KAISER PERMANENTE®

Kaiser Foundation Health Plan of Washington

Clinical Review Criteria
Magnetic Resonance Spectroscopy (MRS)

- ADHD
- Autism
- Cerebral Tumors
- Differentiating Tumors from Non-Tumors
- Epilepsy

Criteria

For Medicare Members

Source	Policy
CMS Coverage Manuals	None
National Coverage Determinations (NCD)	Magnetic Resonance Spectroscopy (220.2.1) **RETIRED** 06/08/2021 NCD Magnetic Resonance Spectroscopy (220.2.1) has been retired. These services still need to meet medical necessity as outlined in the NCD and will require review. NCDs are retired due to lack of evidence of current problems, or in some cases because the material is addressed by a National Coverage Decision (NCD), a coverage provision in a CMS interpretative manual or an article. Most NCDs are not retired because they are incorrect. Therefore, continue to use NCD 220.2.1.
Local Coverage Determinations (LCD)	None

For Non-Medicare Members

There is insufficient evidence in the published medical literature to show that this service/therapy is as safe as standard services/therapies and/or provides better long-term outcomes than current standard services/therapies.

If requesting review for this service, please send the following documentation:

- Last 6 months of clinical notes from requesting provider &/or specialist

The following information was used in the development of this document and is provided as background only. It is provided for historical purposes and does not necessarily reflect the most current published literature. When significant new articles are published that impact treatment option, Kaiser Permanente will review as needed. This information is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

Background

Magnetic resonance spectroscopy (MRS) is a non-invasive technique that provides chemical information on metabolites in tissues. It uses strong magnetic fields to generate an exchange of energy between external magnetic fields and protons within tissues. The energy exchange is transmitted back to the machine as a radiofrequency signal which is decoded by computer software. The software produces a waveform with peaks corresponding to the relative concentration of various chemicals. In addition, the specific chemicals that are present are identified--they appear at different locations on a horizontal axis. MRS utilizes the magnetic property of atomic nuclei. The proton is the most commonly studied nucleus. Proton (^{1}H) MRS defines approximately 15 brain metabolites. These include lipids, lactate, N-acetylaspartate (NAA), glutamate/glutamine (Glx), creatine (Cr), choline (Cho) and myinositol (mI) (Gulati et al., 2003; Lin et al., 2005; BlueCross BlueShield Association, 2005).

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A potential use of MRS is to diagnose conditions when other tests have been negative or inconclusive, or to refine existing diagnoses. For example, an increased Cho signal is believed to indicate the presence of cancerous cells. MRS can be used alone or in combination with magnetic resonance imaging (MRI) which produces anatomic images. In addition, MRS can be used to monitor metabolites to evaluate the effectiveness of therapy by seeing if levels change from elevated back to normal (Lin et al., 2005).

MRS has been used to study various neurologic diseases, including epilepsy, multiple sclerosis, HIV-related neurologic disorders and brain tumors, as well as cerebrovascular and metabolic diseases. One review article stated that MRS's most important use in neurology is quantifying neuronal loss and demonstrating reversible neuronal damage. (Rudkin & Arnold, 1999).

Other imaging tests used for epilepsy include EEG, MRI, FDG PET and CT scanning. ADHD and autism are diagnosed mainly by clinical evaluation. EEG and MRI are sometimes used to provide additional information on autism.

Cerebral Tumors

More than 190,000 people in the United States are diagnosed with primary or metastatic cerebral tumors annually. It is challenging to diagnose and treat cerebral tumors due to the similarity of these lesions to other types of pathologies on conventional imaging, the inaccessibility of the lesions and their proximity to complex brain structures. An accurate non-invasive method for diagnosing cerebral tumors is desirable, especially one that could replace biopsy which has a reported morbidity of 3-4% (AHRQ, 2003, Sibtain et al., 2007; National Brain Tumor Foundation).

Imaging procedures for diagnosing cerebral tumors include CT, MRI, SPECT and PET. CT uses x-rays and MRI uses non-ionizing radio frequency to acquire images. Both methods can generate multiple two-dimensional cross-sections of tissue as well as three-dimensional reconstructions and are generally used in conjunction with stereotactic biopsy. PET scans measure glucose activity which can be translated to a moving picture of the brain. SPECT imaging uses gamma rays to acquire multiple two-dimensional images from multiple angles, which can produce true three-dimensional information.

Magnetic resonance spectroscopy (MRS), a technique related to MRI, is also proposed for imaging cerebral tumors. MRS is a non-invasive technique that provides chemical information on metabolites in tissues. It uses strong magnetic fields to generate an exchange of energy between external magnetic fields and protons within tissues. The energy exchange is transmitted back to the machine as a radiofrequency signal which is decoded by computer software. The software produces a waveform with peaks corresponding to the relative concentration of various chemicals. In addition, the specific chemicals that are present are identified--they appear at different locations on a horizontal axis. MRS utilizes the magnetic property of atomic nuclei. The proton is the most commonly studied nucleus. Proton (1H) MRS defines approximately 15 brain metabolites. These include lipids, lactate, N-acetylaspartate (NAA), glutamate/glutamine (Glx), creatine (Cr), choline (Cho) and myinositol (mI). A chemical profile that may be characteristic of brain tumors includes an increase in Cho, and a reduction in Cr and NAA (Sibtain et al., 2007; Lin et al., 2005; BlueCross BlueShield Association, 2005).

Potential areas in which MRS may contribute diagnostic information include distinguishing abscesses from tumors, providing a more accurate way to determine the grade of primary tumors than conventional MRI, distinguishing single metastatic brain lesions from primary tumors, providing guidance for biopsy and gamma knife therapy, determining tumor recurrence and differentiating between radiation necrosis and tumor recurrence. MRS can be used alone, or in combination with MRI (AHRQ, 2003; Sibtain et al., 2007).

Several factors may limit the performance of MRS in identifying cerebral tumors. Sudden dramatic changes in the composition of tissue can cause inaccuracies in the magnetic fields. This is relevant for lesions adjacent to bone or air-filled structures such as the sinuses. Moreover, lesions that lie near areas of old infarcts or ischemic changes, or concurrent demyelinatin disease, can distort the chemical ratios used in interpretation. In addition, visual interpretation of spectra is difficult and requires special training (AHRQ, 2003; Sitbain et al., 2007).

Medical Technology Assessment Committee (MTAC)

Magnetic Resonance Spectroscopy (MRS)

12/05/2005: MTAC REVIEW

Evidence Conclusion: No published studies were identified on the accuracy of magnetic resonance spectroscopy for diagnosing ADHD or autism. One study was identified on the accuracy of MRS for lateralization

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of patients with medically refractory temporal lobe epilepsy. This study (Cendes et al., 1997) included 100 patients and used EEG as the gold standard. Lateralization based on MRS agreed with EEG findings in 87% of cases. Lateralization based on the results of MRS and MRI combined agreed with EEG findings in 86% of cases.
Articles: The ideal study of diagnostic accuracy would report the sensitivity and specificity of MRS and compare this to an independent blinded comparison to a "gold standard" diagnosis.
ADHD and autism None of the studies on ADHD, or ADHD and autism reported the sensitivity and specificity of MRS diagnosis compared to a "gold standard" such as clinical evaluation. The empirical studies reported on preliminary research using MRS to measure the concentrations of various chemicals in the brains of children with ADHD compared to healthy children. One of the articles included children with autism, in addition to children with ADHD and healthy controls. *Epilepsy* None of the studies on epilepsy reported the sensitivity and specificity of MRS diagnosis compared to a "gold standard". There were several studies examining the correlations between concentrations of chemicals identified by MRS and seizure duration, seizure severity or surgical outcome. One study compared chemical concentrations in patients with epilepsy and normal controls. These were all descriptive studies and were not evaluated further. One study was identified that compared the performance of MRI, MRS and the combination of the two in the lateralization of temporal lobe epilepsy (TLE). This article (Cendes et al., 1997) was critically appraised. No other studies on the diagnostic accuracy of MRS in patients with epilepsy were identified and no studies were identified on diagnostic or therapeutic impact.
The study critically appraised was: Cendes F, Caramanos Z, Andermann F et al. Proton magnetic resonance spectroscopic imaging and magnetic resonance imaging volumetry in the lateralization of temporal lobe epilepsy: A series of 100 patients. Ann Neurol 1997; 42: 737-746. See Evidence Table.

The use of Magnetic resonance spectroscopy (MRS) in diagnosing autism, ADHD and epilepsy does not meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

10/02/2006: MTAC REVIEW
Magnetic Resonance Spectroscopy (MRS)
Evidence Conclusion: No new published studies were identified on the accuracy of magnetic resonance spectroscopy for diagnosing ADHD, epilepsy or autism. No new studies were identified that validate specific chemical profiles that are diagnostic of particular conditions.
Articles: The ideal study of diagnostic accuracy would report the sensitivity and specificity of MRS and include an independent blinded comparison to a "gold standard" diagnosis. *ADHD and autism* - 2005 Review: None of the studies on ADHD, or ADHD and autism reported the sensitivity and specificity of MRS diagnosis compared to a "gold standard" such as clinical evaluation. The empirical studies reported on preliminary research using MRS to measure the concentrations of various chemicals in the brains of children with ADHD compared to healthy children. One of the articles included children with autism in addition to children with ADHD and healthy controls. 2006 Review: The newer studies were similar to those identified in the 2005 search. Studies reported on use of MRS to measure the concentrations of chemicals (i.e. Cho, CR and NAA) in children with autism or ADHD compared to healthy children. None of the studies reported the ability of MRS to diagnose autism or ADHD (i.e. sensitivity and specificity of MRS findings). *Epilepsy* - 2005 Review: None of the studies on epilepsy reported the sensitivity and specificity of MRS diagnosis compared to a "gold standard". Several studies examined the correlations between concentrations of chemicals identified by MRS and seizure duration, seizure severity or surgical outcome. One study compared chemical concentrations in patients with epilepsy and normal controls. These were all descriptive studies and were not evaluated further. One study compared the performance of MRI, MRS and the combination of the two in the lateralization of temporal lobe epilepsy (TLE). This article (Cendes et al., 1997) was critically appraised. 2006 Review: One meta-analysis was identified. This study (Willmann et al., in press, 2006) assessed the pre-operative value of MRS in identifying the epileptogenic zone (EZ) for epilepsy surgery. Preoperative evaluation of epilepsy patients is outside the scope of the current review and the study was thus not evaluated further.

The use of Magnetic resonance spectroscopy (MRS) in diagnosing autism, ADHD and epilepsy does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

12/03/2007: MTAC REVIEW
Magnetic Resonance Spectroscopy (MRS)
Evidence Conclusion: Three studies were reviewed that reported the sensitivity and specificity of MRS for distinguishing brain tumors from non-tumors, compared to a reference standard. All had relatively small sample sizes, especially as regards the number of patients without tumors, so estimates may not be reliable. One of the studies used combined MRS/MRI findings. Sensitivity ranged from 81% to 90% and specificity from 86% to 100%. The size of the studies was too small to draw conclusions about the accuracy of MRS for differentiating between brain tumors and any specific alternate condition such as radiation necrosis or abscess. There is a lack of

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evidence on the diagnostic accuracy of MRS alone compared to conventional imaging, or on MRS plus conventional imaging versus conventional imaging alone. Thus, it is difficult to draw conclusions about the ability of MRS to replace other diagnostic tests. Two studies addressed the impact of MRS on clinical decision-making. Both were case series; Lin et al., 1999 was limited in that it had only 15 patients, and Adamson et al. was retrospective. In the Adamson et al., study, MRS was seen as having a potential positive impact on treatment in 23/78 (29%) of cases. In 2 cases, MRS was seen as having a potential negative impact on treatment. For the remainder of the cases, MRS was viewed as neutral, or patients were lost to follow-up. In the Lin study, which only included 15 patients, MRS was used in place of biopsy in 7 cases, and MRS was correlated with clinical course in 6 cases. MRS did not correlate with clinical course in only 1 patient.

Articles: *Accuracy of MRS* the ideal study of diagnostic accuracy would report the sensitivity and specificity of MRS and include an independent blinded comparison to a "gold standard" diagnosis. Several studies met these criteria and were critically appraised. All had relatively small sample sizes. Rand et al., 1997 and McKnight et al., 2002 evaluated MRS alone and Gajewicz et al., 2003 evaluated MRS in combination with MRI. Rand SD, Prost P, Haughton V et al. Accuracy of single-voxel proton MR spectroscopy in distinguishing neoplastic from nonneoplastic brain lesions. AJRN 1997; 18: 1685-1704. See Evidence Table. McKnight TR, von dem Bussche BS, Vigneron DB. et al., Histopathological validation of a three-dimensional magnetic resonance spectroscopy index as a predictor of tumor presence. J Neurosurg 2002; 97: 794-802. See Evidence Table. Gajewicz W, Papierz W, Szymczak W et al. The use of proton MRS in the differential diagnosis of brain tumors and tumor-like processes. Med Sci Monit 2003; 9: MT97-105. See Evidence Table. Diagnostic impact (does MRS contributes substantially to improved diagnosis and/or replace other diagnostic tests or procedures). There were no studies comparing diagnosis with MRS to diagnosis with conventional imaging. Therapeutic impact of MRS (is more appropriate therapy is used after application of MRS than would be used if the test were not available). Two studies that evaluated the impact of MRS on clinical decision-making were identified and critically appraised: Adamson AJ, Rand SD, Prost RW et al. Focal brain lesions: Effect of single-voxel proton MR spectroscopic findings on treatment decisions. Radiol 1998; 209: 73-78. See Evidence Table**.** Lin A, Blum s, Mamelak AN. Efficacy of proton magnetic resonance spectroscopy in clinical decision making for patients with suspected malignant brain tumors. J Neuro-Oncol 1999; 45: 69-81. See Evidence Table.

The use of Magnetic resonance spectroscopy (MRS) in diagnosing cerebral tumors and differentiating tumors from non-tumors does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

Applicable Codes

Considered Not Medically Necessary:

CPT® Codes	Description
76390	Magnetic resonance spectroscopy

***Note:** Codes may not be all-inclusive. Deleted codes and codes not in effect at the time of service may not be covered.

****To verify authorization requirements for a specific code by plan type, please use the **Pre-authorization Code Check.**

Date Created	Date Reviewed	Date Last Revised
12/23/2005	05/03/2011 MDCRPC, 08/02/2011 MDCRPC, 06/05/2012 MDCRPC, 04/02/2013 MDCRPC, 02/04/2014 MPC, 12/02/2014MPC, 10/06/2015MPC, 08/02/2016MPC, 06/06/2017MPC, 04/03/2018MPC, 04/02/2019MPC, 04/07/2020MPC, 04/06/2021MPC, 04/05/2022MPC, 04/04/2023MPC	11/18/2021

MDCRPC Medical Director Clinical Review and Policy Committee

MPC Medical Policy Committee

Revision History	Description
02/04/2020	MPC approved to remove MCG guideline A-0482 and to retain policy of non-coverage. Also added language that states, Clinical Review physician should consult with KP Neuroradiology on any requests received.
11/18/2021	Medicare Retired NCD (220.2.1) Magnetic Resonance Spectroscopy

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