ACR–ASNR POSITION STATEMENT ON THE USE OF GADOLINIUM CONTRAST AGENTS

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Following U.S. Food and Drug Administration (FDA) approval in 1988, gadolinium-based contrast agents (GBCAs) have been used for diagnosis and treatment guidance in more than 300 million patients worldwide. GBCAs increase the conspicuity of diseased tissues. All GBCAs share a common structure of an organic ligand that tightly binds to and improves the stability, solubility, and safety of the central gadolinium heavy metal ion. In typical patients, the chelate is mostly eliminated via the kidneys, with some amount of liver excretion demonstrated for a few of the agents.

Since 2006, radiologists have withheld some GBCAs from patients with acute kidney injury and/or severe chronic kidney disease, if the estimated glomerular filtration rate (GFR) is <30 mL/min/1.73 m2, because of the increased risk of nephrogenic systemic fibrosis (NSF). NSF is a rare but serious systemic disease characterized by fibrosis of the skin and other tissues throughout the body in renally impaired individuals. As a result of judicious use of GBCAs among patients with compromised renal function and a decrease in utilization of those GBCAs that are more highly associated with NSF, there has been a drastic reduction in the number of cases encountered since restrictive guidelines were put into place after the association of NSF with GBCAs was identified in 2006.

Recently, residual gadolinium has been found within the brain tissue of patients who received multiple doses of GBCAs over their lifetimes. For reasons that remain unclear, gadolinium deposition appears to occur preferentially in certain specific areas of the brain, even in the absence of clinically evident disease and in the setting of an intact blood brain barrier. Such deposition is not expected, and led the FDA to publish a Safety Alert in July of 2015 indicating that they were actively investigating the risk and clinical significance of these gadolinium deposits. To date, no adverse health effects have been uncovered, but the radiology community has initiated a rigorous investigation.

Gadolinium deposition in the brain may be dose dependent and can occur in patients with no clinical evidence of kidney or liver disease. Fortunately, there have been no reports to date to suggest these deposits are associated with histologic changes that would suggest neurotoxicity, even among GBCAs with the highest rates of deposition. Although there are no known adverse clinical consequences associated with gadolinium deposition in the brain, additional research is warranted to elucidate the mechanisms of deposition, the chelation state of these deposits, the relationship to GBCA stability and binding affinity, and theoretical toxic potential, which may be different for different GBCAs. Until we fully understand the mechanisms involved and their clinical consequences, the safety and tissue deposition potential of all GBCAs must be carefully evaluated.

GBCAs provide crucial, life-saving medical information. Each time a gadolinium-enhanced MRI study is considered, it would be prudent to consider the clinical benefit of the diagnostic information or treatment result that MRI or MRA may provide against the unknown potential risk of gadolinium deposition in the brain for each individual patient. Particular attention should be paid to pediatric and other patients who may receive many GBCA-enhanced MRI studies over the course of their lifetimes. If the decision for an individual patient is made to use a GBCA for an MRI study, multiple factors need to be considered when selecting a GBCA, including diagnostic efficacy, relaxivity, rate of adverse reactions, dosing/concentration, and propensity to deposit in more sensitive organs such as the brain. As this gadolinium deposition

phenomenon remains a relatively undefined clinical phenomenon, and accurate and complete data may be useful as investigations proceed, the identity and dose of GBCA used should be recorded after each intravenous administration.

The radiology community will continue to assess the safety of GBCAs and modify clinical practice recommendations accordingly as new data becomes available.