



THE UNIVERSITY OF ARIZONA
MEDICAL CENTER

RADIOLOGY DEPARTMENT

POLICIES, PROCEDURES AND PROTOCOLS

Subject: MRI Administration of Gadolinium Based Contrast Media
Policy: MR008

Author: Diego Martin, MD, PhD; Bobby Kalb, MD
Effective Date: 10/01/11
Revision Dates: 10/01/11

PURPOSE: To provide guidelines to reduce the incidence of adverse effects from gadolinium based contrast agents in patients who undergo contrast-enhanced magnetic resonance imaging.

POLICY: Patients with severe kidney disease and on dialysis are at higher risk for experiencing adverse effects, specifically the fibrosing skin condition termed “Nephrogenic Systemic Fibrosis”, or NSF. Consideration in this policy is being given to the data as we best understand NSF to date. This policy is based on recommendations approved by the University of Arizona Quality Committee, after consultation with members of the MRI Safety Committee and extensive research of the peer-reviewed literature.

Certain gadolinium chelate agents have been associated with a ~2-5% risk of NSF in patients with severe renal failure, and mostly in patients on dialysis (estimated glomerular filtration rate < 15 ml/min). Gadodiamide (Omniscan) accounts for >90% of all un-confounded cases of NSF in peer-reviewed publications where NSF was diagnosed by accepted standards, including skin biopsy; other gadolinium agents that have been associated with NSF include Optimark (gadoversetamide) and Magnevist (gadopentetate). The risk of NSF using gadolinium chelates with higher conditional stability, specifically the linear, high-relaxivity agent gadobenate dimeglumine (MultiHance), or the macrocyclic agents gadoteridol (ProHance) or gadobutrol (Gadavist), remains immeasurably small based on the global body of evidence, even in centers where these agents are given routinely to patients on dialysis. Based on the recommendation of the University of Arizona Quality Committee, Omniscan is not available from the pharmacy formularies in the University of Arizona Health Network. This action was taken to avoid any possibility of inadvertent administration of this agent to patients with renal insufficiency.

In well documented peer-reviewed studies as of 2011, the patients developing NSF are almost all on dialysis, and those who are not typically have Stage 4 or 5 chronic kidney disease (CKD) (usually GFR less than 15 ml/min) **AND** received Omniscan. Repeated (frequently > 3), high doses of gadolinium contrast were also associated with increased risk of NSF in patients with severe (Stage 4 or 5 CKD), and prompt dialysis after gadolinium administration was found to confer some reduction in risk of developing the disease. Subsequent longitudinal, institutional studies following replacement of Omniscan with a more stable, linear agent (Multihance), at lower overall dose, resulted in the reduction of the rate of NSF to 0%, despite continued administration of gadolinium-based contrast to patients with renal disease, including

nearly 800 patients with end stage renal disease on dialysis. With changes in contrast administration protocols, predominately related to dose reduction and the use of more stable gadolinium agents, there have been no additional, documented cases of NSF in the peer reviewed literature world-wide since 2008.

POLICY- Dosage of Gadolinium Based Contrast Media

1. All patients will be screened, using the MRI Screening Form, for severe acute or chronic renal disease. (For the purposes of this policy, based on the published data of patients most at risk for NSF, *severe acute or chronic renal disease is defined as **requiring dialysis.***)
2. Those patients without the indication of severe acute or chronic renal disease requiring dialysis will follow standard protocol for contrast enhanced exams.
3. If the patient is unclear on their history of severe renal disease / dialysis, and this information is unavailable from the medical records available or the ordering MD, at the radiologist's discretion an estimated GFR may be obtained prior to scanning. Note that it would be *exceptional* that a non-emergent patient could have severe acute or chronic renal insufficiency and be on dialysis without being able to provide this history.
4. When a contrast-enhanced MRI is ordered in those patients with a history of severe acute or chronic renal disease requiring dialysis, the technologist will follow the protocol outlined as follows:

The technologist will call the radiologist for a determination on contrast usage only if the following two criteria are *both* met:

- a) the patient has severe renal disease (i.e. the patient is on dialysis)

AND

- b) This would be the fourth or more lifetime contrast-enhanced MR exam for this patient.
5. If none of the above criteria are met, for clinical cases requiring contrast, the technologist will proceed with the imaging protocol. This protocol calls for using a low dose, higher relaxivity agent (MultiHance), or higher stability macrocyclic agent (Gadavist or ProHance). The alternate agents may be used due to the requirements of the clinical study impacting diagnostic results or secondary to any prior adverse reaction to the primary agent. Gadolinium contrast administration will be dosed by weight.
6. For the patients on dialysis, the technologists will verify, prior to giving any gadolinium based contrast agent, that the patient or ordering MD confirms that the patient is scheduled for dialysis no later than 24-36 hours after injection. In any case where the dialysis arrangements are not documented prior to scanning, the technologist must contact the Radiologist responsible for MRI service at the time of scanning and the Radiologist/Technologist must ensure that the referring service is taking responsibility for arranging the dialysis, prior to the MRI scan being performed.

References:

1. Thomsen, H. S., S. K. Morcos and P. Dawson (2006). "Is there a causal relation between the administration of gadolinium based contrast media and the development of nephrogenic systemic fibrosis (NSF)?" Clin Radiol **61**(11): 905-906.
2. Lauenstein, T. C., K. Salman, R. Morreira, S. Tata, D. Tudorascu, G. Baramidze, S. Singh-Parker and D. R. Martin (2007). "Nephrogenic systemic fibrosis: center case review." J Magn Reson Imaging **26**(5): 1198-1203.
3. Broome, D. R. (2008). "Nephrogenic systemic fibrosis associated with gadolinium based contrast agents: A summary of the medical literature reporting." Eur J Radiol **66**(2): 230-234.
4. Prince, M. R., H. Zhang, M. Morris, J. L. MacGregor, M. E. Grossman, J. Silberzweig, R. L. DeLapaz, H. J. Lee, C. M. Magro and A. M. Valeri (2008). "Incidence of nephrogenic systemic fibrosis at two large medical centers." Radiology **248**(3): 807-816.
5. Thomsen, H. S. and P. Marckmann (2008). "Extracellular Gd-CA: Differences in prevalence of NSF." Eur J Radiol.
6. Wertman, R., E. Altun, D. R. Martin, D. G. Mitchell, J. R. Leyendecker, R. B. O'Malley, D. J. Parsons, E. R. Fuller, 3rd and R. C. Semelka (2008). "Risk of nephrogenic systemic fibrosis: evaluation of gadolinium chelate contrast agents at four American universities." Radiology **248**(3): 799-806.
7. Martin, D. R., R. C. Semelka, A. Chapman, H. Peters, P. J. Finn, B. Kalb and H. Thomsen (2009). "Nephrogenic systemic fibrosis versus contrast-induced nephropathy: Risks and benefits of contrast-enhanced MR and CT in renally impaired patients." J Magn Reson Imaging **30**(6): 1350-1356.