

CMR Safety: *Magnetic Fields, Devices, Contrast*

Carlos El-Tallawi, MD
Houston Methodist DeBakey Heart & Vascular Center

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VASCULAR CENTER

Lecture Overview

- Advanced MRI Safety
- Implants & Devices Safety
- Contrast Safety



Advanced MR Safety

Electromagnetic Effects

- Static field effects
- Gradient field effects
- Radiofrequency effects

Electromagnetic Effects

- Static field effects
- Gradient field effects
- Radiofrequency effects

Like a planet, only stronger

Magnetic field strength in teslas (T)

Earth's magnetic field



45 μ T

Standard MRI machine



1,5T

33,000 x
Earth's magnetic field

Modern MRI machine



3T

66,000 x
Earth's magnetic field

Research MRI machine

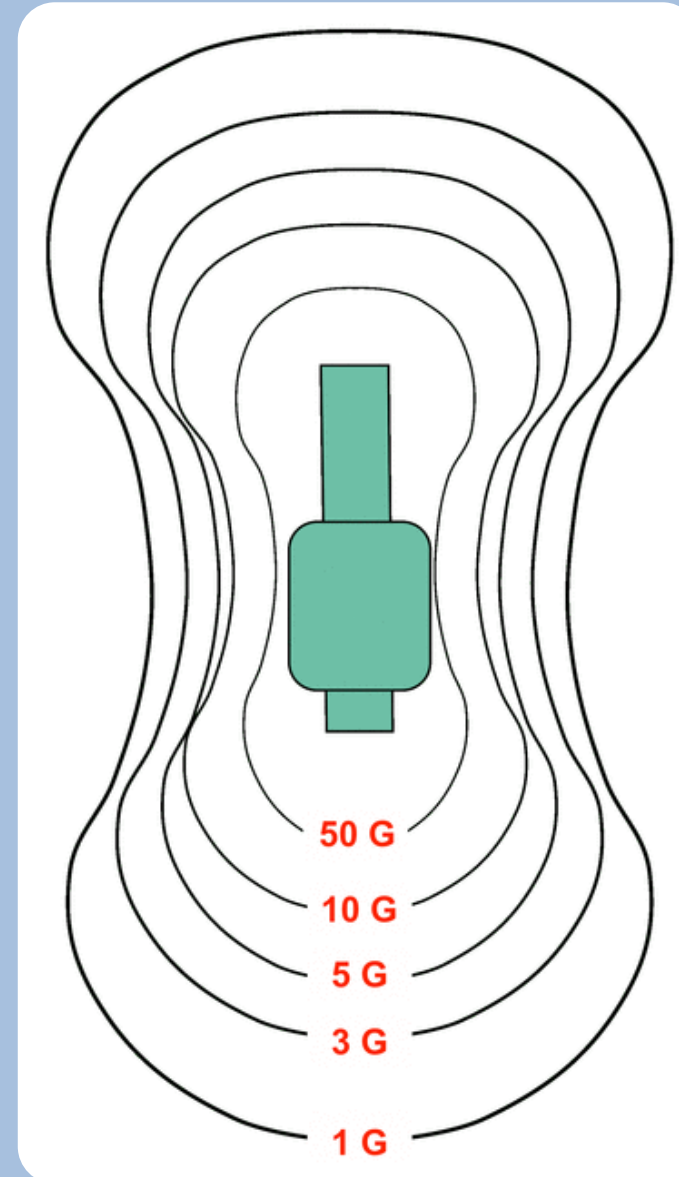
7T

150,000 x
Earth's magnetic field



Static Fields

- Missile injuries/fatalities
- Implants/devices
- Biological effects

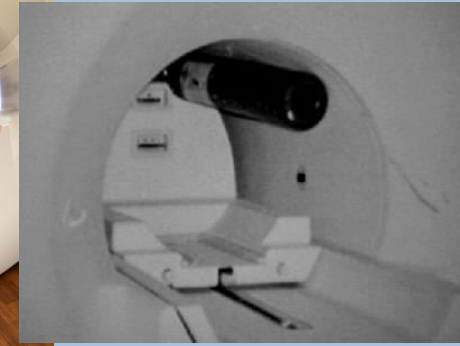


Static Fields: Missile Injuries/Fatalities



<https://www.youtube.com/watch?v=MMP8gt4nZ6I>

- Factors:
 - Metal Type
 - Object Size
 - Magnetism



Employees of the Westchester Medical Center in Valhalla, N.Y., gather outside after learning of the deadly MRI incident. (ABCNEWS.com)

Hospital Nightmare Boy, 6, Killed in Freak MRI Accident

July 31 — A 6-year-old boy died after undergoing an MRI exam at a New York-area hospital when the machine's powerful magnetic field jerked a metal oxygen tank across the room, crushing the child's head.

- Common Objects:
 - Wheelchair
 - IV Poles
 - Oxygen Tanks
 - Hospital Beds
 - Scissors
 - Pens
 - Bras
- Special MR safe items usually labeled

Static Fields: Biologic Effects

- Headaches
- Vertigo
- Metallic Taste
- Nausea



33-year-old male volunteer in a 7 Tesla magnet

Static Field: Safety Measures

- Trained individuals

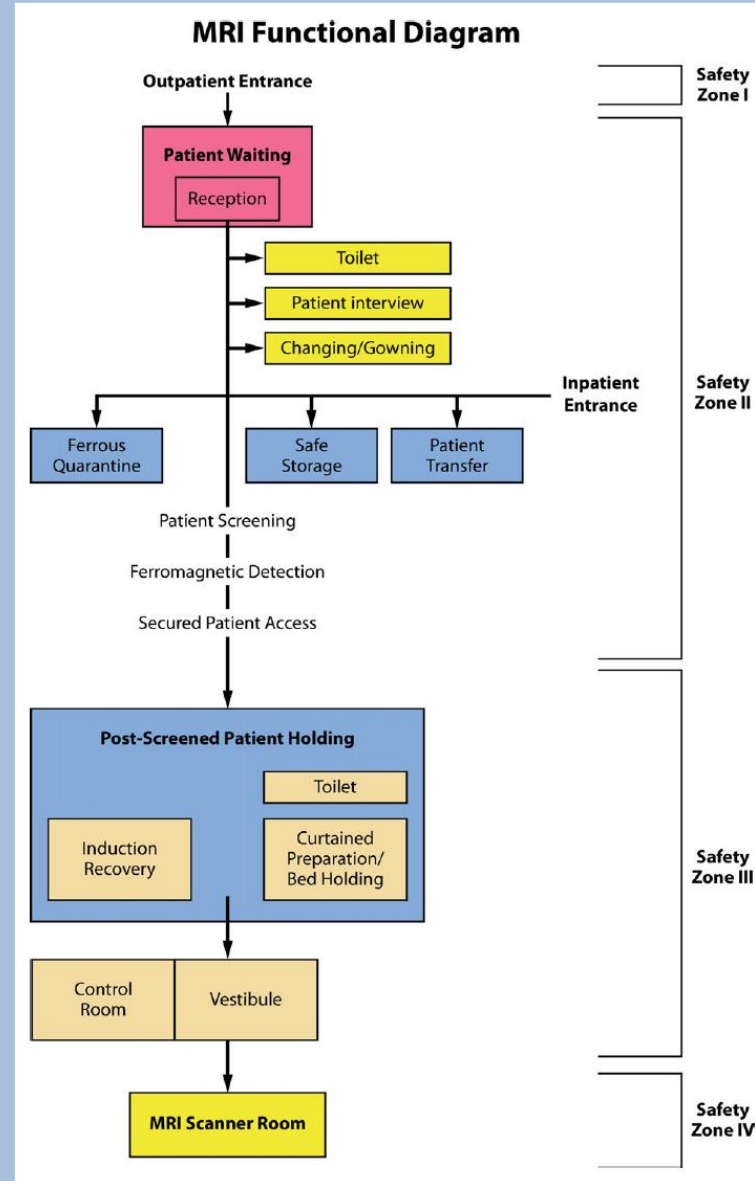
- Specialized doors

- Danger signs



- Ferromagnetic Detection Systems

- Zones

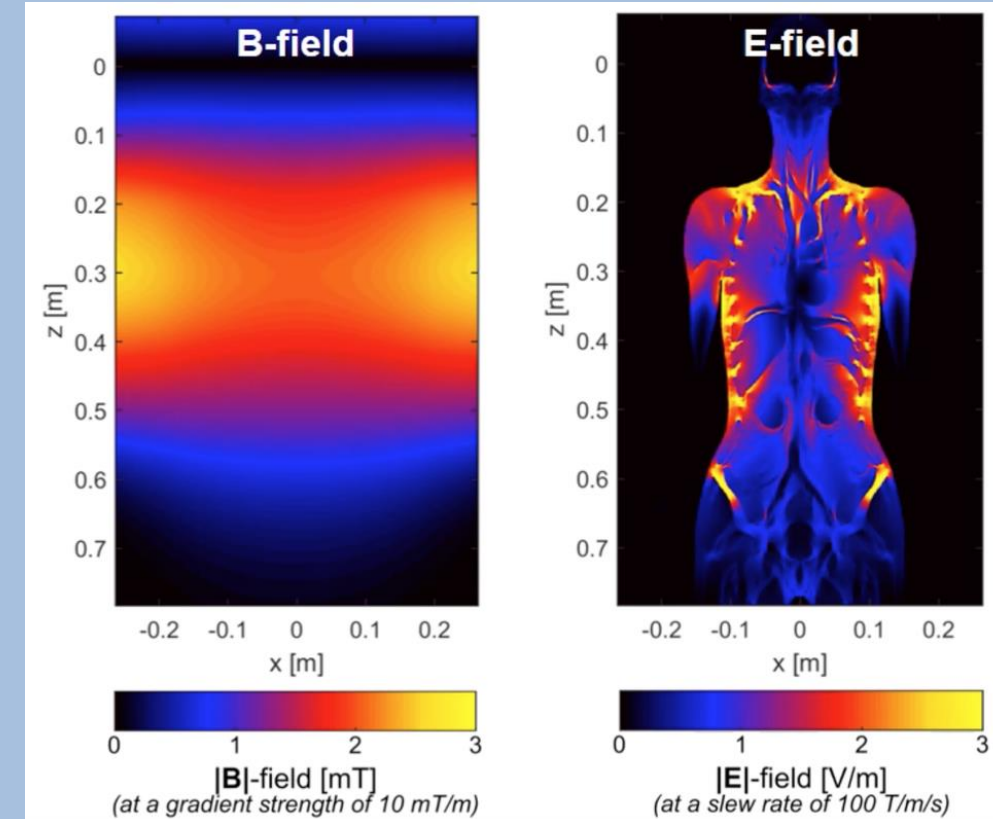


Electromagnetic Effects

- Static field effects
- Gradient field effects
- Radiofrequency effects

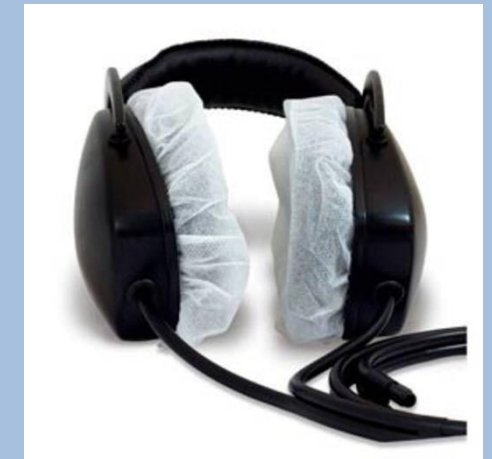
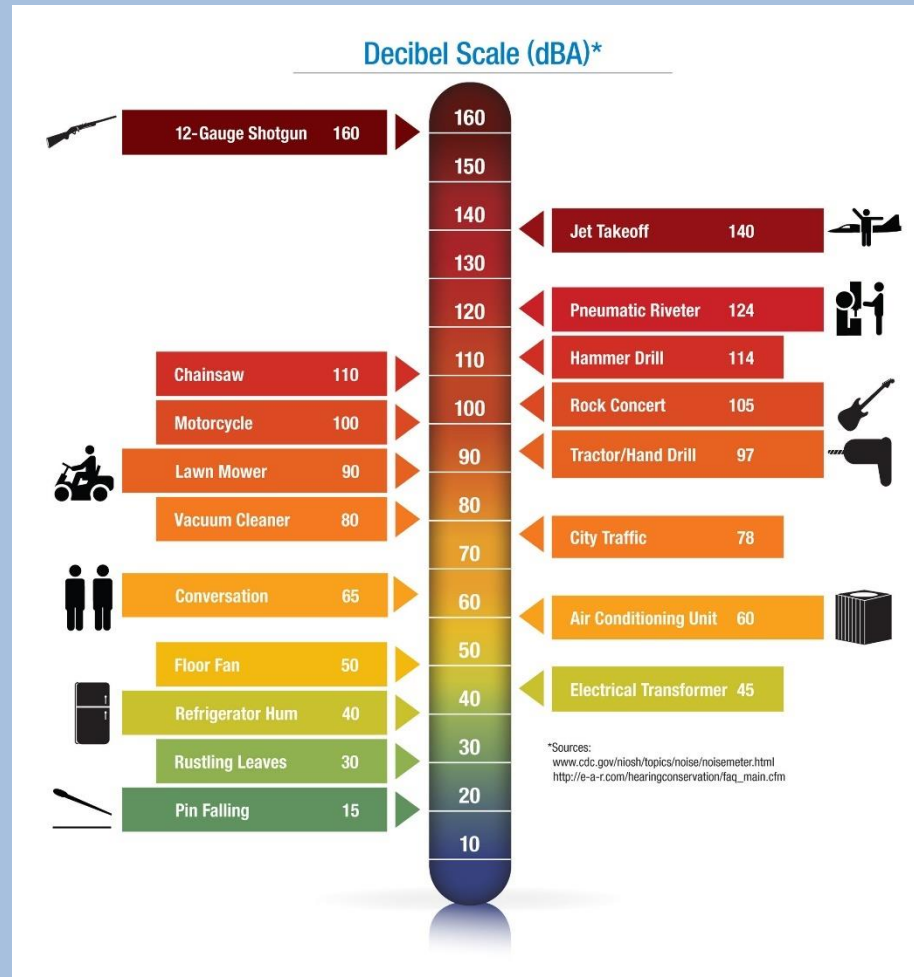
Gradient Field Effects: Peripheral Nerve Stimulation

- PNS Depends on:
 - Peak gradient amplitude
 - Current density
 - Duration of induced voltage
 - Gradient field orientation
 - Body size
 - Tissue sensitivity
 - Other factors
- Symptoms
 - Tingling sensation
 - Muscle twitching
 - Can cause pain



Gradient Field Effects: Acoustic Noise

- MRI >130 dB
- Factors
 - Field strength
 - Pulse sequence
 - Imaging parameters
 - Physical features of scanner & environment



Electromagnetic Effects

- Static field effects
- Gradient field effects
- Radiofrequency effects

Radiofrequency (RF) Fields

TABLE 1: International Electrotechnical Commission Standards for MRI [2]

| Operating Mode | Whole-Body SAR (W/kg) | Head SAR (W/kg) | Maximum Rise of Core Temperature (°C) |
|--|-----------------------|-----------------|---------------------------------------|
| Normal | 2 | 3.2 | 0.5 |
| First-level controlled (medical supervision) | 4 | 3.2 | 1 |

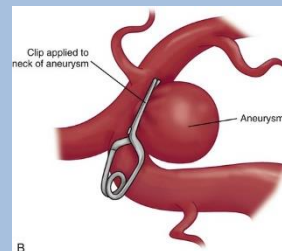
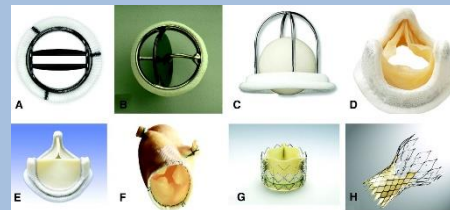
Note—SAR = specific absorption rate.

- Radiofrequency:
 - Goal to excite protons
 - Energy absorbed by tissues
 - Local & whole-body heating
- Specific Absorption Rate (SAR) is the RF power absorbed per unit mass of tissue (W/kg)
- Complex function of numerous variables (calculated by scanner software)
- Dependent on body mass → accurate patient weight is vital.
- The MRI scanner will restrict SAR dependent on scanning mode.
- SAR increases 9-fold from 0.5T to 1.5T.

Implants & Device Safety

Implant & Device Safety: Screening

- EVERYONE needs to be screened
- Written & verbal



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Radiology-MRI Department

MRI Safety Questionnaire Form

MRI Departmental Form / Revised 02-2015

01. Do you have any of the following:

| | | | |
|---------------------------------|-------------|---|-------------|
| HEART PACEMAKER / DEFIBRILLATOR | Y ___ N ___ | METAL INJURY TO EYE(S) / BODY | Y ___ N ___ |
| DEEP BRAIN STIMULATOR | Y ___ N ___ | COCHLEAR (INNER EAR) IMPLANTS | Y ___ N ___ |
| SPINAL CORD STIMULATOR | Y ___ N ___ | TISSUE EXPANDER | Y ___ N ___ |
| VAGAL NERVE/ BLADDER STIMULATOR | Y ___ N ___ | PILLCAM (Endoscopic camera pill w/in 30 days) | Y ___ N ___ |

STOP IF you have selected YES to any of the questions above. Please inform MRI personnel IMMEDIATELY

02. Pregnant or suspect pregnancy? Y ___ N ___

03. Date of last menstrual cycle: _____

04. Do you have any of the following:

| | | | |
|--|-------------|---|-------------|
| Brain Aneurysm Clips (documentation required) | Y ___ N ___ | Coil, Filter, Stents | Y ___ N ___ |
| Shunt (programmable?) | Y ___ N ___ | Implanted Pump (insulin, baclofen, chemo) | Y ___ N ___ |
| Appointment with MD to reprogram programmable shunt or implanted Pump? | Y ___ N ___ | Electronic / Mechanical Implant | Y ___ N ___ |
| Eyelid Spring | Y ___ N ___ | Bone Stimulator | Y ___ N ___ |
| Artificial Eyes | Y ___ N ___ | Shrapnel, Bullet, BB | Y ___ N ___ |
| Ear Implant | Y ___ N ___ | Implants Held by Magnets | Y ___ N ___ |
| Hearing Aids | Y ___ N ___ | Miscellaneous Implant(s) | Y ___ N ___ |
| Removable Dentures / Partial Plates | Y ___ N ___ | Tattoos / Tattooed Eyeliner | Y ___ N ___ |
| Internal Electrodes or Wires | Y ___ N ___ | Body Piercing | Y ___ N ___ |
| Artificial Limbs / Joints (prosthesis) | Y ___ N ___ | Radiation Seeds | Y ___ N ___ |
| Halo Vest / Spinal Fixation Device | Y ___ N ___ | Medication Patch | Y ___ N ___ |
| Surgical Clips or Skin Staples | Y ___ N ___ | Penile Implant | Y ___ N ___ |
| Implanted Items (pins, screws, rods, etc) | Y ___ N ___ | | |

05. In your own words, what made your doctor order this MRI today? _____

06. Have you ever had a surgical operation or procedure? Y ___ N ___ If yes, list surgeries: _____

07. (a) Have you had an MRI examination before? Y ___ N ___
(b) Did you experience any problems? Y ___ N ___ If Yes, please explain: _____

08. What is your approximate weight _____ lbs _____ Kilos

Patient Signature _____ Date _____

Parent / Guardian Signature _____ Relationship _____ Date _____

FOR MRI OFFICE USE ONLY

MRI Safety Qualified Representative Signature
Preliminary Review - Level 1 or 2 Personnel

MRI Safety Qualified Representative Signature
Final Review - Level 2 Only

☐ Phone Assessment ☐ Phone number _____
☐ Date _____ ☐ RT Initials _____

ADHERE
PATIENT LABEL
WITHIN THIS
AREA

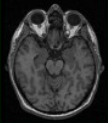
Implant & Device Safety Website

***MRI**SAFETY.COM*


YOUR INFORMATION RESOURCE FOR MRI SAFETY, BIOEFFECTS, & PATIENT MANAGEMENT

The Development of this site was
supported by an Unrestricted
Educational Grant From





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MRI
SAFETY.COM

Search THE LIST. All parameters below are optional. Click Search button.

Keywords and/or Object Name and/or Manufacturer Name

Select ALL (default) means search results will contain "ALL" words you type above. Selecting ANY returns records having "ANY" words above. (more recs returned)

Result Status ☐ Safe ☐ Unsafe 1 ☐ Unsafe 2 ☐ Conditional 1 ☐ Conditional 2 ☐ Conditional 3 ☐ Conditional 4 ☐ Conditional 5 ☐ Conditional 6 ☐ Conditional 7 ☐ Conditional 8

Object Category

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Records: 4584 [Click Here for Search HELP](#)

Per page: First Prev 1 2 3 4 5 6 7 8 9 10 of 153 [Next](#) [Last](#)

| Object | Status | Strength | Reference | Safety Info |
|---|----------------------------------|----------|-----------|--|
| Regulator and Aluminum Cylinder System AirTOTE MTS-303 Western Scott Fetzer, Inc. Westlake, OH | Conditional 7 | 3 | | Miscellaneous Implants and Devices |
| Tita Jet Light Arterial II Vascular Access Port Clinical Plastic Products SA La Chaux-de-Fonds, Switzerland | Conditional 6 | 3 | | Vascular Access Ports, Infusion Pumps*, Catheters, and Accessories |
| 11" Microfiber Flexi Frame, FGQ85500BK00 Rubbermaid, www.rubbermaidhealthcare.com | Safe | 1.5,3 | | Miscellaneous Implants and Devices |
| 18" Quick Connect Wet/Dry Frame, FGQ56000YL00 Rubbermaid, www.rubbermaidhealthcare.com | Conditional 7 | 3 | | Miscellaneous Implants and Devices |
| 2D Helical, 35 Fibered Platinum Coil. Boston Scientific, www.bostonscientific.com | Conditional 5 | 1.5, 3 | | Coils, Filters, Stents, and Grafts |
| 3/4" Socket Wrench 2 1/2" x 1 1/2" x 1 1/2" | Conditional 7 | 3 | | Miscellaneous Implants and Devices |

Implant & Device Safety: MRI Item Labeling

Understanding MRI Safety Labeling

The MR environment has unique safety hazards for patients with implants, external devices and accessory medical devices. Implants, medical devices and other equipment used in or near the MR environment should be labeled as **MR Unsafe**, **MR Conditional**, or **MR Safe**.

MR Unsafe items should not enter the MRI scanner room. Patients with MR Unsafe devices should not be scanned.

MR Conditional items may safely enter the MRI scanner room only under the very specific conditions provided in the labeling. Patients should not be scanned unless the device can be positively identified as MR Conditional AND the conditions for safe use are met.

The conditions for safe use will be different based on the intended use of the device.

For **items intended to enter the bore of the MRI system**, the MRI Safety labeling should be matched with the MRI system for:

- Static field strength
- Maximum spatial field gradient
- dB/dt limitations (usually only applicable to active implants)
- SAR limits
- Any other conditions needed for safe use of the device, for example restrictions on the types of coils that may be used

When present, information about expected temperature rise and artifact extent may inform the risk/benefit decision of whether or not a patient should undergo an MRI examination. Expected temperature rise and artifact extent information are not conditions that must be met.

Items NOT intended to enter the bore of the MRI system usually have gauss line positioning restrictions or requirements to tether or affix the device to an unmovable part of the room.

MR Safe items pose no safety hazards in the MR environment. They may be placed anywhere in the MR environment. Patients with MR Safe devices have no scanning restrictions.

- **MR Unsafe:**
 - Should NOT enter scanner room
- **MR Conditional:**
 - Only under specific conditions
 - Check safety labeling
- **MR Safe:**
 - NO safety hazards, restrictions


Implants & Device Safety: CONDITIONAL

- Know MR **conditions** approved on labeling:
 - Static magnetic field strength
 - Type of transmit RF coil
 - Acceptable whole body/local SAR
 - MRI Conditions
 - maximum spatial field gradient
 - Expected maximum temperature rise
 - Other requirements
 - Patient position, device programming/settings

Implant & Device Safety: Heating → Burns




Implant & Device Safety: Burn Prevention





MRI BURN PREVENTION

Tips for Keeping Patients Safe


Screen patients for implants, devices, and other metallic objects. Assume anything unknown is MR Unsafe.






Screen objects to ensure that anything entering the scan room is MR Conditional or MR Safe. Match conditions on MR Conditional devices with your scanner. All metals, even non-ferromagnetic ones, have the potential to heat up and cause burns.


Have patients change out of street clothes whenever possible.






Position patients to avoid skin-to-skin contact (e.g. no hands on hips, no crossed arms, no crossed legs, etc.).


Always use the manufacturer-provided padding to insulate the patient. Sheets and blankets may be added for patient comfort but are not a substitute for manufacturer-provided padding.









Route cables out of the scanner in a straight line. Don't coil cables or allow them to touch the patient.

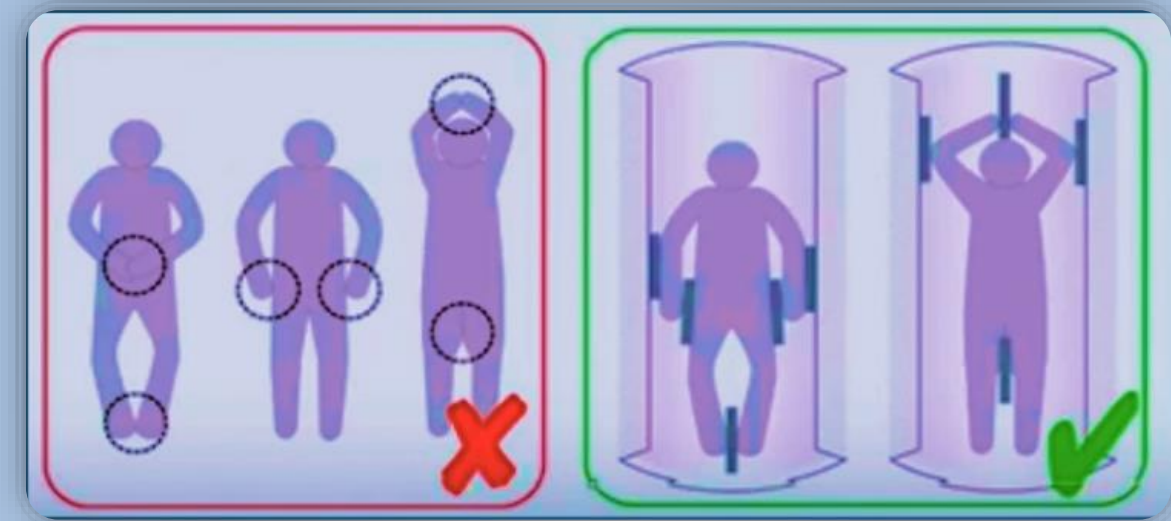
Use only Normal Operating Mode and the lowest SAR, whenever possible.



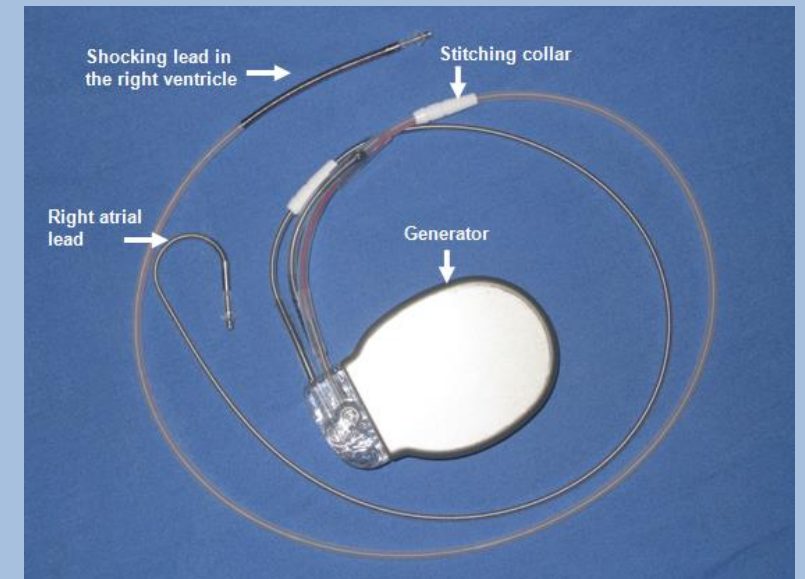
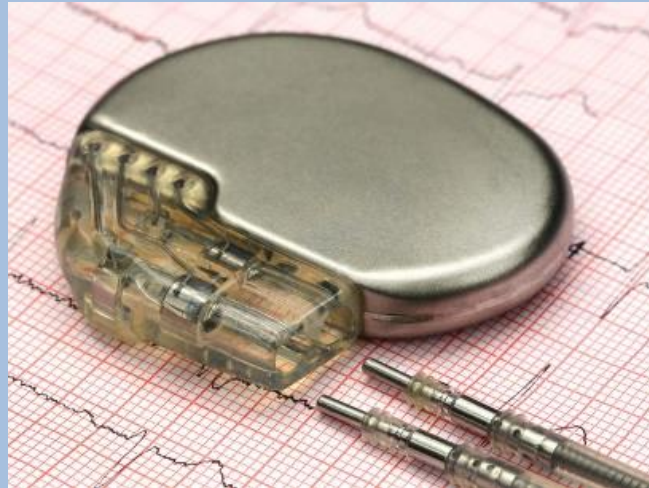


Keep your eyes and ears on the patient at all times. Stay in communication with patients to identify warming. Monitor sedated patients using MR Conditional monitoring equipment.





Implant & Device Safety: Cardiac Devices



Implant & Device Safety: Pacemakers/Defibrillators

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Assessing the Risks Associated with MRI in Patients with a Pacemaker or Defibrillator

Robert J. Russo, M.D., Ph.D., Heather S. Costa, Ph.D., Patricia D. Silva, M.S., Jeffrey L. Anderson, M.D., Aysha Arshad, M.D., Robert W.W. Biederman, M.D., Noel G. Boyle, M.D., Ph.D., Jennifer V. Frabizzio, M.D., Ulrika Birgersdotter-Green, M.D., Steven L. Higgins, M.D., Rachel Lampert, M.D., Christian E. Machado, M.D., Edward T. Martin, M.D., Andrew L. Rivard, M.D., Jason C. Rubenstein, M.D., Raymond H.M. Schaerf, M.D., Jennifer D. Schwartz, M.D., Dipan J. Shah, M.D., Gery F. Tomassoni, M.D., Gail T. Tominaga, M.D., Allison E. Tonkin, M.D., Seth Uretsky, M.D., and Steven D. Wolff, M.D., Ph.D.

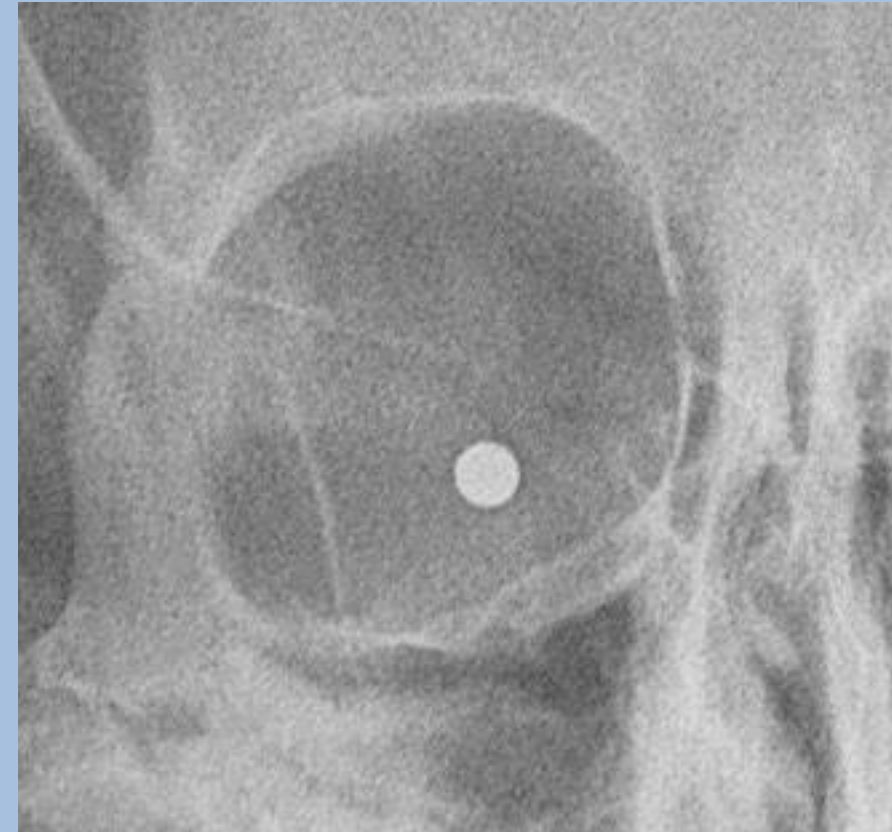
- MRI in 1000 pacemaker and 500 ICD cases
- Device or lead failure did not occur in any patient with a non-MRI-conditional pacemaker or ICD
- Scans were at 1.5 tesla, pts appropriately screened, and devices reprogrammed

N Engl J Med 2017; 376:755-764

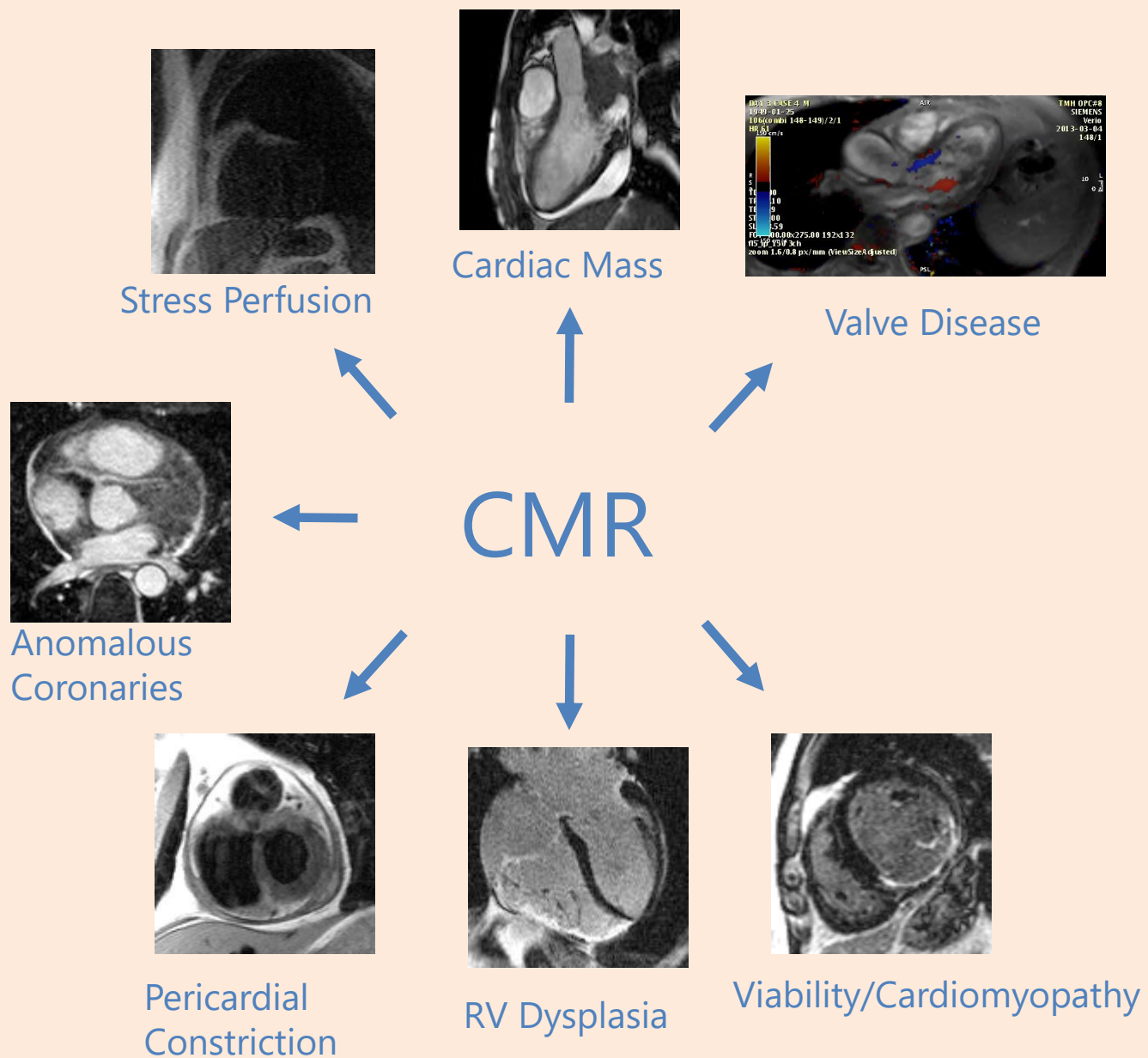
- Setup:
 - Implant >6 weeks prior to scan
 - Only on 1.5T system
 - Onsite cardiologist & device tech
- Modes:
 - NOT dependent: ODO/OVO
 - Dependent: VOO/DOO
- Abort if the following:
 - Abandoned lead/fractures lead
 - Patient discomfort
 - Cardiac stimulation/arrhythmias

Implants & Device Safety: Foreign Bodies

- **Screen all patients**
- *“Have you previously been struck in the eye by a piece of metal (shavings, shrapnel, BB...)?”*
- *“If so, was it removed?”*
- Occupational exposure to metal fragments alone usually not sufficient to warrant additional radiographic workup.
- If reasonable suspicion or patient seems unsure:
 - Review prior head imaging
 - If imaging not available → X-ray
 - Check proximity to vital neurovascular structures



Contrast Safety



RESEARCH

Open Access

2015 Update on Acute Adverse Reactions to Gadolinium based Contrast Agents in Cardiovascular MR. Large Multi-National and Multi-Ethnical Population Experience With 37788 Patients From the EuroCMR Registry



O. Bruder¹, S. Schneider², G. Pilz³, A.C. van Rossum⁴, J. Schwitter⁵, D. Nothnagel⁶, M. Lombardi⁷, S. Buss⁸, A. Wagner⁹, S. Petersen¹⁰, S. Greulich¹², C. Jensen¹, E. Nagel¹¹, U. Sechtem¹² and H. Mahrholdt^{12*}

Abstract

Objectives: Specifically we aim to demonstrate that the results of our earlier safety data hold true in this much larger multi-national and multi-ethnic population.

Background: We sought to re-evaluate the frequency, manifestations, and severity of acute adverse reactions associated with administration of several gadolinium-based contrast agents during routine CMR on a European level.

Methods: Multi-centre, multi-national, and multi-ethnic registry with consecutive enrolment of patients in 57 European centres.

Results: During the current observation 37788 doses of Gadolinium based contrast agent were administered to 37788 patients. The mean dose was 24.7 ml (range 5–80 ml), which is equivalent to 0.123 mmol/kg (range 0.01 - 0.3 mmol/kg). Forty-five acute adverse reactions due to contrast administration occurred (0.12 %). Most reactions were classified as mild (43 of 45) according to the American College of Radiology definition. The most frequent complaints following contrast administration were rashes and hives (15 of 45), followed by nausea (10 of 45) and flushes (10 of 45). The event rate ranged from 0.05 % (linear non-ionic agent gadodiamide) to 0.42 % (linear ionic agent gadobenate dimeglumine). Interestingly, we also found different event rates between the three main indications for CMR ranging from 0.05 % (risk stratification in suspected CAD) to 0.22 % (viability in known CAD).

Conclusions: The current data indicate that the results of the earlier safety data hold true in this much larger multi-national and multi-ethnic population. Thus, the “off-label” use of Gadolinium based contrast in cardiovascular MR should be regarded as safe concerning the frequency, manifestation and severity of acute events.

Keywords: Gadolinium, Safety, Cardiovascular magnetic resonance, “Off-label use”

37788 doses of Gadolinium based contrast agent were administered

Mean dose:

24.7 ml (range 5–80 ml)

0.123 mmol/kg (range 0.01 - 0.3 mmol/kg)

- 45 acute adverse reactions (0.12 %)
- Most classified as mild (43 of 45)

What Strategies Can Be Employed?

- Contrast Agent Selection
- Patient Selection
- Dose Minimization
- Use of non-contrast Imaging Techniques
- Use of non-Gd based MRI Contrast Alternatives

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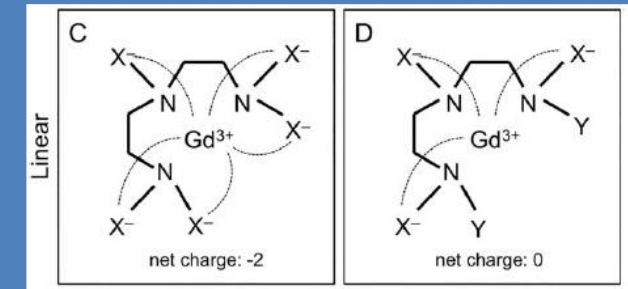
Gd Based Contrast Agents

Group I: Agents **associated with the greatest number of NSF cases:**

Gadodiamide (Omniscan® – GE Healthcare)

Gadopentetate dimeglumine (Magnevist® – Bayer)

Gadoversetamide (OptiMARK® – Guerbet)



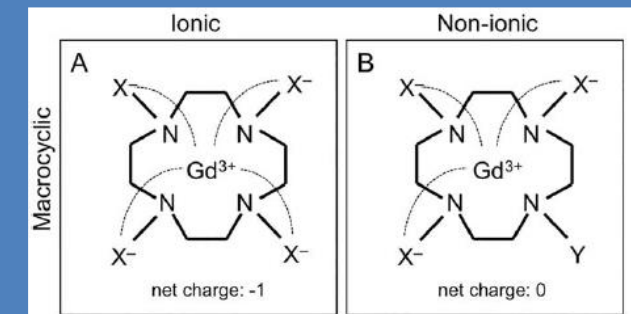
Group II: Agents **associated with few, if any, unconfounded NSF cases:**

Gadobenate dimeglumine (MultiHance® – Bracco Diagnostics)

Gadobutrol (Gadavist® – Bayer)

Gadoterate meglumine (Dotarem® – Guerbet)

Gadoteridol (ProHance® – Bracco Diagnostics)



What Strategies Can Be Employed?

- Contrast Agent Selection
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Patient selection

Vulnerable Populations?

- Pediatric Patients
 - Fetus (pregnancy)
 - Infants
- Comorbidities that might affect biodistribution:
 - Diabetes
 - Renal Insufficiency
 - Osteoporosis
- Patients needing repeated imaging over lifetime
 - E.g., Aortic aneurysm

Special safety: Pregnancy



JAMA | **Original Investigation**

Association Between MRI Exposure During Pregnancy and Fetal and Childhood Outcomes

Joel G. Ray, MD, MSc, FRCPC; Marian J. Vermeulen, BScN, MHSc; Aditya Bharatha, MD, FRCPC;
Walter J. Montanera, MD, FRCPC; Alison L. Park, MSc

CONCLUSIONS AND RELEVANCE Exposure to MRI during the first trimester of pregnancy compared with nonexposure was not associated with increased risk of harm to the fetus or in early childhood. Gadolinium MRI at any time during pregnancy was associated with an increased risk of a broad set of rheumatological, inflammatory, or infiltrative skin conditions and for stillbirth or neonatal death. The study may not have been able to detect rare adverse outcomes.

JAMA. 2016;316(9):952-961. doi:10.1001/jama.2016.12126

Special safety: Pregnancy

TABLE 3. Professional Society Guidelines for GBCA Use in Pregnancy and Lactation

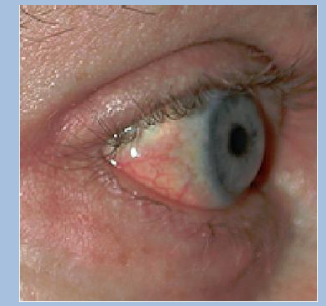
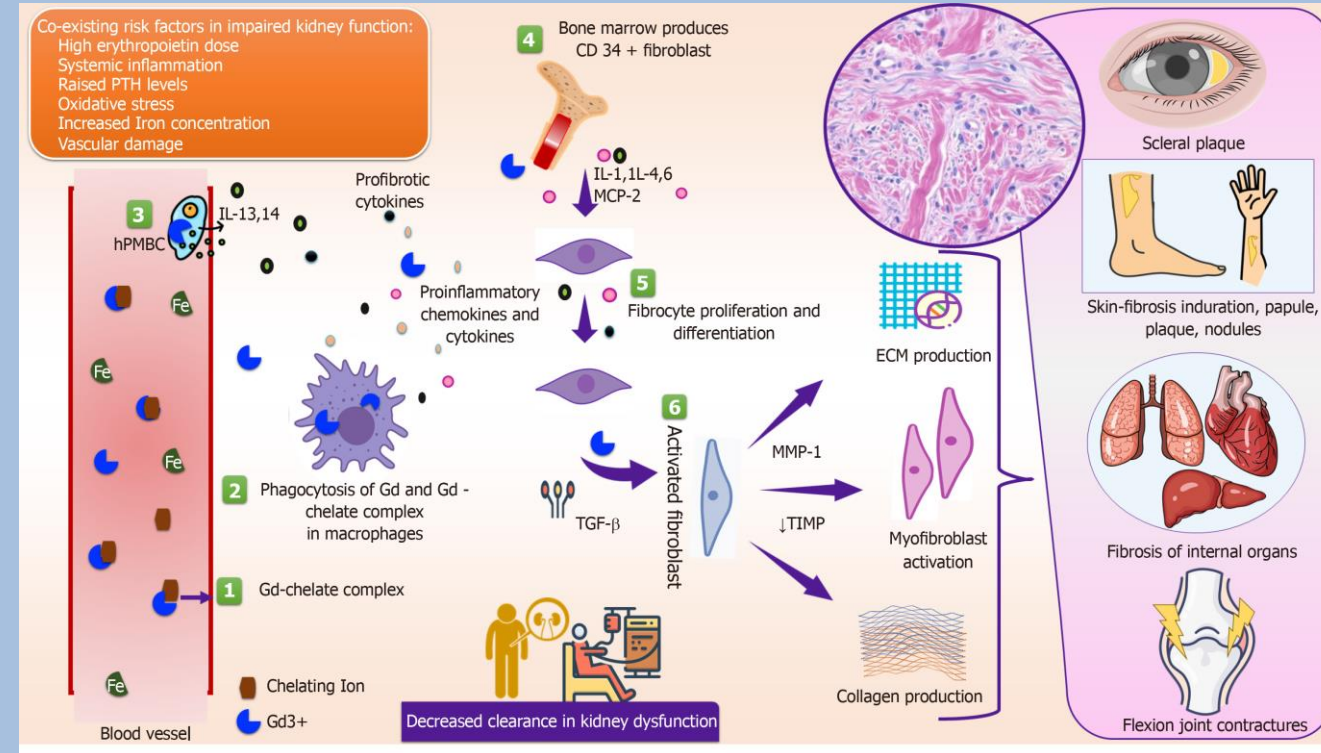
| | GBCAs in pregnancy | GBCAs in lactation |
|----------------------------------|---|---|
| ACR ¹⁰ Year: 2016 | “Each case should be reviewed carefully by members of the clinical and radiology service groups, and a GBCA should be administered only when there is a potential significant benefit to the patient or fetus that outweighs the possible but unknown risk of fetal exposure to free gadolinium ions.” | “Because of the very small percentage of gadolinium-based contrast medium that is excreted into the breast milk and absorbed by the infant’s gut, we believe that the available data suggest that it is safe for the mother and infant to continue breast-feeding after receiving such an agent.” |
| ESUR ⁸ Year: 2015 | “When there is a very strong indication for enhanced MR, the smallest possible dose of one of the most stable gadolinium contrast agents . . . may be given to the pregnant female.” “Following administration of gadolinium-based agents to the mother during pregnancy, no neonatal tests are necessary.” | “Breast feeding should be avoided for 24 hours after contrast medium if high-risk agents are used.” |
| ACOG ⁴³ Year: 2016 | “The use of gadolinium contrast with MRI should be limited; it may be used as a contrast agent in a pregnant woman only if it significantly improves diagnostic performance and is expected to improve fetal or maternal outcome.” | “Breastfeeding should not be interrupted after gadolinium administration.” |

ACOG = American Congress of Obstetricians and Gynecologists; ACR = American College of Radiology; ESUR = European Society of Urogenital Radiology; GBCA = gadolinium-based contrast agent.

Nephrogenic Systemic Fibrosis

Risk Factors:

- History of kidney disease:
 - Dialysis
 - Renal transplant
 - Single kidney
 - Kidney surgery
 - Renal cancer
- Hypertension
- Diabetes mellitus



Assessment of Renal Function Prior to Imaging

TABLE 2. eGFR Evaluation of Renal Function to Group I or Group III GBCA Administration

| Patient Condition | eGFR Requirement |
|---|---|
| Patient on dialysis (any type) | No eGFR required — eGFR is not helpful in this situation. |
| Patient with AKI | No eGFR required — eGFR is not helpful in this situation. |
| Inpatient | Obtain eGFR within 2 days of the MRI study. |
| Outpatient/ED with no prior eGFR at the time the MR exam is scheduled | If NO risk factors [1], no eGFR required. WITH risk factors [1], obtain eGFR.* |
| Outpatient/ED with most recent prior eGFR of 45 or above | If NO risk factor [1] and eGFR of 60 or above, no new eGFR required. WITH risk factors [1] and/or eGFR 45-59, if most recent prior eGFR is within 6 weeks of the MRI, no new eGFR is needed; otherwise obtain a new eGFR.* |
| Outpatient/ED with most recent prior eGFR of 44 or below | Obtain eGFR within 2 days of the MRI study |

Gadolinium and ESRD

Using Highly Concentrated Gadobutrol as an MR Contrast Agent in Patients Also Requiring Hemodialysis: Safety and Dialysability

Bernd Tombach¹
Christoph Bremer¹
Peter Reimer²
Fritz Matzkies³
Roland M. Schaefer³
Wolfgang Ebert⁴
Viviane Geens⁴
Jeffrey Eisele⁴
Walter Heindel¹

OBJECTIVE. The purpose of our study was to assess the safety and dialysability of gadobutrol, a new, electrically neutral, and highly concentrated MR contrast agent, in patients who require hemodialysis.

SUBJECTS AND METHODS. Eleven patients with end-stage renal failure who required ongoing hemodialysis were enrolled in our prospective study. Gadobutrol (1 mol/L) was injected IV at randomly assigned doses of either 0.1 or 0.3 mmol of gadolinium per kilogram of body weight for contrast-enhanced MR imaging. Hematology, clinical chemistry, and vital signs were closely monitored at baseline and during an observation period of 120 hr after the IV injection of gadobutrol. To calculate the dialysability, blood samples were drawn before and after each of three hemodialysis sessions. Additional arterial and venous blood sampling was performed during the first hemodialysis session after 30 and 90 min.

RESULTS. No gadobutrol-related changes in hematology, clinical chemistry, or vital signs were detected at either dose level during the observation period. The mean and the standard deviation for the eliminated fraction of gadobutrol was $68.2\% \pm 12.7\%$ after a 3-hr hemodialysis session using a 1.2 m^2 low-flux polysulfone membrane. After three consecutive hemodialysis sessions, the total amount of gadobutrol eliminated increased to $98.0\% \pm 1.8\%$. The mean clearance rates of gadobutrol were $126.1 \pm 17.8 \text{ mL/min}$ and $126.6 \pm 24.5 \text{ mL/min}$ at 30 and 90 min, respectively.

CONCLUSION. Gadobutrol is effectively removed by three hemodialysis sessions using a low-flux polysulfone membrane. Our study documents initial evidence that gadobutrol can be used safely in hemodialysis patients.

AJR 2002;178:105–109

JAMA Internal Medicine | Original Investigation

Risk of Nephrogenic Systemic Fibrosis in Patients With Stage 4 or 5 Chronic Kidney Disease Receiving a Group II Gadolinium-Based Contrast Agent: A Systematic Review and Meta-analysis

Sean A. Woolen, MD, MS; Prasad R. Shankar, MD; Joel J. Gagnier, ND, MSc, PhD; Mark P. MacEachern, MLIS; Lisa Singer, MD, PhD; Matthew S. Davenport, MD

IMPORTANCE Risk of nephrogenic systemic fibrosis (NSF) to individual patients with stage 4 or 5 chronic kidney disease (CKD; defined as estimated glomerular filtration rate of $<30 \text{ mL/min/1.73 m}^2$) who receive a group II gadolinium-based contrast agent (GBCA) is not well understood or summarized in the literature.

OBJECTIVE To assess the pooled risk of NSF in patients with stage 4 or 5 CKD receiving a group II GBCA.

DATA SOURCES A health sciences informationist searched the Ovid (MEDLINE and MEDLINE Epub Ahead of Print, In-Process & Other Non-Indexed Citation, and Daily and Versions), Embase, Cochrane Central Register of Controlled Trials, Web of Science, and Open Grey databases from inception to January 29, 2019, yielding 2700 citations.

STUDY SELECTION Citations were screened for inclusion in a multistep process. Agreement for final cohort inclusion was determined by 2 blinded screeners using Cohen κ . Inclusion criteria consisted of stage 4 or 5 CKD with or without dialysis, administration of an unconfounded American College of Radiology classification group II GBCA (gadobenate dimeglumine, gadobutrol, gadoterate meglumine, or gadoteridol), and incident NSF as an outcome. Conference abstracts, retracted manuscripts, narrative reviews, editorials, case reports, and manuscripts not reporting total group II GBCA administrations were excluded.

DATA EXTRACTION AND SYNTHESIS Data extraction was performed for all studies by a single investigator, including publication details, study design and time frame, patient characteristics, group II GBCA(s) administered, total exposures for patients with stage 4 or stage 5 CKD, total cases of unconfounded NSF, reason for GBCA administration, follow-up duration, loss to follow-up, basis for NSF screening, and diagnosis.

MAIN OUTCOMES AND MEASURES Pooled incidence of NSF and the associated upper bound of a 2-sided 95% CI (risk estimate) for the pooled data and each of the 4 group II GBCAs.

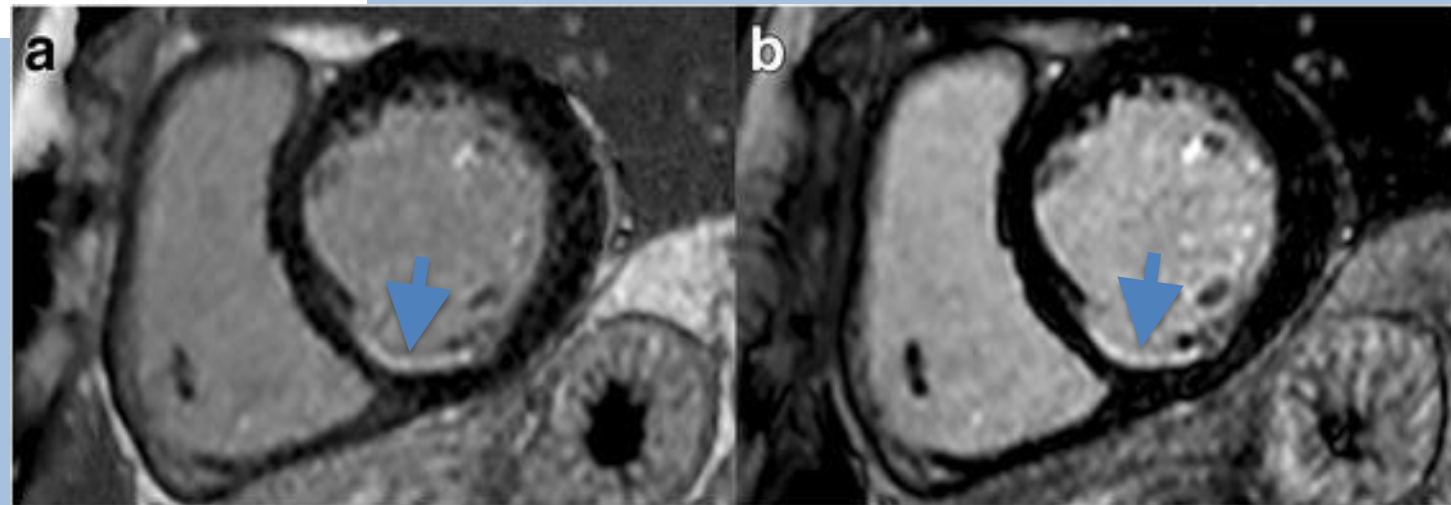
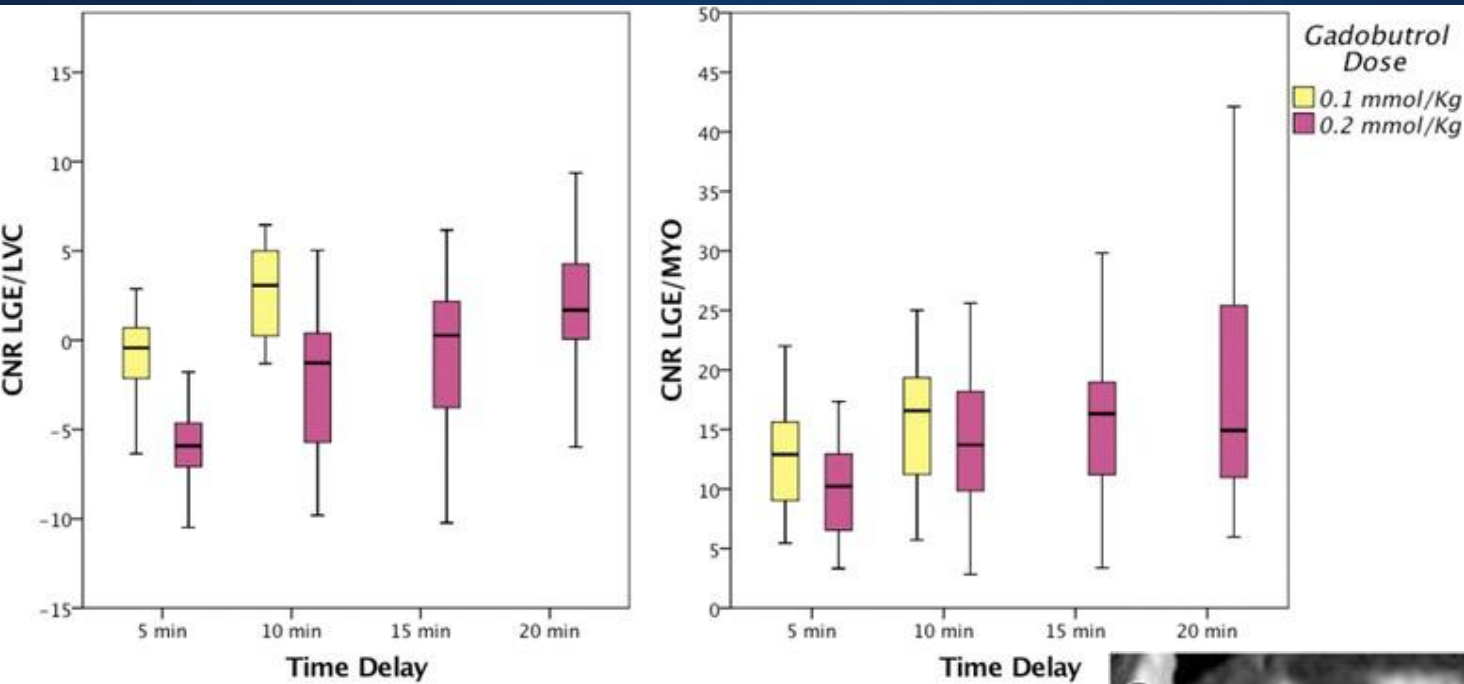
RESULTS Sixteen unique studies with 4931 patients were included ($\kappa = 0.68$) in this systematic review and meta-analysis. The pooled incidence of NSF was 0 of 4931 (0%; upper bound of 95% CI, 0.07%). The upper bound varied owing to different sample sizes for gadobenate dimeglumine (0 of 3167; upper bound of 95% CI, 0.12%), gadoterate meglumine (0 of 1204; upper bound of 95% CI, 0.31%), gadobutrol (0 of 330; upper bound of 95% CI, 1.11%), and gadoteridol (0 of 230; upper bound of 95% CI, 1.59%).

CONCLUSIONS AND RELEVANCE This study's findings suggest that the risk of NSF from group II GBCA administration in stage 4 or 5 CKD is likely less than 0.07%. The potential diagnostic harms of withholding group II GBCA for indicated examinations may outweigh the risk of NSF in this population.

What Strategies Can Be Employed?

- Contrast Agent Selection
- Patient Selection
- Dose Minimization
- Use of non-contrast Imaging Techniques
- Use of non-Gd based MRI Contrast Alternatives

Contrast Dose Minimization



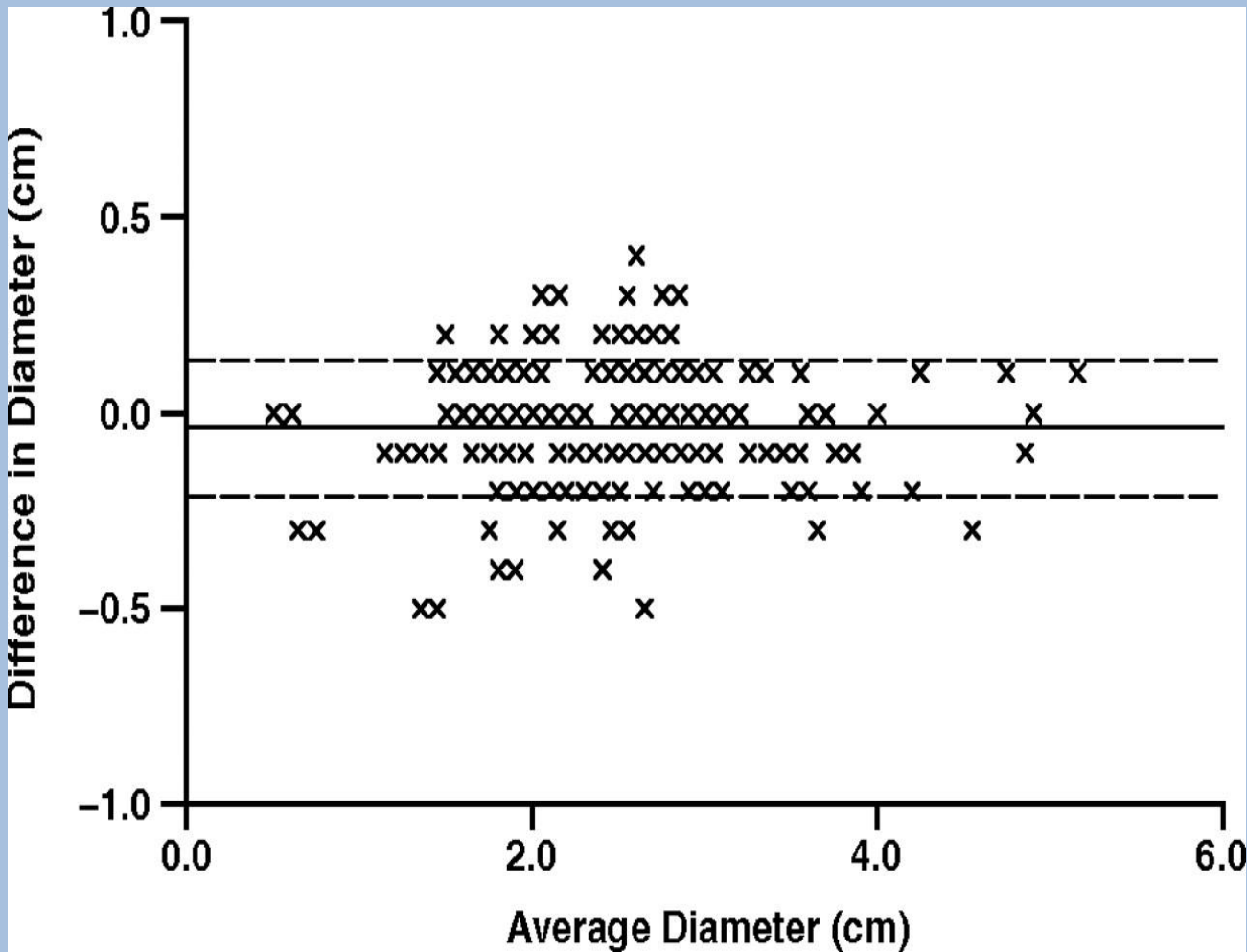
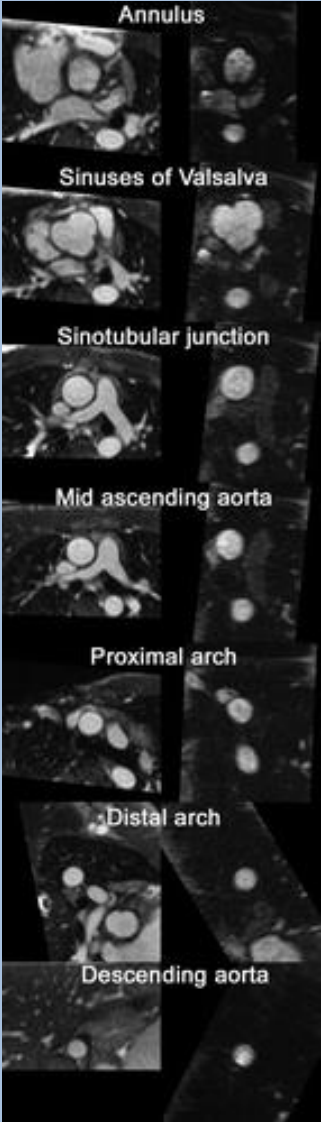
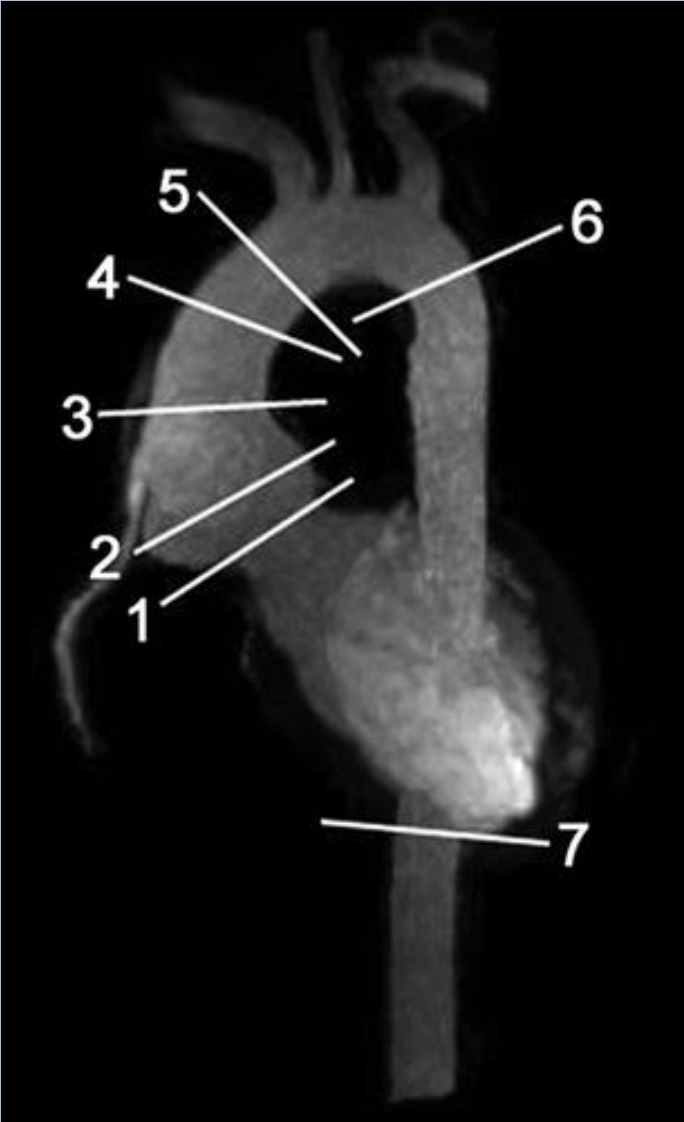
a) 0.1 mmol/kg after 10 min

b) 0.2 mmol/kg after 20 min

What Strategies Can Be Employed?

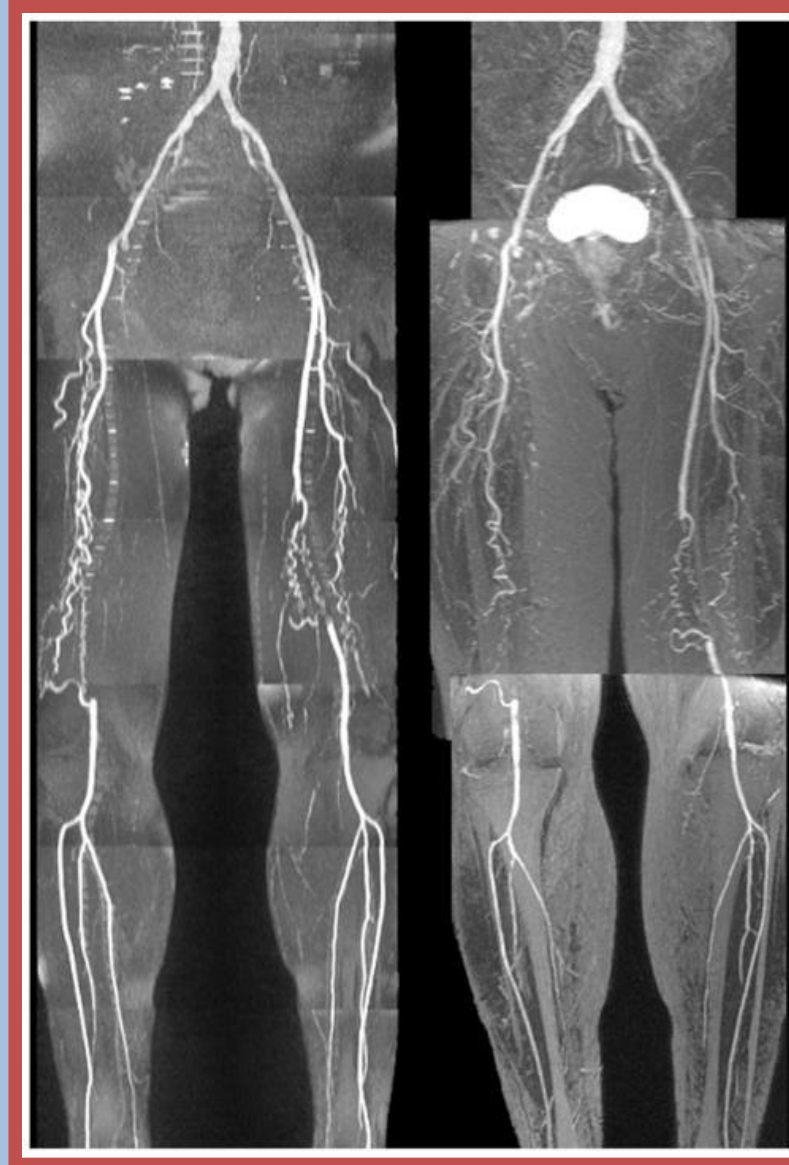
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Non-contrast 3D SSFP Acquisition of Thoracic Aorta



Quiescent-Interval Single-Shot (QISS) Unenhanced MRA

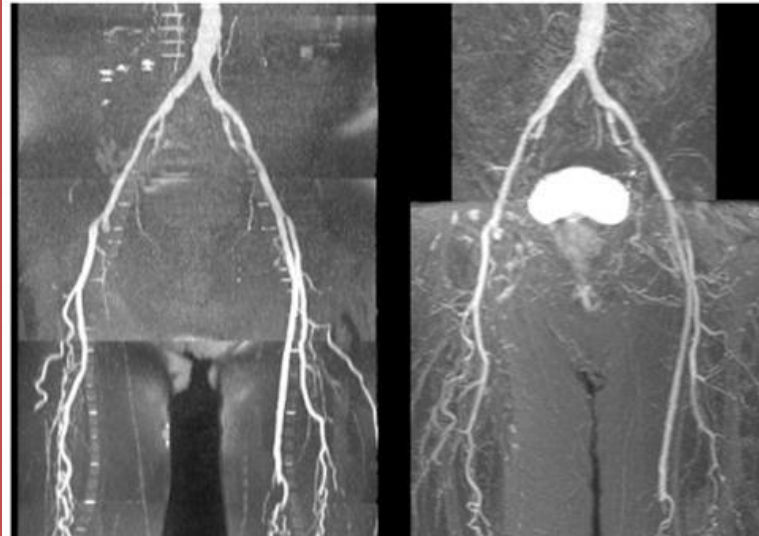
Non-Contrast QISS



Contrast Enhanced

Quiescent-Interval Single-Shot (QISS) Unenhanced MRA

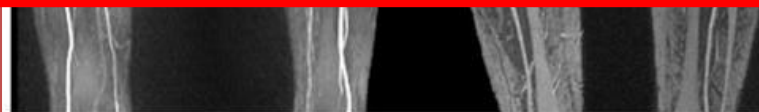
Non-Contrast QISS



Contrast Enhanced

| | Per segment | Per region | Per limb |
|-----------------|------------------|------------------|--------------------|
| Sensitivity (%) | 94.1 (89.8–96.7) | 97.0 (83.3–99.4) | 100.0 (91.6–100.0) |
| Specificity (%) | 97.8 (95.8–98.8) | 96.7 (84.7–99.5) | 100.0 (91.6–100.0) |
| PPV (%) | 95.1 (91.2–98.3) | 97.0 | 100.0 |
| NPV (%) | 97.2 (95.1–98.6) | 96.7 | 100.0 |

Numbers in brackets are 95% confidence intervals. NPV: negative predictive value; PPV: positive predictive value.
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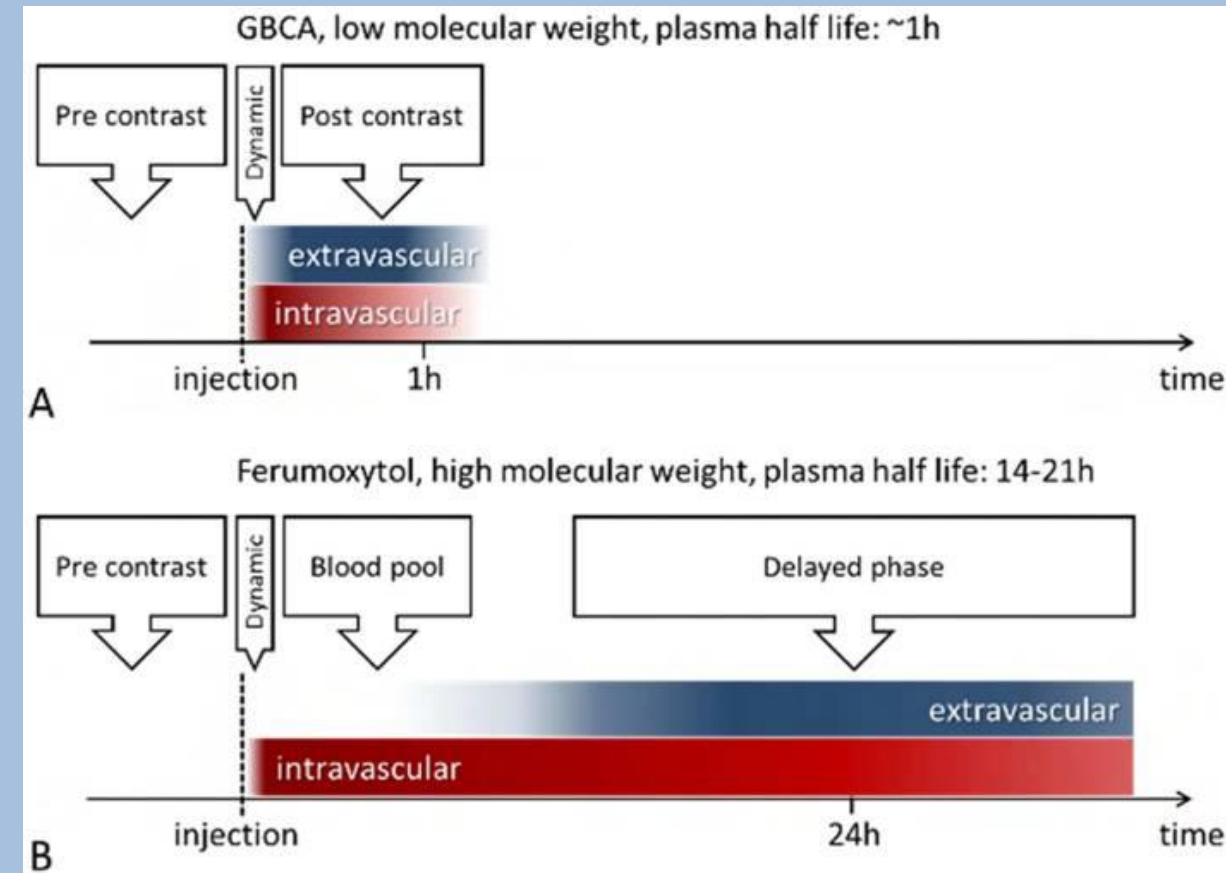
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Ferumoxytol Properties



- IV iron formulation
- Can be used for "off-label" MR imaging of patients with renal failure or allergic to gadolinium
- Ultrasmall (~20 nm) super paramagnetic iron oxide particles which shorten T1 and T2/T2*
- Long intravascular half-life of 14 hours → suitable for MRA
- Later uptake into liver, spleen, bone marrow and lymph nodes



Summary on Optimal Utilization of GBCA

- Contrast agent selection
- Vulnerable patients
 - Very young
 - Renal/Metabolic disorders
 - Need for repeated imaging
- Dose Minimization
- Use of non-contrast Imaging Techniques
- Use of non-Gd based MRI contrast alternatives

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