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ACR–ASNR–SPR PRACTICE PARAMETER FOR THE PERFORMANCE OF INTRACRANIAL MAGNETIC RESONANCE PERFUSION IMAGING

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 care¹. 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 in light of 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 the condition of the patient, limitations of available resources, or advances in knowledge or technology subsequent to publication of this document. However, a practitioner who employs an approach substantially different from the guidance in this document is advised to document in the patient record information sufficient to explain the approach taken.

The practice of medicine involves not only the science, but also 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 sole 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, ___ N.W.2d ___ (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 perfusion imaging is a proven and useful tool for the evaluation, assessment of severity, and follow-up of diseases of the central nervous system. It can be performed with contrast administration using dynamic susceptibility contrast (DSC) or dynamic contrast enhancement (DCE) techniques or without contrast administration using arterial spin-labeling (ASL) techniques.

II. INDICATIONS

Primary indications for perfusion magnetic resonance imaging (MRI) include, but are not limited to, the following:

- A. Diagnosis and Characterization of Mass Lesions
 1. Differential diagnosis (tumor versus tumor mimic)
 2. Diagnosis of primary neoplasms (may include grading)
 3. Surgical planning (biopsy or resection)
 - a. Targeting locations for biopsy
 - b. Guiding resection extent
 4. Therapeutic follow-up
 - a. Radiation necrosis versus recurrent or residual tumor
 - b. Chemonecrosis versus recurrent or residual tumor
 - c. Pseudoprogression and pseudoresponse
 - d. Monitor potential transformation of non-resectable low grade neoplasms to higher grade
- B. Assessment of Neurovascular Disease
 1. Acute stroke (assessment of ischemic penumbra)
 2. Assessment of the hemodynamic significance of cervical or intracranial vascular stenosis
 3. Assessment of cervical or intracranial revascularization efficacy
 4. Assessment of vasospasm
- C. Neurodegenerative Disease

III. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

See the [ACR Practice Parameter for Performing and Interpreting Magnetic Resonance Imaging \(MRI\)](#) [1].

IV. SAFETY GUIDELINES AND POSSIBLE CONTRAINDICATIONS

See the [ACR Practice Parameter for Performing and Interpreting Magnetic Resonance Imaging \(MRI\)](#) [1], the [ACR Guidance Document on MR Safe Practices](#) [2], the [ACR-SPR Practice Parameter for the Use of Intravascular Contrast Media](#) [3], and the [ACR Manual on Contrast Media](#) [4].

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

V. SPECIFICATIONS OF THE EXAMINATION

The written or electronic request for MRI perfusion 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's scope of practice requirements. (ACR Resolution 35, adopted in 2006)

The supervising physician must have complete understanding of the indications, risks, and benefits of the examination, as well as alternative imaging procedures. The physician must be familiar with potential hazards associated with MRI, including potential adverse reactions to contrast media. The physician should be familiar with relevant ancillary studies that the patient may have undergone. The physician performing MRI interpretation must have a clear understanding and knowledge of the anatomy and pathophysiology relevant to the MRI examination.

The supervising physician must also understand the pulse sequences to be used and their effect on the appearance of the images, including the potential generation of image artifacts. Standard imaging protocols may be established and varied on a case-by-case basis when necessary. These protocols should be reviewed and updated periodically.

A. Patient Selection

The physician responsible for the examination should supervise patient selection and preparation, and be available for consultation. Patients should be screened and interviewed prior to the examination to exclude individuals who may be at risk by exposure to the MR environment.

Bolus perfusion studies require the intravenous (IV) administration of gadolinium-based contrast agents (GBCAs). GBCAs should be administered using appropriate injection protocols and in accordance with the institution's policy on IV contrast utilization. Although GBCAs are widely used in pediatric patients, the physician responsible for administration should be aware that safety and efficacy of GBCAs are not as well established in children younger than 2 years as they are in older children and adults (see the [ACR-SPR Practice Parameter for the Use of Intravascular Contrast Media](#) [3] and the [ACR Manual on Contrast Media](#) [4]).

Pediatric patients or patients suffering from anxiety or claustrophobia may require sedation or additional assistance. Administration of moderate sedation or general anesthesia may be needed to achieve a successful examination, particularly in young children. If moderate sedation is necessary, refer to the [ACR-SIR Practice Parameter for Sedation/Analgesia](#) [5].

B. 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.

C. Examination Technique

1. Dynamic susceptibility contrast MRI (DSC MRI) T2* perfusion

a. Technique

The DSC MRI perfusion technique is typically used in the setting of infarct and tumor, as well as other conditions with altered cerebrovascular hemodynamics, since it estimates cerebral blood flow and volume. The most common method to perform DSC MRI is a single shot gradient-echo echoplanar sequence, which permits acquisition of an entire image slice with only a single

radiofrequency excitation. TE should be based on optimization of T2* contrast for the field strength at which imaging is performed. In DSC, images are acquired dynamically during the passage of GBCA through the brain. Image contrast is based on gadolinium's magnetic susceptibility effect. Typically, approximately 10 seconds after the beginning of image acquisition, 0.1 mmol/kg of a GBCA is administered via a peripheral intravenous catheter. The injection rate in adults is typically 4-5 cc/s, using a power injector to assure standard, reproducible GBCA bolus administration. Ideally, images should be obtained at least once every 1.5 seconds. Sufficient number of repetitions should be acquired to capture the entire first pass of the contrast bolus – typically 40 repetitions at a TR=1.5 seconds. Examples may be found in the literature [6-8].

The specific protocol may vary depending on the manufacturer and field strength. For imaging neoplasms, an initial GBCA dose of approximately 0.05 mmol/kg may be injected prior to the DSC injection in order to correct for anticipated leakage effects. Alternatively, intravascular blood pool agents may be considered to evaluate perfusion, although these agents limit evaluation of blood-brain barrier leakage.

To assess the hemodynamic significance of an arterial stenosis or occlusion, pharmacologic challenge testing may be useful. In general, such testing entails comparison of DSC performed with and without prior administration of a vasodilatory agent such as acetazolamide. The decision to perform challenge testing should be made in light of the patient's overall cardiovascular status and should take place under physician supervision.

b. Data processing

A signal intensity versus time curve is extracted from each voxel over the time series and computationally converted to contrast agent concentration-versus-time curves. Pre-injection points are typically averaged to produce an estimate of baseline signal intensity, S_0 . Following the arrival of the bolus, the concentration of gadolinium in a voxel can be derived from signal intensity by the

$$\text{equation } C(t) = -k \ln \left(\frac{S_t}{S_0} \right),$$

in which $C(t)$ is the contrast agent concentration at a particular time t , S_t is the signal intensity at that time, S_0 is the baseline signal intensity before the arrival of the contrast agent, and k is a constant whose value depends on the pulse sequence used, the manner in which the contrast is injected, and complex characteristics of the patient's circulatory system that are difficult to model. Because the value of k is difficult to estimate, most perfusion maps provide only relative quantification of perfusion parameters. Cerebral blood volume (CBV) is generally calculated by numerically integrating the area under the entire $C(t)$. Some researchers have attempted to extract the first pass of the contrast bolus by fitting gamma variates to the first portion of $C(t)$, but no particular model has been shown to reflect the first pass reliably. Calculation of cerebral blood flow (CBF) requires incorporation of the concentration-versus-time curve not just in any voxel but also in the arteries that supply blood to that voxel, the arterial input function (AIF). An AIF is calculated by measuring $C(t)$ in voxels near an artery or arteries that are clearly identifiable and preferably supplying the region impacted by pathology. $C(t)$ functions are then averaged either manually or automatically over the selected arterial voxels. Other parameters such as relative cerebral blood volume (rCBV), relative peak height (rPH), and peak signal recovery (PSR) may also be calculated.

A mathematical process called deconvolution is used to derive a scaled residue function in each voxel from the AIF and the voxel's $C(t)$ function. The amplitude of the deconvolved signal is measured as the CBF, and the time at which this maximum value is reached is called Tmax. Mean transit time is calculated by dividing CBV by CBF. Time to peak (TTP) is the time at which contrast concentration reaches its maximum.

2. Dynamic contrast enhanced magnetic resonance imaging (MRI) (DCE MRI) – T1 permeability mapping [9-14]

a. Technique

The DCE MRI perfusion technique is typically used in the setting of tumor evaluation since it allows estimation of tissue permeability. The most common method to perform DCE MRI uses a fast T1-weighted gradient-echo sequence with short TE (<1.5 ms) and TR (<7 ms) and flip angle around 30 degrees. A temporal resolution of 5 to 10 seconds for obtaining a series of two-dimensional (2-D) slices or a single three-dimensional (3-D) slab is possible with current technology while preserving spatial resolution. Obtaining a T1 map, commonly using a precontrast lower flip angle dataset, improves the accuracy of GBCA concentration calculations and quantification. The use of a power injector for bolus (2 to 5 cc/second) or infusion (30 to 60 seconds) technique ensures reproducible and standardized GBCA administration. As there is potential for leakage effects that can cause the (rCBV) measurements performed for DSC MRI to be overestimated or underestimated (see V.C.1.a), DCE MRI is typically performed before the DSC MRI. This ordering also allows for saturation of the extravascular space, providing for more accurate quantification of metrics such as rCBV from DSC MRI.

b. Data processing

The determination of an AIF to obtain more accurate $C(t)$ can be a challenge in DCE imaging. Ideally, the AIF would be determined in each patient using the dynamic curve of the carotid or middle cerebral artery. However, if this is not possible, the AIF can be approximated from the superior sagittal sinus, with the understanding that this will introduce some error in the compartmental model output. The plasma concentration curve can be further fitted—eg, to biexponential form (as in the Tofts model).

There are also “reference tissue” models that attempt to estimate the vascular tracer concentration from one or more normal-appearing surrounding tissues. DCE can be reviewed qualitatively by characterizing the T1 signal intensity curves over time, or various DCE MRI quantitative metrics can also be estimated. The typical parameters that can be estimated from the DCE MRI include K^{trans} (vascular permeability), EES (extravascular, extracellular space), V_p (plasma volume), and the K_{ep} (K^{trans}/EES). In general, malignant neoplasms will have a very high K^{trans} and V_p but lower EES, and more benign pathologies, including radiation necrosis and chemonecrosis, will have lower K^{trans} and V_p but higher EES.

3. Arterial spin-labeling perfusion MRI

a. Technique

Arterial spin-labeling (ASL) perfusion MRI uses magnetically labeled endogenous blood water as a tracer to derive information on cerebral hemodynamics. This is accomplished by manipulating the longitudinal magnetization of intravascular blood water in order to differentiate it from the tissue magnetization. ASL does not require the use of an exogenous contrast agent, can be performed within about a 5 minute acquisition time, and provides both qualitative and quantitative measures of cerebral blood flow (CBF). Moreover, unlike contrast-based approaches, ASL can be repeated multiple times, for example, under different physiological conditions. Although either pulsed labeling (PASL) with an instantaneous spatially selective saturation or inversion pulse, or continuous labeling (CASL), most typically by flow driven adiabatic fast passage, have been used, pseudocontinuous (P-CASL) is now widely available and provides the important advantage of relative insensitivity to transit time variability [15]. The ASL images are acquired both with and without magnetization labeling of arterial blood water. The subtle difference between images acquired with (labeled) and without (control) ASL can be modeled to derive a calculated cerebral blood flow image showing perfusion in ml/min/100 g-tissue at each voxel.

b. Data processing

Analysis of the acquired ASL images can be performed using readily available software. The qualitative CBF map is created by subtracting the labeled images from the control images, resulting in an image with intensity proportional to CBF. The quantitative CBF in units of ml/min/100 g-tissue is much more challenging to measure and requires sophisticated software. Briefly, the equilibrium magnetization $M_{0,a}$ of the arterial blood is estimated by fitting the control or unlabeled signal in the brain tissue to a saturation-recovery curve. The CBF is calculated by a fit of the signal difference (ΔM) to the perfusion model with the following values for the physical constants: R_1 (longitudinal relaxation rate of tissue); R_{1a} (longitudinal relaxation rate of blood); and λ (brain/blood partition coefficient of water).

4. Perfusion imaging in pediatric patients [16,17]

The need for small caliber IVs, intravenous access in hands and feet, and small caliber PICC lines in infants and small children limits the use of automated power injectors, and in such situations, manual injection should be considered to avoid extravasation of contrast and damage to precarious IV access. The radiologist should carefully consider whether GBCA should be given, conferring with the providers participating in the direct care of the patient, as needed. ASL should always be considered as an alternative, given the potential repeated exposures to GBCAs for children over their lifetime and the unknown potential risk of gadolinium deposition in brain tissue.

Perfusion models based on parameters derived from adults have been applied to children and age-related normative values for CBF in children are just starting to be established [18]. The effects of general anesthesia or conscious sedation on cerebral perfusion are not clear. ASL may be preferable to contrast-enhanced perfusion imaging in pediatric patients, especially in neonates, given the theoretical advantage in SNR due to higher velocities of flow in children and because GBCA administration is not required.

Special considerations in interpreting perfusion studies in infants and young children include congenital heart disease involving right to left shunts, age-related changes in flow velocity, and sickle cell anemia in which flow velocity is typically elevated. The use of rCBV has limited application in pediatric brain tumors due to predominance of astrocytic tumors of low-grade and high prevalence of non-astrocytic tumors. Similarly, the utility of perfusion metrics in determination of penumbra in pediatric stroke is not known.

VI. DOCUMENTATION

Reporting should be in accordance with the [ACR Practice Parameter for Communication of Diagnostic Imaging Findings](#) [19].

Reports should specify the perfusion technique employed, volume of contrast and rate of injection. Specification of the hemodynamic parameters (eg, CBV, MTT, etc) examined and whether qualitative review of parameter maps and/or extraction of time-intensity curves or quantitative values were employed should be specified. Relevant post-processed images/maps depicting hemodynamic parameters should be archived in the same manner as the study images.

VII. EQUIPMENT SPECIFICATIONS

The MRI equipment specifications and performance must meet all state and federal requirements. The requirements include, but are not limited to, specifications of maximum static magnetic strength, maximum rate of change of the magnetic field strength (dB/dt), maximum radiofrequency power 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 (<http://www.acr.org/guidelines>).

Specific policies and procedures related to MRI safety should be in place along with documentation that is updated annually and compiled under the supervision and direction of the supervising MRI physician. Guidelines should be provided that deal with potential hazards associated with the MRI 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 MRI examination.

Equipment monitoring should be in accordance with the [ACR–AAPM Technical Standard for Diagnostic Medical Physics Performance Monitoring of Magnetic Resonance Imaging \(MRI\) Equipment](#) [20].

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