Memorandum: Guidelines on the Use of Magnetic Resonance Angiography (MRA) for the Diagnosis of Pulmonary Embolus at the University of Wisconsin

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To: The Departments of Emergency Medicine, Obstetrics and Gynecology, and Radiology

Purpose: The purpose of this memorandum is to describe the appropriate use of pulmonary MRA for the diagnosis of pulmonary embolus in patients with dyspnea and/or chest pain, including the appropriate use of pulmonary MRA in pregnant patients.

Background: Pulmonary embolus (PE) is a potentially life-threatening condition with notoriously nonspecific presentation making it challenging to diagnose on presentation and physical exam alone. For this reason, cross-sectional imaging, most commonly computed tomographic angiography (CTA), is widely accepted as the standard of care in patients with a clinical suspicion of PE. However, CTA requires the use of ionizing radiation and iodinated contrast media, which is potentially nephrotoxic.

In response to these drawbacks of pulmonary CTA, the Department of Radiology has made available pulmonary magnetic resonance angiography (MRA) as a safe and effective alternative for the diagnosis of PE, avoiding the need for ionizing radiation and iodinated contrast media. Available since 2008 at UW-Madison, pulmonary MRA is well established as the local standard of care in adolescents and young adults with a clinical suspicion of PE. Recent data from UW-Madison demonstrate that pulmonary MRA is a clinically-effective exam. In a recent retrospective case-control study of clinical outcomes in 1173 patients, the 6-month rate of bleeding, venous thromboembolism (VTE) or all-cause mortality following pulmonary MRA was no worse than (and possibly better than) that following pulmonary CTA in the emergency setting (manuscript under review). Thus, the purpose of this document is to codify guidelines for appropriate use of pulmonary MRA in the emergency setting.

Regarding evaluation for PE in pregnant women: Unfortunately, gadolinium-based contrast agents are strictly contraindicated in pregnant patients due to potential teratogenic effects shown in animal studies. For this reason, gadolinium-enhanced MRA is not offered in pregnant patients. In recent years, however, there has been increasing use of ferumoxytol (Feraheme, AMAG) as an off-label alternative to gadolinium-based contrast agents for contrast-enhanced MRA. Ferumoxytol is an FDA-approved intravenously-administered iron-based agent used to treat anemia in patients with renal failure. There is a substantial and growing body of literature demonstrating the diagnostic efficacy of ferumoxytol as an MRI contrast agent, including for use in pulmonary MRA. Ferumoxytol is available on the formulary at UWHC as an option for contrast-enhanced MRA in those patients with a contraindication to gadolinium-based contrast agents. Ferumoxytol is an intravascular “blood pool” agent and steady-state pulmonary MRA and/or MR venography of the deep pelvic veins and lower extremities can be performed for several hours after the infusion of this agent.

Notably, ferumoxytol is listed as a pregnancy category C agent (no human safety studies performed). Despite the lack of data establishing clear safety in pregnancy, ferumoxytol is widely regarded as a safe agent for the treatment of anemia in pregnant women, and is used by obstetricians at many institutions, including UW-Madison and Meriter Unity-Point Hospital. For this reason, ferumoxytol-enhanced MRA is now available as an option to assess pregnant women with suspected PE.

Guidelines: The following describe the appropriate use of pulmonary MRA at UW-Madison.

1. Pulmonary MRA is available 24/7 at UWHC for patients with a clinical suspicion of PE. Pulmonary MRA is recommended as the first line test to exclude PE in patients:
   a. under 40 years of age
   b. without a complicated history of acute or chronic pulmonary disease
   c. able to hold their breath for approximately 15 seconds
   d. able to undergo MRI without the need for sedation
   e. without contraindications to MRI
   f. with contraindications to iodinated contrast media (eg. allergy, impaired renal function)
2. For pregnant patients, or patients with known severe allergy to gadolinium-based contrast agents, ferumoxytol-enhanced MRA is now offered as an alternative to pulmonary CTA to exclude PE. For patients in whom ferumoxytol-enhanced MRA is being considered:
   a. Discussion between the patient's physician (resident or attending) with a radiology physician (resident, fellow, or attending) should take place prior ordering a ferumoxytol-enhanced MRA study in any patient.
   b. MRI safety screening must take place prior to administration of ferumoxytol.
   c. First-pass imaging using ferumoxytol will not be performed for the purpose of pulmonary MRA. Steady-state imaging is adequate for the diagnosis of pulmonary embolus.
   d. Per Department of Radiology guidelines for ferumoxytol administration (https://www.radiology.wisc.edu/fileShelf/contrastCorner/UW_ferumoxytol_guidelines.pdf?buster=1471712972), ferumoxytol will be administered by slow infusion and will include heart rate and blood pressure monitoring. For patients in the Emergency Department, infusion can be performed in the Emergency Department prior to transport for MRI, as ferumoxytol is an intravascular agent, and administration can occur up to two hours prior to imaging, if needed.
   e. A typical dose for ferumoxytol-enhanced MRI is 1-5 mg/kg, never to exceed 510mg (full bottle). A dose of 1-3 mg/kg is recommended in pregnant patients. Please note that the therapeutic dose is a full bottle (510mg), thus, typical doses for MRI are substantially lower than therapeutic doses.
   f. Patients with known allergies to ferumoxytol or other IV iron-based pharmaceutical agents are not eligible for ferumoxytol-enhanced MRA.
   g. These guidelines were reviewed by the MRI Safety Committee on 9/14/2016.
   h. The use of ferumoxytol for MRI/MRA in pregnant patients was approved by the UWHC Pharmacy and Therapeutics committee on 9/15/2016.

Summary: The Department of Radiology aims to offer the safest and most effective imaging alternatives for our patients. The use of pulmonary MRA is a safe and effective means of diagnosing clinically-significant PE in young patients, who are most sensitive to the effects of ionizing radiation. The use of ferumoxytol is a recent advance, enabling the use of MRA without the need for gadolinium-based contrast agents that are contraindicated in pregnancy. Please do not hesitate to contact Drs. François, Reeder, Repplinger, Schiebler, Nagle or Shah should you have any questions regarding the details of these guidelines.