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Medical Policy Manual

Topic: Magnetic Resonance Spectroscopy

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

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; i.e., 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 grey 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, termed the voxel. 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.

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. For example, proton MRS of the healthy brain reveals 5 principal spectra arising from:

- N-acetyl groups, especially n-acetylaspartate (NAA)

  NAA intensity is thought to be a marker of neuronal integrity and is the most important proton signal in studying CNS pathology. Decreases in the NAA signal are associated with neuronal loss.

- Choline-containing phospholipids (Cho) such as membrane phospholipids (e.g., phosphocholine and glycerophosphocholine)

  Choline levels increase in acute demyelinating disease. Brain tumors may also have high signals from Cho.

- Creatinine and phosphocreatinine

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

- Lipid

  The presence of lipids is indicative of a severe pathological process in which membrane lipids are liberated.

- 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, in both 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 Cho levels and reduced NAA levels. 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.

Regulatory Status

Since 1993, multiple software packages for performing proton MRS have received clearance by the Food and Drug Administration (FDA) through the 510(k) process.

MEDICAL POLICY CRITERIA

Magnetic resonance spectroscopy (MRS) is considered **investigational** for all indications, including but not limited to evaluation of the following:

- Brain Tumor
- Breast Tumor
- Dementia
- Liver

- DiseaseMitochondrial Disorders
- Prostate Tumor
- Treatment Response

SCIENTIFIC EVIDENCE

Validation of a new imaging technique involves the following steps:

1. Demonstration of its technical feasibility, including assessment of its reproducibility and precision. For comparison among studies, a common standardized protocol is necessary.

2. Establishment of normal and abnormal values as studied in different clinical situations. For accurate interpretation of study results, sensitivities, specificities, and positive and negative predictive values compared to a gold standard must be known.

3. Assessment of the clinical utility of both positive and negative tests. The clinical utility of an imaging study is related to how the results of that study can be used to benefit patient management. Relevant outcomes of a negative test (i.e., suspected pathology is not present) may be avoidance of more invasive diagnostic tests or avoidance of ineffective therapy. Relevant outcomes of a positive test (i.e., suspected outcome is present) may also include avoidance of a more invasive test plus the institution of specific, effective therapy.

Literature Appraisal

There are a variety of potential indications for MRS, both for cancer and non-cancer conditions. The clinical utility of MRS will be evaluated separately for each of these indications.

Brain Tumors

Magnetic resonance imaging (MRI) is a sensitive tool for identifying space occupying CNS lesions, but it is relatively nonspecific in distinguishing between benign and malignant lesions. Magnetic resonance spectroscopy (MRS) can provide a chemical profile of the lesions that may help in this determination. In order to understand the impact of the addition of MRS to the diagnostic evaluation of brain tumors, well-designed randomized controlled trials (RCTs) that compare changes in treatment planning and the resulting health outcomes from patients evaluated with MRI alone to those evaluated with MRI and MRS (where MRS is proposed for adjunctive use) are needed. The primary health outcomes associated with evaluation of suspected brain tumors may include avoidance of invasive biopsy procedures. Other measures are typically measured in units of survival past treatment: disease-free survival (DFS), a period of time following treatment where the disease is undetectable; progression-free survival (PFS), the duration of time after treatment before the advancement or progression of disease; and overall survival (OS), the period of time the patient remains alive following treatment. Patient quality of life may be another primary outcome, particularly among patients living with refractory disease.

To date, no randomized controlled trials have been published on the use of MRS in the evaluation of suspected brain tumors. The literature on the use of MRS in patients with suspected or known malignant tumors of the brain consists of two technology assessments and a systematic review, which are the focus

of this literature appraisal. Several non-randomized studies have also been published, examples of which are provided below.

Systematic Reviews

Two technology assessments, both published in 2003, have been performed on the use of MRS in evaluation of suspected brain tumors. Both assessments concluded the use of MRS should undergo further study (due to the limited nature of the evidence).

- In 2003, the BlueCross BlueShield Association Technology Evaluation Center (TEC) conducted an assessment of the published literature on MRS for the evaluation of suspected brain tumors.[1] Seven studies (n=271) were selected for inclusion if the sample size was at least 10, criteria for a positive test were specified, there was a method to confirm MRS diagnosis, and the report provided sufficient data to calculate diagnostic test performance. The assessment identified seven studies meeting these criteria; up to 271 subjects were included. In the assessment, MRS was judged to produce a beneficial effect on health outcomes only when it correctly determined the presence or absence of a tumor and avoided the need for a brain biopsy, an invasive procedure with associated morbidity. Following is a summary of findings from the TEC Assessment:

    - The available studies identified for the assessment all had some degree of shortcomings, and the overall body of evidence did not provide strong and consistent evidence regarding the diagnostic test characteristics of MRS.
    - Studies of diagnostic performance usually mixed together different populations of patients (with clinically important differences) and did not clearly delineate how MRS information was intended to guide patient management.
    - It was not possible to determine from the studies mixing patients with different clinical indications whether MRS provides sufficiently high sensitivity, specificity, and positive and negative predictive values to safely avoid brain biopsy.
    - Differences in MRS technique and methods of analysis across studies made it difficult to synthesize findings from different studies.
    - In sum, further replication of these findings in a prospectively defined population is needed.

- The above findings were confirmed in a 2003 technology assessment commissioned by Medicare from the Agency for Healthcare Research and Quality.[2] This report concluded that while the use of MRS for brain tumors is technically feasible, standardized techniques for acquiring and interpreting MRS spectra are lacking, and there is a paucity of high quality direct evidence demonstrating the effect of MRS on diagnostic thinking and therapeutic decision-making.

- A systematic literature review published in 2006 on MRS for the characterization of brain tumors concluded the following:[3]

    "A number of large diagnostic performance studies have demonstrated that 1H-MR spectroscopy can accurately distinguish between high- and low-grade astrocytomas. This work now needs to be extended to demonstrate: (1) diagnostic thresholds selected a priori, rather than post hoc, can achieve similar diagnostic accuracy, (2) the incremental diagnostic yield of 1H-MR spectroscopy compared with anatomic MR imaging, and (3) that any improvement in tumor grading by 1H-MR spectroscopy leads to a reduction in biopsy rates or changes in therapy."

This review evaluated whether MRS could differentiate malignant from non-malignant lesions; high-grade tumors from low-grade tumors; and metastatic from primary brain tumors. The authors concluded that the evidence on MRS for characterizing brain tumors is promising, but that additional comparative diagnostic studies (MRI with and without MRS), along with randomized controlled trials of primary health outcomes are needed before any conclusions can be made about utility of MRS in diagnosing brain tumors.

Nonrandomized Studies

Other non-randomized studies have attempted to determine whether MRS can differentiate the type of brain tumor.

- In 2013, Vicente and colleagues reported on a multi-center study to evaluate the ability of single voxel, proton MRS to differentiate 78 histologically confirmed pediatric brain tumors (29 medulloblastomas, 11 ependymomas, and 38 pilocytic astrocytomas).[4] Significant metabolic differences in tumor types were identified by MRS when results from short and long echo times were combined, suggesting that MRS may provide non-invasive diagnostic information.

- In a recent study, Wilson et al. evaluated MRS as a prognostic tool. This study reported on single voxel, proton MRS using short echo times to predict survival of patients with pediatric brain tumors in 115 patients followed for a median of 35 months.[5] Metabolic changes were identified that predicted survival. Poor survival was associated with lipids and scyllo-inositol while glutamine and N-acetyl aspartate were associated with improved survival ($p<0.05$).

- Authors evaluated the clinical feasibility of (31)P MRS for making the differential diagnosis of brain tumors.[6] The study included 28 patients with brain tumorous lesions (22 cases of brain tumor and 6 cases of abscess) and 11 normal volunteers. Authors concluded the brain tumor group showed increased PME/PDE ratio compared with that in the normal control group. Authors suggested that clinically applicable (31)P MRS, and the pH, PME/PDE, PDE/Pi, PME/PCr, and PDE/PCr ratios were helpful for differentiating among the different types of brain tumors.

- In 2011, a trial by Amin and colleagues, which compared MRS with single photon emission computed tomography (SPECT) in the identification of residual or recurrent glioma versus radiation necrosis in 24 patients treated with surgery and radiotherapy.[7] MRS and SPECT results differed in 9 cases of recurrence and were more accurate with SPECT. Specificity and positive predictive value were 100% in both MRS and SPECT; however, sensitivity was 61.1% versus 88.8% and negative predictive value was 46.2% versus 75%, respectively. The use of a single voxel rather than multiple voxels is noted as a limitation in interpreting the MRS results in this study.

Examples of other non-randomized studies include several non-comparative observational studies[8-10] and case series.[11] However, due to the lack of comparison with a gold standard, or lack of evaluation of primary health outcomes following testing with MRS, interpretation of these findings is limited.

Conclusion

Although the evidence detailed above adds to the body of literature on the use of MRS in characterization of brain tumors, at present there is insufficient data detailing the positive and negative predictive value of MRS in distinguishing benign and malignant lesions.[12,13] In known malignancies, MRS has been used to assess tumor histology before resection.[14-17] However, there is no discussion of how this information influences treatment decisions. For example, the standard approach to CNS tumors is to initially complete surgical resection, thus the exact tumor histology is not relevant to initial treatment decisions.[18] In this setting, the negative predictive value is probably the most critical statistic; i.e., there is a minimal chance of a missed diagnosis of malignancy. There are no such studies of MRS. After initial treatment, the distinction between tumor recurrence or radiation necrosis is frequently a difficult clinical issue. There is insufficient data on whether MRS can be used to make this distinction.[19]

Breast Tumor

MRS has also been proposed for adjunctive use with MRI for the evaluation or prognostication of breast tumors. As in the characterization of brain tumors (above), evaluation of MRS in breast cancer requires evidence from randomized controlled trials with primary outcomes such as: disease-free survival (DFS), progression-free survival (PFS), overall survival (OS), and patient quality of life, particularly among patients living with refractory disease. Additionally, avoidance of additional testing, particularly invasive testing, may be evaluated.

The evidence on the use of MRS in evaluation of breast tumors consists of non-randomized studies, an example of which is detailed below. No studies of clinical utility have been identified in the peer-reviewed literature.

Systematic review

In 2013, Baltzer and colleagues conducted a systematic review and meta-analysis of 19 studies on MRS for detecting benign versus malignant breast lesions.[20] The combined total number of patients in the studies reviewed was 1,183 and included 452 benign and 773 malignant lesions. In the pooled estimates, sensitivity of MRS was 73% (556 of 761; 95% confidence interval [CI]: 64%, 82%) and specificity was 88% (386 of 439; 95% CI: 85%, 91%). The area under the ROC curve for MRS detecting breast cancers versus benign lesions was 0.88. There was significant heterogeneity between studies and evidence of publication bias, limiting interpretation of findings.

Nonrandomized studies

Bartella and colleagues conducted a preliminary study using MRS to evaluate suspicious lesions 1 cm or larger identified on MR imaging.[21] They found that the addition of MRS increased the specificity of MRI in the specific population examined to 88% (23/26) and could have prevented unnecessary biopsies; the sensitivity was 100% (31/31). As the authors note, these findings need to be confirmed in larger studies and with a more diverse set of lesions. In particular, their sample only included one ductal carcinoma in situ (DCIS), and other studies have suggested that the choline peak they used to indicate a positive MRS result may be less likely to occur with DCIS. Although this study adds to the body of literature on MRS in breast tumors, interpretation of these results is limited by lack of comparative, blinded testing and the failure to control for potential bias in favor of MRS. Additional study of diagnostic accuracy and clinical utility is required to evaluate the effectiveness of MRS in breast tumors.

Conclusion

The current evidence is insufficient to determine if health outcomes are improved following MRS imaging for breast tumors.

Dementia

MRS has been proposed for use in the identification of dementia, especially in its early stages. Primary outcomes associated with treatment of dementia include: improvement in behavioral, emotional or neurological function (as measured by a validated clinical instrument). Identification of improvement in such outcomes associated with diagnosis by MRS is best achieved by conducting randomized controlled clinical trials of appropriate size and duration. However, to date, evidence identified on the use of MRS for diagnosis of dementia consists entirely of non-randomized studies, an example of which is detailed below.

Systematic review

Tumati and colleagues conducted a systematic review and meta-analysis of 29 studies on MRS for mild cognitive impairment (MCI).[22] Included in the analysis were a total of 607 MCI patients and 862 healthy controls. Patterns in metabolite concentration, including N-acetyl aspartate (NAA), creatine (Cr), choline (Cho) and myoinositolin (mI), in various regions of the brain were identified and associated with MCI. For example, levels of creatine were found to be significantly lower in the hippocampus and paratrigonal white matter. NAA was found to be most associated with MCI, but other markers including mI, Cho, and Cr may also contribute to MCI.

Nonrandomized studies

- A community-based study was conducted to evaluate whether MRS could distinguish between patients with normal cognition, dementia, or mild cognitive impairment (MCI) in a population with a low Mini-Mental State Examination (MMSE) score.[23] From an initial population of 1,500 patients, 215 individuals with low MMSE scores were identified. MRS results were obtained for 56 patients. MRS results were associated with identification of patients with dementia, but were not able to distinguish between patients with MCI and those with normal cognition. Diagnostic accuracy was not reported and results from this study were limited by the low participation rate. This potentially biased the results as it was not clear whether the 56 patients able to undergo MRS were representative of the population of interest.

- In a 2012 study, Shiino and colleagues compared proton MRS in 99 patients with Alzheimer's disease (AD), 31 patients with subcortical ischemic vascular dementia (SIVD) and 45 elderly controls.[24] Differences in metabolic patterns were seen in both AD and SVID patients. Especially notable were increases in myoinositol concentration in the hippocampus identified in AD but not in SIVD (0.95 area under the receiver operating characteristic (ROC) curve).

Conclusion

Although a number of studies have examined the use of MRS for identifying and monitoring cognitive impairment and dementia, the cumulative evidence is insufficient to determine any role for MRS outside of the research setting. There are no clear criteria for diagnosing cognitive impairment or dementia with MRS and insufficient data on diagnostic comparators. Additionally, the impact of MRS imaging on clinical management and health outcomes is unknown.

Liver Disease

MRS has been evaluated as a noninvasive alternative to liver biopsy in the diagnosis of hepatic steatosis and/or nonalcoholic fatty liver disease. In order to understand the contribution of MRS in this setting, prospective randomized controlled trials are needed to evaluate long-term health outcomes, such as development of liver fibrosis, risk of mortality, or quality of life.

In a 2013 RCT, authors investigated the utility of magnetic resonance imaging (MRI)-estimated proton-density-fat-fraction (PDFF) to assess quantitative changes in liver fat by three-way comparison between MRI-estimated PDFF and MRS-measured PDFF with liver histology-determined steatosis grade at two-time points in patients with nonalcoholic-fatty-liver-disease (NAFLD).[25] Fifty biopsy-proven NAFLD patients who participated underwent paired evaluation with liver biopsy, MRI-estimated and MRS-measured PDFF of the liver at baseline and 24 weeks. Authors concluded MRI-estimated PDFF correlates well with MRS-measured-PDFF and is more sensitive than histology-determined steatosis grade in quantifying increase or decrease in liver fat content. This RCT includes a small sample size and limited follow-up.

Conclusion

The literature on the use of MRS for diagnosis of hepatic steatosis consists of one small, RCT and several non-randomized studies, examples of which evaluate the diagnostic accuracy of MRS compared with other noninvasive imaging procedures (e.g., computed tomography, dual-gradient echo magnetic resonance imaging, and ultrasonography), and/or invasive biopsy as the reference standard.[26-29] Results from these studies require replication in larger studies with adequate representation of the target population for this type of testing before any conclusions regarding diagnostic accuracy can be established. Additionally, studies of clinical utility are required to demonstrate that any increases in diagnostic accuracy provided by MRS are accompanied by improvements in net health outcomes.

Mitochondrial Disorders

MRS is proposed as an adjunctive diagnostic test in patients with primary mitochondrial cytopathies with CNS involvement. The principle health outcomes associated with improved diagnosis and treatment planning in this population may include increases in quality of life or activities of daily living. Other outcomes important for study include risk of adverse events (including hospitalization) and secondary or intermediate health outcomes may consist of changes in muscle strength or endurance or biochemical markers of disease.[30]

The evidence available on the use of MRS as an adjunctive diagnostic tool in patients with suspected mitochondrial disorders consists of non-comparative observational studies. For example, Bianchi and colleagues reported on the use of MRI and MRS in the evaluation of mitochondrial disease in 15 patients.[31] Both tests were performed on all patients and statistical analysis was used to estimate the correlation between results on MRS and clinical findings (of brain abnormalities). However, this study and others like it failed to report sensitivity, specificity and positive and negative predictive values compared with existing genetic, biochemical, and pathologic tests. In addition, there are no published studies demonstrating the clinical utility of MRS in evaluating mitochondrial disorders, i.e., how test results impact patient management.

Conclusion

MRS has also been utilized in research studies for measurement of study outcomes.[30] Due to limitations such as the lack of a consensus MRS diagnostic protocol, lack of head-to-head comparisons with gold standard diagnostic tests for mitochondrial disorders, and unknown impact of MRS diagnosis on clinical decision-making and primary health outcomes, these studies do not add to the understanding of the net effect of this testing on the diagnosis and treatment of mitochondrial cytopathies.

Prostate Tumor

The utility of MR spectroscopy has also been investigated for identifying whether or not prostate cancer is confined to the prostate, which has implications for prognosis and treatment. Randomized controlled trials (RCTs) studying primary outcomes such as: disease-free survival (DFS), progression-free survival (PFS), and overall survival (OS) are needed. Patient quality of life may be another primary outcome, particularly among patients living with refractory disease. Additionally, avoidance of additional testing or treatment (due to the potential for slow tumor growth and/or extended survival following metastasis)[32] may be evaluated. Several RCTs have been identified and examples of available non-randomized studies are also detailed below.

Systematic Review

In a 2013 Health Technology Assessment, Mowatt and colleagues systematically reviewed 51 studies to evaluate image-guided prostate biopsy with MRS and other enhanced MRI techniques (i.e., dynamic contrast-enhanced MRI and diffusion-weighted MRI) compared to T2-MRI and transrectal ultrasound (TRUS) in patients with suspicion of prostate cancer due to elevated prostate specific antigen (PSA) levels despite a previous negative biopsy.[33] MRS had the highest sensitivity in the meta-analysis of individual tests (92%; 95% CI: 86% to 95%), with an estimated specificity of 76% (95% CI: 61% to 87%). TRUS-guided biopsy had the highest specificity (81%; 95% CI: 77% to 85%).

Randomized Controlled Trials (RCTs)

- A single-institution RCT published in 2010 compared conducting a second randomly selected biopsy (group A) to a biopsy selected partly based on MRS and dynamic contrast-enhanced MRI results (group B).[34] The participants were selected from 215 consecutive men with an elevated prostate-specific-antigen (PSA) (between 4 and 10 ng/mL), an initial negative biopsy result, and a negative digital rectal examination; 180 patients participated in the study. Cancer was detected in 24.4% of group A patients and 45.5% of group B participants. Fifty patients from group A with 2 negative biopsy results agreed to undergo biopsy a third time using MRS and dynamic contrast-enhanced MRI results; 26 more cancers were found. Overall, 61.6% of the cancers detected had Gleason scores 7 (4+3) or more. The cancers detected after using MRS and dynamic contrast-enhanced MRI imaging also lined up with the suspicious areas detected on imaging. The sensitivity and specificity of MRI were 84.6% and 82.3%, respectively; adding MRS increased the sensitivity to 92.6%, and the specificity to 88.8%. Limitations of the study include that it was conducted at a single center, analysis was confined to the peripheral zone of the prostate gland, and more samples were drawn from group B patients than from group A patients (12.17 vs. 10 cores, respectively). Furthermore, given the concerns about potential overtreatment among patients with early stage prostate cancer, the benefits of detecting these additional cancers were not evaluated by examining clinical outcomes for these patients.

- In a similar report from this institution by these authors, 150 patients with a negative prostate biopsy, despite PSA elevations, were randomized to MRS or MRS plus DCE-MRI to locate prostate cancer

foci for a second targeted biopsy.[35] The addition of DCE-MRI to MRS yielded increased sensitivity and specificity over MRS alone (93.7% and 90.7% versus 82.8% and 91.8%, respectively). However, treatment decisions were not based on results of differential testing; therefore, the impact of testing on health outcomes (e.g., clinical utility) was not addressed in this study and awaits future clinical research.

Nonrandomized Studies

Nonrandomized studies on the technical feasibility or diagnostic accuracy of MRS have also been published, an example of which is the study by Pedrona and colleagues on the combined use of MRS and MRI for prostate cancer in 106 patients in a prospective cohort study.[36] The authors reported combined MRS and MRI results yielded unacceptably low positive predictive value of 19%. Negative predictive value was 91%. Sensitivity was 71% and specificity was 48%. The authors indicated the combined MRS and DCE-MRI may be useful in avoiding biopsy since the negative predictive value was 91%.

Results from this study, like several others identified,[37,38] are limited by lack of comparator group (without which it is not possible to isolate the contribution of MRS to the diagnosis). Studies which include long-term follow-up on primary health outcomes, along with randomization to comparative diagnostic groups, are needed to evaluate the clinical utility of MRS in prostate cancer.

Conclusion

Although a number of studies have examined the use of MRS for localizing prostate cancer for biopsy and for monitoring of patients with prostate cancer, the cumulative evidence remains uncertain. Data comparing the diagnostic accuracy of MRS to alternative imaging strategies is limited. Additionally, the impact of MRS imaging compared to other imaging strategies on clinical management and health outcomes is unknown and further study is needed.

Treatment Response

The possibility of using MRS to track treatment response and failure has been explored. As in the evidence required for determination of treatment benefit in detection of malignant tumors (see breast and prostate above), randomized controlled trials measuring clinical outcomes are required.

The evidence on MRS for evaluating treatment response consists of non-comparative observational studies in recurrent gliomas, including a small (n=16), preliminary study of tamoxifen treatment for recurrent gliomas by Sankar and colleagues in 2008.[39] Serial MRS demonstrated that metabolic spectra stabilized after initiation of therapy among responders and then changed in advance of clinical or radiologic treatment failure.

Conclusion

Although available non-randomized studies add to the body of literature on MRS, the lack of a comparative treatment group does not allow for isolation of the independent diagnostic contribution associated with MRS.

Other Indications

The use of MRS has been studied in non-randomized studies of other indications, such as diagnosis of radiation necrosis,[40-48] stroke progression immediately after acute stroke,[49] fetal lung maturity,[50] lipid tissue detection in atherosclerotic coronary or carotid plaques,[51,52] epilepsy,[53,54] differential diagnosis in lymphoma,[55] diagnostic efficacy of stereotactic brain biopsy,[56] diagnosis or disease characterization in multiple sclerosis,[57] systemic lupus erythematosis[58], and to distinguish between tumors and abscesses or other infectious processes.[59] MRS has also been studied in a variety of psychiatric disorders in the research setting but no studies on the clinical use of MRS for the treatment of psychiatric disorders were found.[60,61]

Conclusion

To evaluate the use of MRS in any indication, evidence of clinical utility (from randomized comparative trials) is needed. Current evidence from available studies is unreliable due to inherent design flaws, such as non-random allocation of treatment and lack of appropriate comparison groups, which do not allow for valid and precise estimates of diagnostic accuracy. Studies providing evidence of clinical utility have not been identified.

Clinical Practice Guidelines

Several clinical practice guidelines have been identified which address the use of MRS.

National Comprehensive Cancer Network (NCCN) Guidelines

- NCCN clinical practice guidelines for central nervous system cancers identify MRS as an imaging modality whose optimal use is to differentiate tumor from radiation necrosis.[62]
- NCCN guidelines for prostate cancer list MR spectroscopy as one of the options that patients with a negative biopsy following post-radiation biochemical recurrence may choose for more aggressive workup.[63]

The NCCN recommendations[62,63] are based on 2A level of evidence (lower-level evidence and NCCN consensus).

American College of Radiology (ACR) and American Society of Neuroradiology (ASNR).

- The ACR/ASNR practice guideline on MRS of the central nervous system lists 22 possible indications for MRS imaging, when conventional imaging by MRI or CT is inadequate for answering specific clinical questions.[64] However, these guidelines are not evidence-based and were developed through consensus.

Summary

Magnetic resonance spectroscopy (MRS) is a noninvasive technique that can be used to measure the concentrations of different chemical components within tissues. While MRS has been investigated in a wide variety of clinical situations, there are few studies specifically focusing on its sensitivity and specificity in specific clinical situations. As there are no studies validating how the results of MRS may dictate patient management in prospectively defined patient populations for any indication, it is not possible to determine whether MRS provides relevant clinical information that will safely influence diagnostic thinking and therapeutic choice. Therefore, the use of MRS is considered investigational for all indications.

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CROSS REFERENCES

None

CODES	NUMBER	DESCRIPTION
CPT	76390	Magnetic resonance spectroscopy
HCPCS	None	