

UAB Department of Radiology Guidelines for Administering Gadolinium-based and Iodine-based Intravenous Contrast Agents in Patients with Renal Dysfunction or at Risk for Adverse Reactions

Because Iodinated and Gadolinium-based contrast agents may have adverse effects in patients with renal dysfunction and may cause adverse reactions in other patients, the following guidelines are established to minimize risks of administering these agents. New point-of-service serum creatinine and estimated GFR (eGFR) capability at TKC MRI and CT and new informed consent requirement for MRI patients with eGFR ≤ 30 at TKC and ≤ 40 at University and UAB Highlands Hospitals should be noted by all radiologists involved in IV contrast administration.

The primary Gadolinium-based MR contrast agent at University Hospital, UAB Highlands and the Kirklin Clinic is ProHance®, a macrocyclic agent with high thermodynamic and kinetic stability. The primary Iodinated contrast agents used at University Hospital and UAB Highlands Hospital are differing concentrations of Omnipaque®, and at The Kirklin Clinic are differing concentrations of Isovue®, all nonionic agents.

Topics Addressed in This Document

1. Renal Function Assessment Prior to CT and MRI
2. Notification of Ordering Physician of Renal Dysfunction
3. Strategies in Patients at Risk for Allergic Reactions to IV Contrast for MRI
4. Strategies in Renal Dysfunction Patients for MRI
5. Risk of Developing NSF after IV Gadolinium Administration
6. Informed Consent for Contrast MRI
7. Strategies in Renal Dysfunction Patients for CT
8. Strategies in Patients at Risk for Allergic Reactions to IV Contrast for CT
9. Recommended Reading
10. Appendix: Premedication to Minimize Allergic Contrast Reactions

Renal Function Assessment Prior to CT and MRI

University Hospital and UAB Highlands Hospital:

Serum creatinine is to be obtained within 72 hours prior to scanning on all patients for whom IV contrast administration is anticipated. Any of the following values require that the technologist request the radiologist responsible for protocoling and/or interpreting the examination to decide whether IV contrast should be administered and, if so, what dose:

1. If eGFR (calculated from serum creatinine, patient weight, age and gender) is less than or equal to 60, OR
2. If creatinine is greater than or equal to 1.5 mg/dl, OR
3. If there has been an increase in creatinine of 0.2 mg/dl or greater since the most recently available prior creatinine value.

The Kirklin Clinic:

Serum creatinine values are to be reviewed on all patients for whom IV contrast administration is anticipated. In most cases, a creatinine will be available from the TKC laboratory. However, point-of-service creatinine determinations with an i-STAT device are now available in the TKC MRI and CT laboratories. If the patient arrives at CT and a creatinine value is needed according to the guidelines below, the technologist will either send the patient to the laboratory, or perform a point-of-service determination under ANY ONE of the following conditions:

1. If there is no creatinine value in the UABHS computerized medical record or on a documented (e.g. Faxed or copied) report from an outside institution within the past 90 days,
2. If the most recent creatinine is greater than or equal to 1.5 mg/dl, or if the eGFR is less than or equal to 60 and a creatinine value has not been obtained within the past 2 weeks,
3. The patient has had an increase in creatinine of 0.2 or greater or a substantial change in eGFR values within the previous 6 months,
4. If there is a clinical reason to suspect onset of renal dysfunction since the last renal function determination,
5. At the discretion of the radiologist if the patient is 65 years old or older, even if they have no known or suspected renal dysfunction.

If the eGFR is less than 60, the technologist will request the radiologist responsible for protocoling and/or interpreting the examination to decide whether IV contrast should be administered and, if so, what dose.

Notification of Ordering Physician of Renal Dysfunction

An abnormal creatinine or eGFR obtained with i-Stat in Radiology may be the first indication of significant renal dysfunction. At the discretion of the radiologist, the referring physician or a member of the clinical team may be contacted, and documentation of such contact should be placed in the MRI or CT report. The abnormal value and any resulting alteration of contrast administration should be included in the report.

Strategies in Patients at Risk for Allergic Reactions to IV Contrast for MRI

Although anaphylactoid reactions to intravenous Gadolinium contrast are much less common than to intravenous Iodinated contrast media, they do rarely occur. Most reactions are mild and serious reactions are very unusual.

1. Current recommended treatment is analogous to reactions with similar symptoms as would be used for Iodinated contrast reactions.
2. The only known predictive factor for allergic reaction is a prior reaction to Gadolinium.
3. Although there have been no published studies, if a patient had a prior non-life threatening reaction to a Gadolinium agent, if a contrast enhanced MRI is deemed medically necessary, it is recommended for the patient to be premedicated with

same regimen as for Iodinated contrast (see Appendix), and to use a different contrast agent than the patient reacted to, if possible [4].

4. For patients with normal renal function (e.g. eGFR greater than 60), the alternative Gadolinium-based MR contrast agents that are available at UAB should be considered when there is a history of prior severe nausea or allergic reaction to ProHance. These secondary agents are Optimark at The Kirklin Clinic and Magnevist at University Hospital and UAB Highlands Hospital.
5. No Gadolinium-based agent should be administered if the eGFR is less than 30, unless there is a strong clinical indication for Gadolinium contrast administration, as determined in discussion with the referring clinician.

Strategies in Renal Dysfunction Patients for MRI

When eGFR is ≤ 30 for outpatients and when eGFR is ≤ 40 for inpatients, the supervising radiologist should take into account the following:

1. Is Gadolinium necessary to make the diagnosis?
2. Can an imaging test other than MRI answer the clinical question with less risk to the patient?
3. If Gadolinium is necessary, what is the lowest dose that can be administered to the patient while maintaining diagnostic quality of the MRI?
4. The ordering physician may need to be contacted regarding estimation of relative benefit of contrast use for the suspected clinical abnormality, versus risks (see below).

The UAB Department of Radiology does not have a universal policy of withholding IV Gadolinium when the eGFR is less than 30. The only absolute contraindication to receiving gadolinium is a known diagnosis of NSF.

Standard Gadolinium dose is 0.1 mmol per kilogram, and all doses should be weight-based at University Hospital, UAB Highlands Hospital and TKC. In some unusual circumstances (e.g., depiction of brain metastases, performance of an MR angiogram runoff, and others), reports have indicated that using a “double dose” will improve examination accuracy and will be important to patient management. Such a double-dose technique should only be used for a list of specific indications such as those above and not on an ad hoc basis. Also, a double dose should not be used for patients with renal dysfunction.

If contrast is deemed necessary and the patient can be examined with the 3.0 Tesla unit at the Kirklin clinic, he/she should receive one-half of the standard dose. This can be utilized for patients with stage 4 and 5 chronic kidney disease to decrease the amount of Gadolinium administered. If the patient is on dialysis, the supervising radiologist may determine the next dialysis appointment and contact the patient's nephrologist if there is a significant delay between the Gadolinium administration and the next planned dialysis.

Risk of Developing NSF after IV Gadolinium Administration

A JACR special issue containing material from the first Symposium on Nephrogenic Systemic Fibrosis [1] summarizes the risks for developing NSF in patients with renal dysfunction. This includes valuable information that may be discussed with referring physicians or patients. This symposium is worthwhile reading for all radiologists who cover the MRI service. **Pertinent articles from this journal edition have been placed in MRI reading areas at University Hospital, UAB Highlands Hospital and TKC.**

The summary follows:

1. For hospitalized patients with eGFR less than 60 and a pro-inflammatory condition, the yearly incidence of NSF was 4.6% [2]. This population included mostly patients with renal failure but also two patients with acute failure with eGFR between 30 and 60.
2. For outpatients with renal failure or stage 5 chronic kidney disease (eGFR<15), risk estimate for developing NSF after single Gadolinium dose is 2.4% (1/42 patients) [3]; in this same study the overall incidence was 4.3 cases per 1000 in a population of outpatients with stable end stage renal disease.
3. For outpatients with stage 4 chronic kidney disease (eGFR 15-29), risk estimate for developing NSF after single Gadolinium dose is 0.24% (1/416 patients).
4. For outpatients with stage 3 chronic kidney disease (eGFR 30-60), risk estimate for developing NSF after a single Gadolinium dose is very low (1/170,000 patients). Please note that these estimates are for patients with CHRONIC renal disease; there is not sufficient data for estimation of risk in patients with ACUTE renal failure.
5. There is data that suggests risk of developing NSF increases with larger dose (i.e. double or triple dose) or cumulative dose over time [1].

Informed Consent for Contrast MRI

The summary of data regarding the incidence of NSF for patients with renal dysfunction as well as the new point-of-service serum creatinine/eGFR mechanism at the TKC MRI Suite enables UAB Department of Radiology personnel to engage in *informed consent discussions* with patients who may be at increased risk for developing NSF and who require Gadolinium during MRI examinations. All outpatients with an eGFR \leq 30 or inpatients with an eGRF \leq 40 will be given informed consent prior to Gadolinium administration. This is to be performed by an attending radiologist, radiology resident or radiology fellow. Standard institutional consent forms should be used. After signatures are obtained on the consent form from the patient or her/his representative, the document will be digitized as a component of the MRI examination and become part of the computerized patient record though PACS. The paper informed consent document will be placed in the patient's clinic or hospital chart. Optimum informed consent confirmation and documentation includes 1) having a technologist or other individual present when informed consent is given and 2) documenting the following in the radiology report of the MRI: a) that the risks, benefits and alternatives of the procedure were discussed with the patient or her/his representative and that the opportunity to ask questions was provided,

b) what risks were discussed and c) the content, date and time of any discussion with the referring physician regarding risks and benefits, and this physician's name or role.

Strategies in Renal Dysfunction Patients for CT

Contrast Induced Nephropathy (CIN) is defined as a rise in creatinine of 0.5 mg/dl after contrast administration. Risk factors for CIN include:

1. Preexisting renal impairment
2. Diabetes mellitus
3. Congestive heart failure
4. Higher doses of IV contrast media
5. Dehydration
6. Nephrotoxic drugs

The risk increases with an increasing number of risk factors. The threshold for concern about inducing CIN is an eGFR of 60. The following actions are recommended for patients with some risk factors above for whom IV contrast administration is anticipated:

1. Do NOT place the patient NPO prior to examination unless required for another indication,
2. Encourage oral hydration the day prior to and the day of examination,
3. Allow only clear liquids beginning four hours prior to the examination.

The details of preparation prior to IV contrast administration for patients at risk for CIN is beyond the scope of this document. However, depending on the severity of risk and whether the patient is an inpatient or outpatient, the following may be considered alone or in combination:

1. Intravenous hydration with normal saline prior to and following the examination,
2. Administration of IV Bicarbonate,
3. Administration of Mucomyst®,

The dose of IV Iodinated contrast to be administered within the UAB Department of Radiology is based upon patient weight and other factors. A standard dose of IV contrast may be administered in the following situations:

1. If the eGFR is stable and is 60 or above,
2. If the eGFR is 30 or below, but the patient is on dialysis.

In some patients, a standard dose is not recommended and a reduced dose or avoidance of IV contrast administration should be considered at the discretion of the radiologist. Charts are present at each scanner that list the appropriate dose for patients with renal dysfunction, based on the patient's weight. Situations in which a reduced dose of IV contrast should be considered include:

1. If the eGFR is 30-60,
2. If the eGFR is 60 or above, but has deteriorated,
3. If the eGFR is 60 or above, but the patient has a combination of risk factors for

CIN that puts the patient at higher than average risk.

IV contrast material should be avoided, at the discretion of the radiologist:

1. If the eGFR is 30 or below and the patient is not on dialysis,
2. If the eGFR is 30-60, but has deteriorated,
3. If the eGFR is 30-60, but the patient has a combination of risk factors for CIN that puts the patient at higher than average risk.

Under some acute situations for patients with elevated creatinine and reduced eGFR, Iodinated IV contrast material may be administered. For additional detail, please also refer to the UAB Interdisciplinary Standard: IV Contrast Use in Radiology.

Strategies in Patients at Risk for Allergic Reactions to IV Contrast for CT

A comprehensive discussion of adverse reactions to Iodinated contrast media is beyond the scope of this document. The most recent recommendations for preparation prior to IV contrast injection for patients at risk for allergic reactions are in the appendix below. Studies have demonstrated that premedication is probably not effective unless steroids have been administered at least 12 hours prior to contrast injection.

The following are general guidelines for patients at risk for adverse reactions to Iodinated IV contrast media:

1. No special preparation or precautions are required for patients with an isolated allergy to shellfish,
2. Premedication is recommended for patient with atopic syndrome (a combination of allergic hypersensitivities),
3. Premedication is recommended for patients with a history of minor adverse or allergic reaction to prior administration of IV contrast media,
4. Premedication may be recommended at the discretion of the referring physician or responsible radiologist in patients with a prior history of minor adverse or allergic reaction to administration of IV contrast media, but not during the most recent administration,
5. If the patient has had a prior severe reaction to Iodinated IV contrast media (e.g. difficulty breathing, hypotension, respiratory or cardiac arrest, etc.), avoiding the use of IV contrast should be strongly considered. However, if IV contrast is strongly indicated, the patient should be premedicated.

Recommended Reading

1. Special Issue: Nephrogenic Systemic Fibrosis. JACR 2008; 5:21-56
2. Sadowski et al. Nephrogenic Systemic Fibrosis: risk factors and incidence estimation. Radiology 2007; 243:148-157.
3. Deo et al. Nephrogenic Systemic Fibrosis: A population study examining the relationship of disease development to gadolinium exposure. Clin J Am Soc Nephrol 2007; 2:264-267.
4. Murphy KJ. Adverse Reactions to Gadolinium: a review of 36 cases. AJR 1996; 167:847-849
5. Thomsen HS. Guidelines for Contrast Media from the European Society of Urogenital Radiology. AJR 2003; 181:1463–1471.
6. Lasser EC, Berry CC, Talner LB, et al. Pretreatment with corticosteroids to alleviate reactions to intravenous contrast material. NEJM 1987; 317:845-849.

Policy approved by:

Franklin Tessler, M.D.
Chief, Body Imaging

Date

Reginald Munden, D.M.D., M.D.
Chairman, Department of Radiology

Date

Version, Revised: July 14, 2009

Appendix: Premedication to Minimize Contrast Reactions

<u>PREMEDICATION FOR CONTRAST REACTIONS</u>	
Circumstance	Protocol
<i>Routine Option A</i> (PO <u>OR</u> IM route)	<ul style="list-style-type: none"> •Prednisone (Deltasone) 50 mg PO – 13, 7, & 1 hr before exam •Diphenhydramine (Benadryl) 50 mg PO/IM night before & 1 hr before •Use low osmolar nonionic contrast medium
<i>Routine Option B</i> (PO route)	<ul style="list-style-type: none"> •Methylprednisilone (Medrol) 32 mg PO – 12 & 2 hrs before exam •Use low osmolar nonionic contrast medium
<i>NPO Patients</i> <i>IV <u>OR</u> IM routes</i>	<ul style="list-style-type: none"> •H₁ blocker: Diphenhydramine (Benadryl) 25-50 mg IM/IV night before & on call •H₂ blocker: Ranitidine (Zantac) 50mg IM/IV night before & on call •Methylprednisilone (Solu-Medrol) 100 mg IV 13 & 7 hours before exam and on call
<i>Emergency</i> (IV <u>OR</u> IM routes)	<ul style="list-style-type: none"> •H₁ blocker: Diphenhydramine (Benadryl) 50 mg IM/IV STAT •H₂ blocker: Ranitidine (Zantac) 50 mg IM/IV STAT •Methylprednisilone (Solu-Medrol) 100 mg IV STAT •Ordering clinician/team responsible for patient outcome