Revised 2019 (Resolution 16)*

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

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.

[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. While 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. Adherence to these practice parameters optimizes the benefit of MRS for patients.

II. 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)
2. Grading of primary glial neoplasm, particularly high-grade versus low-grade glioma [5,6]
3. Evidence or suspicion of brain infection, especially cerebral abscess (pretreatment and posttreatment) and HIV-related infections
4. Seizures, especially temporal lobe epilepsy
5. Evidence or suspicion of neurodegenerative disease, especially Alzheimer's disease, Parkinson's disease, and Huntington's disease [7-9]
6. Evidence or suspicion of subclinical or clinical hepatic encephalopathy
7. Evidence or suspicion of an inherited metabolic disorder, such as Canavan disease, mitochondrial encephalopathies, and other leukodystrophies [10,11]
8. Suspicion of acute brain ischemia or infarction, including birth asphyxia [12]
9. Evidence or suspicion of a demyelination or dysmyelination disorder [13-16]
10. Evidence or suspicion of traumatic brain injury
11. Evidence or suspicion of brain developmental abnormality and cerebral palsy
12. Evidence or suspicion of other neurodegenerative diseases, such as amyotrophic lateral sclerosis
13. Evidence or suspicion of chronic pain syndromes
14. Evidence or suspicion of chromosomal and inherited neurocutaneous disorders, such as neurofibromatosis and tuberous sclerosis
15. Evidence or suspicion of neurotoxicity, such as misuse of medications, and exposure to environmental hazards, such as carbon monoxide and inhalants
16. Evidence or suspicion of hypoxic ischemic encephalopathy
17. Evidence or suspicion of spinal cord disorders, such as tumors, demyelination, infection, and trauma
18. Evidence of neuropsychiatric disorders, such as depression, posttraumatic stress syndrome, and schizophrenia [17-26]
19. Differentiation between recurrent tumor and treatment-related changes or radiation injury
20. Differentiation of cystic lesions (eg, abscess versus cystic metastasis or cystic primary neoplasm)
21. Evidence or suspicion of cerebral vasculitis, systemic lupus erythematosus (SLE), and neuropsychiatric systemic lupus erythematosus (NPSLE)
22. Evaluation of response to treatment of neurological disorders (eg, tumor evaluation)
23. Detection of 2-hydroxyglutarate (2-HG) in suspected IDH1 mutant gliomas
24. Developmental delay
25. Evaluation of response to treatment of metabolic disorders

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

See the ACR Practice Parameter for Performing and Interpreting Magnetic Resonance Imaging (MRI) [27].

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. SAFETY GUIDELINES AND POSSIBLE CONTRAINDICATIONS

See the ACR Practice Parameter for Performing and Interpreting Magnetic Resonance Imaging (MRI), the ACR Manual on Contrast Media, and the ACR Guidance Document on MR Safe Practices [27-29].

Peer-reviewed literature pertaining to MR safety should be reviewed on a regular basis.

V. 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/spectroscopist at the time of the study.

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.

Certain indications require administration of intravenous (IV) contrast media. IV contrast enhancement should be performed using appropriate injection protocols and in accordance with the institution's policy on IV contrast utilization. (See the ACR–SPR Practice Parameter for the Use of Intravascular Contrast Media [30].)

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 Sedation/Analgesia [31]).

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.

D. Examination Technique

Physicians and/or spectroscopists 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:

1. STEAM (stimulated echo acquisition mode) that uses three 90° radiofrequency (RF) pulses for volume selection.
2. PRESS (point-resolved spectroscopy) that uses a 90° excitation pulse plus two 180° refocusing RF pulses for volume selection.

The physician and/or spectroscopist should understand the differences between the PRESS and STEAM techniques.

Other basic pulse sequences for spectral data acquisition are available commercially.

The physician and/or spectroscopist performing the study should understand how the history and physical examination affect the choice of technique (including location of voxel placement), repetition time (TR), and echo time (TE) for the examination and how the metabolite peaks are affected by changes in the TE. The physician and/or spectroscopist performing and the physician 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. All examinations are interpreted by physicians.

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

1. Short echo time (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, such as tumors, metabolic and neurodegenerative disorders, seizures, chronic pain syndrome, and disorders of myelination. They are also useful in monitoring therapy for these diseases. 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 a number of 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 to 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. While lactate peak inversion is a reasonably consistent phenomenon at 1.5T field strength, it is variable at 3T, which could cause a false-negative results [32].
   b. Better-defined baseline and less baseline distortion compared with short TE.
   c. No artifactual n-acetylasparate (NAA). Peak in the 2.0 to 2.05 range can only be attributed to NAA rather than superimposed Glx complex peaks in the 2.05 to 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 2-HG in IDH1 mutant glioma imaged at 3T.

3. Long echo time (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 [32].

4. Chemical shift imaging (CSI) or MRS imaging (MRSI)
   MRSI or 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 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.

   The physician, technologist, or spectroscopist 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, as 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, as 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.

   The physician and/or spectroscopist 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.

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 the ventricle in a voxel should be avoided. The MRS 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 [33].

   MRS is routinely performed with short TE (35 ms versus 20-40 ms), intermediate TE (144 ms versus 97-144 ms), and/or long TE (288 ms versus 270-288 ms); short TE technique provides for higher SNR and

depiction of all metabolites. Preferred voxel size is 2 × 2 × 2 cm or 2 cm cubed (8 cc). Smaller voxels may be needed to avoid partial volume effects; voxel size should be at least 4 cc.

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 while glycine does not, and intermediate or long TE, in addition to short TE, should be acquired in neonates with clinical suspicion of nonketotic hyperglycinemia [34].

   The 2016 World Health Organization (WHO) CNS classification presents major restructuring of the diffuse gliomas, medulloblastomas, and other embryonal tumors and incorporates new entities that are defined by both histology and molecular features, including glioblastoma, IDH-wildtype, and glioblastoma, IDH-mutant. The reclassification 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 is important [35].

   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 until 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). It is recommended that multinuclear MRS be performed using a field strength of at least 3T. Some of the reasons for the recommendation to use higher field strength are:
   a. Lower gyromagnetic ratio compared with ^{1}H.
   b. Lower sensitivity that will be mitigated by the higher SNR provided by higher B0.
   c. Longer measurement times at 1.5T.
   d. Low spatial resolution at 1.5T.
   e. Multiplets – needed to decouple to demonstrate the metabolites adequately.

      Phosphorus-31, ^{19}F, and ^{13}C have demonstrated some utility in neuro-oncologic evaluations [36]. Phosphorus-31 MRS provides information on cellular energy metabolism, membrane phosphates, and intracellular pH. Compared with proton spectroscopy (^{1}H MRS), the clinical utility of ^{31}P MRS has been limited, which is due in part to the necessity for hardware modifications (coils), the relatively large volumes of tissue required (resulting in partial volume effects through necrotic regions), and the sometimes subtle metabolite changes when the spectra are reviewed visually. Cellular energy metabolism is represented by adenosine triphosphate (ATP), phosphocreatine (PCr), and inorganic phosphate (Pi). The phosphodiester (PDE) and phosphor monoester (PME) compounds are from membrane phospholipids. In high-grade glial tumors (HGGT), such as glioblastoma multiforme, there is alkalization (pH: 7.12), an increase in PME, and a decrease in PDE/α-ATP with no significant changes in PCr/α-ATP or PCr/Pi ratios. The metabolite resonances in HGGT may sometimes be reduced by the presence of necrosis. As expected, HGGT will express higher levels of phosphatidylcholine compared with low-grade glial tumors. Meningiomas are characterized by an alkalinity (pH: 7.16), a decrease in phosphocreatine, and decreased PDEs. Proton-decoupled ^{31}P (^{31}P-[^{1}H]) and ^{1}H MRS may eventually be used in a multinuclear, multi-TE approach to neurologic diseases.

8. Ultra-high-field MRS (beyond 3T)
   MRS is FDA approved and can be performed clinically at field strengths up to 7T for neurological and extremity applications and up to 3T for other sites. The safety and efficacy of MRS beyond these field strengths are still under investigation.

VI. DOCUMENTATION

Reporting should be in accordance with the ACR Practice Parameter for Communication of Diagnostic Imaging Findings [37].

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.

VII. EQUIPMENT SPECIFICATIONS

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 RFpower deposition (specific absorption rate), and maximum acoustic noise levels.

VIII. 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).

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.

Equipment monitoring should be in accordance with the ACR–AAPM Technical Standard for Diagnostic Medical Physics Performance Monitoring of MRI Equipment [38].

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.

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*Practice parameters and standards are published annually with an effective date of October 1 in the year in which amended, revised, or approved by the ACR Council. For practice parameters and technical standards published before 1999, the effective date was January 1 following the year in which the practice parameter or technical standard was amended, revised, or approved by the ACR Council.

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