSA Medical Policy Reference Manual [Electronic Version] 6.01.24, 12/12/13

Specialty Matched Consultant Advisory Panel 7/2014

BCBSA Medical Policy Reference Manual [Electronic Version] 6.01.24, 12/11/14

Specialty Matched Consultant Advisory Panel 6/2015

BCBSA Medical Policy Reference Manual [Electronic Version] 6.01.24, 12/10/15

BCBSA Medical Policy Reference Manual [Electronic Version] 6.01.24, 9/14/2017

BCBSA Medical Policy Reference Manual [Electronic Version] 6.01.24, 9/13/2018

Policy Implementation/Update Information

12/97	Original Policy developed. Reviewed by the Plan's Medical Director
9/99	Reformatted, Description of Procedure or Service changed, Medical Term Definitions added.
12/99	Medical Policy Advisory Group
2/00	Coding system change
10/00	Specialty Matched Consultant Advisory Panel review. No change recommended in criteria. System coding changes. Medical Policy Advisory Group review. No change in criteria. Approve.
9/02	Specialty Matched Consultant Advisory Panel review 8/2002. Added source to Scientific Background and Reference Sources section. No changes in criteria.
8/26/04	Specialty Matched Consultant Advisory Panel review 7/15/2004 with no changes made to policy criteria. References added. Benefits Application and Billing/Coding sections updated for consistent policy language.
6/5/06	Description of procedure expanded for clarification. Rationale added to Policy Guidelines. Policy number added to Key Words. References updated. Specialty Matched Consultant Advisory Panel review 5/3/06 with no changes to policy coverage criteria.
10/2/06	Policy statement changed to indicate BCBSNC will not provide coverage for MRS. It is considered investigational. Information in the "When MRS is Covered" section replaced with the statement "not applicable." Information in the "When MRS is Not Covered" section replaced with the statement "The use of Magnetic Resonance Spectroscopy is considered investigational for all applications. BCBSNC does not provide coverage for investigational services." Policy Guidelines section updated to include the following rationale for noncoverage: The available studies all have some degree of shortcomings, and the overall body of evidence does not provide strong and consistent evidence regarding the diagnostic test characteristics or clinical utility of MRS for any condition. Studies of diagnostic performance often included a heterogeneous mix of patients that had clinically important differences and did not clearly delineate how MRS information would be used to guide patient management. Furthermore, there were differences in MRS technique and methods of analysis across studies that make it difficult to synthesize findings from different studies. References added. Notification date 10/2/06. Effective date 12/11/06.
6/16/08	Specialty Matched Consultant Advisory Panel review 5/15/08. No change in policy statement. (adn)
6/22/10	Policy Number(s) removed (amw)
9/28/10	Description section extensively revised. Investigational statement reworded but intent is unchanged. Specialty Matched Consultant Advisory Panel review 8/25/10. Draft policy accepted as written. (adn)

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- 7/19/11 Policy Guidelines updated. Specialty Matched Consultant Advisory Panel review 6/29/11. Policy accepted as written. (adn)
- 7/10/12 Summary statement added. Specialty Matched Consultant Advisory Panel review 6/20/12. No change in policy statement. (sk)
- 1/29/13 Reference added. No change to policy statement. (sk)
- 7/30/13 Specialty Matched Consultant Advisory Panel review 7/17/13. No change to policy statement. (sk)
- 4/1/14 Reference added. No change to Policy statement. (sk)
- 8/12/14 Specialty Matched Consultant Advisory Panel review 7/29/14. No change to policy statement. (sk)
- 2/10/15 Updated Description section. Reference added. No change to policy statement. (lpr)
- 7/28/15 Specialty Matched Consultant Advisory Panel review 6/24/2015. No change to policy statement. (lpr)
- 2/29/16 Updated Policy Guidelines section. Reference added. No change to policy statement. (lpr)
- 7/26/16 Specialty Matched Consultant Advisory Panel review 6/29/2016. No change to policy statement. (an)
- 6/30/17 Specialty Matched Consultant Advisory Panel review 5/31/2017. No change to policy statement. (an)
- 6/29/18 Reference added. Specialty Matched Consultant Advisory Panel review 5/23/2018. No change to policy statement. (an)
- 6/11/19 Updated Policy Guidelines. Reference added. Specialty Matched Consultant Advisory Panel review 5/15/2019. No change to policy statement. (an)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.