

Date: June 15, 2017
To: Referring Physicians Ordering Gadolinium-enhanced MRI Exams at UW Health
Re: Deposition of Gadolinium-based Contrast Agents
From: Scott Reeder, MD, PhD, Chief, Magnetic Resonance Imaging
Howard Rowley, MD, UW MRI Safety Committee Chair

**Purpose:** provide an update on the recently reported phenomenon of gadolinium deposition in the brain, and to provide guidance to referring physicians ordering gadolinium-enhanced MRI studies at UW Health.

Recent reports in the literature describe subtle increased signal intensity in deep brain nuclei in patients who have received multiple doses of gadolinium-based contrast agents (GBCAs), including agents that are currently in routine use for clinical care and research at UW-Madison. Emerging data indicate a dose relationship with signal intensity correlating with a number of lifetime administrations of GBCAs. Autopsy studies and animal studies have als o demonstrated the presence of gadolinium in brain tissue using biochemical assays, although the chemical form of deposited gadolinium is currently unknown. Given the known toxicity of free gadolinium ions, these observations have raised legitimate concerns about possible adverse consequences of gadolinium deposition in the brain.

However, to date, there are no reports of any adverse biological or clinical effects resulting from gadolinium deposition. Approximately 30 million doses of GBCAs are administered to humans every year and over 300 million doses have been administered since these agents were first introduced in the 1980's. Notably, there is no relationship between gadolinium deposition and renal failure, and this phenomenon is unrelated to nephrogenic systemic fibrosis (NSF), a form of gadolinium toxicity associated with certain GBCAs administered to patients with renal failure.

The International Society for Magnetic Resonance in Medicine (ISMRM) has recently published a detailed overview of the current stage of knowledge on gadolinium deposition in the brain in <u>Lancet Neurology</u>. Importantly, specific recommendations for clinical and research use of gadolinium are provided as part of this paper. The American Society of Neuroradiology (ASNR) and the American College of Radiology (ACR) have also published a similar position paper available at <u>www.acr.org/Quality-Safety/Resources/Contrast-Manual</u>. Further, on 5/22/2017, the <u>FDA made similar recommendations</u> based on a lack of any evidence of adverse health effects related to gadolinium deposition.

The UW MRI Safety Committee has discussed this issue in detail and concurs with the ISMRM recommendations. Specifically, for clinical care, the white paper states the following: "The ISMRM urges caution in the utilization of any medications, including GBCAs. Per standard practice, GBCAs should be avoided when not required. The data on gadolinium deposition emphasize, but do not alter this practice, and GBCAs should not be withheld from patients with a clinical indication for gadolinium enhanced MRI. The physician responsible for the administration of contrast should understand the benefits and risks of the agent." Given the extraordinary safety profile of GBCAs and the absence of any data indicating any adverse outcomes from gadolinium deposition, the UW MRI Safety Committee recommends adherence to the ISMRM guidelines.

However, we understand that questions may arise from our patients regarding our approach on the use of GBCAs in clinical practice. It is for this reason, that we have provided this information. Further, we have provided an online information sheet for patients who may have questions regarding the phenomena of gadolinium deposition at the <u>following link</u>. Further, we would be pleased to provide any additional information to you and your colleagues who may have questions regarding this phenomenon. As always, please do not hesitate to contact either of us should you have any questions regarding MRI safety or GBCAs.

Sincerely,

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