ACR–ASNR–SPR PRACTICE PARAMETER FOR THE PERFORMANCE AND INTERPRETATION OF MAGNETIC RESONANCE SPECTROSCOPY OF THE CENTRAL NERVOUS SYSTEM

Revised 2024 (Resolution 2)

PREAMBLE

This document is an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. Practice Parameters and Technical Standards are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care[1]. For these reasons and those set forth below, the American College of Radiology and our collaborating medical specialty societies caution against the use of these documents in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the practitioner considering all the circumstances presented. Thus, an approach that differs from the guidance in this document, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in this document when, in the reasonable judgment of the practitioner, such course of action is indicated by variables such as the condition of the patient, limitations of available resources, or advances in knowledge or technology after publication of this document. However, a practitioner who employs an approach substantially different from the guidance in this document may consider documenting in the patient record information sufficient to explain the approach taken.

The practice of medicine involves the science, and the art of dealing with the prevention, diagnosis, alleviation, and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. Therefore, it should be recognized that adherence to the guidance in this document will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The purpose of this document is to assist practitioners in achieving this objective.

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[1] *Iowa Medical Society and Iowa Society of Anesthesiologists v. Iowa Board of Nursing, 831 N.W.2d 826 (Iowa 2013) Iowa Supreme Court refuses to find that the "ACR Technical Standard for Management of the Use of Radiation in Fluoroscopic Procedures (Revised 2008)" sets a national standard for who may perform fluoroscopic procedures in light of the standard's stated purpose that ACR standards are educational tools and not intended to establish a legal standard of care. See also, Stanley v. McCarver, 63 P.3d 1076 (Ariz. App. 2003) where in a concurring opinion the Court stated that "published standards or guidelines of specialty medical organizations are useful in determining the duty owed or the standard of care applicable in a given situation" even though ACR standards themselves do not establish the standard of care.*

I. INTRODUCTION

This practice parameter was revised collaboratively by the American College of Radiology (ACR), the American Society of Neuroradiology (ASNR), and the Society for Pediatric Radiology (SPR).

Magnetic resonance spectroscopy (MRS) is a proven and useful method for the evaluation, assessment of severity, therapeutic planning, posttherapeutic monitoring, and follow-up of diseases of the brain and other regions of the body [1-4]. It should be performed only for a valid medical reason. Although, MRS can be useful in the diagnosis and management of patients, its findings may be misleading if not closely correlated with clinical history, physical examination, laboratory results, and diagnostic imaging studies including MRI. Adherence to these practice parameters optimizes the benefit of MRS for patients.

II. INDICATIONS AND CONTRAINDICATIONS

A. Indications

When conventional imaging by magnetic resonance imaging (MRI) or computed tomography (CT) provides limited information regarding specific clinical questions, indications for MRS in adults and children include, but are not limited to, the following:

1. Evidence or suspicion of primary or secondary neoplasm (pretreatment and posttreatment), including for detection of metabolites that may allow for differentiation of tumor histologies, differentiation of tumors from tumor mimics and differentiation of tumor recurrence from treatment-related injury
2. Grading of primary glial neoplasm, particularly high-grade versus low-grade glioma [5,6]
3. Differentiation of cystic lesions (eg, abscess versus cystic metastasis or cystic neoplasm)
4. Evidence or suspicion of brain infection, including cerebral abscess (pretreatment and posttreatment)
5. Seizures, including temporal lobe epilepsy and metabolic epilepsy
6. Evidence or suspicion of neurodegenerative disease, including Alzheimer's disease, Parkinson's disease, Huntington's disease [7-9], amyotrophic lateral sclerosis, and other genetic diseases
7. Suspicion of subclinical or clinical metabolic encephalopathy
8. Suspicion of an inherited metabolic disorder, such as leukodystrophies and mitochondrial encephalopathies [10,11], and for monitoring response to treatment
9. Suspicion of acute brain ischemia or infarction, including hypoxic ischemic encephalopathy [12], and for the prediction of neurologic outcomes following cardiac arrest [13]
10. Suspicion of a demyelinating or dysmyelinating disorder [14-17]
11. Suspicion of neurotoxicitydue to medications, and exposure to environmental hazards, such as carbon monoxide and inhalants
12. Suspicion of spinal cord disorders, such as tumors, demyelination, infection, and trauma

B. Contraindications

Contraindications to MRI in general also serve as contraindications to MRS.

C. Safety Guidelines

See the ACR Practice Parameter for Performing and Interpreting Magnetic Resonance Imaging (MRI), the ACR Manual on Contrast Media, and the ACR Manual on MR Safety [28-30].
Peer-reviewed literature pertaining to MR safety should be reviewed on a regular basis.

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

See the ACR Practice Parameter for Performing and Interpreting Magnetic Resonance Imaging (MRI) [29].

The physician supervising and interpreting MRS must understand the specific questions to be answered before the procedure in order to plan and perform the study safely and effectively.

IV. SPECIFICATIONS OF THE EXAMINATION

A. Written Request for the Examination

The written or electronic request for MRS of the central nervous system (CNS) should provide sufficient information to demonstrate the medical necessity of the examination and allow for its proper performance and interpretation.

Documentation that satisfies medical necessity includes 1) signs and symptoms and/or 2) relevant history (including known diagnoses). Additional information regarding the specific reason for the examination or a provisional diagnosis would be helpful and may at times be needed to allow for the proper performance and interpretation of the examination.

The request for the examination must be originated by a physician or other appropriately licensed health care provider. The accompanying clinical information should be provided by a physician or other appropriately licensed health care provider familiar with the patient's clinical problem or question and consistent with the state scope of practice requirements. (ACR Resolution 35, adopted in 2006 – revised in 2016, Resolution 12-b)

Reasonable efforts should be made to ensure that all pertinent prior imaging of the region in question is available to the interpreting physician at the time of the study.

IV. SPECIFICATIONS OF THE EXAMINATION

B. Patient Selection

The physician responsible for the examination should supervise patient selection and preparation and be available in person or by phone for consultation. Patients and all other persons entering the MRI safety zone must be screened and interviewed (if their condition permits) before the examination to exclude individuals who may be at risk by exposure to the MR environment.

If MRS is performed along with a structural contrast-enhanced MRI, the MRS should preferentially be acquired before contrast administration. (See the ACR–SPR Practice Parameter for the Use of Intravascular Contrast Media [31] if contrast is to be administered.)

Patients suffering from anxiety or claustrophobia may require sedation or additional assistance. Administration of sedation may be needed to achieve a successful examination. If sedation is necessary, it should be administered by appropriately certified personnel (see the ACR–SIR Practice Parameter for Minimal and/or Moderate Sedation/Analgesia [32]). For pediatric patients, support from child life specialists may be beneficial and may avoid sedation in some cases.

IV. SPECIFICATIONS OF THE EXAMINATION

C. Facility Requirements

Appropriate emergency equipment and medications must be immediately available to treat adverse reactions associated with administered medications. The equipment and medications should be monitored for inventory and drug expiration dates on a regular basis. The equipment, medications, and other emergency support must also be appropriate for the range of ages and sizes in the patient population.

IV. SPECIFICATIONS OF THE EXAMINATION

D. Examination Technique

Physicians using MRS should understand the artifacts and limitations of the MR pulse sequences. MRS involves the application of various MR pulse sequences that are designed to provide a range of capabilities. These include the following techniques:

1. Stimulated echo acquisition mode (STEAM), which uses three 90° radiofrequency (RF) pulses for volume selection.
2. Point-resolved spectroscopy (PRESS), which uses a 90° excitation pulse plus two 180° refocusing RF pulses for volume selection.
3. Chemical shift imaging (CSI), which uses phase encoding for spatial location and is used for multivoxel MRS.

The physician should understand the differences between the PRESS and STEAM techniques [33].

Other basic pulse sequences for spectral data acquisition are available commercially, including a variety of sequences that have been developed specifically to address the technical challenges of ultra-high-field MRS.

The physician performing the study should understand how the history and physical examination affect the choice of technique (including location of voxel placement), repetition time, and echo time (TE) for the examination and how the metabolite peaks are affected by changes in the TE. The physician(s) planning and interpreting the examination should be knowledgeable about the normal metabolites and their relative concentrations, as well as the spectra that could be anticipated for the diagnostic entities being considered in the patient. The physician interpreting the examination must also be familiar with the ways in which metabolite concentrations vary across age groups and brain anatomic regions. All examinations are interpreted by physicians.

IV. SPECIFICATIONS OF THE EXAMINATION

E. Guidelines for Performing MRS, Including the Choice of Echo Time

1. Short TE (eg, 20–40 ms)

   Short TE is useful in demonstrating myoinositol (MI), glutamine/glutamate (Glx), amino acids, lactate, and lipids. These metabolites are useful in characterizing most neurological diseases, including tumors, metabolic and neurodegenerative disorders, seizures, and disorders of myelination. They are also useful in monitoring therapy for these diseases although technical variations between exams should be considered during interpretation. The choice of TE depends on the clinical indication. For example, in the characterization of neurodegenerative disorders such as Alzheimer's disease, short TE MRS is recommended to ensure that information on metabolites only detected with short TE MRS, such as MI and the Glx complexes, is obtained.

2. Intermediate echo (eg, 97–144 ms)

   Intermediate TE has certain advantages over short TE MRS but provides information on fewer metabolites. Intermediate TE can be performed for the following reasons:

   a. In differentiating lactate and alanine from lipids around 1.3–1.4 ppm by J-modulation/inversion of the lactate and alanine doublet peaks. However, it should be noted that J-modulation is field-strength dependent. Although lactate peak inversion is a reasonably consistent phenomenon at 1.5T field strength, it is variable at 3T, which could cause a false-negative result [34].
   b. Better-defined baseline and less baseline distortion compared with short TE.
   c. No artifactual N-acetylaspartate (NAA). Peak in the 2.0–2.05 range can only be attributed to NAA rather than superimposed Glx complex peaks in the 2.05–2.5 ppm range.
   d. Presence of lipids may imply more significance than when observed at short TE.
   e. More reproducibility and accuracy, particularly for quantifying Cho and NAA peaks.
   f. Provide optimal identification of 2HG in IDH1 mutant glioma imaged at 3T [35].

3. Long TE (eg, 270–288 ms)

   At longer TE (longer than 144 ms), there is less signal from NAA, Cho, and Cr relative to the baseline noise; hence, the signal-to-noise ratio (SNR) is lower than that at short and intermediate TE measurements

because of the T2 decay of metabolites. The recommendation is to acquire MRS data at short TE and, time permitting, to include an intermediate echo time acquisition for the reasons stated above. Long TE can be used if the user has experience and normative data for comparison. However, a long TE MRS may be primarily performed on 3T scanners for a more accurate depiction of lactate levels [34].

4. CSI or MRS imaging (MRSI)

MRSI and CSI, either 2-D or 3-D, obtain spectroscopic information from multiple adjacent volumes over a large volume of interest in a single measurement. They have better spatial resolution and sample metabolites over a larger region of interest than other techniques, facilitating evaluation for focal as well as global neurological processes. CSI can be combined with conventional MRI because spectral patterns and metabolite concentrations can be overlaid on grayscale conventional imaging to compare voxels containing normal parenchyma and voxels containing pathology and also to obtain distributional patterns of specific metabolites. It also allows for comparison and normalization of pathologic spectra to spectra in normal tissue. However, caution must be exercised regarding artifacts, such as chemical-shift artifact, voxel bleeding, and voxel contamination, when using commercially available CSI sequences. In addition, SNR is typically decreased with CSI due to smaller voxel size.
The physician or technologist performing the examination must understand how voxel placement and regional variation can impact the distribution and relative concentration of the metabolites in different parts of the brain. The placement of voxels over the ventricles and near the bony calvarium can also affect the water suppression and cause susceptibility, affecting the shim and quality of the spectra.
When investigating focal disease, it is recommended that multivoxel MRSI be used, because this will provide MRS samples from heterogeneous areas within a focal lesion as well as some normal tissue voxels for a comparison. If multivoxel is not available, single voxel can be used; having a second voxel in normal tissue for comparison would also be recommended.
When investigating diffuse brain or spinal cord disease, single-voxel MRS can be used, because the MRS changes should be found diffusely.
The voxel size, thickness, and matrix should be determined by the disease process, the extent of disease, its location, and a compromise between obtaining sufficient SNR and reducing volume averaging through normal tissue. For focal diseases, if only a small single voxel is possible, the Number of Excitations can be adjusted, increasing the SNR at the expense of increased scan time.
The physician performing and the physician interpreting MRS should recognize artifacts that are due to poor shimming, improper water suppression, lipid contamination, chemical shift artifact/misregistration, and/or poor voxel placement.
MRS can be used in the setting of contrast without significant detriment to the quality of the spectra for qualitative analysis. If spectroscopy is performed for the evaluation of D-2 hydroxyglutate 2HG), it should be done before intravenous contrast.

5. Technical consideration in MRS

Adequate shimming narrows peak widths, increases SNR, and improves water suppression. Single-voxel spectra are easier to shim than multivoxel spectra, and higher shimming is needed with voxels placed at the periphery compared to the center of the brain.
Single-voxel PRESS MRS is used most often in routine clinical practice for pediatrics. Appropriate placement of voxel requires knowledge of the clinical indications for the MRS and region of the brain potentially affected by the disease process. An incorrect voxel placement may result in nondiagnostic MRS. Inclusion of CSF or fat in a voxel should be avoided. The MRS, including voxel placement, should be reviewed by the radiologist in conjunction with the routine MR image and preferably before the patient has been removed from the scanner.
Pediatric MRS can be acquired at 1.5T and 3T; the higher SNR of 3T potentially allows for decreases in image acquisition time and/or smaller voxel size with the marginal compromise of somewhat wider metabolite peaks using short TEs at 3T [36].
Preferred voxel size is 2 × 2 × 2 cm or 2 cm $(8\ cc)^3$. Smaller voxels may be needed to avoid partial volume effects; voxel size should be at least 4 cm^3.

6. Detection of specific metabolites

   Glycine and MI resonate at 3.5 ppm and 3.56 ppm, respectively, and pathologic evaluations of glycine in nonketotic hyperglycinemia may be masked by myo-inositol at short TE. At intermediate TE values, myo-inositol normally decreases whereas glycine does not, and intermediate or long TE, in addition to short TE, should be acquired in neonates with clinical suspicion of nonketotic hyperglycinemia [37].
   The 2021 5th edition of the WHO Classification of Tumors of the Central Nervous System ushered in the use of molecular diagnostics with histology in effort to provide the most accurate classification of CNS tumors [38]. The classification of glioblastoma and gliomas based on IDH mutation acknowledges significant differences in glioma biology, therapeutic triage, and outcome. As a result, the application of MRS in characterizing the molecular subtypes of glioma can be important in situations in which tumor biopsy is undesirable or challenging [39]. The detection of D-2-hydroxyglutate (2HG) can be used for preoperative prediction of *IDH* mutation [35], and detection may be improved by use of an edited MRS pulse sequence [40]. The addition of MRS to conventional MRI improves diagnosis of pediatric brain tumors [41]. For the detection of 2HG, the placement of a voxel ideally larger than 8 cm^3 in a homogeneous portion of the lesion, avoiding areas of cystic degeneration, necrosis or partial volume, is highly correlated to the sensitivity and specificity [42]. MRS has potential for preoperative prediction of molecular subtype of medulloblastoma [43]. Following brain tumor treatment, MRS can be used in addition to other modalities to aid in differentiation of tumor recurrence from pseudoprogression or radiation necrosis [44]. For those physicians interpreting MRS in neonates and young infants, the physician should be familiar with MRS in this age group. Age-related differences in metabolites in normal neonates include high myo-inositol levels. The NAA levels are also lower in neonates up to 24 months. In these early years, macromolecules/lipids at 0.8 and 1.3 ppm may also be present as the brain myelinates.

7. Multinuclear MRS

   Besides proton hydrogen-1 (^{1}H) MRS, other nuclei for MRS that can be used include helium-3 (^{3}HE), lithium-7 (^{7}Li), carbon-13 (^{13}C), oxygen-17 (^{17}O), fluorine-19 (^{19}F), sodium-23 (^{23}Na), phosphorus-31 (^{31}P), and xenon-129 (^{129}Xe). Although several of these show promise for research purposes, proton MRS remains the dominant technique in clinical practice.

8. Ultra-high-field MRS (beyond 3T)

   MRS can be performed clinically at field strengths up to 7T for neurological and other applications. The safety and efficacy of MRS beyond these field strengths are still under investigation.

V. DOCUMENTATION

Reporting should be in accordance with the ACR Practice Parameter for Communication of Diagnostic Imaging Findings [46].

The report should describe the peaks visualized in the spectrum, the relative heights of the peaks, or relative concentrations of the metabolites. It should attempt to address the potential etiologies suggested by any abnormities found.

Follow-up pathology and laboratory results and diagnoses are needed to correlate radiology and pathology findings and should be actively sought whenever possible as part of any quality control or quality improvement program.

VI. EQUIPMENT SPECIFICATIONS

Equipment monitoring should be in accordance with the ACR–AAPM Technical Standard for Diagnostic Medical Physics Performance Monitoring of Magnetic Resonance (MR) Imaging Equipment [47].

The MR equipment specifications and performance must meet all state and federal requirements. These requirements include,

but are not limited to, specifications of maximum static magnetic field strength, maximum rate of change of magnetic field strength, maximum RF power deposition (specific absorption rate), and maximum acoustic noise levels.

Specific policies and procedures related to MR safety should be in place with documentation that is updated annually and compiled under the supervision and direction of the supervising MR physician. Guidelines should be provided that deal with potential hazards associated with the MR examination of the patient as well as to others in the immediate area. Screening forms must also be provided to detect those patients who may be at risk for adverse events associated with the MR examination.

VII. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION

Policies and procedures related to quality, patient education, infection control, and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education appearing under the heading *Position Statement on QC & Improvement, Safety, Infection Control*, *and Patient Education* on the ACR website https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Quality-Control-and-Improvement).

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