CORSO DI LAUREA
TECNICHE DI RADIOLOGIA MEDICA, PER IMMAGINI E RADIOTERAPIA

CORSO INTEGRATO
«FISICA E APPARECCHIATURE TC E RM – RMX012»

ANNO ACCADEMICO 2023/2024

Gemelli

UNIVERSITAS CATHOLICA SACRI CORDIS JESV MEDIOLANI

Insegnamento:
APPARECCHIATURE RISONANZA MAGNETICA
RMX054 - 13 ore MED/50 CFU 1

Formazione per l'eccellenza

nov. '23

2° anno I semestre

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1° OSPEDALE IN ITALIA
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Formazione per l'eccellenza

Insegnamento:
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RMX054 - 13 ore MED/50 CFU 1

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Argomenti del Corso

- Introduzione
- Sicurezza in RM
- **Mdc e sicurezza**
- Passato, presente e futuro della RM
- Fenomeno «RM» e principi fisici di base
- Magnete e i vari componenti
- Radiofrequenza e Bobine
- Gradienti
- Generazione di un'immagine RM
- Tecniche di acquisizione – *Parallel Imaging*
- Intelligenza artificiale – *Deep Learning*
- Artefatti
- Esame RM
- Apparecchiature Fondazione

Formazione per l'eccellenza

Insegnamento:
APPARECCHIATURE RISONANZA MAGNETICA
RMX054 - 13 ore MED/50 CFU 1

MRI – MdC e sicurezza

Gemelli

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Conoscenza e libertà

CORSO DI LAUREA
TECNICHE DI RADIOLOGIA MEDICA, PER IMMAGINI E RADIOTERAPIA

ADO RMX102
«Angio-RM in neuroradiologia»

ANNO ACCADEMICO 2023/2024

Gemelli

MEZZI DI CONTRASTO IN RM

Formazione per l'eccellenza

nov. '23

3° anno II semestre

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Perché il MdC?

I mezzi di contrasto per la RM sono usati per migliorare la delineazione dei tessuti patologici.

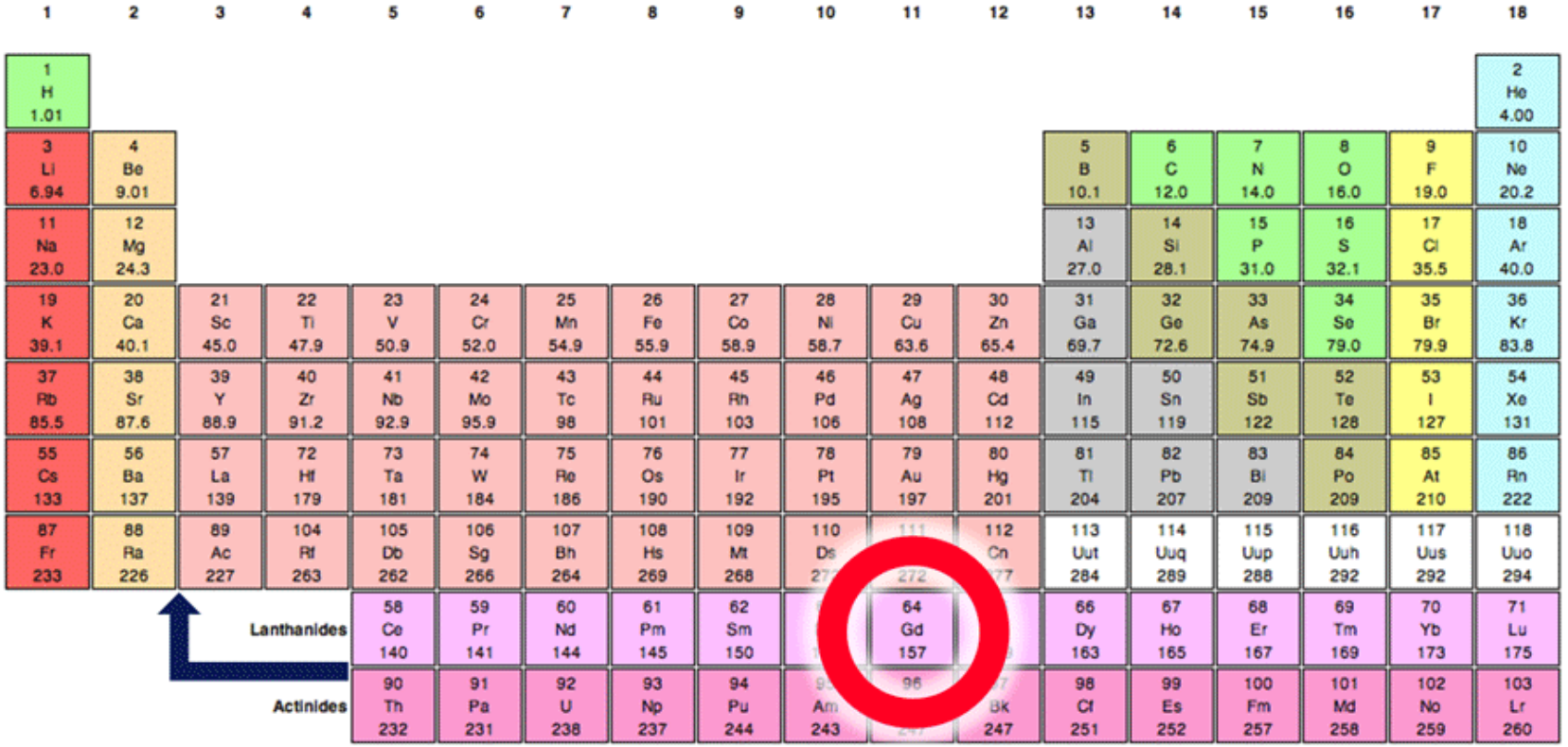
I complessi dell'elemento **gadolinio (Gd)** sono gli agenti di contrasto MR più utilizzati. A causa della sua struttura elettronica unica (descritta di seguito), Gd è **fortemente paramagnetico**. Il paramagnetismo è una proprietà intrinseca di alcuni materiali che si magnetizzano temporaneamente quando vengono posizionati in un campo magnetico esterno. In effetti, Gd è uno dei soli quattro elementi che possono essere magnetizzati a temperatura ambiente (gli altri tre sono il ferro, il nichel e il cobalto).

Le potenti proprietà paramagnetiche di Gd lo rendono estremamente utile come agente di contrasto MR. Il gadolinio non è visibile direttamente in un'immagine RM, ma manifesta indirettamente la sua presenza facilitando il rilassamento dei protoni dell'idrogeno nelle vicinanze. Gd preferibilmente accorcia i valori di T1 nei tessuti in cui si accumula rendendoli **iperintensi** sulle immagini pesate in T1.

Perché il MdC?

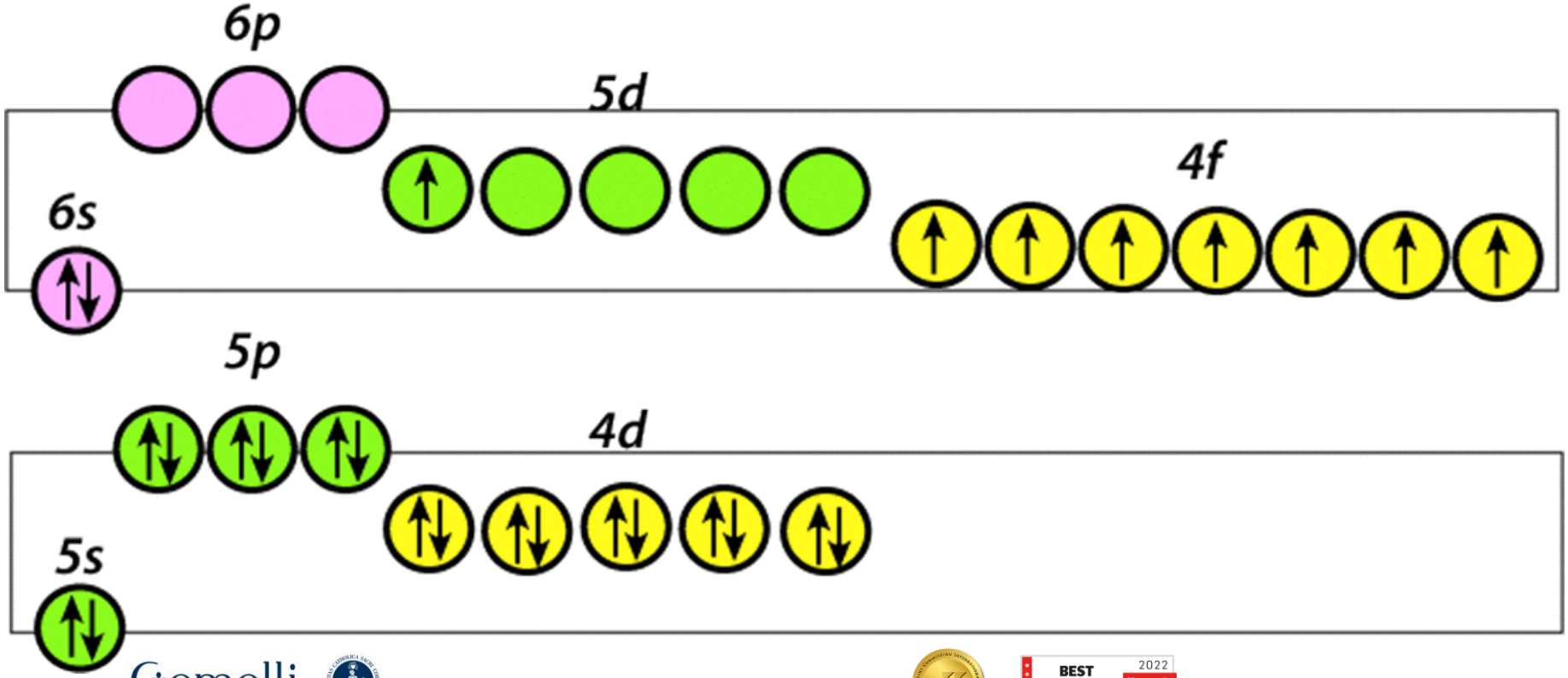
Formazione per l'eccellenza

Gadolinio ha il numero atomico 64 nella tavola periodica. Occupa la posizione centrale nella serie di elementi in lantanide. I lantanidi sono metalli delle terre rare raggruppati chimicamente perché possiedono shells interni di elettroni parzialmente riempiti (subshells 4f e 5d).

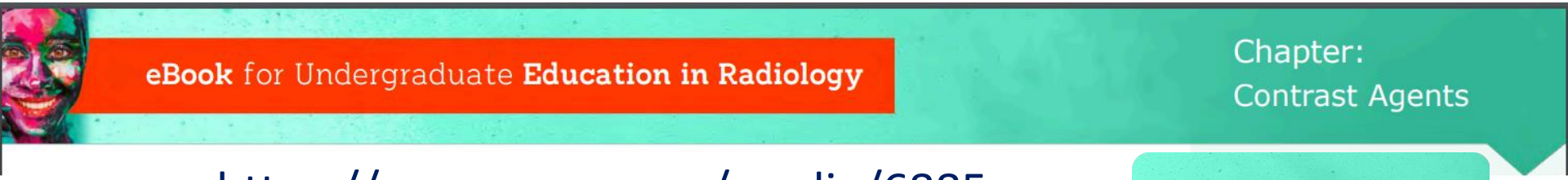


Perché il MdC?

La struttura elettronica dell'atomo Gd neutro è mostrata sotto. Nota i **7 elettroni spaiati** nella sua subshell 4f che spiegano il forte paramagnetismo dell'elemento. Nel suo stato ionizzato, Gd + 3 dona i suoi elettroni $6s^2$ e $5d^1$ per il legame, lasciando intatto il suo shell di elettroni 4f7. Il potente momento magnetico di Gd è quindi ampiamente mantenuto anche quando chelato a un ligando come DTPA in una formulazione di agente di contrasto.



MdC - ESR



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ESR eBook for Undergraduate Education in Radiology – 03 Contrast Agents

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Formazione per l'eccellenza

Magnetic Resonance Contrast Agents

Magnetic resonance imaging (MRI) contrast agents are diagnostic pharmaceutical compounds that affect the **nuclear magnetic resonance signal of the ^{1}H-hydrogen nuclei (protons) of water molecules** contained in the surrounding tissue.

The contrast of an MR image results from a complex interplay of various factors such as proton density, the longitudinal (spin-lattice) relaxation time T_1 and the transverse (spin-spin) relaxation time T_2, and on the applied MRI sequences.

Contrast agents (CAs) used in MRI either consist of **paramagnetic metal ions or of superparamagnetic particles**, and they act to modify T_1 and T_2 of water protons present in the tissue.

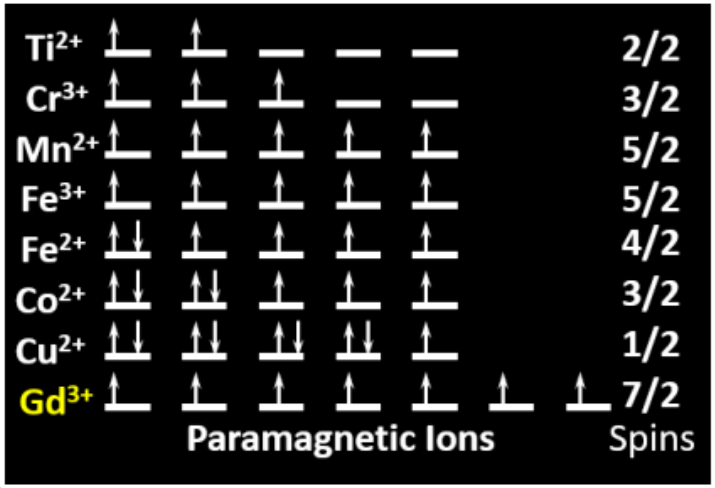


Fig. 22. Single spins (here electrons) are magnetised in the MR and interact with protons thus changing the tissue signal.

CHAPTER
Contrast Agents

Paramagnetic contrast agents

Paramagnetic CAs contain metal ions that have unpaired electrons in their outer shell, which implies a resultant electron spin and a permanent magnetic moment.

The magnetic moment of a tumbling paramagnetic CA molecule induces an additional, time-variable magnetic field in the hydrogen nuclei of the surrounding water molecules, which in turn can increase the rate r_1 of longitudinal spin-lattice relaxation and the rate r_2 of transverse spin-spin relaxation.

The increase in relaxation rate caused by a CA leads to a corresponding shortening of T_1 and T_2 in the region of interest, producing hyperintense signals in T_1-weighted images and hypointense signals in T_2-weighted images.

The effect on T_1 is already evident at low concentrations of the contrast agent, whereas the effect on T_2 becomes increasingly significant at higher concentrations.

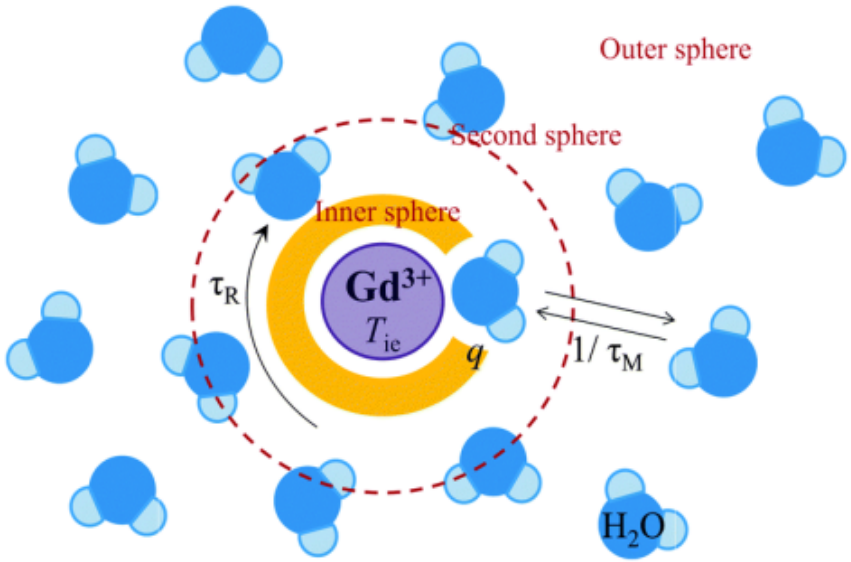


Fig. 23. Gadolinium interacting with the surrounding water protons at different levels. Usually 1-2 water protons get closer to the central atom surrounded by a ligand.

CHAPTER
Contrast Agents

Relaxivity

The efficacy of a MR contrast agent is expressed in terms of relaxivity R, which refers to the ability of the CA to enhance the proton relaxation rate. It is generally measured experimentally in water and is defined as the increase in relaxation time of the solvent (water) induced by 1 mmol L^{-1} of the active ion of the contrast agent:

$$R_1 = 1 / T_1 \text{ (1 Mol, 20°C)}$$

The contrast efficiency is expressed as the r_2/r_1 ratio: the higher the ratio, the greater the relative effect on T_2 and vice versa on T_1.

Manganese-based contrast agents

Manganese-based CAs contain bivalent manganese, a transition metal with five unpaired electrons, which is also naturally present in the body.

Paramagnetic manganese is available either in the form of small molecules or as the more recently developed nanometer sized materials.

Mangafodipir trisodium (Mn-DPDP) is a liver specific CA in which a manganese ion Mn^{2+} is chelated with a dipyridoxyldiphosphate ligand.

Gadolinium-based contrast agents

Gadolinium-based CAs, which contain trivalent gadolinium – a metal from the lanthanide series with seven unpaired electrons – **are the most clinically used CAs in MRI** because of their high magnetic moment and long electronic spin relaxation time.

However, the cytotoxicity of gadolinium in its free ionic form Gd^{3+} makes it necessary to mask the gadolinium by providing **chelating ligands** which form chemically stable complexes.

Administering gadolinium as an inert and stable coordination complex prevents the cellular uptake of free Gd^{3+} and maintains the biodistribution within the extracellular space, thereby enhancing renal filtration and urinary excretion.

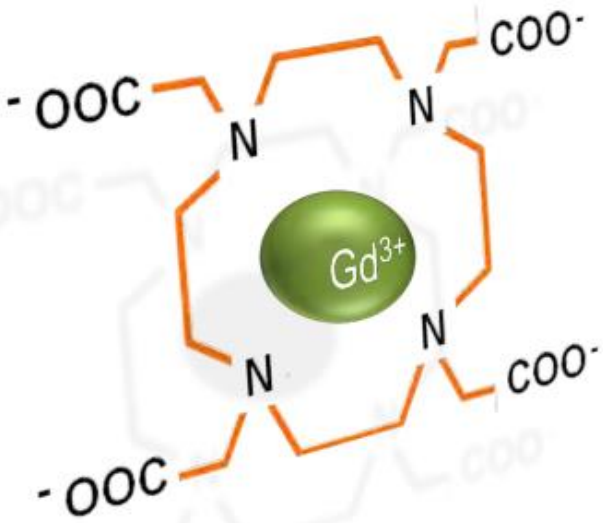


Fig. 24. Macrocyclic gadolinium complex with Gd^{3+} as the central atom bound tightly to a lignd presenting a ring-like structure

Structure of the Gd complexes

The currently available Gd-based contrast agents can be classified into four main categories according to their structure, particularly the nature of the chelating moiety, and to their ionicity.

In **linear complexes**, the gadolinium ion is only partially surrounded by a chain-like structure of the ligand, whereas in **macrocyclic complexes**, the gadolinium ion is enclosed within a cage-like structure formed by the ligand.

Both, the linear and the macrocyclic gadolinium complexes can either be **non-ionic or ionic**. In the ionic gadolinium complexes, the remaining anionic groups are salified with meglumine or sodium cations.

The molecular characteristics of the four classes of gadolinium complexes have a significant impact on some key properties such as **osmolality and viscosity**, but also on their **relaxivity and biodistribution.**

The molecular characteristics are also responsible for the differences between the various gadolinium complexes regarding their **thermodynamic stability constants and kinetic rate constants**.

MdC - ESR

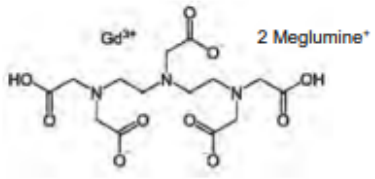
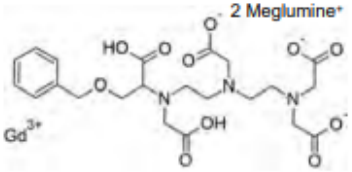
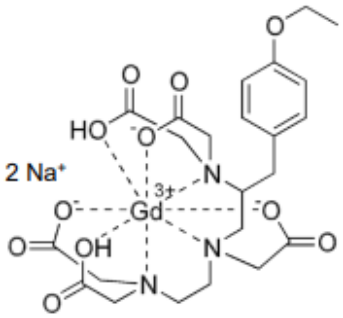
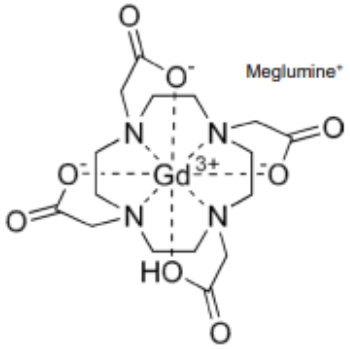
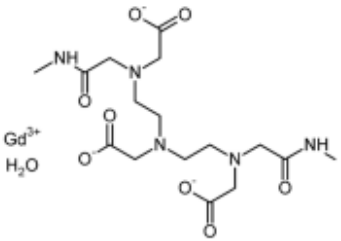
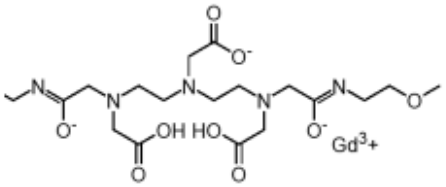
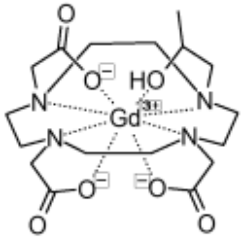
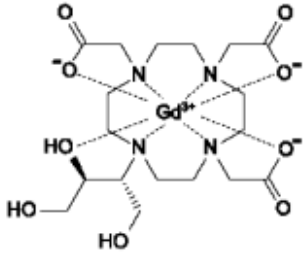
	Linear		Macrocyclic
Ionic	 Gd-DTPA  Gd-BOPTA	 Gd-EOB-DTPA	 Gd-DOTA
Non-ionic	 Gd-DTPA-BMA	 Gd-DTPA-BMEA	 Gd-HP-DO3A  Gd-BT-DO3A

Fig. 25. Classification and structure of Gd-based CAs

Stability of Gd complexes

In solutions of Gd-containing CAs, there is always an equilibrium between complexed gadolinium (Gd-Ligand) and free gadolinium ions (Gd^{3+}):

$$Gd^{3+} + Ligand \leftrightarrow Gd\text{-}Ligand$$

The equilibrium state can be characterized by the thermodynamic stability constant

$$K_{TD} = \frac{[Gd\text{-}Ligand]}{[Gd^{3+}] \cdot [Ligand]}$$

which is often expressed in logarithmic form log K_{TD}. For the Gd complexes used as contrast agents, this equilibrium strongly favors the side of the complexed gadolinium, with log K_{TD} ranging from 16.6 to 25.6.

MdC - ESR

Table 2. Stability of gadolinium complexes

Complexes	Structure	Thermodynamic stability -log K	Kinetic stability at pH 7.4	Dissociation half-life at 25°C, pH 1.0
Gd-DOTA	macrocyclic-ionic	25.6	high	338 hours
Gd-HP-DO3A	macrocyclic-non-ionic	23.8	high	3.9 hours
Gd-BT-DO3A	macrocyclic-non-ionic	21.8	high	43 hours
Gd-BOPTA	inear-ionic	22.6	medium	< 5 sec
Gd-DTPA	linear-ionic	22.1	low	< 5 sec
Gd-DTPA-BMA	linear-non-ionic	16.9	low	< 5 sec
Gd-DTPA-BMEA	linear-non-.ionic	16.6	low	< 5 sec

The thermodynamic stability of Gd complexes decreases with **decreasing pH**, so that in acidic environment the complexes are more prone to decomplexation.

Macrocyclic complexes generally have a **higher** thermodynamic and kinetic stability than linear complexes.

Ionic compounds tend to have a slightly **higher** thermodynamic and kinetic stability than non-ionic compounds.

Transmetallation

Decomplexation of the Gd complexes may result from **reactions with other metal ions that are present in human body fluids.**

In particular, the Gd^{3+} ion in a chelate complex may be replaced by Zn^{2+}, which leads to release of toxic Gd^{3+} ions and to formation of zinc complexes resulting in an undesirable zinc washout via renal elimination.

An important reason for the toxicity of free Gd^{3+} ions is the size similarity and resulting competition with Ca^{2+} ions in cellular and biochemical processes, leading to an inhibition of calcium channels and a blockage of Ca^{2+} dependent enzymes.

A further factor contributing to the toxicity of Gd^{3+} ions is their tendency to bind to endogenous anions, particularly phosphates and carbonates, creating insoluble salts which are taken up by the reticuloendothelial system (RES) through phagocytosis and accumulate in human tissues. This process is accompanied by a stimulation of local macrophages to initiate an inflammatory response with the release of cytokines and cytokine triggered transcription factors.

Biodistribution

After intravenous administration, gadolinium complexes are **rapidly distributed into the intravascular space and then passed**, through the capillaries, **into the interstitial space**, with the intravascular half-life time being dependent on the molecular weight and on the extent of plasma protein binding.

Depending on its structure, a gadolinium complex may also be **partially distributed in the liver** through passive diffusion or through a selective uptake by hepatocytes via carrier-mediated transport across the cell membranes.

Gadolinium contrast agents **do not penetrate the intact blood-brain barrier.**

Low molecular weight gadolinium complexes are generally not metabolized.

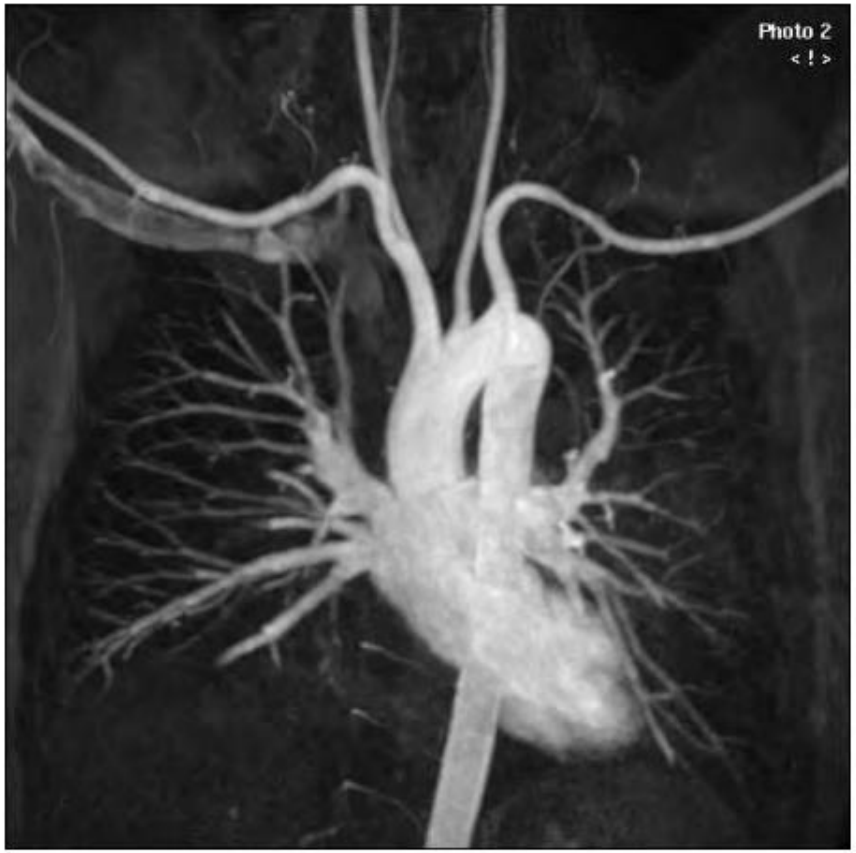


Fig. 26. Early vascular distribution of the iv injected Gd contrast agent

MdC - ESR

The gadolinium complexes are **excreted either almost exclusively via the kidneys**, or they have a **dual elimination** pathway via the kidneys and via the hepatobiliary system.

Patients with **normal renal function** eliminate more than 90% of low molecular weight gadolinium CAs within the first 12 hours after injection and more than 90% of high molecular weight CAs within 72 hours after injection.

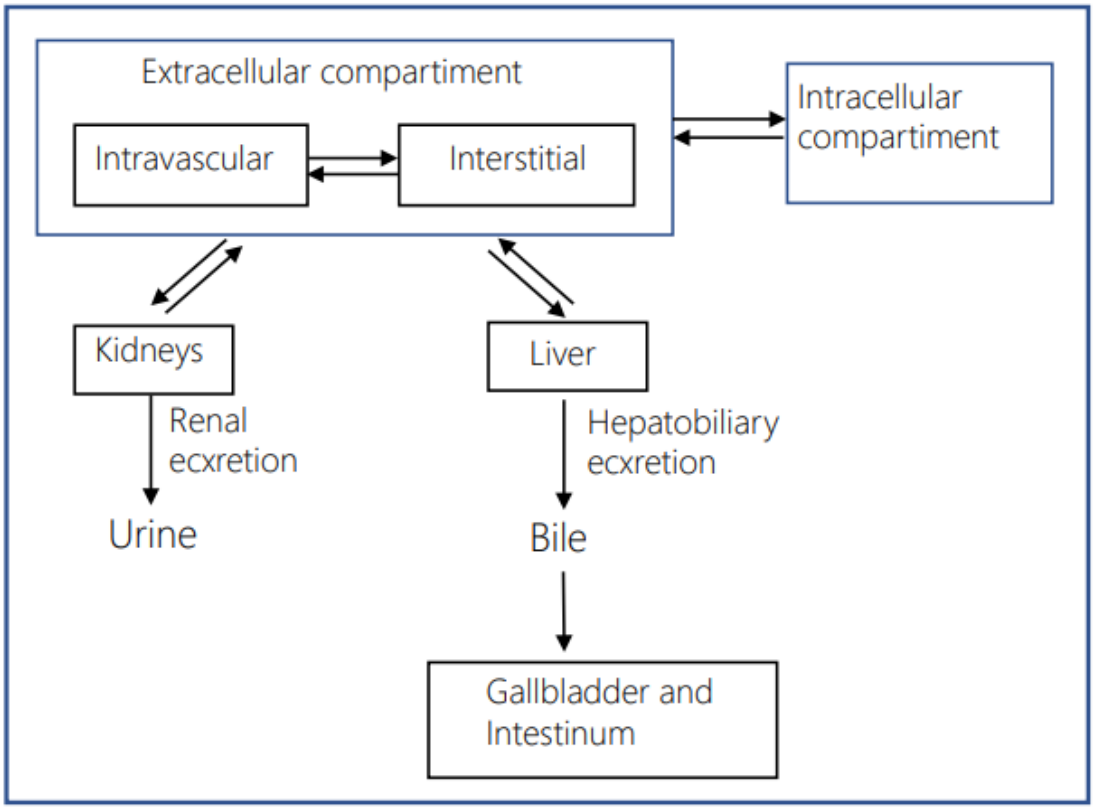


Fig. 27. Distribution sites and elimination pathways for intravenously administered gadolinium complexes

Superparamagnetic contrast agents

Superparamagnetic contrast agents consist of **iron oxide nanoparticle cores** coated with a protective layer of a biocompatible material like polyethylene glycol, dextran, heparin or albumin.

The magnetic moment of the superparamagnetic cores tends to align with the external magnetic field, inducing local magnetic field gradients that dephase the transverse magnetization of water protons, which predominantly leads to a shortened T_2 and concomitant negative contrast enhancement in pathologically relevant T_2-weighted images. With decreasing size of the superparamagnetic particles, shortening of T_1 becomes more pronounced, so that small superparamagnetic particles with core diameters of less than 10 nm can produce positive contrast in anatomically relevant T_1-weighted images.

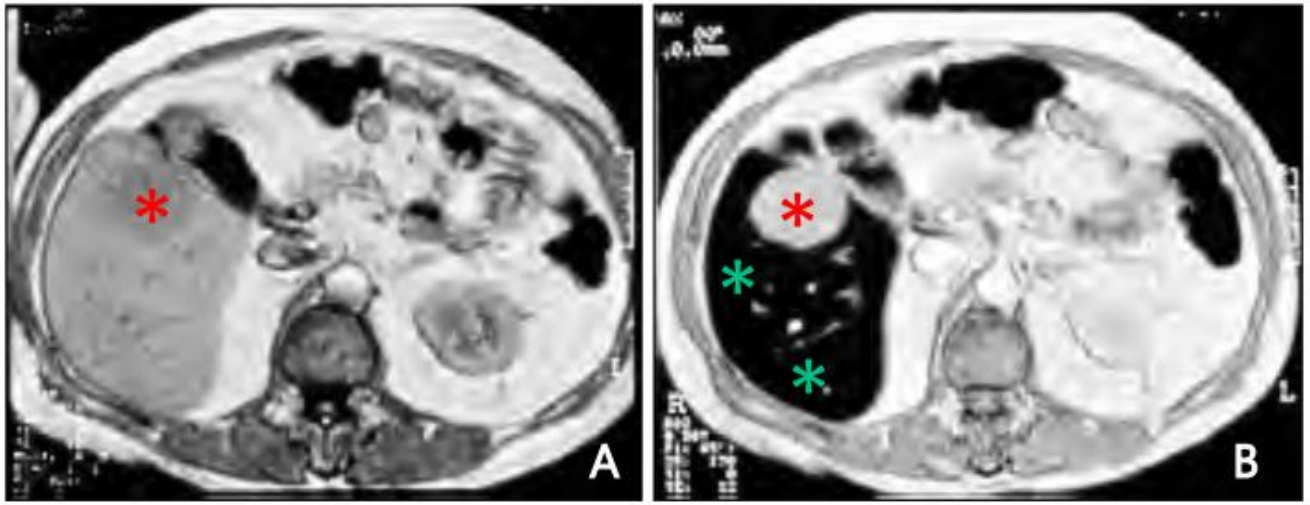


Fig. 28. Liver MRI pre (A) and post (B) iv administration of iron oxide nanoparticles with no uptake in the hepatocellular carcinoma (red asterisk) and uptake in normal liver tissue (green asterisks).

Indications

MR contrast agents can be classified according to their biodistribution pattern and the consequent applications in the morphological and functional diagnostic practice.

Non-specific extracellular contrast agents

Extracellular MR contrast agents are **low molecular weight gadolinium complexes** which, after injection, rapidly diffuse from the intravascular space into the extracellular space, from where they are then gradually eliminated by the kidneys.

These contrast agents circulate freely in the extracellular space but do not penetrate into tissues with specialized vascular barriers. Accordingly, they tend to accumulate in **tissues with abnormal perfusion or capillary permeability and in regions where the blood-brain barrier permeability is altered**.

The extracellular MR contrast agents are mainly applied for **CNS examinations** aimed at the detection of various neoplasms, the assessment of demyelinating diseases, infectious and inflammatory processes, the characterization of vascular anomalies and the diagnosis of cerebral ischemia and infarction. These agents are also **extensively used in body imaging** to asses certain pathologic processes, such as hepatocellular carcinoma or renal cell carcinoma and also for certain muskuloskeletal applications (see next page).

Some extracellular MR contrast agents can also be employed in MR angiography but due to their short residence time in the intravascular space, the imaging acquisition time window is very limited.

For the use as extracellular nonspecific contrast agents, most gadolinium complexes are equally effective because of their similar relaxivities and biodistributions.

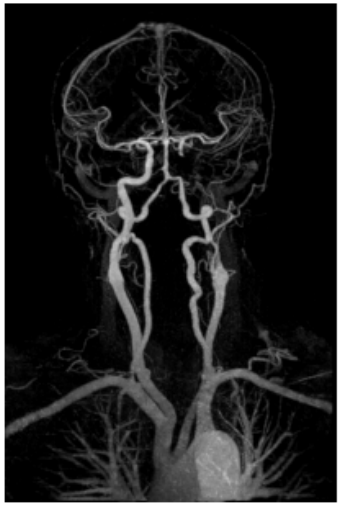


Fig. 29. Gd-enhanced MRI of the carotid arteries

Indications for non-specific extracellular CAs

Central nervous system
Detection of primary neoplasms and brain metastases, assessment of demyelinating diseases, detection of infectious and inflammatory processes, characterization of vascular anomalies and diagnosis of cerebral ischemia and infarction

Abdomen and pelvis
Detection and characterization of lesions, and determination of the extent of malignant tumor dissemination

MR angiography
Assessment of vascular anatomy and disease

Breast
Differentiation of malign and benign lesions, detection of multicentric malignancies, recurrent local breast cancer or benign post therapeutic fibrosis

Musculoskeletal system
Detection and characterization of mass lesions and inflammatory processes and evaluation of the extent of disease

Blood pool agents

Blood pool agents are high molecular weight gadolinium compounds which have a slow diffusion rate from the intravascular into the extracellular space because of their albumin binding and which require metabolization of their macromolecular moiety before renal excretion, so that **their concentration in plasma remains stable for over one hour.**

Blood pool agents cause a significant reduction in the T_1 relaxation time of circulating blood; thus, these agents are used for **MR angiography**, including coronary artery imaging, and for assessing tumor angiogenesis.

Organ-specific Gd-based contrast agents

The two linear ionic complexes **Gd-BOPTA and Gd-EOB-DTPA** exhibit **liver specificity because of their selective uptake by hepatocytes and their partial hepatobiliary excretion.**

After intravenous administration, these CAs have an initial extracellular phase, which allows imaging of **hepatic vasculature,** followed by a **delayed hepatocytic uptake and biliary elimination phase**, which permits the evaluation of **hepatic tissue with altered functionality**.

The uptake by hepatocytes selectively increases the signal intensity of normal liver parenchyma, while focal lesions containing mutated cells or altered structure do not uptake the CA and will appear hypointense, enhancing the visualization of the lesion and helping to characterize its nature.

They can also be useful to improve detection of metastases and hepatocellular carcinoma.

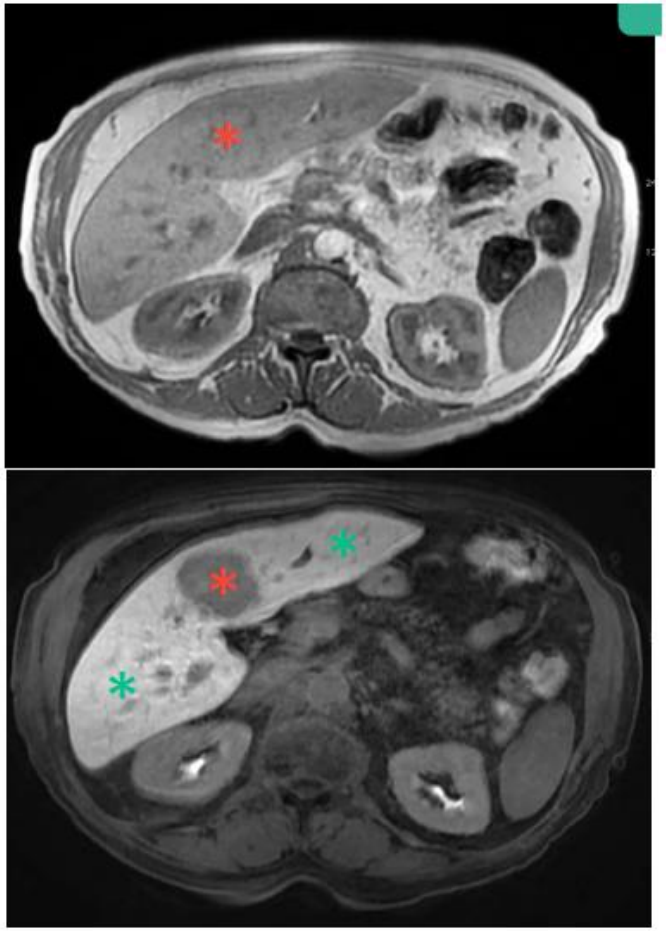


Fig. 30. Liver MRI pre and 20 min post iv administration of Gd-EOB-DTPA with no uptake in an adenoma (red asterisk) and contrast agent uptake in normal liver tissue (green asterisk).

Tissue specific reticuloendothelial and lymph node agents

Superparamagnetic iron oxide particles (SPIO) are selectively taken up by the reticuloendothelial system (RES) through phagocytosis, with the size of the particles determining the tissue specificity.

Large SPIO are rapidly metabolized by phagocytic cells like Kupffer cells in the liver and spleen, producing negative contrast in T_2 weighted images. Since most liver lesions, including metastases and the vast majority of hepatocellular carcinomas, do not have an intact RES, their signal intensity is unchanged by administration of SPIO, so that the contrast between normal and abnormal liver tissue is increased as the lesion appears hyperintense relative to the normal tissue.

Large SPIO particles can be used in **liver and spleen imaging**.

Small SPIO with a core size under 10 nm enter the lymphatic system and are metabolized by phagocytes in normal lymph nodes, whereas metastatic lymph nodes retain a certain quantity of the CA, allowing to differentiate between normal tissue, which has a negative contrast enhancement in T_2 weighted images, and metastatic tissue, which maintaining high signal intensity.

Small SPIO particles are utilized in the study of **lymph nodes and bone marrow** (limited availability).

Formazione per l'eccellenza

Direct MR arthrography

Direct MR arthrography involves the injection of a contrast agent into a joint region under fluoroscopic or ultrasound guidance, followed by magnetic resonance imaging. MR arthrography provides clearer images of the tendons, ligaments and cartilage in the affected region.

The low concentrated solutions correspond to 1:200-250 fold dilutions (2-2.5 mM) of the iv approved products (500-1000 mM).

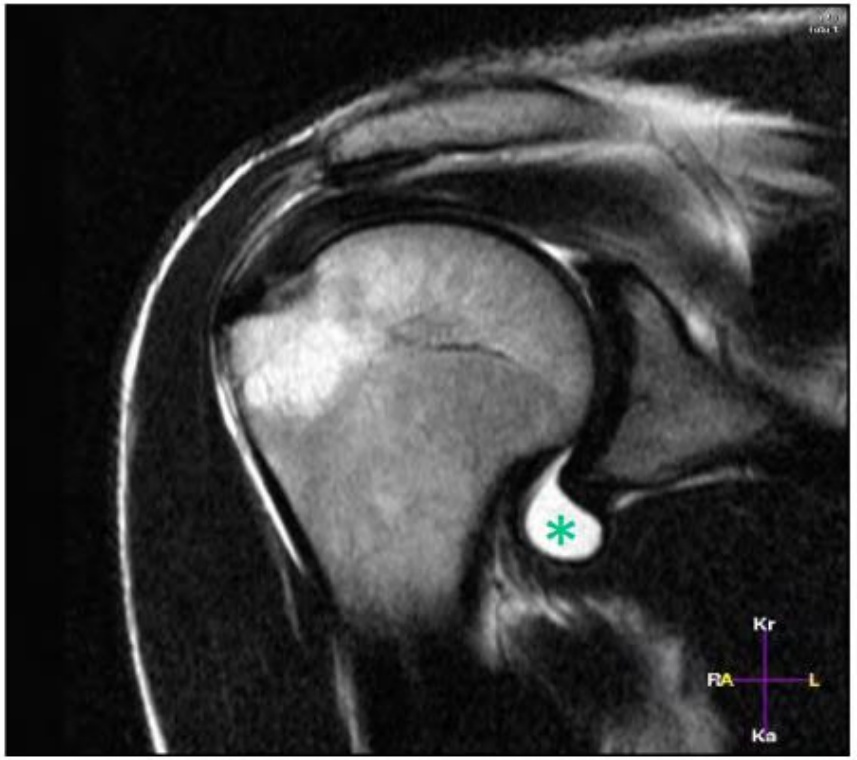


Fig. 31. Direct MR arthrography of the shoulder using a 2.5 mM GBCA (Artirem®). GBCA in the joint space is indicated by an asterisk.

Dosage of gadolinium contrast agents

For clinical use, the recommended dose of extracellular MR contrast agents is 0.1 mmol/kg of body weight for most of body imaging examinations. When used in MR angiography and CNS imaging, the extracellular MR contrast agents may be utilized with a higher dose up to 0.3 mmol/kg body-weight.

Liver-specific contrast agents are effective in lower doses of 0.05 to 0.1 mmol/kg for Gadobenate (Gd-BOPTA) and 0.025 mmol/kg for Gadoxetate (Gd-EOB-DTPA).

Formazione per l'eccellenza

Adverse reactions

The most frequently reported adverse events of gadolinium contrast agents are rated as **mild** and include coldness, warmth or pain at the injection site, nausea, vomiting and headache, paresthesias and dizziness.

Allergic-like reactions with gadolinium complexes, which occur only **very rarely,** consist of sweating, rash, urticaria, itching and facial swelling.

Risk factors for developing an allergic-like reaction are a previous moderate or severe acute reaction to a gadolinium-based or iodinated contrast agent, asthma, and various other allergies.

Hypersensitivity is the major risk

Pregnancy and lactation

In pregnant women, when there is a very strong indication for an enhanced MRI, a macrocyclic gadolinium contrast agent may be administered using the smallest possible dose.

Breast feeding may be continued normally when macrocyclic gadolinium-based contrast agents are given to the mother.

Nephrogenic systemic fibrosis (NSF)

Nephrogenic systemic fibrosis (NSF) is a rare but highly disabling disorder, which can occur in patients with impaired renal function exposed to less stable gadolinium-based CAs.

Clinical manifestations of NSF are extensive thickening and hardening of the skin and subcutaneous tissues associated with erythematous papules, as well as muscle weakness, bone pain and joint contractures.

Progressed NSF may also involve other organs, such as the liver, lungs, esophagus, heart, and skeletal muscle.

Symptoms develop and progress rapidly, are irreversible and can lead to extreme disability and death because of scarring alterations of the organs with consequent loss of function.

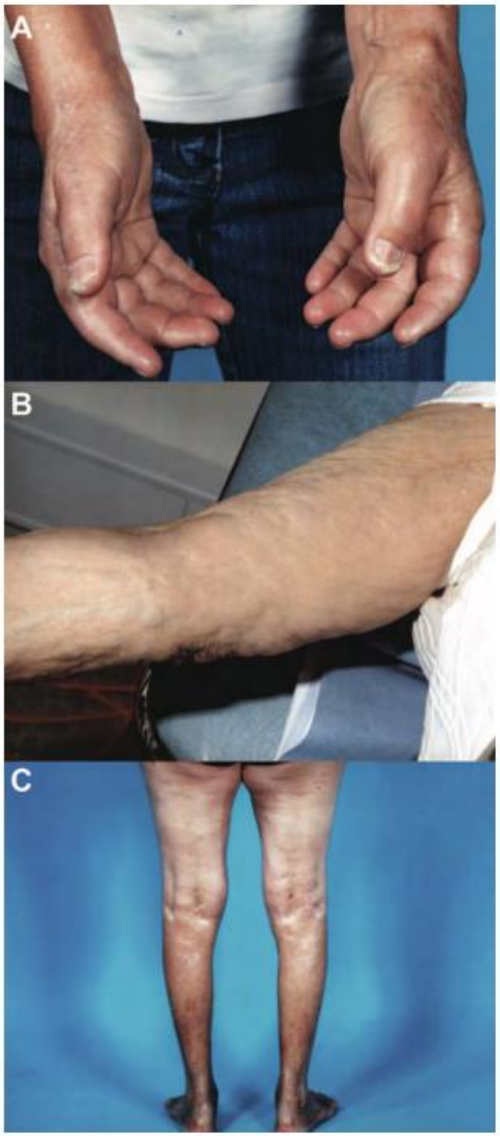


Fig. 32. Manifestations of nephrogenic systemic fibrosis. A: Tightness and hardness of the hands combined with joint contractures. B: Firm nodules establishing a cobblestone configuration. C: Tight and firm skin on lower legs.

Reproduced from: Elmholdt TR et al., Nephrogenic Systemic Fibrosis in Denmark– A Nationwide Investigation. PLOS ONE 2013; 8(12): e82037. doi:10.1371/iournal.pone.0082037.0001

MdC - ESR

As a pathophysiological mechanism, it is assumed that a reduced renal function, which is associated with a considerably prolonged tissue exposure to the gadolinium complex, increases the probability for precipitation of insoluble, toxic gadolinium salts. This process is supposed to stimulate a subsequent proinflammatory cascade of events leading to the fibrosing process.

Risk factors for the development of NSF

The greatest risk factors for the development of NSF are a **reduced renal function**, particularly with a glomerular filtration rate of eGFR < 15 ml/min/1.73 m^2, and patients on dialysis.

The risk for developing NSF is substantially more pronounced after the administration of non-ionic and ionic linear gadolinium complexes, and it increases with contrast agent dose and multiple exposure.

Further risk factors include metabolic acidosis, elevated blood levels of iron, calcium or phosphate, a high-dose erythropoietin therapy, immunosuppression, vasculopathy, and infection or other acute proinflammatory events.

Formazione per l'eccellenza

Gadolinium retention in the brain

Repeated administration of gadolinium-based contrast agents is associated with gadolinium accumulation in the brain regions of the dentate nucleus and globus pallidus even in subjects with normal renal function.

While such deposits have been reported for all gadolinium-based agents, the highest levels found after the administration of **linear agents** were substantially higher than after the use of macrocyclic agents.

A significant positive correlation exists between the amount of gadolinium accumulated and the cumulative dose of previous administrations of gadolinium-based contrast agents.

To date, **no neurological symptoms associated with gadolinium retention in the brain** have been reported.

Gadolinium deposits may also occur in the **bone, liver and skin, independently of renal function**.

Bone and liver retention do not produce any clinical symptoms, whereas skin deposits manifest as red skin plaques.

Safety recommendation

The **European Medicines Agency (EMA)** has classified the linear complexes Gd-DTPA-BMA, Gd-DTPA and Gd-DTPA-BMEA as high risk agents and suspended their intravenous usage, with the exception that Gd-DTPA may still be employed for direct MR arthrography.

The linear complexes Gd-BOPTA and Gd-EOB-DTPA, which are rated as intermediate risk agents, remain approved by EMA for hepato-biliary imaging only.

The macrocyclic agents are considered as low-risk and are maintained by EMA as non-specific Gd contrast agents. However, they should be used with caution in patients with GFR < 30 ml/min, observing a period of at least 7 days between two injections.

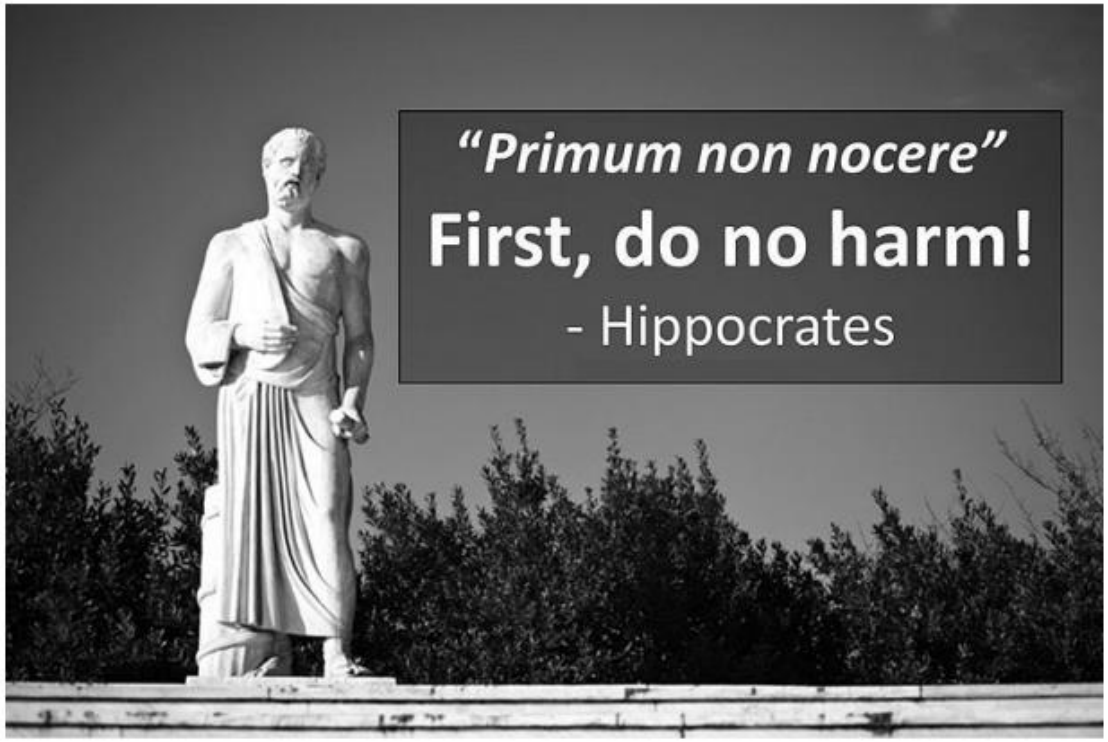


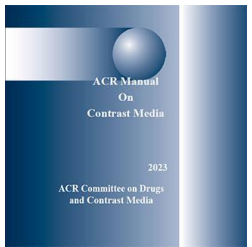
Fig. 33. Image from Wikimedia Commons https://commons.wikimedia.org/wiki/File:Primum_Non_Nocere.jpg#filelinks

Table 3. Recommendation of the use of gadolinium-based CAs according to the European Medicines Agency (EMA)

Type	Ionicity	Product	Complex	EMA recommendation
Linear		Gd-DTPA	gadopentetate dimeglumine	restricted use for direct MR arthrography
	ionic	Gd-BOPTA	gadobenate dimeglumine	restricted use as for hepato-biliary imaging
		Gd-EOB-DTPA	gadoxetate	restricted use as for hepato-biliary imaging
	non-ionic	Gd-DTPA-BMA	gadodiamide	suspended
		Gd-DTPA-BMEA	gadoversetamide	suspended
Macrocyclic	ionic	Gd-DOTA	gadoterate meglimine	maintained as non-specific GdCA
	non-ionic	Gd-HP-DO3A	gadoteridol	maintained as non-specific GdCA
		Gd-BT-DO3A	gadobutrol	maintained as non-specific Gd-CA

GADOLINIUM-BASED INTRAVASCULAR

Product	Chemical Structure and Class	Anion	Cation	Viscosity+ 25° C (cp or mPa.s)	Viscosity+ 37° C (cp or mPa.s)	Relaxivity 1.5T (3T)	Osmolality (mOsm/ kgH2O)	Log k Therm (cond7.4)
Magnevist® (Bayer Healthcare)	Gd-DTPA Linear Ionic	Gadopentetate	Dime-glumine	4.9*	2.9	4.1(3.7)	1960	22.5 (18.4)
Prohance® (Bracco)	Gd-HP-D03A Macrocyclic Non-ionic	Gadoteridol	None	2.0*	1.3	4.1(3.7)	630	23.8 (17.2)
Multihance® (Bracco)	Gd-BOPTA Linear Ionic	Gadobenate	Dime-glumine	9.2*	5.3	6.3(5.5)	1970	22.6 (18.4)
Omniscan™ (GE Healthcare)	Gd-DTPA-BMA Linear Non-ionic	Gadodiamide	None	2.0	1.4	4.3 (4)	789	16.9 (14.9)
Optimark™ (Guerbet)	Gd-DTPA-BMEA Linear Non-ionic	Gadoverset-amide	None	2.8**	2.0	4.7(4.5)	1110	16.8 (15)
EOVIST/Primovist® (Bayer Healthcare)	Gd-EOB-DTPA Linear Ionic	Gadoxetate	Disodium		1.19	6.9(6.2)	688	23.5 (18.7)
Gadavist/Gadovost™ (Bayer Healthcare)	Gd-BT-D03A Macrocyclic Non-Ionic	Gadobutrol	None		4.96	5.2 (5)	1603	21.8 (15.5)
Dotarem® (Guerbet) Clariscan™ (GE Healthcare)	Gd-DOTA Macrocyclic Ionic	Gadoterate	Meglu - mine	3.4*	2.4	3.6(3.5)	1350	25.6 (19.3)



NOTA INFORMATIVA 19.2.2018

Agenzia Italiana del Farmaco

In accordo con l'Agenzia Europea dei Medicinali (EMA) e l'Agenzia Italiana del Farmaco (AIFA), le aziende farmaceutiche Agfa HealthCare Imaging Agents GmbH, Bayer S.p.A., Bracco Imaging S.p.A., GE Healthcare Srl, Guerbet S.p.A. desiderano informarLa di quanto segue:

Una revisione condotta dall'EMA ha confermato che, a seguito dell'uso di mezzi di contrasto a base di gadolinio, si ha un accumulo di piccole quantità di gadolinio nei tessuti cerebrali.

È stato osservato che vi è un maggior accumulo a seguito dell'uso dei mezzi di contrasto lineari rispetto agli agenti macrociclici.

NOTA INFORMATIVA 19.2.2018

Agenzia Italiana del Farmaco

Non esiste attualmente alcuna evidenza che i depositi di gadolinio nel cervello abbiano causato danni ai pazienti, tuttavia, non essendo noti i rischi a lungo termine l'EMA ha raccomandato che i mezzi di contrasto **lineari** per uso endovenoso siano sospesi nell'UE ad eccezione dell'acido gadoxetico e dell'acido gadobenico, che continueranno a essere disponibili esclusivamente per l'impiego nelle scansioni epatiche.

NOTA INFORMATIVA 19.2.2018

Formazione per l'eccellenza

Panoramica delle prescrizioni per i mezzi di contrasto a base di gadolinio autorizzati nell'UE		
Prodotto	**Struttura (forma farmaceutica)**	**Stato autorizzativo dal 28 febbraio***
Artirem/Dotarem/Dotarem Arthro (*acido gadoterico*)	macrociclico (intra-articolare)	mantenuto
Dotarem (*acid gadoterico*)†	macrociclico (endovenoso)	mantenuto
Gadovist (*gadobutrolo*)	macrociclico (endovenoso)	mantenuto
Magnevist (*acido gadopentetico*)	lineare (intra-articolare)	mantenuto
Magnevist (*acido gadopentetico*) ‡	lineare (endovenoso)	sospeso
Multihance (*acido gadobenico*)	lineare (endovenoso)	limitato alle scansioni del fegato
Omniscan (*gadodiamide*)	lineare (endovenoso)	sospeso
Optimark (*gadoversetamide*)	lineare (endovenoso)	AIC decaduta per mancata presentazione rinnovo
Primovist (*acido gadoxetico*)	lineare (endovenoso)	mantenuto§
Prohance (*gadoteridolo*)	macrociclico (endovenoso)	mantenuto

* Gli stampati dei prodotti dei quali l'A.I.C. viene mantenuta sono stati aggiornati.
† Compresi i rispettivi prodotti generici (Cyclolux, Claricyclic, Dotagita, Dotagraf, Dotamulti, Dotaspin, DotaVision, Gadoteerzuur Guerbet Gadotersäure Sanochemia).
‡ Compresi i rispettivi prodotti generici (Gadocon, Gadolan, Gadopent, Gadopentat, Gadopur, Gadothek, Magnegita, Magnetolux, Magnevision, Magnograf, MR-Lux).
§ L'acido gadoxetico è autorizzato solo per le scansioni epatiche.

Stability Concerns

- Retention
- Vulnerable Populations
  - Repeat Studies
  - Pediatric Patients

2023 MRI Safety: What the Radiologist Needs to Know

Gadolinium Retention: A Research Roadmap from the 2018 NIH/ACR/RSNA Workshop on Gadolinium Chelates

Robert J. McDonald, MD, PhD • Deborah Levine, MD • Jeffrey Weinreb, MD • Emanuel Kanal, MD • Matthew S. Davenport, MD • James H. Ellis, MD • Paula M. Jacobs, PhD • Robert E. Lenkinski, PhD • Kenneth R. Maravilla, MD • Martin R. Prince, MD, PhD • Howard A. Rowley, MD • Michael F. Tweedle, PhD • Herbert Y. Kressel, MD

From the Division of Neuroradiology, Department of Radiology, Mayo Clinic, Rochester, Minn (R.J.M.); Department of Radiology, Beth Israel Deaconess Medical Center, 330 Brookline Ave, Boston, MA 02215 (D.L., H.Y.K.); Department of Radiology & Biomedical Imaging, Yale School of Medicine, New Haven, Conn (J.W.); Department of Radiology, University of Pittsburgh Medical Center, Pittsburgh, Pa (E.K.); Department of Radiology, University of Michigan Health System, Ann Arbor, Mich (M.S.D., J.H.E.); Cancer Imaging Program, National Institutes of Health, National Cancer Institute, Bethesda, Md (P.M.J.); Department of Radiology, UT Southwestern Medical Center, Dallas, Tex (R.E.L.); Department of Radiology, University of Washington, Seattle, Wash (K.R.M.); Department of Radiology, Cornell and Columbia Universities, New York, NY (M.R.P.); Department of Radiology, University of Wisconsin, Madison, Wis (H.A.R.); and Department of Radiology, The Ohio State University, Columbus, Ohio (M.F.T.). Received May 14, 2018; revision requested June 5; revision received June 27; accepted July 27. **Address correspondence to** H.Y.K. (e-mail: *hkressel@bidmc.harvard.edu*).

Conflicts of interest are listed at the end of this article.

Radiology 2018; 00:1–15 • https://doi.org/10.1148/radiol.2018181151 • Content codes: SQ MR

Gadolinium-based contrast agents (GBCAs) have revolutionized MRI, enabling physicians to obtain crucial life-saving medical information that often cannot be obtained with other imaging modalities. Since initial approval in 1988, over 450 million intravenous GBCA doses have been administered worldwide, with an extremely favorable pharmacologic safety profile; however, recent information has raised new concerns over the safety of GBCAs. Mounting evidence has shown there is long-term retention of gadolinium in human tissues. Further, a small subset of patients have attributed a constellation of symptoms to GBCA exposure, although the association of these symptoms with GBCA administration or gadolinium retention has not been proven by scientific investigation. Despite evidence that macrocyclic GBCAs show less gadolinium retention than linear GBCAs, the safety implications of gadolinium retention are unknown. The mechanism and chemical forms of gadolinium retention, as well as the biologic activity and clinical importance of these retained gadolinium species, remain poorly understood and underscore the need for additional research. In February 2018, an international meeting was held in Bethesda, Md, at the National Institutes of Health to discuss the current literature and knowledge gaps about gadolinium retention, to prioritize future research initiatives to better understand this phenomenon, and to foster collaborative standardized studies. The greatest priorities are to determine *(a)* if gadolinium retention adversely affects the function of human tissues, *(b)* if retention is causally associated with short- or long-term clinical manifestations of disease, and *(c)* if vulnerable populations, such as children, are at greater risk for experiencing clinical disease. The purpose of the research roadmap is to highlight important information that is not known and to identify and prioritize needed research.

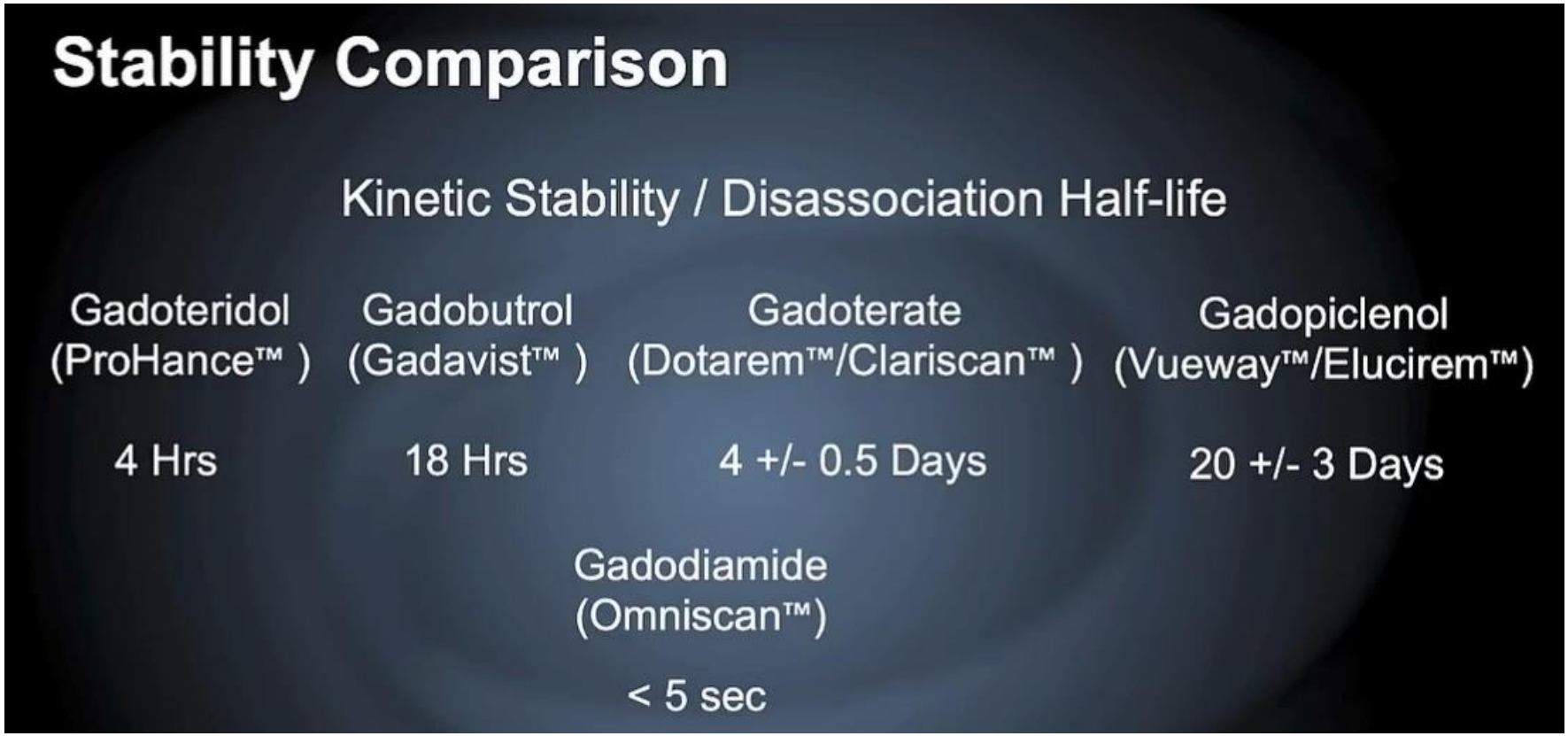
Online supplemental material is available for this article.

Since initial regulatory approval, over 450 million doses of gadolinium-based contrast agents (GBCAs) have been administered worldwide (1). The historic safety profile of GBCA use has been highly favorable, with very low rates of immediate adverse side effects when compared with other pharmaceuticals, including iodinated contrast agents (2–4). GBCA use in patients with severely compromised renal function has been associated with development of the rare condition nephrogenic systemic fibrosis (NSF), in which fibrotic changes may be seen in many tissues, predominately skin, and muscle contractures may occur (5–9). Fortunately, rapid changes in clinical practice in the use of GBCAs within the renally impaired population have essentially eradicated this clinical entity.

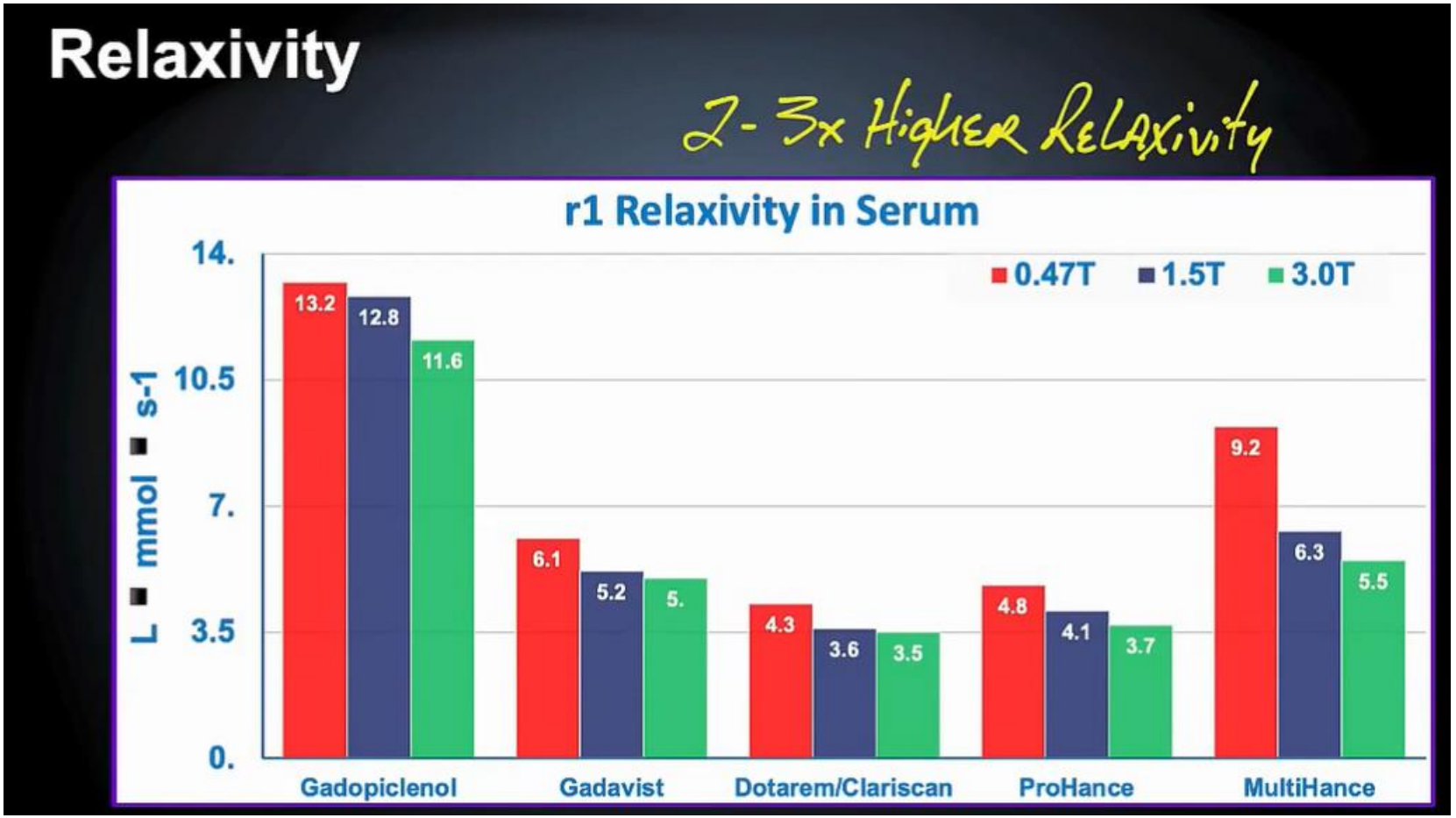
At the time of initial regulatory approval in 1988, it was widely thought that the gadolinium ion remained in the chelated state after intravenous administration of a GBCA and that it was rapidly excreted. However, scientific evidence has been mounting that traces of gadolinium remain in the bone, brain, and other organs in patients with nor-

24 hours] and long term [>1 month after exposure]) tends to show an association with cumulative dose. Although tissue retention appears to be highest with linear GBCAs, all agents (linear and macrocyclic) demonstrate some degree of tissue retention of gadolinium in some form, and existing data suggest there may be intraclass variability in this retention (17,22–25). The causal relationship between GBCA exposure, retention, and symptoms remains unclear due to inconsistencies in the timing of symptom onset relative to GBCA administration, dose thresholds, and heterogeneity in presumed associated symptoms (26).

Nine GBCAs have been approved for use in the United States, each with unique chemical and physical properties (Table 1, Figure) (27–32). However, in the European Union, the linear GBCAs have recently been restricted or removed from the market due to concerns regarding gadolinium retention. This difference may, in part, be reflective of the differences in the regulatory approach across countries, and it also attests to the limitations in the available research on these agents, their biodistribution, and the ef-



2023 MRI Safety: What the Radiologist Needs to Know



2023 MRI Safety: What the Radiologist Needs to Know

Adverse Events

- Rate at clinical doses: 0.07% to 2.4%
  Most reactions are mild and physiologic, including coldness, warmth, or pain at the injection site; nausea with or without vomiting; headache; paresthesias; and dizziness.
- Allergic-like reactions: 0.004% to 0.7%
  Similar to those of an allergic-like reaction to an iodinated contrast medium
- Severe life-threatening anaphylactic: 0.001% to 0.01%

SALA MAGNETE – Iniettore automatico

Formazione per l'eccellenza

MEDRAD® Spectris Solaris EP

MR Injection System

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SALA MAGNETE – Iniettore automatico

Formazione per l'eccellenza

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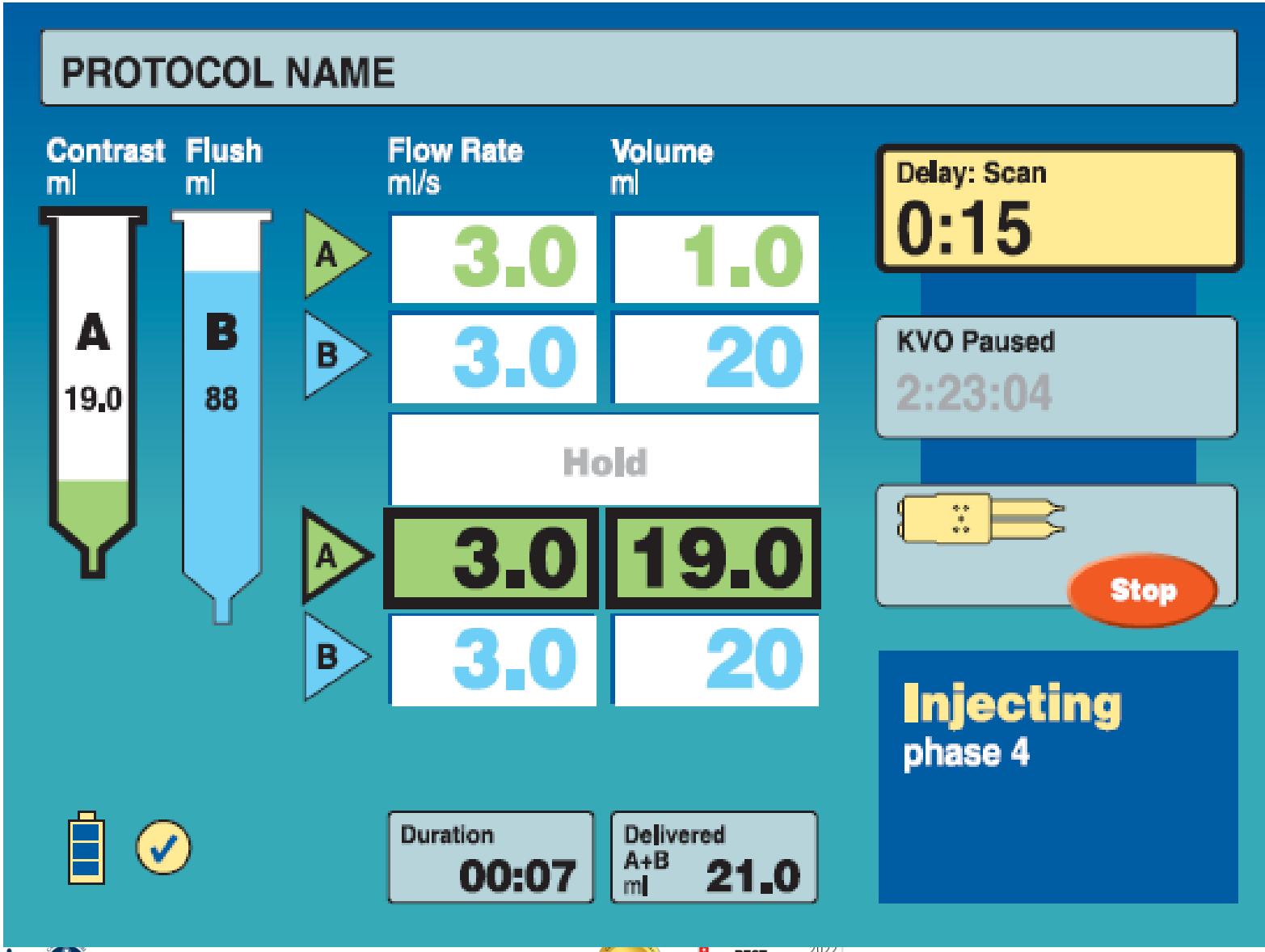
SALA MAGNETE – Iniettore automatico

TVP → KVO keep vein open



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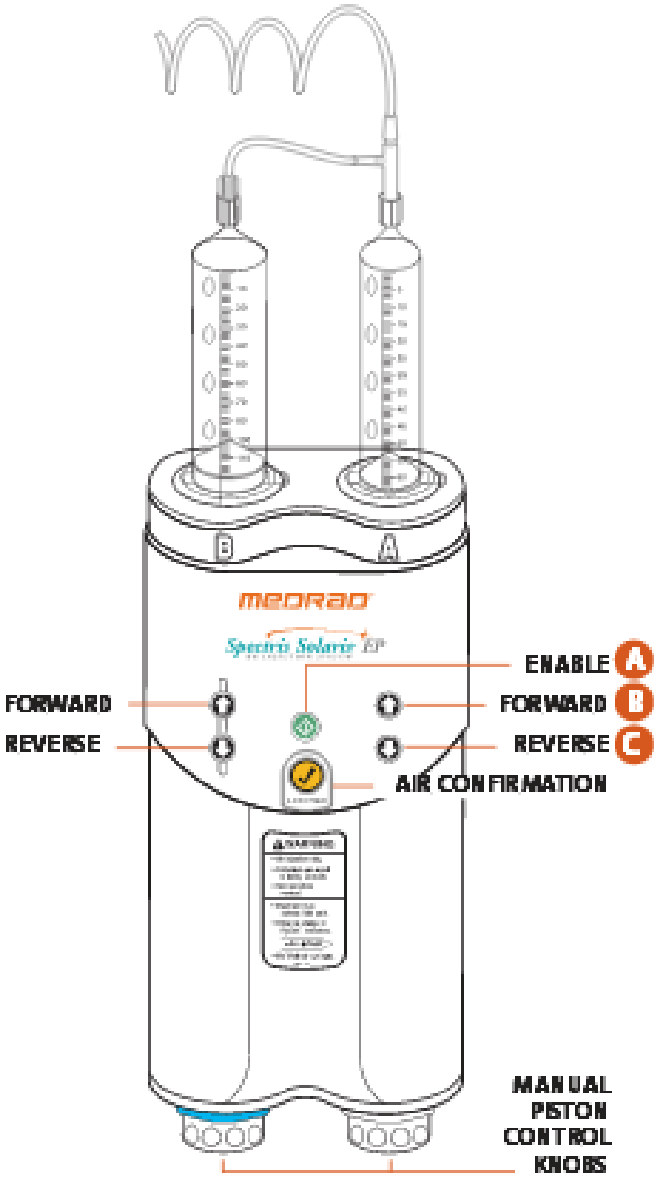

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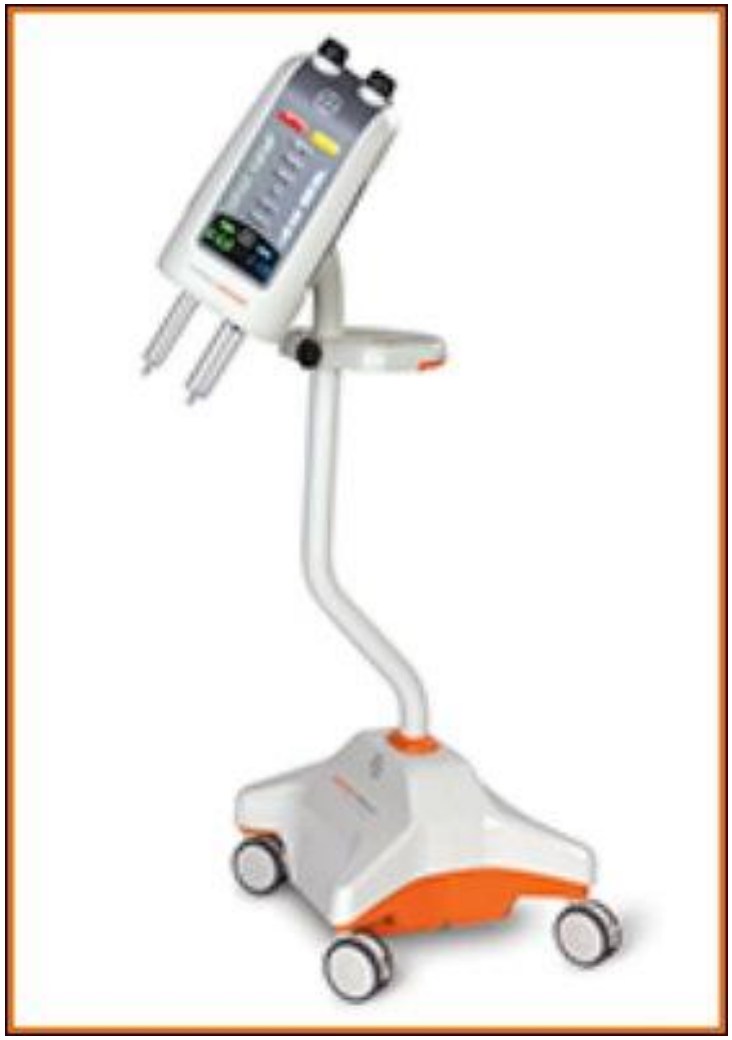
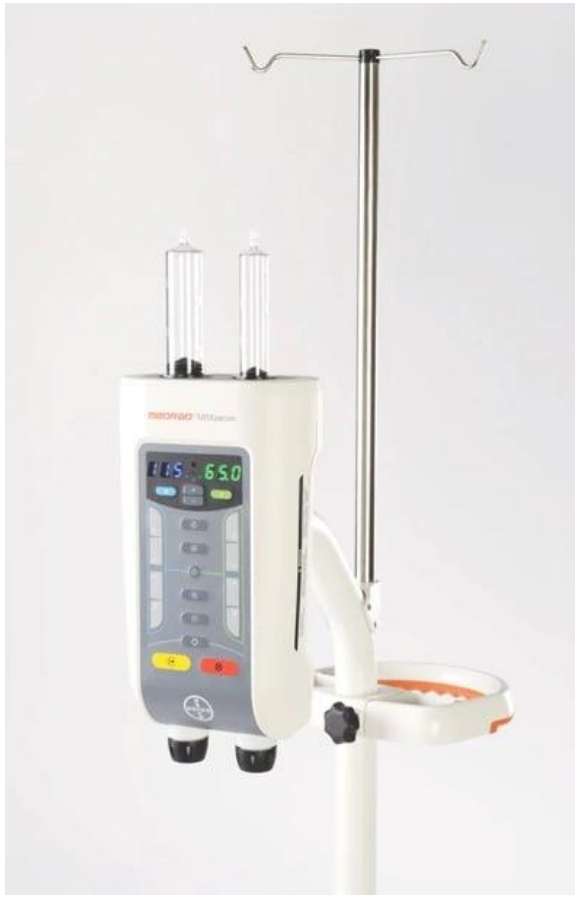


medrad® MRXperion

MR Injection System



SALA MAGNETE – Iniettore automatico

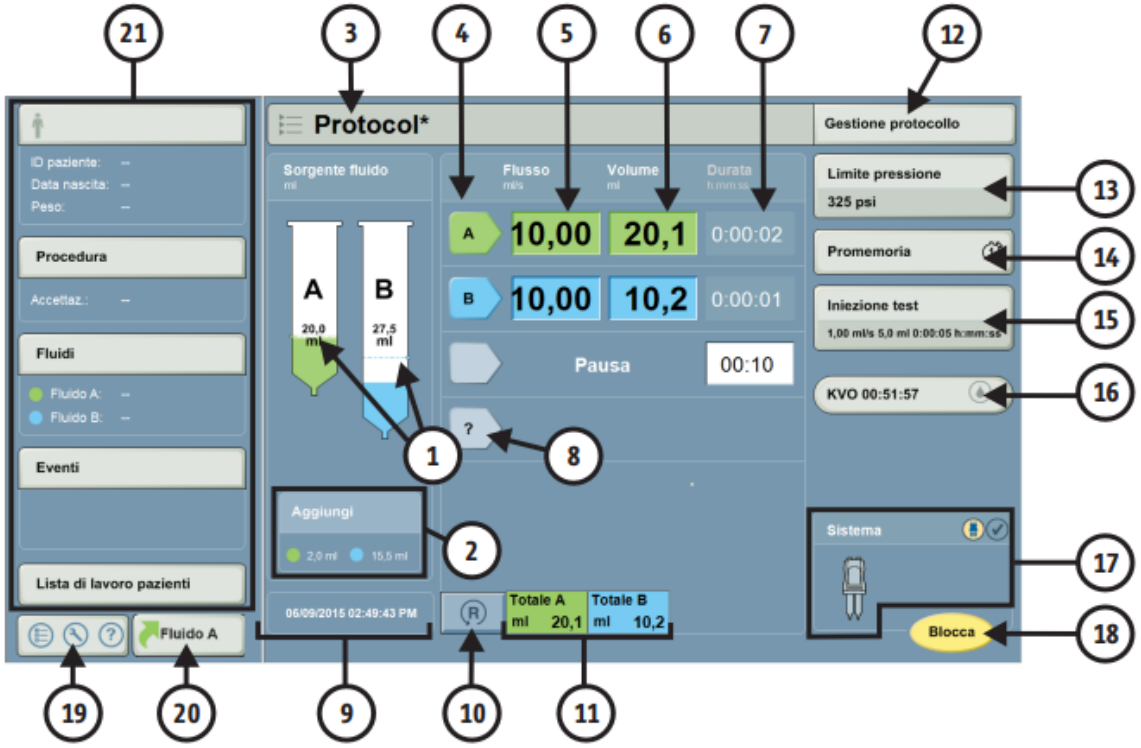


Figura 5 - 1: Schermata iniziale

1 Informazioni sul volume delle siringhe
2 Indicatore di aggiunta volume (se pertinente)
3 Protocollo
4 Pulsante Fase (modifica fase)
5 Portata
6 Volume
7 Durata
8 Pulsante Fase (nuova fase)
9 Data e ora correnti
10 Ripristina i valori predefiniti di fabbrica del protocollo.
11 Visualizza il volume totale programmato per siringa o il volume totale combinato in entrambe le siringhe.

MEDRAD® MRXperion
MR Injection System

SALA MAGNETE – Iniettore automatico

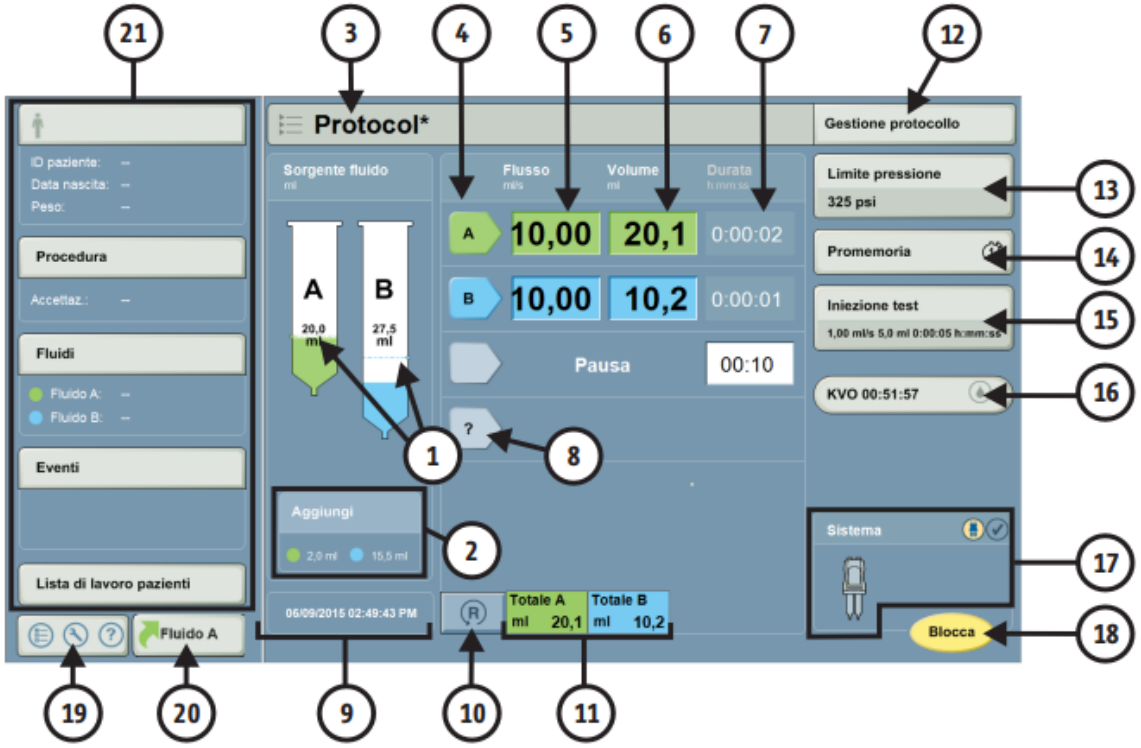


Figura 5 - 1: Schermata iniziale

12 Apre Gestione protocollo.
13 Visualizza il limite di pressione corrente.
14 Visualizza il numero di promemoria impostati.
15 Iniezione test. Indica i parametri dell'iniezione test definiti dall'operatore.
16 KVO Somministra piccoli boli di soluzione di lavaggio comune prima e dopo l'iniezione e nelle fasi di attesa o di pausa. Si illumina di blu quando la funzione KVO è attivata.
17 Informazioni sul sistema
18 Blocca/Arma/ Disarma
19 Menu di avvio
20 Fluido A: visualizza i valori più recenti immessi per Fluido A
21 Visualizza il pannello informatico.

SALA MAGNETE – Iniettore automatico

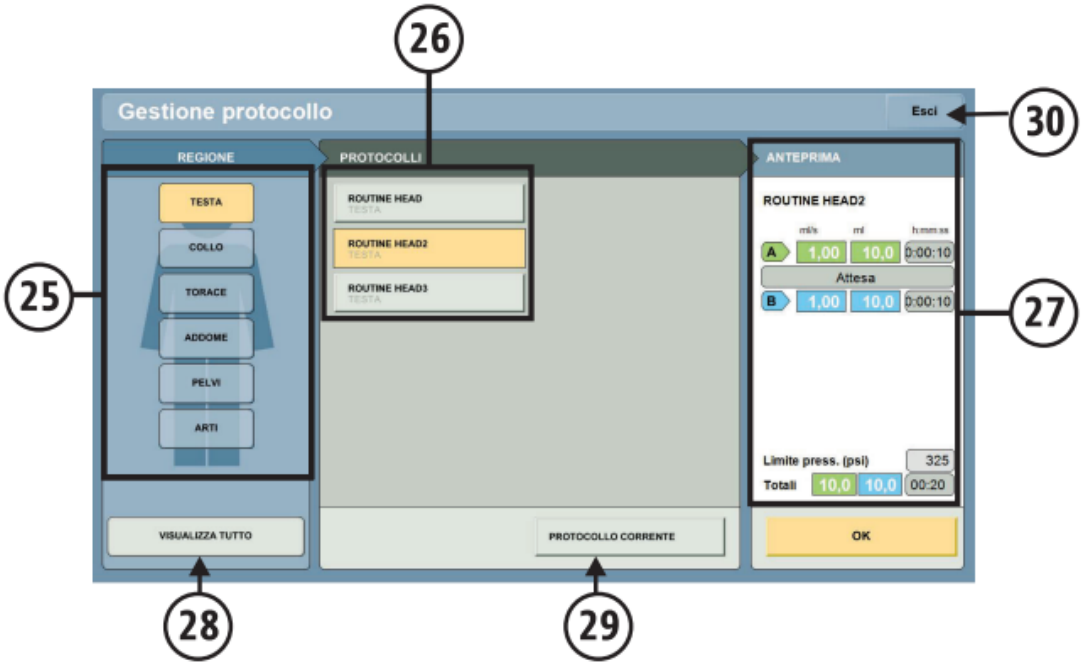


Figura 5 - 3: Gestione protocollo

25 Regione di interesse Mostra l'elenco di regioni in cui sono memorizzati i protocolli

26 Elenco di protocolli Elenco di protocolli memorizzati nella regione di interesse evidenziata.

27 Anteprima protocollo Visualizza i dettagli del protocollo selezionato.

28 Visualizza tutto Visualizza tutti i protocolli memorizzati

29 Protocollo corrente Mostra i dettagli relativi al protocollo corrente in uso.

30 Esci Ritorna alla schermata iniziale.

SALA MAGNETE – Iniettore automatico

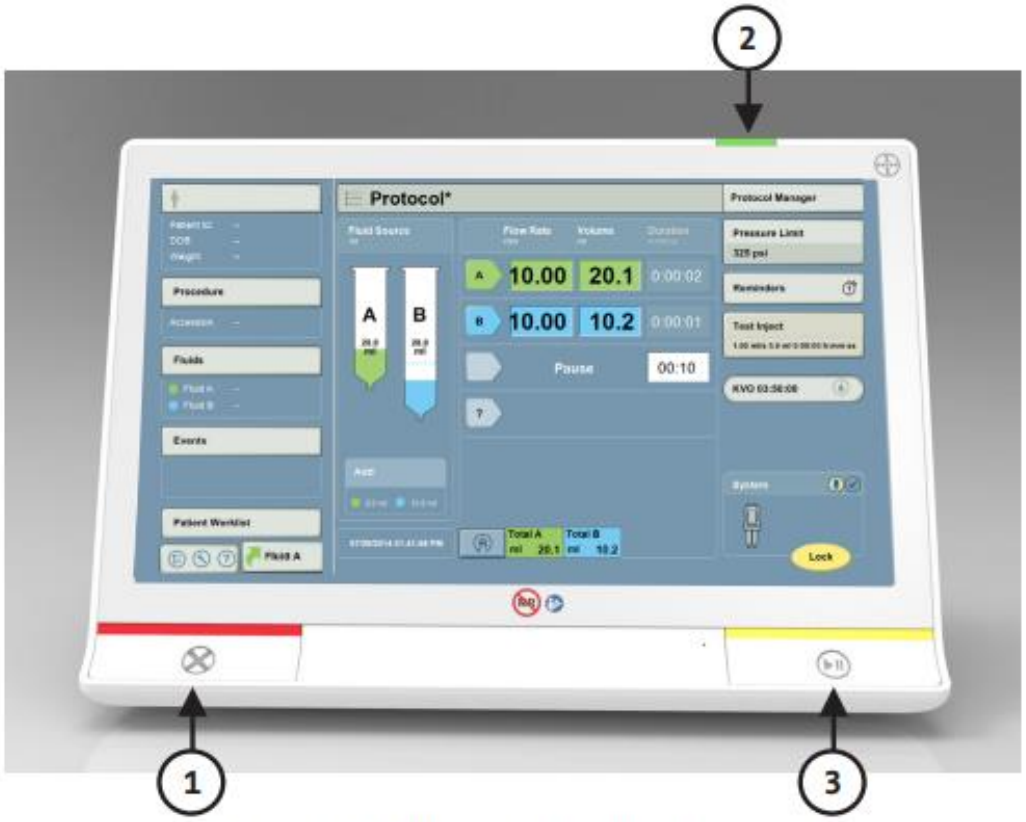


Figura 5 - 5: Workstation, vista frontale

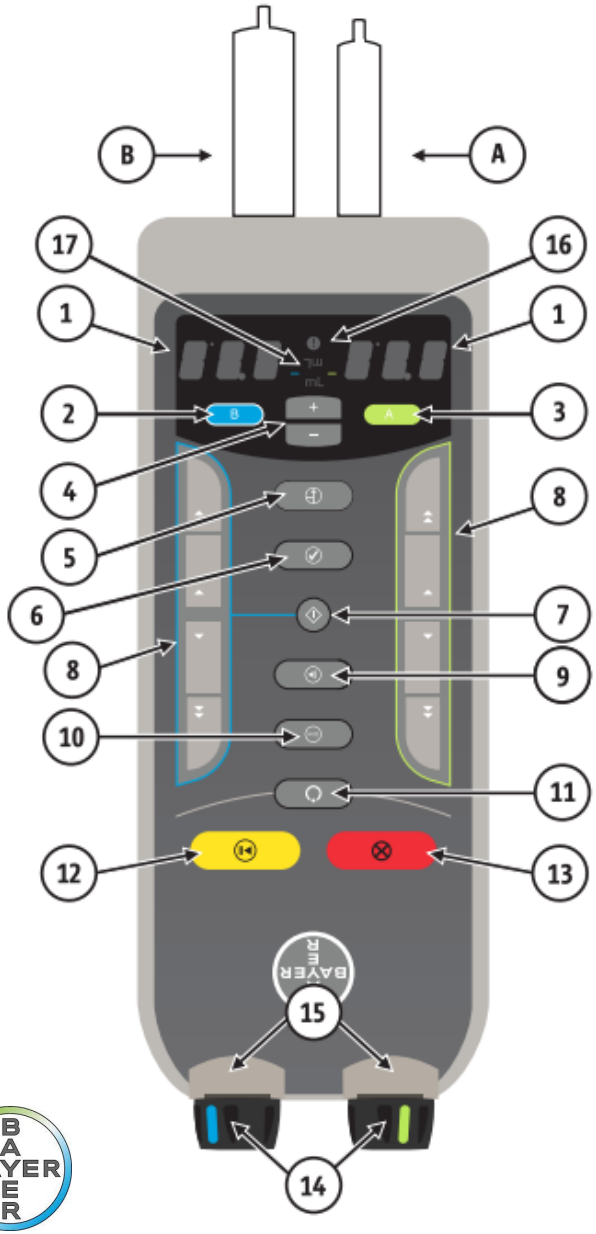
1 Interrompi Termina l'iniezione e disarma il sistema.

2 Alimentazione Accende e spegne il sistema. Lampeggia o si illumina con luce fissa gialla o verde, a seconda dello stato dell'alimentazione.

3 Avvio/ Attesa Avvia l'iniezione. Sospende l'iniezione per un massimo di 20 minuti.

SALA MAGNETE – Iniettore automatico

A Siringa A Siringa per il mezzo di contrasto
B Siringa B Siringa per la soluzione fisiologica
1 Indicatore del volume (lato A o B)
2 Pulsante B Premere due volte puntando la testa dell'iniettore verso l'alto: riempie la siringa B (soluzione fisiologica) fino al volume visualizzato (riempimento automatico).
3 Pulsante A Premere due volte puntando la testa dell'iniettore verso l'alto: riempie la siringa A (mezzo di contrasto) fino al volume visualizzato (riempimento automatico).
4 Pulsanti +/- Regolano il volume di riempimento automatico in incrementi/ decrementi di 1 ml. È possibile utilizzarli dopo una singola pressione del pulsante A o del pulsante B. Si illuminano per indicare che l'operatore può iniziare il riempimento automatico.



5 Riempi Se premuto, attiva la funzione di riempimento. Si illumina per indicare che l'operatore può iniziare il riempimento.
6 Pulsante di conferma Controllo aria
7 Pulsante Attiva comandi pistone
8 Comandi di avanzamento e arretramento pistone (lato A o B)
9 Iniezione test Se premuto, avvia un'iniezione test in base a parametri definiti dall'operatore. Quando lampeggia, indica che l'operatore può eseguire un'iniezione test per determinare la pervietà della connessione del paziente.
10 KVO Se premuto, attiva la funzione KVO (Tieni vena pervia).

SALA MAGNETE – Iniettore automatico

11 Arma Per usare questa funzione la testa deve essere orientata puntando le siringhe verso il basso ed è necessario confermare il Controllo aria.

12 Avvio/Pausa Se premuto, avvia un'iniezione quando il sistema è armato. Se premuto durante un'iniezione, la mette in pausa.

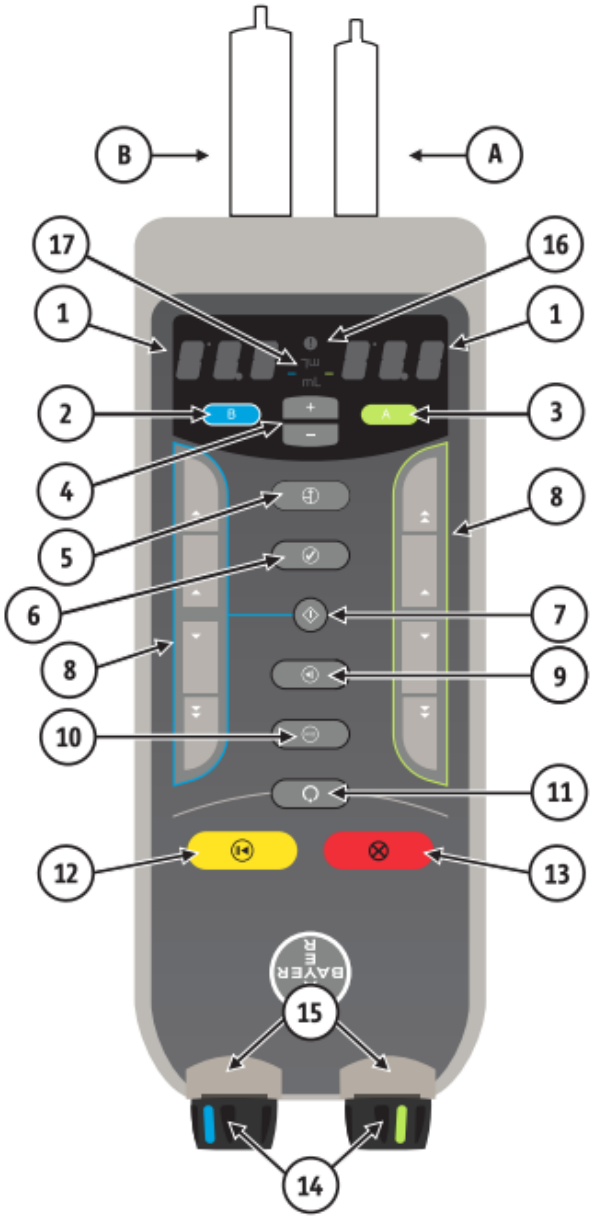
13 Interrompi Se premuto, termina l'iniezione e disarma l'iniettore.

14 Manopole manuali Consente all'operatore di spostare manualmente il pistone quando l'iniettore non è armato.

15 Indicatori di stato dell'iniettore Indicatori di armamento e di stato dell'iniezione.

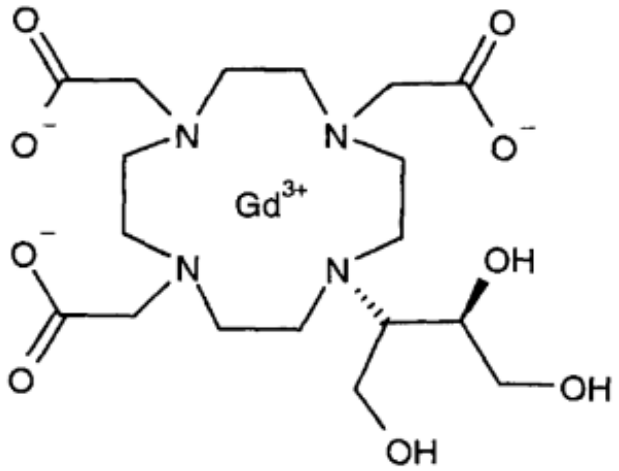
16 Indicatore di attenzione Si illumina per avvisare l'operatore

17 ml Indica l'unità di volume di fluido indipendentemente dall'orientamento della testa dell'iniettore.



MEZZI DI CONTRASTO

Gadovist® 1.0 – Now also approved for children from 0 years onwards



Composition: 1 mL solution for injection contains 604.72 mg gadobutrol (equiv. 1.0 mmol) as active ingredient. Excipients: calcobutrol sodium, tromethamol, hydrochloric acid, water for injections.

MEZZI DI CONTRASTO

Indications: For diagnostic use only. Gadovist® 1.0 is indicated in adults, adolescents, and children of all ages (including term neonates) for:

1.Contrast enhancement in cranial and spinal magnetic resonance imaging (MRI);

2.Contrast enhanced MRI of liver or kidneys in patients with high suspicion or evidence of having focal lesions to classify these lesions as benign or malignant;

3.Contrast enhancement in magnetic resonance angiography (MRA).

Gadovist® can also be used for MR imaging of pathologies of the whole body.

MEZZI DI CONTRASTO

Formazione per l'eccellenza

BRACCO

LIFE FROM INSIDE

ProHance® (Gadoteridol) Injection, 279.3 mg/mL is the first macrocyclic gadolinium MRI contrast agent approved in the United States for CNS MRI.

ProHance®
(Gadoteridol) Injection, 279.3 mg/mL

MEZZI DI CONTRASTO

Formazione per l'eccellenza

BRACCO
LIFE FROM INSIDE

ProHance®
(Gadoteridol) Injection, 279.3 mg/mL

ProHance (Gadoteridol) injection, 279.3 mg/mL is safe for use in children **(> 2 years)** or those with renal insufficiency. It is the only agent still FDA approved for a cumulative dose of 0.3 mmol/kg. The ACR categorizes ProHance (Gadoteridol) injection, 279.3 mg/mL as a group 2 agent. In fact, there are no unconfounded cases of nephrogenic systemic fibrosis (NSF) with ProHance (Gadoteridol) injection, 279.3 mg/mL in published, peer reviewed literature.

Generalmente la dose raccomandata è di 0,1 mmoli/Kg (0,2 ml/kg).

MEZZI DI CONTRASTO

Formazione per l'eccellenza

BRACCO
LIFE FROM INSIDE

ProHance®
(Gadoteridol) Injection, 279.3 mg/mL

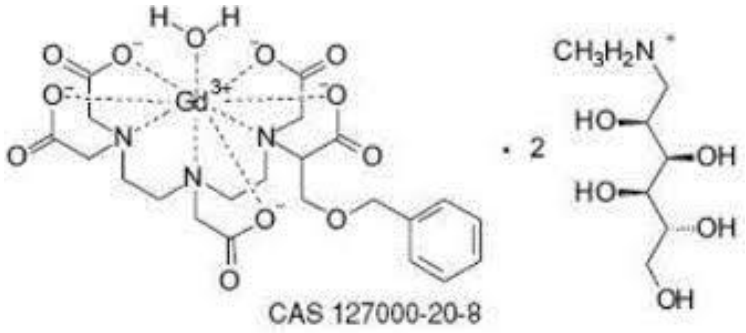
Non usare Prohance nei bambini di età inferiore a 6 mesi.
Poiché la funzionalità renale non è ancora matura nei bambini fino a 1 anno di età Prohance dovrà essere utilizzato nei pazienti da 6 a 12 mesi solo dopo un'attenta valutazione da parte del medico.
Nel neonato o nel bambino, l'esame con il mezzo di contrasto non deve essere ripetuto prima di **7 giorni**.

https://farmaci.agenziafarmaco.gov.it/aifa/servlet/PdfDownloadServlet?pdfFileName=footer_002988_029055_FI.pdf&sys=m0b1l3

MEZZI DI CONTRASTO

BRACCO

multihance
(gadobenate dimeglumine)
injection, 529 mg/mL



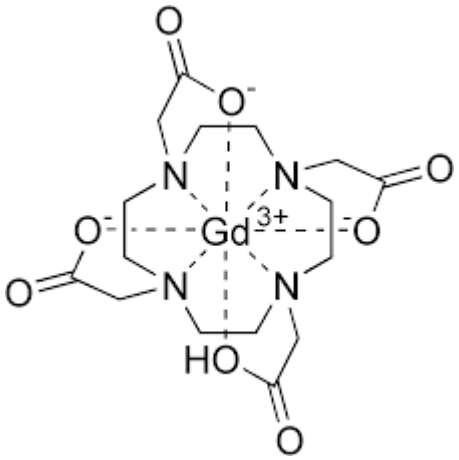
MULTIHANCE INDICATIONS AND USAGE:

MultiHance is a gadolinium-based contrast agent indicated for use in:

•Magnetic resonance imaging (MRI) of the central nervous system (CNS) in adults and children **over 2 years** of age to visualize lesions with abnormal blood-brain barrier or abnormal vascularity of the brain, spine, and associated tissues and

•Magnetic resonance angiography (MRA) to evaluate adults with known or suspected renal or aorto-ilio-femoral occlusive vascular disease.

MEZZI DI CONTRASTO



Il principio attivo è l'acido gadoterico (complesso di gadolinio dell'acido 1, 4, 7, 10 tetra-azaciclo-dodecano N, N', N'', N''' tetra-acetico). 100 ml contengono 27,932 g di Acido gadoterico corrispondente a 20,246 g di DOTA e 9,062 g di ossido di gadolinio.

Guerbet

MEZZI DI CONTRASTO

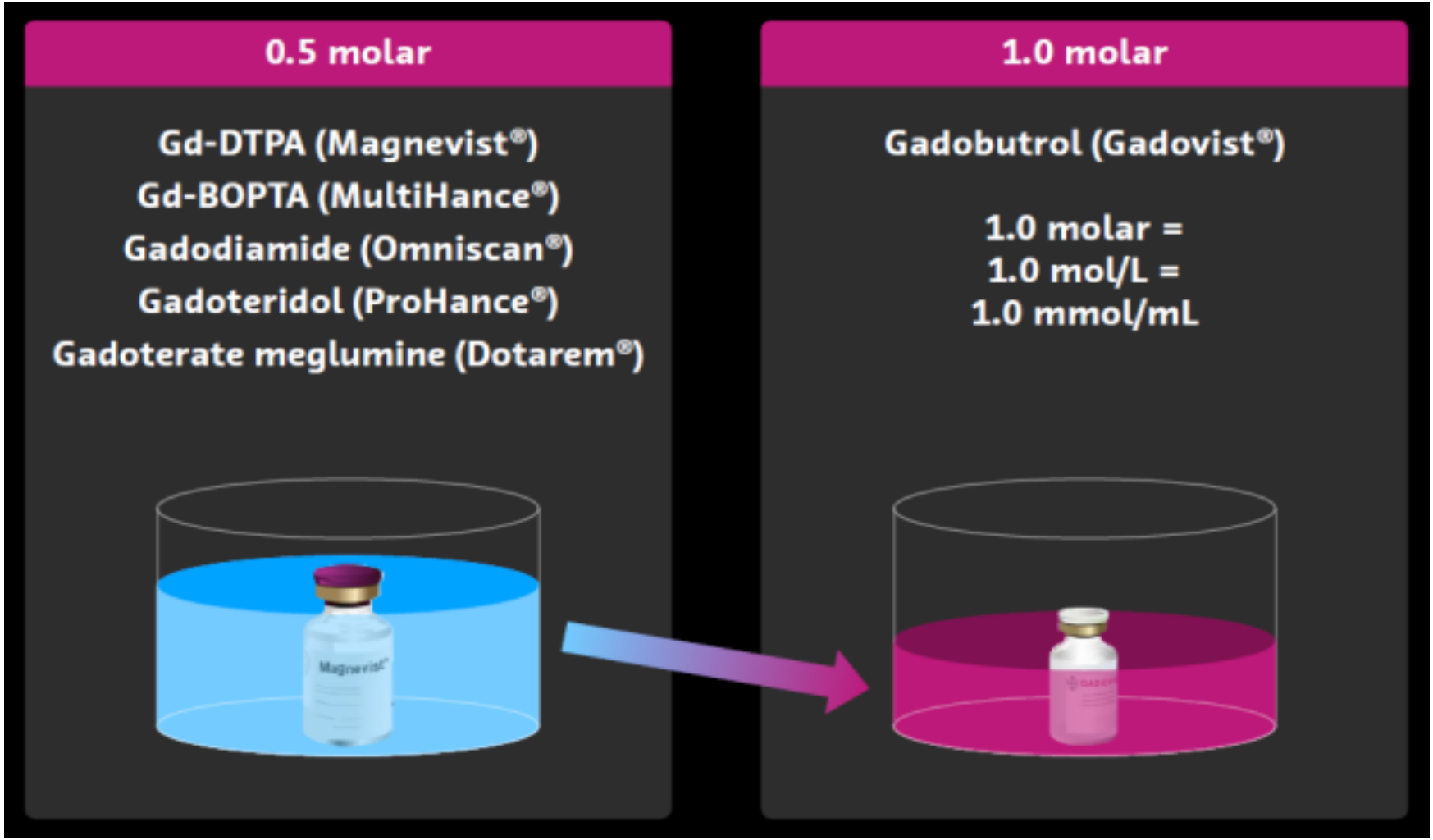
MEZZI DI CONTRASTO

Central Nervous System: Magnevist® (gadopentetate dimeglumine) injection is indicated for the use with magnetic resonance imaging (MRI) in adults and pediatric patients (2 years of age and older) to visualize lesions with abnormal vascularity in the brain (intracranial lesions), spine and associated tissues. Magnevist® has been shown to facilitate visualization of intracranial lesions including but not limited to tumors.

Extracranial/Extraspinal Tissues: Magnevist® is indicated for use with MRI in adults and pediatric patients (2 years of age and older) to visualize lesions with abnormal vascularity in the head and neck.

Body: Magnevist® is indicated for use with MRI in adults and pediatric patients (2 years of age and older) to visualize lesions with abnormal vascularity in the body (excluding the heart).

MEZZI DI CONTRASTO



QUANTITA' MdC

[concentrazione]

0,5 MOLARE

- 0,2 ml/Kg
- (Multihance, Prohance, Magnevist, Dotarem …

1 MOLARE

- 0,1 ml/Kg
- (Gadovist)

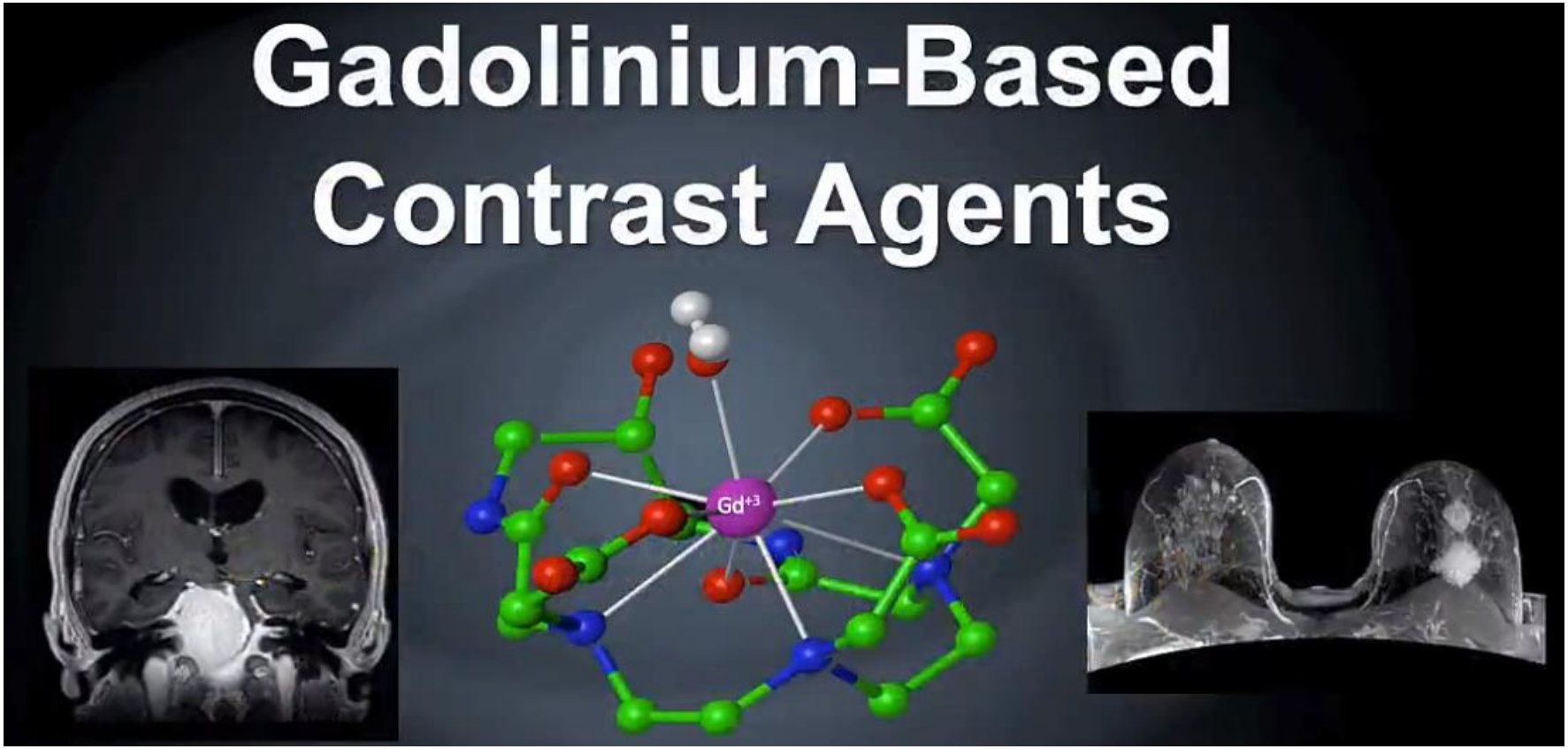
MdC

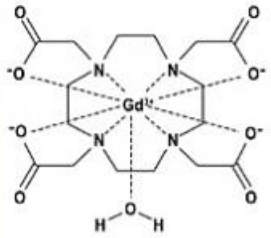
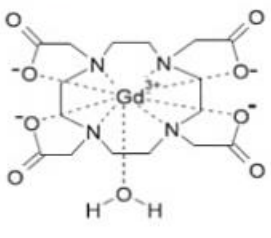
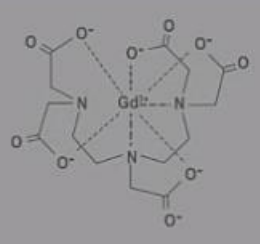
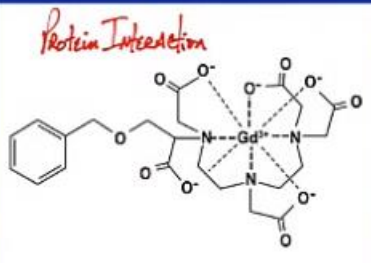
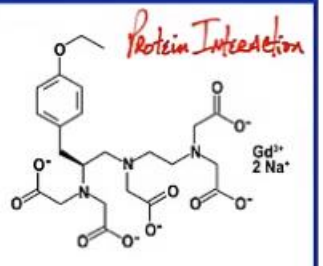
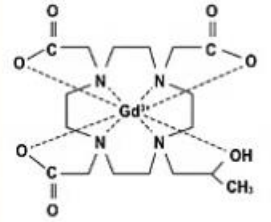
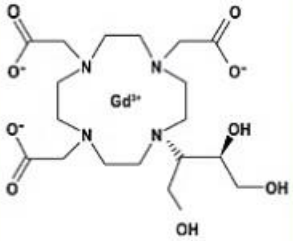
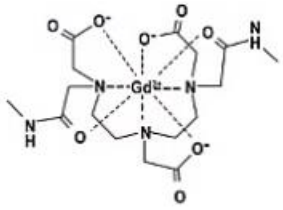
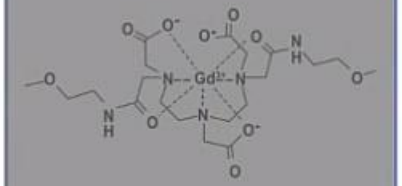
Formazione per l'eccellenza

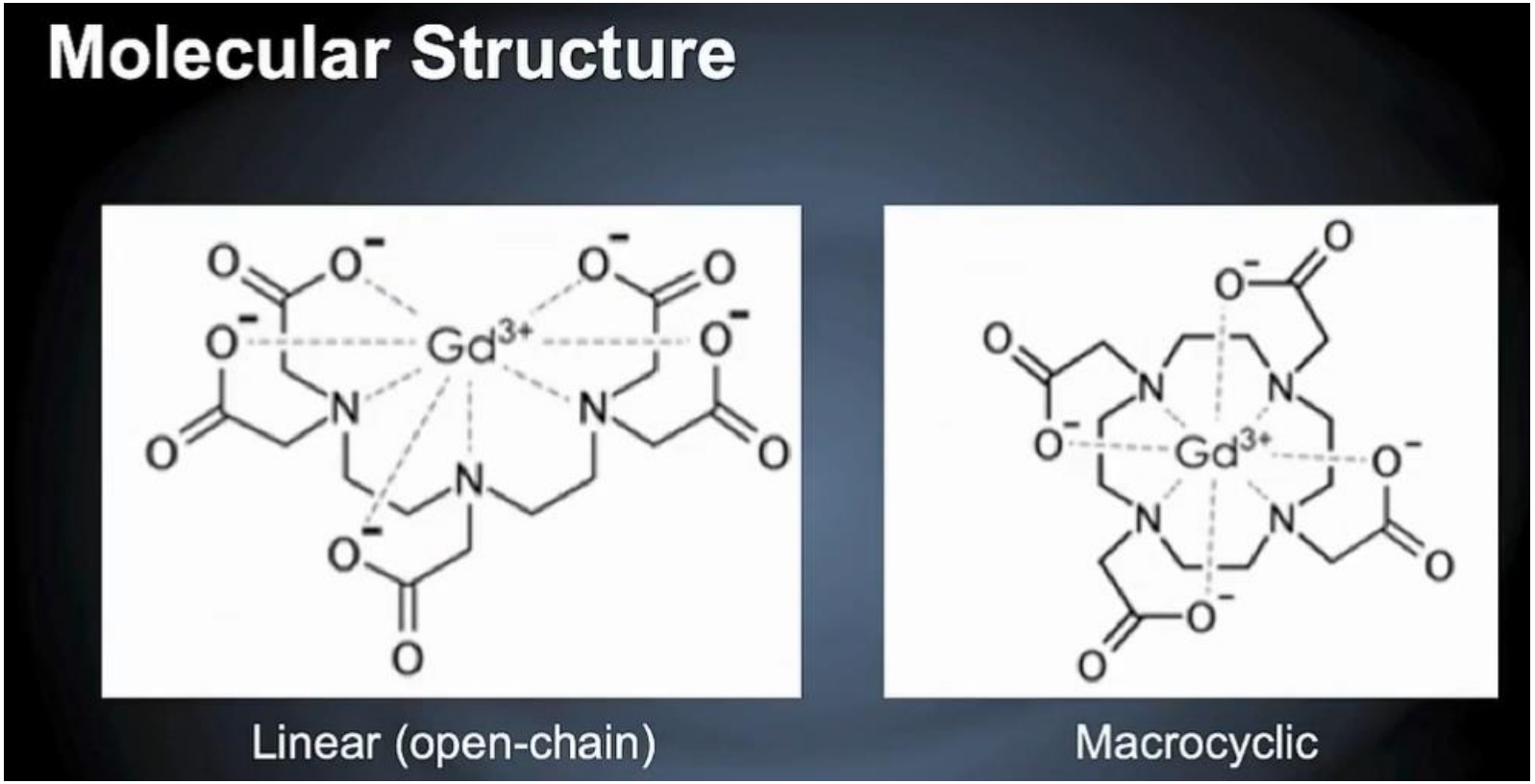
Applied Radiology 50

MRI Safety: What the Radiologist Needs to Know

Expert Forums



	Macrocyclic		Open-chain		
Ionic	 Gd-DOTA, gadoterate meglumine, Dotarem	 Gd-DOTA gadoterate meglumine, Clariscan	 Gd-DTPA, gadopentetate dimeglumine, Magnevist	 Gd-BOPTA, gadobenate dimeglumine, MultiHance	 Gd-EOB-DTPA, gadoxetic acid disodium salt, Eovist
Non-ionic	 Gd-HP-DO3A, gadoteridol, ProHance	 Gd-BT-DO3A, gadobutrol, Gadavist	 Gd-DTPA-BMA, gadodiamide, Omniscan	 Gd-DTPA-BMEA, gadoversetamide, OptiMARK	



2023 MRI Safety: What the Radiologist Needs to Know

Formazione per l'eccellenza

FDA Approved Agents (ECF)

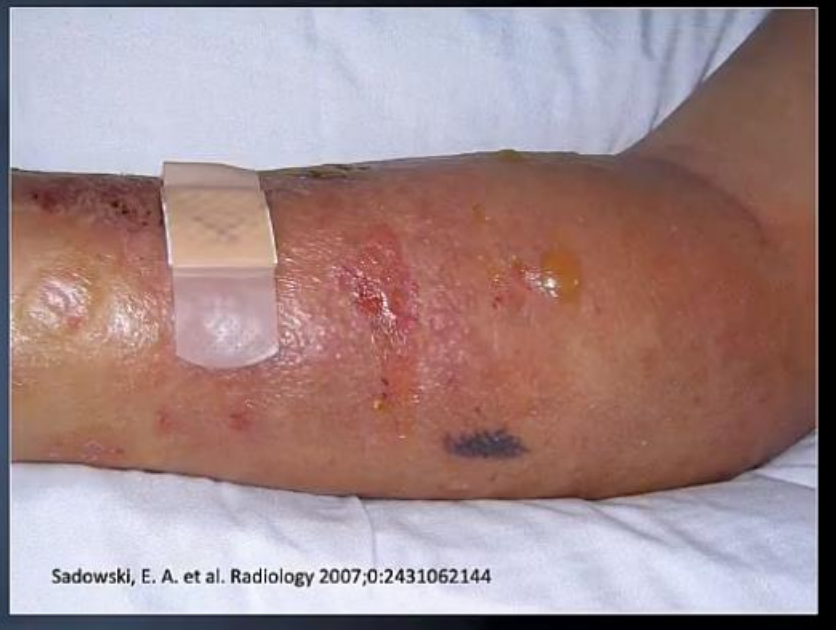
Trade Name	Chemical Name	Design	Ionicity	Molar Concentration	Standard Dose
ProHance	Gd-HP-DO3A gadoteridol	Macrocyclic	Non-ionic	0.5	0.1 mmol/kg
Gadavist	Gd-BT-DO3A gadobutrol	Macrocyclic	Non-ionic	1.0	0.1 mmol/kg
Dotarem / Clariscan	Gd-DOTA gadoterate meglumine	Macrocyclic	Ionic	0.5	0.1 mmol/kg
Vueway / Elucerim	gadopiclenol	Macrocyclic	Non-ionic	0.5	0.05 mmol/kg
MultiHance	Gd-BOPTA gadobenate dimeglumine	Linear	Ionic	0.5	0.1 mmol/kg
Omniscan	Gd-BTPA-BMA gadodiamide	Linear	Non-ionic	0.5	0.1 mmol/kg

Stability Metrics

- Thermodynamic Stability: Energy required to release the Gd^{3+} ion (measured at a pH 1 or pH 7 as "conditional stability")
- Kinetic Stability: Rate/speed at which the gadolinium dissociates (measured at a pH 1)

Nephrogenic Systemic Fibrosis (NSF)

"Nephrogenic systemic fibrosis (NSF) is a fibrosing disease, primarily involving the skin and subcutaneous tissues but also known to involve other organs, such as the lungs, esophagus, heart, and skeletal muscles."



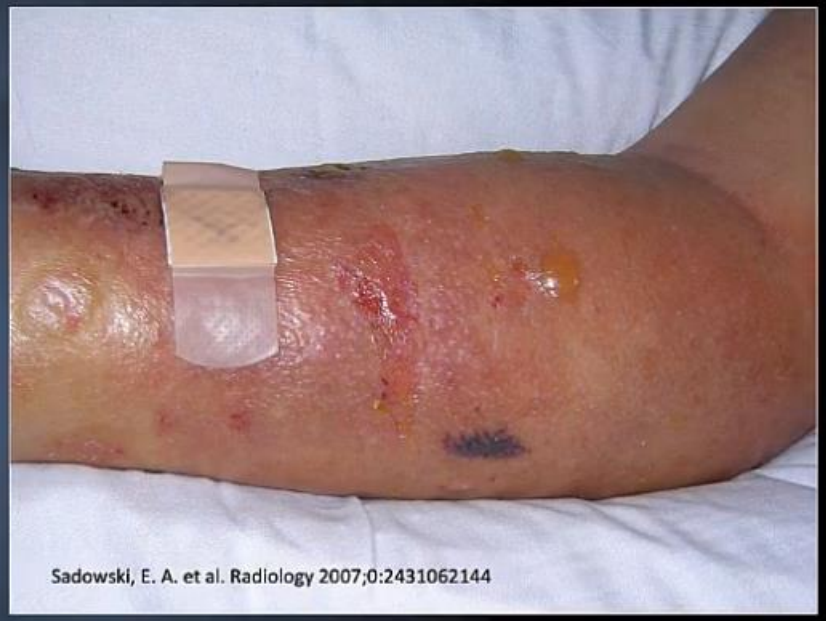
Sadowski, E. A. et al. Radiology 2007;0:2431062144

Nephrogenic Systemic Fibrosis (NSF)

"… generally accepted that GBCA exposure is a necessary factor in the development of NSF, although in rare instances NSF can be diagnosed without known GBCA exposure*."

GBCA exposure not the only trigger for NSF

Am J Transplant 2007; 7:2425-2432
Australas J Dermatol. 2008:49:44-7
J Cutan Pathol. 2009; 1(36 suppl): 31-34



Currently, the exact pathophysiology of NSF remains unknown

TABLE 1. ACR Manual Classification of Gadolinium-Based Agents Relative to Nephrogenic Systemic Fibrosis

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

Gadodiamide (Omniscan® – GE Healthcare)

Gadopentetate dimeglumine (Magnevist® – Bayer HealthCare Pharmaceuticals)

Gadoversetamide (OptiMARK® – Guerbet)

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

Gadobenate dimeglumine (MultiHance® – Bracco Diagnostics)

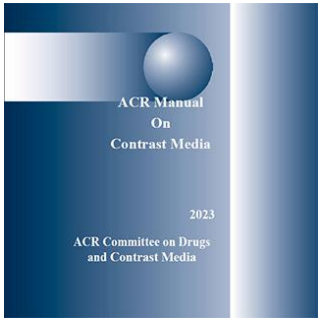
Gadobutrol (Gadavist® – Bayer HealthCare Pharmaceuticals; Gadovist in many countries) Gadoteric acid

(Dotarem® – Guerbet, Clariscan – GE Healthcare)

Gadoteridol (ProHance® – Bracco Diagnostics)

Group III: Agents for which data remains limited regarding NSF risk, but for which few, if any unconfounded cases of NSF have been reported:

Gadoxetate disodium (Eovist – Bayer HealthCare Pharmaceuticals; Primovist in many countries)



Group II Agents

Based on the most recent scientific and clinical evidence [30-37] the ACR Committee on Drugs and Contrast Media considers the risk of NSF among patients exposed to standard or lower than standard doses of group II GBCAs is sufficiently low or possibly nonexistent such that assessment of renal function with a questionnaire or laboratory testing is optional prior to intravenous administration. As in all instances, group II GBCAs should only be administered if they are deemed necessary by the supervising radiologist, and the lowest dose needed for diagnosis should be used as deemed necessary by the supervising radiologist.[1]

Based on the most recent scientific and clinical evidence [30-37] the ACR Committee on Drugs and Contrast Media considers the risk of NSF among patients exposed to standard or lower than standard doses of group II GBCAs is sufficiently low or possibly nonexistent such that assessment of renal function with a questionnaire or laboratory testing is optional prior to intravenous administration. As in all instances, group II GBCAs should only be administered if they are deemed necessary by the supervising radiologist, and the lowest dose needed for diagnosis should be used as deemed necessary by the supervising radiologist.[1]

Gadolinium Retention

- Retention in bone and other tissues known for some time
- Recently discovered retention in certain areas of the brain in patients without clinically evident disease and intact blood brain barrier
- To date, no adverse health effects have been demonstrated in both animal and human brain tissues
- FDA recommendations include limiting the use of GBCAs to cases where it is clinically warranted
- Assess the necessity of repeated exams GBCAs

Formazione per l'eccellenza

Adverse Events

- Rate at clinical doses: 0.07% to 2.4%
  Most reactions are mild and physiologic, including coldness, warmth, or pain at the injection site; nausea with or without vomiting; headache; paresthesias; and dizziness.
- Allergic-like reactions: 0.004% to 0.7%
  Similar to those of an allergic-like reaction to an iodinated contrast medium
- Severe life-threatening anaphylactic: 0.001% to 0.01%

Adverse Events

Medical Emergencies

- Medical emergencies in the MRI environment present unique challenges - Quenching the magnet IS NOT an appropriate response
- Do not attempt to treat a medical emergency in the scan room (Zone IV)
- The patient should be immediately removed to a predetermined MR safe area for treatment
- Practice codes and emergent patient removal at least once a year and under all staffing scenarios
- Level 2 MR personnel are to remain in control of the MRI environment at all times

La Fibrosi Sistemica Nefrogenica (NSF, dall'inglese Nephrogenic Systemic Fibrosis), nota anche con il nome di dermatopatia nefrogenica fibrosante, è una malattia sistemica descritta esclusivamente in pazienti con grave disfunzione renale. È caratterizzata da un interessamento fibrotico della pelle simile alla sclerodermia, interessamento che successivamente coinvolge anche altri organi.

Da quando la NFS è stata per la prima volta riconosciuta nel 1997, i ricercatori hanno prospettato diverse teorie sulle possibili cause della malattia. Tuttavia solo all'inizio del 2006 è stata ipotizzata una correlazione tra l'NSF ed i mezzi di contrasto contenenti Gadolinio.

BioSpace®

New Gadolinium-Free MRI Contrast Agent Advances Safer Patient CareReveal Pharmaceuticals doses first subjects in **Phase 1 Clinical Trial of RVP-001**

Published: Jun 13, 2022

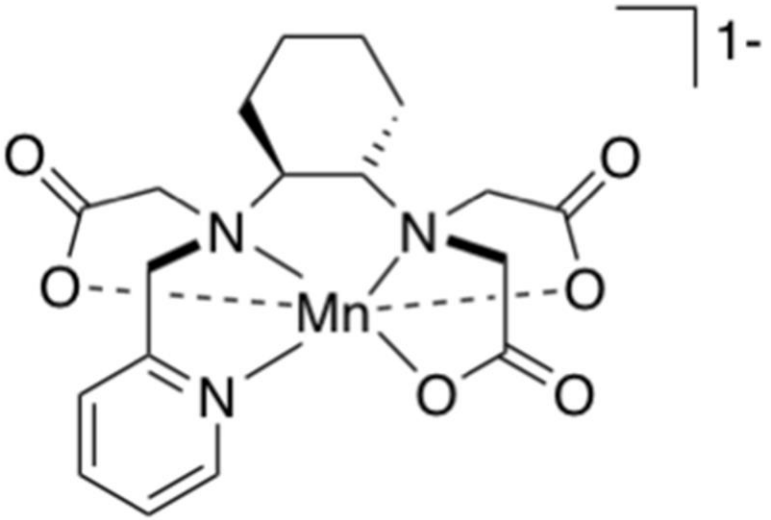
Reveal Pharma

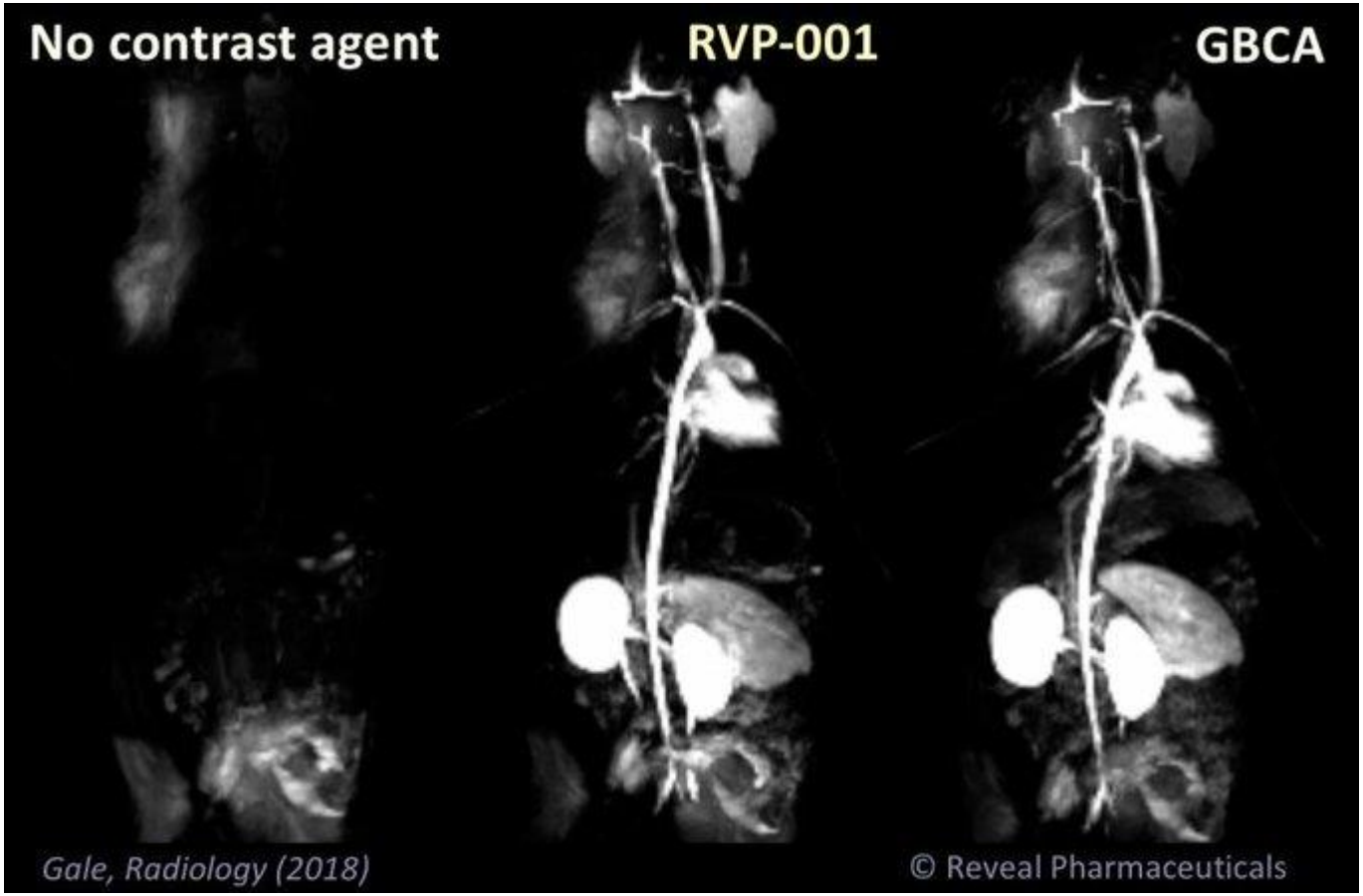
RVP-001 was invented by Peter Caravan and Eric Gale at Harvard Medical School / Massachusetts General Hospital. The National Cancer Institute, part of the National Institutes of Health, is funding the US-based clinical trial.

BioSpace®

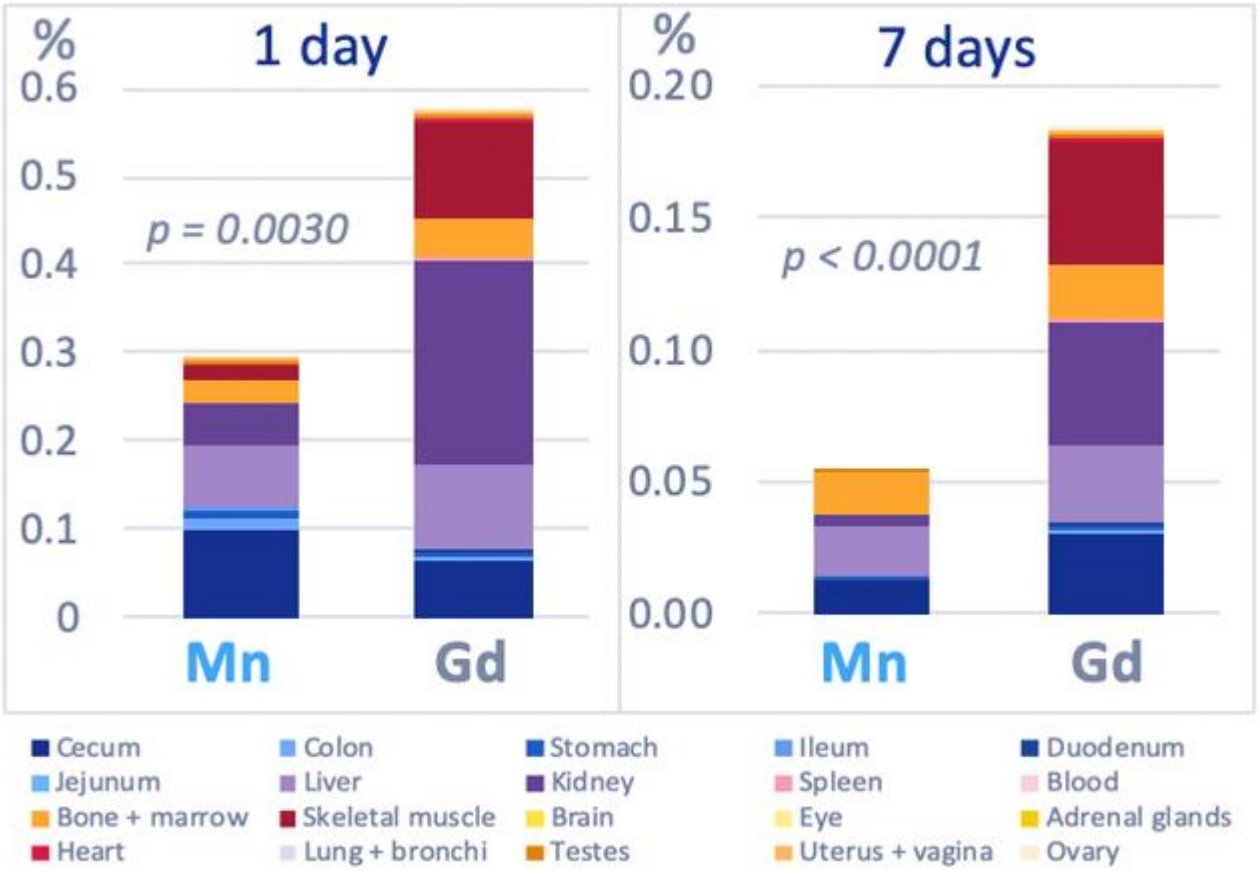
"RVP-001 promises to directly replace gadolinium-based contrast agents and use established radiology protocols developed over decades of CE-MRI," said Srinivasan Mukundan, Reveal's medical director and former chief of MRI and Neuroradiology at Brigham Health.

RVP-001 is based on **manganese**, an essential element. It was designed to produce equivalent images for the same indications as current gadolinium based contrast agents, using existing radiology protocols.




No contrast agent
RVP-001
GBCA
Gale, Radiology (2018)
© Reveal Pharmaceuticals

Reveal vs Gd-DOTA Residual Metal

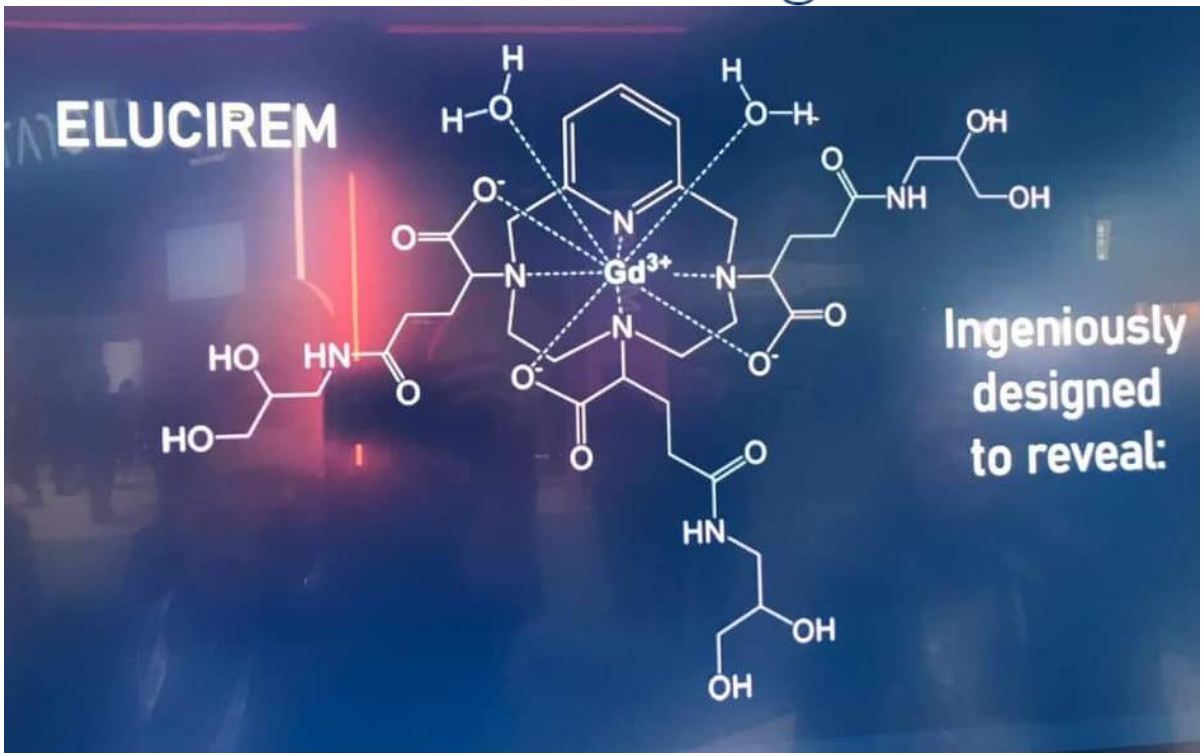


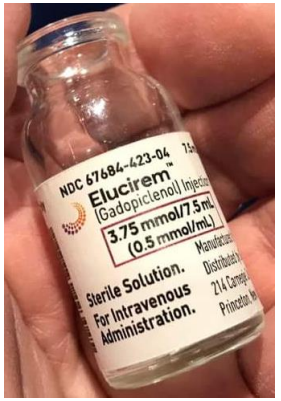
 Gale, Investigative Radiology 2019

Elucirem™ (gadopiclenol) injection

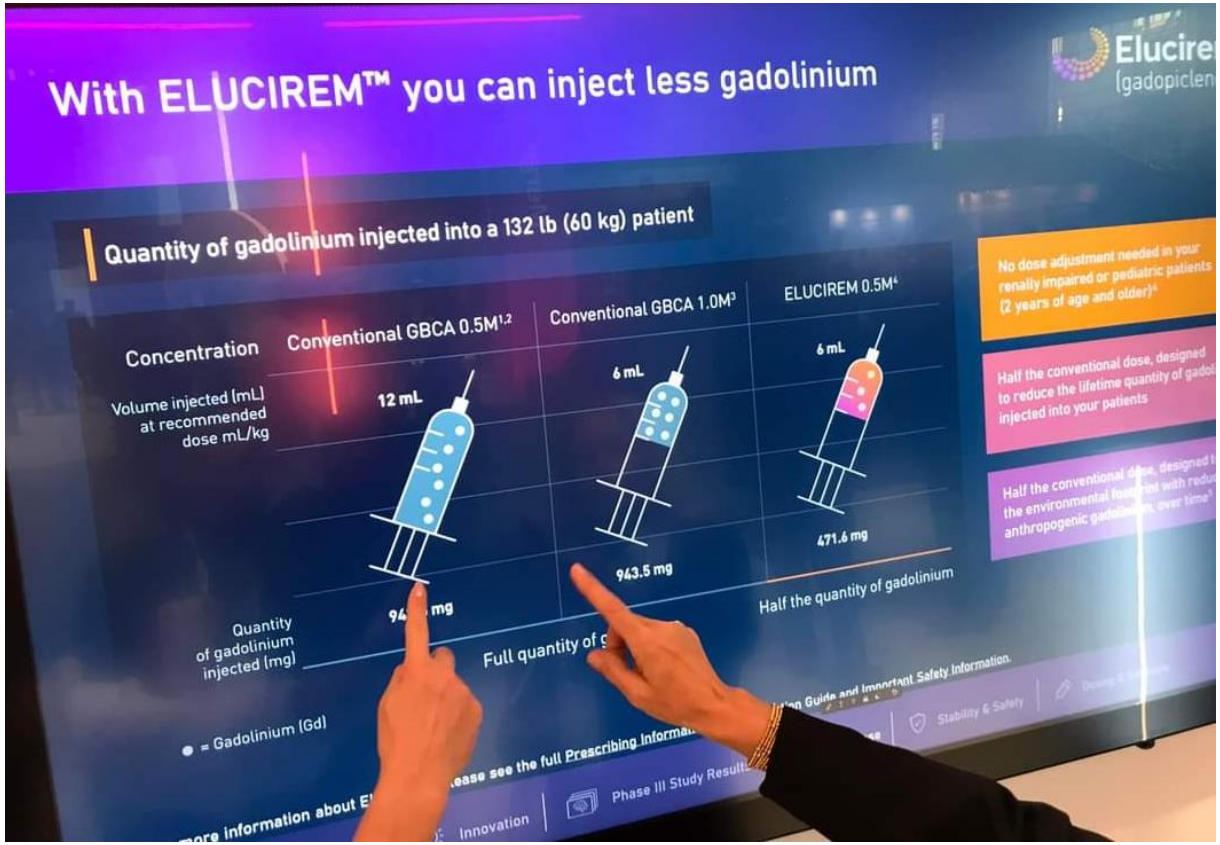
RSNA – Chicago 2022

ELUCIREM illuminates high-quality images at half the conventional dose of gadolinium[1]





Elucirem™ (gadopiclenol) injection



← Health Imaging 🔍

New MRI contrast agent Gadopiclenol (Elucirem) was developed to cut gadolinium doses in half from current agents. It was just cleared by the FDA and is not yet released in the market, pending the creation of packet inserts.

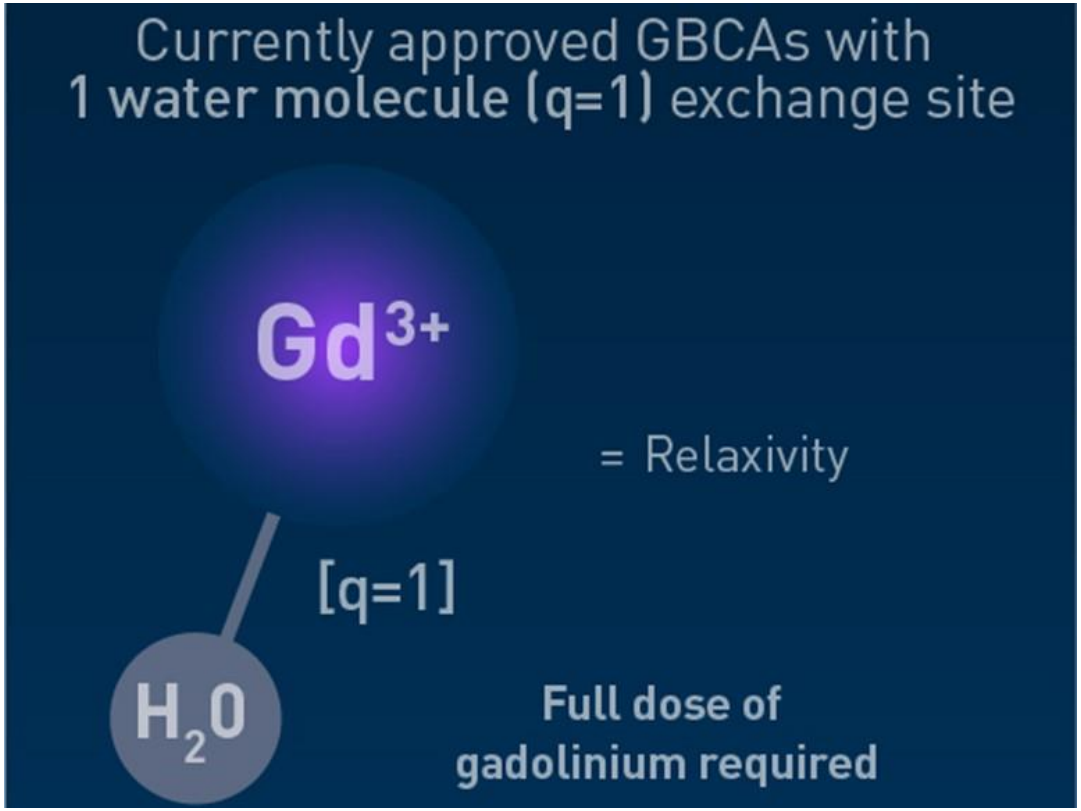
It has a molecular structure with two water molecules rather than one found on all othe gadolinium agents. This allows it to bind with tissues in the body for easier and morerapid uptake. The molecules are also large, which slows relaxation during MRI scanning.

The contrast agent was co-developed by Guebet and Bracco. Guebet will be producing it domestically in the U.S. in Ralghie, North Carolina, for itself and Bracco. The two companies were selling the product under different brand names.

Guebet said the lower dose gadolinium agent was developed over the past several year out of concerns about the possible long term health issues retained gadolinium. For this reason, Guebet said it will be targeted for pediatrics and

Elucirem™ (gadopiclenol) injection

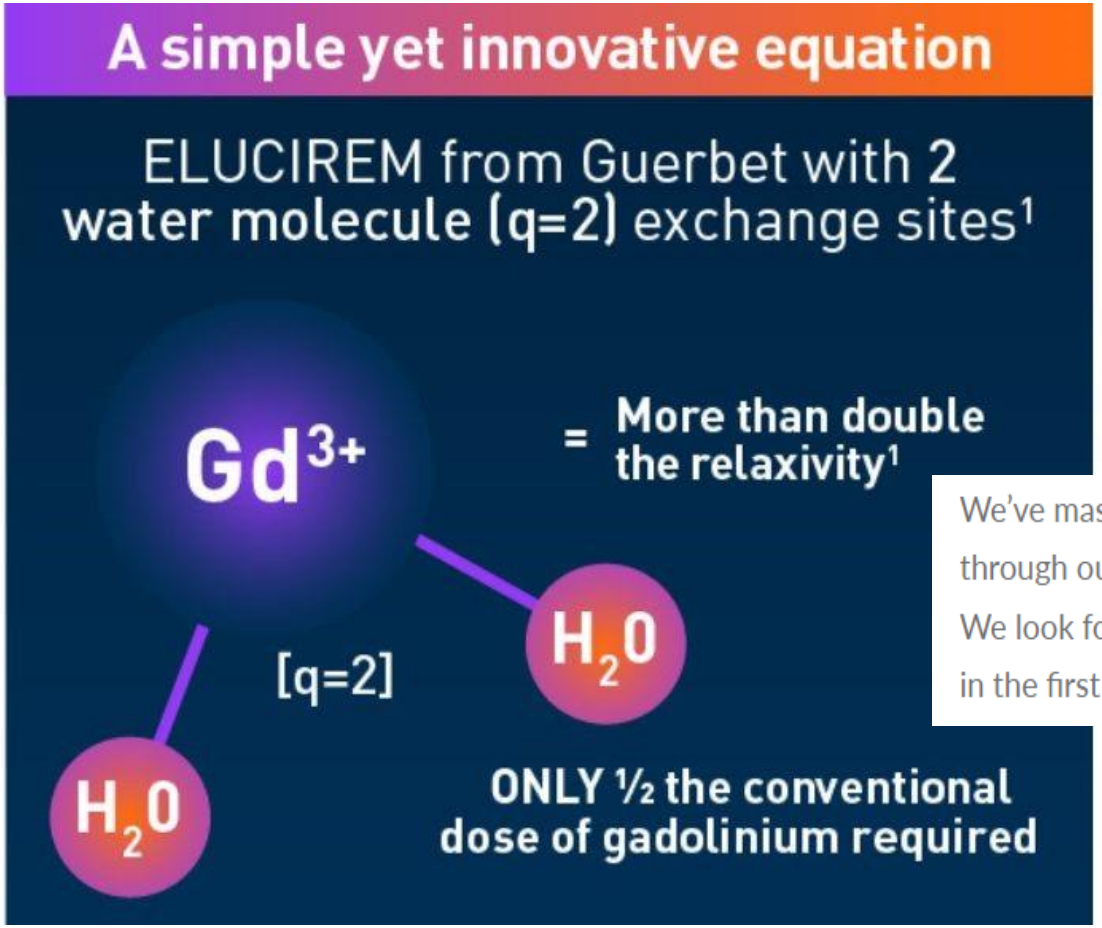
Guerbet



Most GBCAs have 1 water molecule exchange site, which provides relaxivity and contrast enhancement with a conventional dose of gadolinium

Formazione per l'eccellenza

Elucirem™ (gadopiclenol) injection



ELUCIREM is designed with 2 water molecule exchange sites, which doubles the relaxivity and amplifies contrast enhancement, allowing the use of 50% less gadolinium than conventional GBCAs[1]

We've mastered the gadopiclenol manufacturing process through our history of macrocyclic GBCA innovation.
We look forward to making ELUCIREM commercially available in the first quarter of 2023.

Guerbet

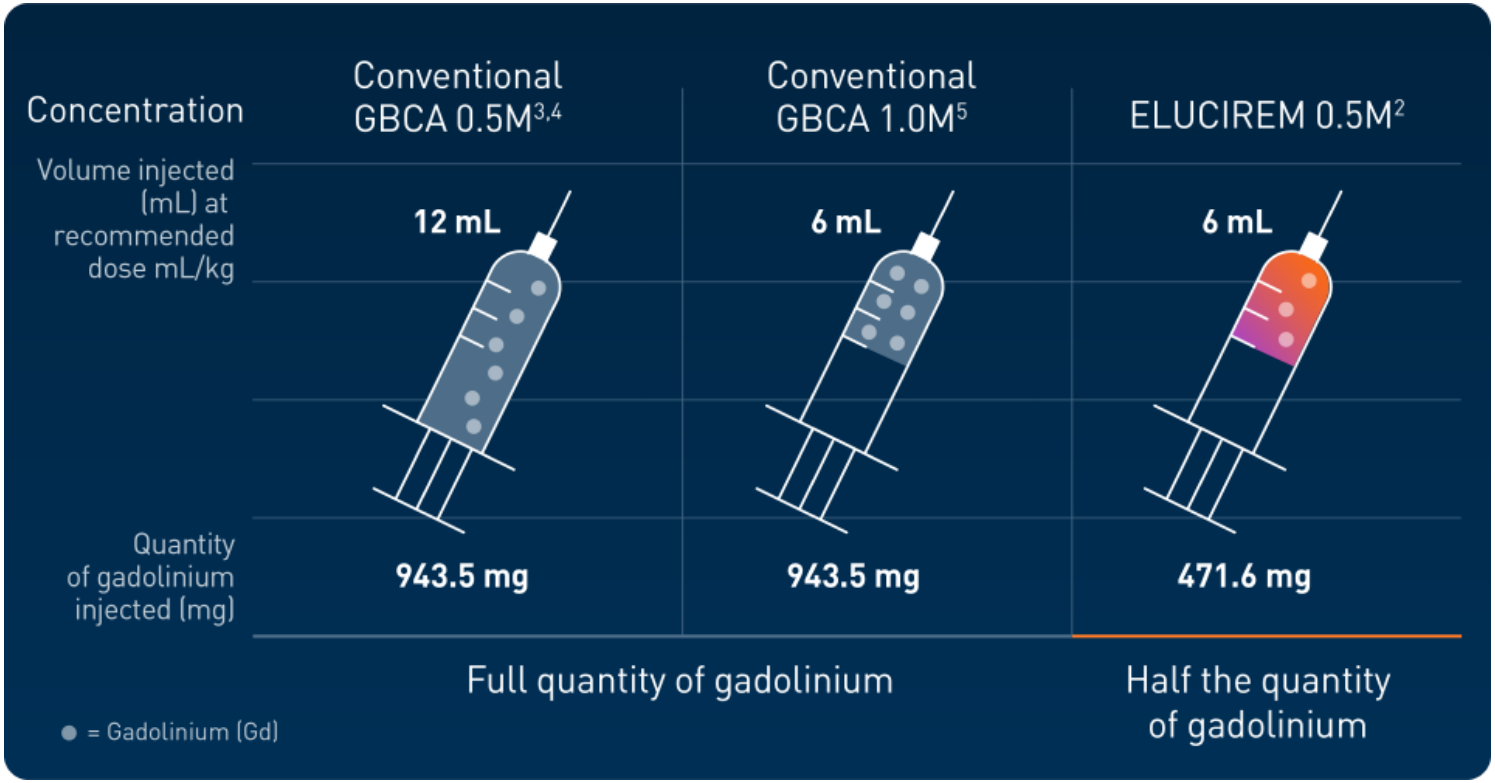
Gemelli

https://www.elucirem.com/

Formazione per l'eccellenza

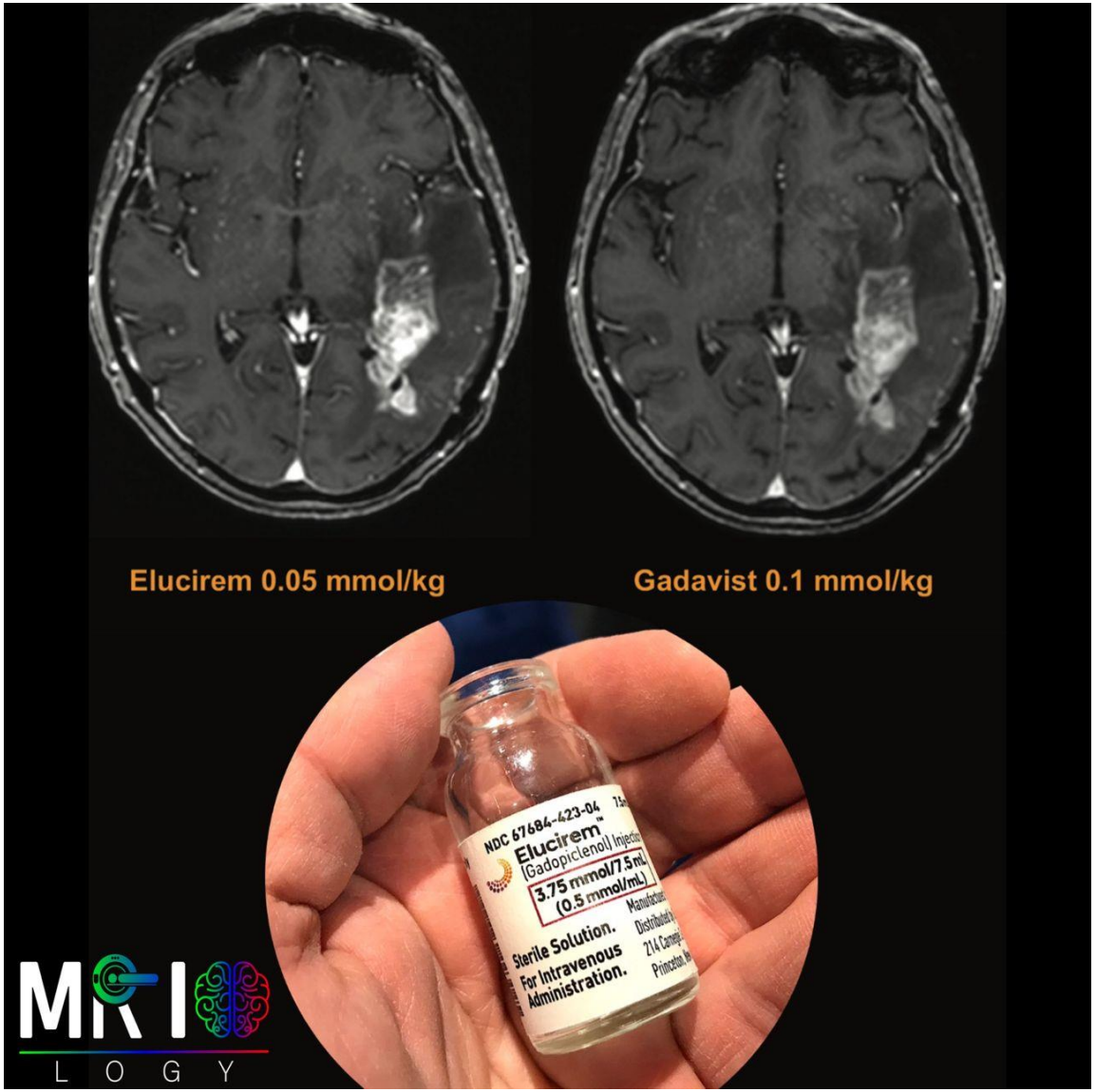
Elucirem™ (gadopiclenol) injection

Guerbet



Elucirem™ (gadopiclenol) injection

Guerbet



Gemelli

Elucirem™ (gadopiclenol) injection

Guerbet

ELUCIREM™ (gadopiclenol) injection Important Safety Information

Indications and Usage

ELUCIREM™ (gadopiclenol) injection is indicated in adult and pediatric patients aged 2 years and older for use with magnetic resonance imaging (MRI) to detect and visualize lesions with abnormal vascularity in the central nervous system (brain, spine, and associated tissues), and the body (head and neck, thorax, abdomen, pelvis, and musculoskeletal system).

AR Connect MRI Pediatric Imaging Portal Nov 20, 2023

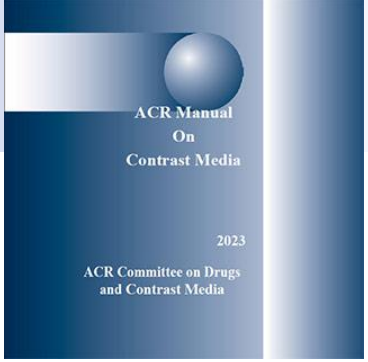
Celebrating the First Clinical Administration of Elucirem™ (Gadopiclenol) Injection for MRI

Guerbet

Following FDA approval of Elucirem™ (gadopiclenol) injection in 2022, the first clinical injection of the GBCA in the United States took place in February 2023 at the Hospital of the University of Pennsylvania in Philadelphia. Laurie A. Loevner, MD, Chief of the Division of Neuroradiology, and Professor of radiology at the Perelman School of Medicine at the University of Pennsylvania, was involved in the clinical trials for gadopiclenol, and administered that first dose.

Villepinte (France), June 13 2022 (8:30 CET) – Guerbet (FR0000032526 GBT), a global leader in medical imaging, announces today that Elucirem™, the proposed Guerbet brand name for Gadopiclenol, has been accepted by the European Medicines Agency (EMA). Gadopiclenol is an investigational macrocyclic gadolinium-based contrast agent.

AGO-CANNULA



Intravenous contrast media should be administered by power injector through a flexible plastic cannula. Use of metal needles for power injection should be avoided whenever possible. In addition, the flow rate should be appropriate for the gauge of the catheter used. Although 22-gauge catheters may be able to tolerate flow rates up to 5 ml/sec, a **20-gauge** or larger catheter is preferable for **flow rates of 3 ml/sec or greater**. An antecubital or large forearm vein is the preferred venous access site for power injection. If a **more peripheral** (e.g., hand or wrist) venipuncture site must be used, flow rates should be reduced if feasible (e.g., **1-2 mL/sec**).

AGO-CANNULA

Formazione per l'eccellenza

Ago cannula di sicurezza Jelco IntuitIV Safety Catheter™

Codice ordine	Lunghezza	Calibro/Colore introduttore	Materiale ago cannula
7138	32 mm	14G, Arancione	FEP
7188	45 mm	14G, Arancione	FEP
7131	32 mm	16G, Grigio	FEP
7132	45 mm	16G, Grigio	FEP
7135	32 mm	18G, Verde	FEP
7134	45 mm	18G, Verde	FEP
7137	25 mm	20G, Rosa	FEP
7136	32 mm	20G, Rosa	FEP
7139	45 mm	20G, Rosa	FEP
7130	25 mm	22G, Blu	FEP
7133	19 mm	24G, Giallo	FEP

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AGO-CANNULA

Formazione per l'eccellenza

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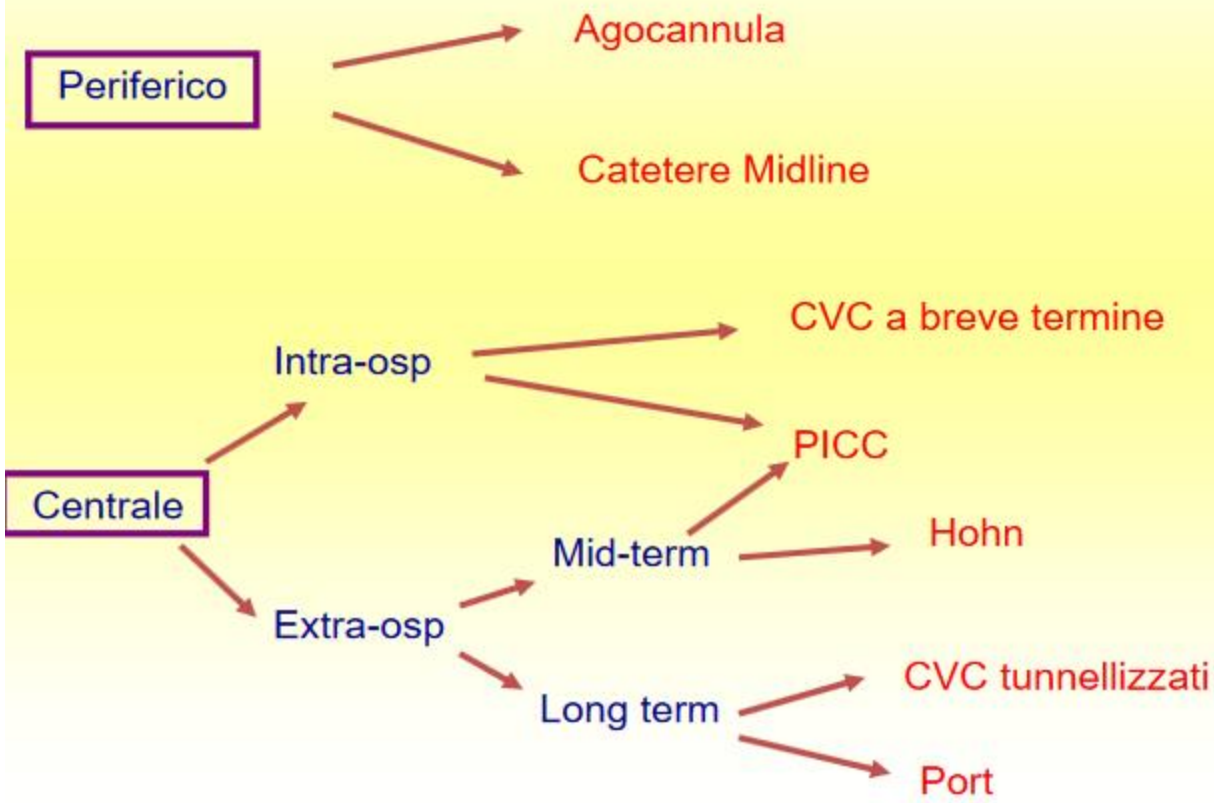
BARD ADVANCING LIVES AND THE DELIVERY OF HEALTH CARE™

Il **PowerPort* isp M.R.I.* Delrin** garantisce i benefici dell'infusione del mezzo di contrasto ad alta pressione (quando utilizzato con il set di infusione sicura PowerLoc*) con la proprietà di vedere attraverso il port senza alcun artefatto. Il PowerPort* isp M.R.I.* è radio-translucente, aiuta l'identificazione di un port capovolto e permette ai pazienti di ricevere le terapie E.V e le procedure TAC-MC senza la necessità di ripetute venipunture periferiche.

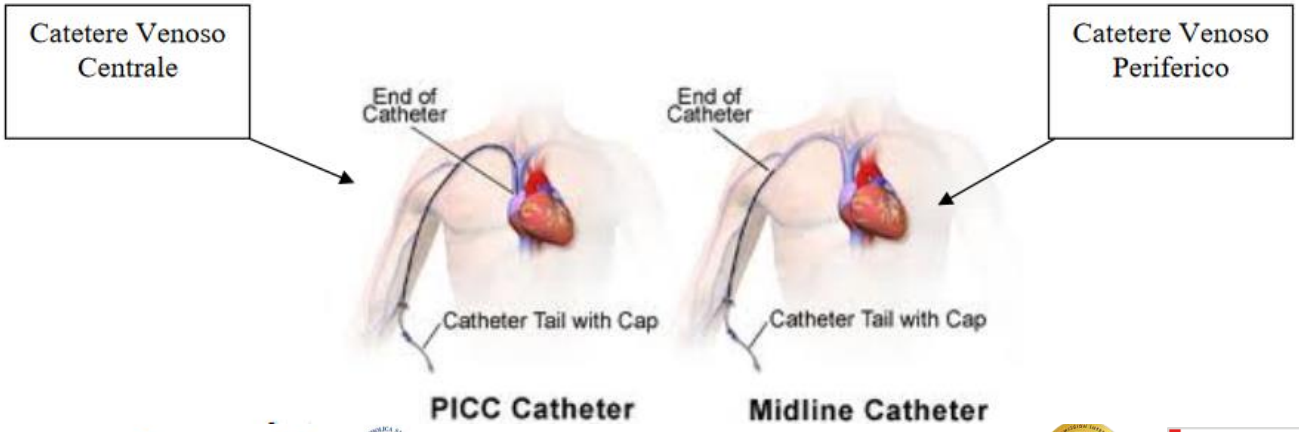
Formazione per l'eccellenza

Algoritmo per la scelta dell'accesso venoso nell'adulto

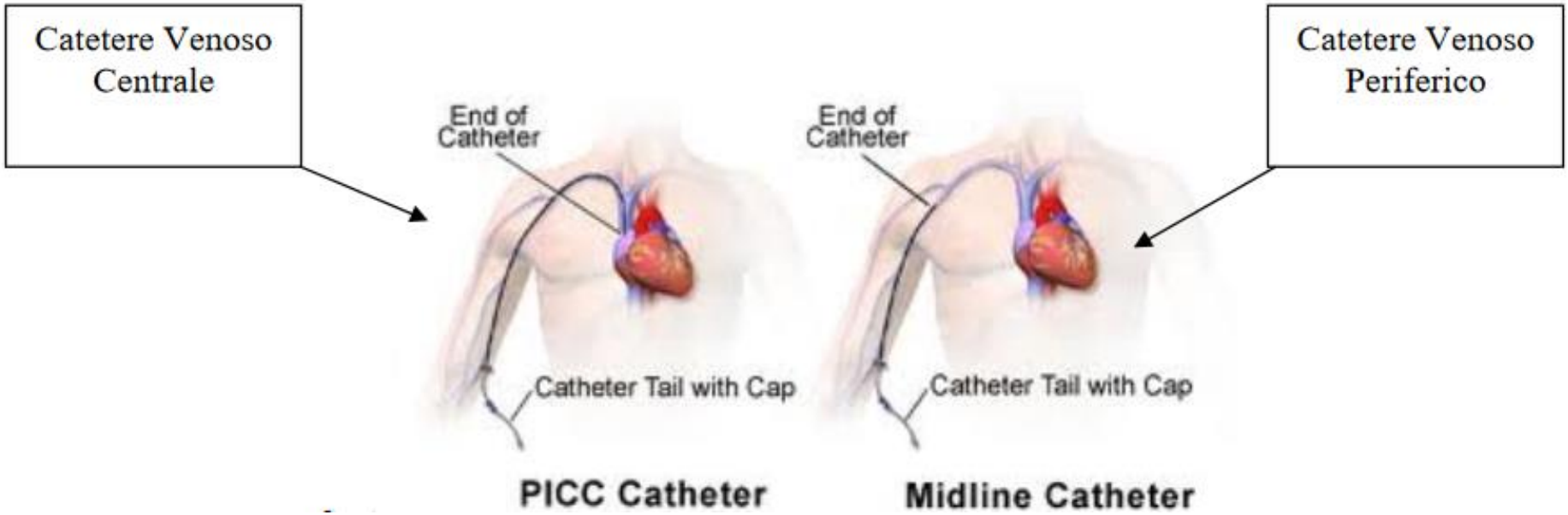


Per definizione un catetere venoso è "periferico" quando la sua punta, indipendentemente dal sito di accesso, non raggiunge la prossimità della giunzione tra vena cava superiore ed atrio destro

Un catetere venoso lo si definisce «centrale» quando la sua punta viene posizionata in prossimità della giunzione tra vena cava superiore ed atrio destro.



POWER-PICC



Da alcuni anni sono stati messi sul mercato una nuova tipologia di PICC detti **Power PICCs**, contraddistinti da un'elevata resistenza alle alte pressioni in infusione come quelle generate dalle pompe per mezzo di contrasto durante una TAC o una RM.

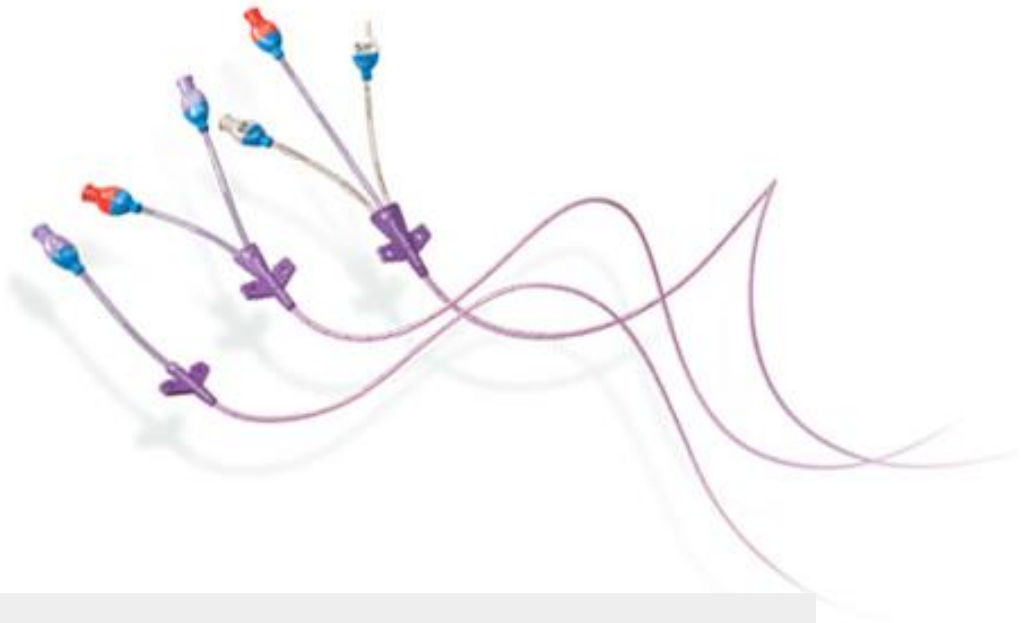
Formazione per l'eccellenza

Comparazione dei flussi tramite i PICC

- Per gravità
  - 4 Fr — 2-3 ml/min
  - 5 Fr — 3-4 ml/min
- Con pompa
  - 4 Fr — 10-11 ml/min
  - 5 Fr — 11-13 ml/min
- Pompa + PICC power injectable
  - 4 – 5 - 6 Fr — fino a 300 ml/min

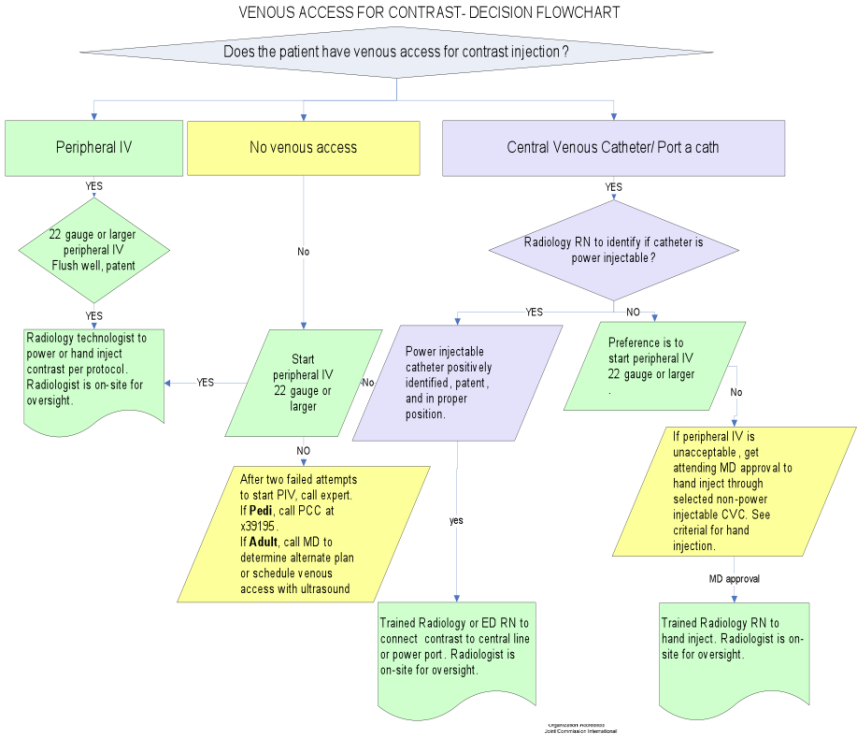
POWER-PICC

Available sizes:4 Fr. & 5 Fr. Single-Lumen, 5 Fr. Dual-Lumen, and 5 Fr. & 6 Fr. Triple-Lumen

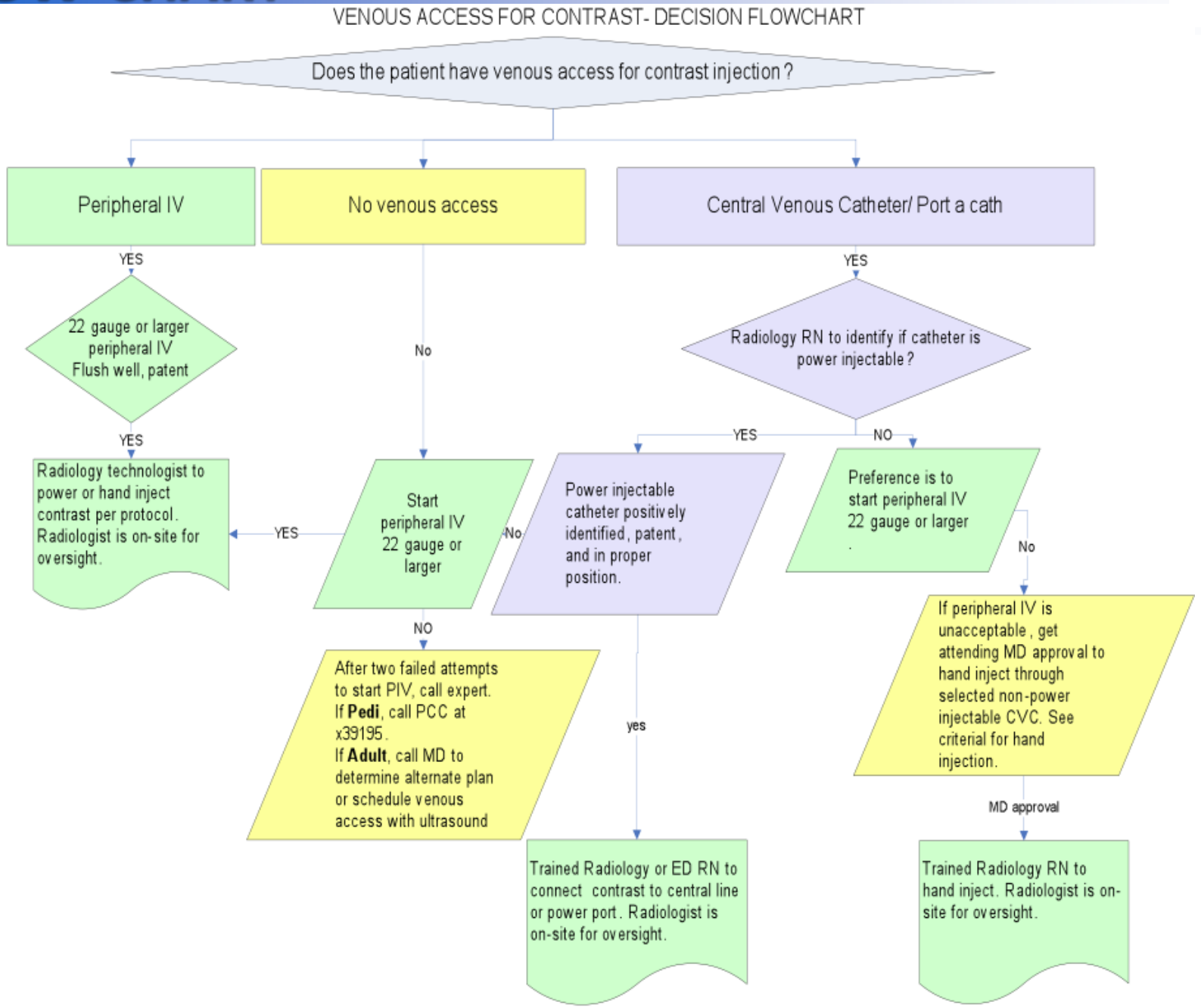


POWER-PICC

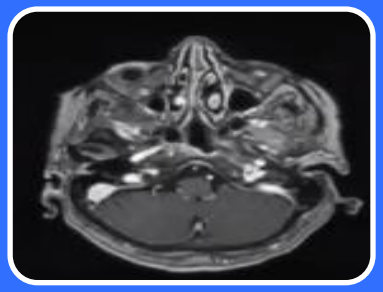

5Fr PowerPICC
5mL/sec MAX
POWERINJECTABLE


VENOUS ACCESS FOR CONTRAST- DECISION FLOWCHART
Does the patient have venous access for contrast injection ?
Peripheral IV
No venous access
Central Venous Catheter/ Port a cath
YES
22 gauge or larger peripheral IV Flush well, patent
No
YES
Radiology RN to identify if catheter is power injectable?
YES
NO
YES
Radiology technologist to power or hand inject contrast per protocol. Radiologist is on-site for oversight.
YES
Start peripheral IV 22 gauge or larger
No
Power injectable catheter positively identified, patent, and in proper position.
Preference is to start peripheral IV 22 gauge or larger .
No
NO
After two failed attempts to start PIV, call expert.
If Pedi, call PCC at x39195.
If Adult, call MD to determine alternate plan or schedule venous access with ultrasound
yes
If peripheral IV is unacceptable , get attending MD approval to hand inject through selected non-power injectable CVC. See criterial for hand injection.
MD approval
Trained Radiology or ED RN to connect contrast to central line or power port . Radiologist is on-site for oversight.
Trained Radiology RN to hand inject. Radiologist is on-site for oversight.

FLOW-CHART

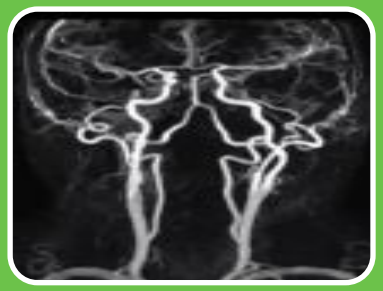

VENOUS ACCESS FOR CONTRAST- DECISION FLOWCHART
Does the patient have venous access for contrast injection?
Peripheral IV
No venous access
Central Venous Catheter/ Port a cath
YES
22 gauge or larger peripheral IV Flush well, patent
YES
Radiology technologist to power or hand inject contrast per protocol. Radiologist is on-site for oversight.
No
YES
Start peripheral IV 22 gauge or larger
No
NO
After two failed attempts to start PIV, call expert. If **Pedi**, call PCC at x39195. If **Adult**, call MD to determine alternate plan or schedule venous access with ultrasound
YES
Radiology RN to identify if catheter is power injectable?
YES
NO
Power injectable catheter positively identified, patent, and in proper position.
Preference is to start peripheral IV 22 gauge or larger .
No
If peripheral IV is unacceptable, get attending MD approval to hand inject through selected non-power injectable CVC. See criterial for hand injection.
yes
Trained Radiology or ED RN to connect contrast to central line or power port. Radiologist is on-site for oversight.
MD approval
Trained Radiology RN to hand inject. Radiologist is on-site for oversight.

FLUSSO MdC



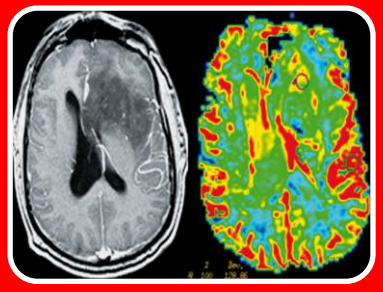
ENCEFALO STANDARD con MdC

- Flusso 1 ml/sec
- Agocannula 22-24G



ANGIO CRANIO/ANGIO COLLO

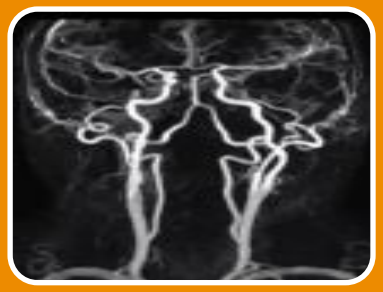
- Flusso 2 ml/sec, Angio-cranio ritardo 20 sec.
- Agocannula 20-22G



PERFUSIONE DSC (T2*) ENCEFALO

- Flusso 4-5 ml/sec, ritardo ≅ 10 scansioni basali
- Agocannula 18-20G (piega del gomito)

FLUSSO MdC

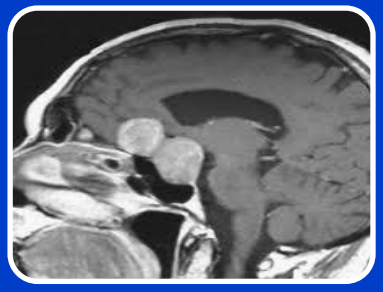


PERFUSIONE DCE (T1)

- Flusso 2 ml/sec, in contemporanea
- Agocannula 20-22G

ENCEFALO DINAMICA IPOFISI

- Flusso 2 ml/sec, 1 acq. basale, poi ritardo o cont.
- Agocannula 20-22G (valutare ½ dose)



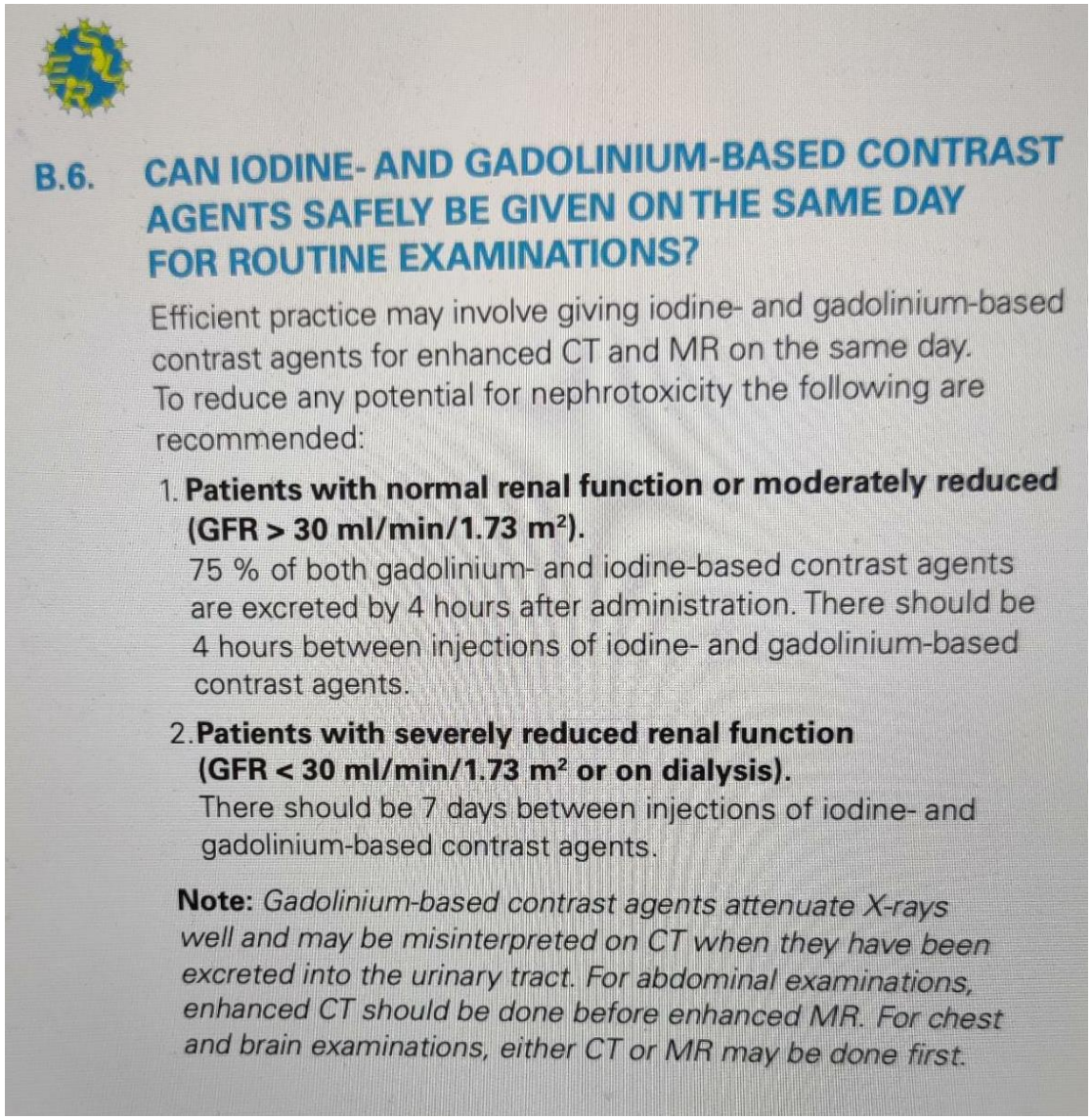
ENCEFALO IPOFISI

- Flusso 1 ml/sec
- Agocannula 22-24G

n.b. dove non è specificato eventuale ritardo, la scansione va effettuata alla fine della iniezione totale. Quindi solo dopo aver somministrato il mezzo di contrasto e la fisiologica.

Generalmente la quantità minima di fisiologica da iniettare dopo il mezzo di contrasto per l'adulto è di **20ml**.

CONTRASTO TC e RM



B.6. CAN IODINE- AND GADOLINIUM-BASED CONTRAST AGENTS SAFELY BE GIVEN ON THE SAME DAY FOR ROUTINE EXAMINATIONS?

Efficient practice may involve giving iodine- and gadolinium-based contrast agents for enhanced CT and MR on the same day. To reduce any potential for nephrotoxicity the following are recommended:

1. **Patients with normal renal function or moderately reduced (GFR > 30 ml/min/1.73 m²).**
   75 % of both gadolinium- and iodine-based contrast agents are excreted by 4 hours after administration. There should be 4 hours between injections of iodine- and gadolinium-based contrast agents.
2. **Patients with severely reduced renal function (GFR < 30 ml/min/1.73 m² or on dialysis).**
   There should be 7 days between injections of iodine- and gadolinium-based contrast agents.

Note: *Gadolinium-based contrast agents attenuate X-rays well and may be misinterpreted on CT when they have been excreted into the urinary tract. For abdominal examinations, enhanced CT should be done before enhanced MR. For chest and brain examinations, either CT or MR may be done first.*

Formazione per l'eccellenza

Use of both iodine- and gado-based contrast boosts kidney injury risk

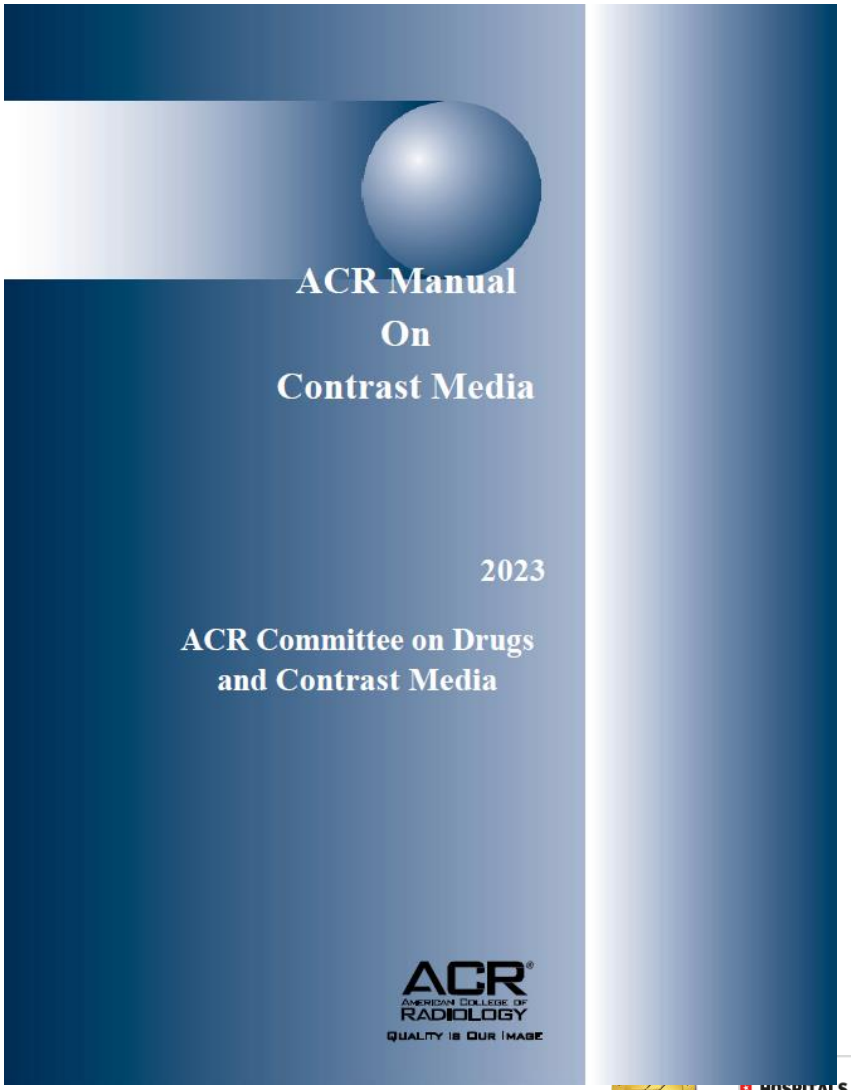
AuntMinnie.com

team led by Dr. Changshin Kang of Chungnam NationalUniversity Hospital in Daejeon, South Korea. The results were published April 26 in *KidneyResearch and Clinical Practice*.

April 28, 2023 -- Patients who present in the emergency department (ED) and undergo advanced CT and MR imaging with both iodine- and gadolinium-based contrast are at higher risk of postcontrast acute kidney injury (PC-AKI).

Sicurezza e MdC

https://www.acr.org/Clinical-Resources/Contrast-Manual

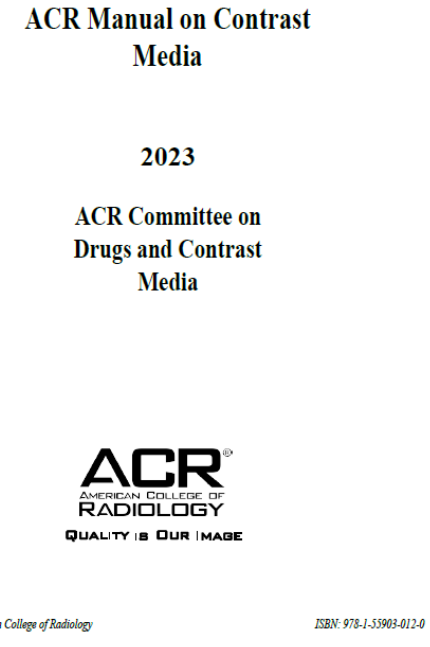


Formazione per l'eccellenza

Gemelli

Manual on Contrast Media

https://www.acr.org/Clinical-Resources/Contrast-Manual



Manual on Contrast Media

Download Your Copy of the Contrast Manual Today »

Contrast Reaction Cards

Contrast Reaction Card **(Adult)**

Download the Adult Contrast Reaction Card »

Contrast Reaction Card **(Pediatric)**

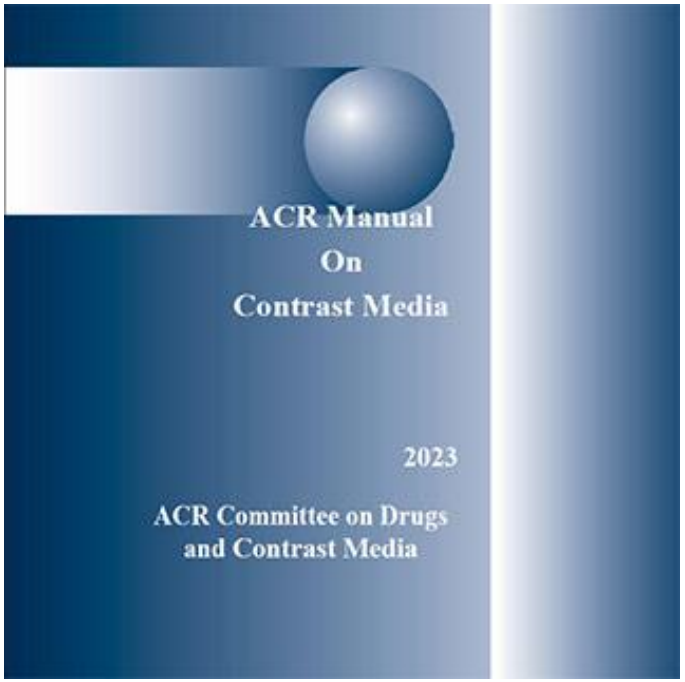
Download the Pediatric Contrast Reaction Card »

Updated chapters:

- Extravasation of Contrast Media (Evidence Based Update) – 2022
- Gadolinium Pregnancy Screening Statement – 2022

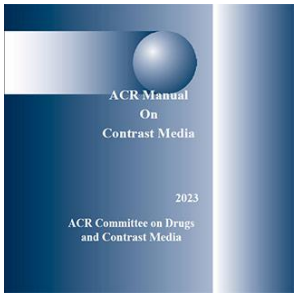
Reazioni al MdC

Le reazioni di tipo allergico ai moderni mezzi di contrasto iodati e a base di gadolinio sono rare (iodato: 0,6% aggregato, 0,04% grave; a base di gadolinio: 0,01-0,22% aggregato, 0,008% grave). Esistono fattori di rischio che aumentano il rischio di una reazione di contrasto.



Reazioni al MdC

Allergia: i pazienti che hanno avuto una precedente reazione di tipo allergico o di tipo sconosciuto (ovvero una reazione di manifestazione sconosciuta) al mezzo di contrasto hanno un rischio circa 5 volte maggiore di sviluppare una futura reazione di tipo allergico se esposti ancora una volta alla stessa classe del mezzo di contrasto. Una precedente reazione di tipo allergico o di tipo sconosciuto alla stessa classe di mezzo di contrasto è considerata il maggior fattore di rischio per la previsione di futuri eventi avversi. In generale, i pazienti con allergie non correlate corrono un rischio da 2 a 3 volte maggiore di una reazione di tipo allergico al mezzo di contrasto, ma a causa del modesto aumento del rischio, non è raccomandato limitare l'uso del mezzo di contrasto o premedicare esclusivamente sulla base di allergie non correlate .

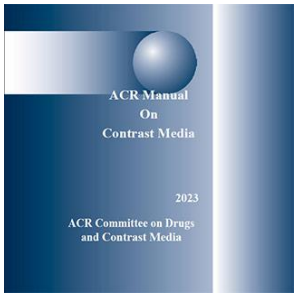


Reazioni al MdC

Asma: una storia di asma aumenta la probabilità di una reazione di contrasto di tipo allergico

Stato cardiaco: i pazienti con cardiopatia grave possono essere maggiormente a rischio di un evento cardiaco non allergico se si verifica una reazione di contrasto di tipo allergico o non allergico. Questi includono pazienti sintomatici (ad esempio, pazienti con angina o sintomi di insufficienza cardiaca congestizia con uno sforzo minimo) e anche pazienti con grave stenosi aortica, aritmie cardiache, ipertensione polmonare primaria o cardiomiopatia grave ma compensata.

Ansia: ci sono alcune prove che le reazioni di contrasto sono più comuni nei pazienti ansiosi. Rassicurare un paziente ansioso prima dell'iniezione del mezzo di contrasto può mitigare la probabilità di una lieve reazione di contrasto.

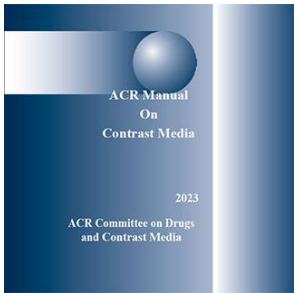


Reazioni al MdC

Età e sesso: neonati, bambini e anziani hanno tassi di reazione inferiori rispetto ai pazienti di mezza età. I pazienti di sesso maschile hanno tassi di reazione inferiori rispetto alle pazienti di sesso femminile.

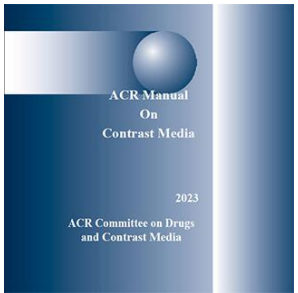
Beta-bloccanti: alcuni hanno suggerito che l'uso di beta-bloccanti abbassa la soglia per le reazioni di contrasto, aumenta la gravità delle reazioni di contrasto e riduce la risposta al trattamento con epinefrina. I pazienti in terapia con beta-bloccanti non devono sospendere il/i farmaco/i prima della somministrazione del mezzo di contrasto.

Tratto/malattia falciforme: alcuni hanno suggerito che l'esposizione al mezzo di contrasto nei pazienti con tratto falciforme o anemia falciforme potrebbe aumentare il rischio di una crisi falciforme acuta; tuttavia, non ci sono prove che ciò avvenga con i moderni mezzi di contrasto iodati o a base di gadolinio.



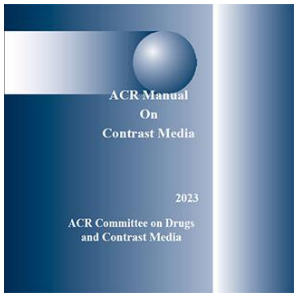
Reazioni al MdC

Feocromocitoma: non ci sono prove che la somministrazione EV di moderni mezzi di contrasto iodati o a base di gadolinio aumenti il rischio di crisi ipertensive nei pazienti con feocromocitoma. L'iniezione diretta di qualsiasi tipo di mezzo di contrasto nelle arterie surrenali o renali in un paziente con feocromocitoma non è stata adeguatamente studiata ed è di rischio sconosciuto.



Reazioni al MdC

Miastenia grave: esiste una relazione discutibile tra il mezzo di contrasto iodato EV e le riacutizzazioni dei sintomi miastenici nei pazienti con miastenia grave. Mentre uno studio retrospettivo non ha mostrato alcun aumento immediato dei sintomi miastenici in seguito alla somministrazione di mezzo di contrasto iodato o a base di gadolinio, un altro che ha cercato le riacutizzazioni miasteniche che si verificano fino a 45 giorni dopo una scansione TC ha rilevato che il mezzo di contrasto iodato non ionico IV era associato a una riacutizzazione miastenica acuta (entro 1 giorno dalla somministrazione del mezzo di contrasto) in circa il 6% dei pazienti (rispetto a un tasso di esacerbazione acuta dell'1% nei pazienti sottoposti a TC senza mezzo di contrasto, p=0,01). Tuttavia, quello studio era retrospettivo e il numero di eventi era piccolo. È controverso se il mezzo di contrasto iodato debba essere considerato una controindicazione relativa nei pazienti con miastenia grave.

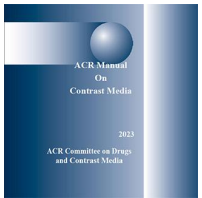


Reazioni al MdC

Ipertiroidismo: i pazienti con una storia di ipertiroidismo possono sviluppare tireotossicosi dopo esposizione a mezzo di contrasto iodato, ma questa complicanza è rara. Pertanto, si sconsiglia di limitare l'uso del mezzo di contrasto o premedicare esclusivamente sulla base di una storia di ipertiroidismo.

Tuttavia, due situazioni speciali possono influire su questo:

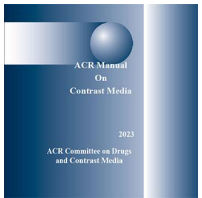
1. Nei pazienti con tempesta tiroidea acuta, l'esposizione al mezzo di contrasto iodato può potenziare la tireotossicosi; in tali pazienti, il mezzo di contrasto iodato deve essere evitato. È improbabile che la premedicazione con corticosteroidi in questo contesto sia utile.
2. Nei pazienti che stanno prendendo in considerazione la terapia con iodio radioattivo o nei pazienti sottoposti a imaging con iodio radioattivo della ghiandola tiroidea, la somministrazione di mezzo di contrasto iodato può interferire con l'assorbimento del trattamento e la dose diagnostica. Se è stato somministrato mezzo di contrasto iodato, si suggerisce un periodo di sospensione per ridurre al minimo questa interazione. Il periodo di washout è idealmente di 3-4 settimane per i pazienti con ipertiroidismo e di 6 settimane per i pazienti con ipotiroidismo.



Reazioni al MdC

Funzionalità tiroidea normale: il mezzo di contrasto iodato non influisce sui risultati dei test di funzionalità tiroidea nei pazienti con una ghiandola tiroidea normalmente funzionante. Diversi studi hanno dimostrato che una singola dose di mezzo di contrasto iodato somministrato a una madre incinta non ha alcun effetto sulla funzione tiroidea neonatale.

Angiografia: i mezzi di contrasto per iso-osmolalità (IOCM) sono associati alla minima quantità di vasospasmo e al minor disagio periferico per gli angiogrammi periferici. L'uso concomitante di mezzo di contrasto iodato con alcuni farmaci intra-arteriosi (ad es. papaverina) può portare alla precipitazione del mezzo di contrasto e alla formazione di cristalli o trombi. Le decisioni sull'uso e la tempistica di tali farmaci non rientrano nell'ambito di questo documento.



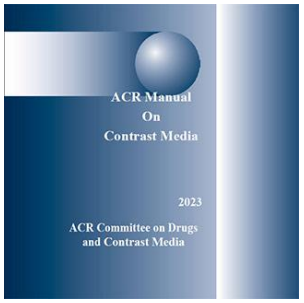
Reazioni al MdC

Table 1: CATEGORIES OF ACUTE REACTIONS

Mild

Signs and symptoms are self-limited without evidence of progression. Mild reactions include:

Allergic-like	Physiologic
Limited urticaria / pruritis	Limited nausea / vomiting limited
Cutaneous Edema	Transient flushing / warmth / chills
Limited "itchy"/"scratchy" throat	Headache / dizziness / anxiety / altered taste
Nasal congestion	Mild hypertension
Sneezing / conjunctivitis / rhinorrhea	Vasovagal reaction that resolves spontaneously



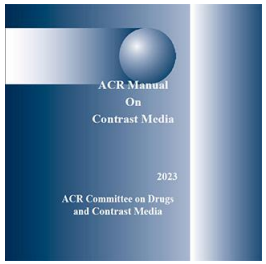
Reazioni al MdC

Table 1: CATEGORIES OF ACUTE REACTIONS

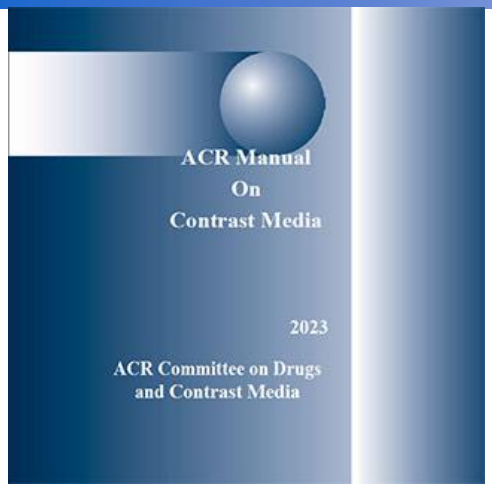
Moderate

Signs and symptoms are more pronounced and commonly require medical management. Some of these reactions have the potential to become severe if not treated. Moderate reactions include:

Allergic-like	**Physiologic**
Diffuse urticaria / pruritis	Protracted nausea / vomiting
Diffuse erythema, stable vital signs	Hypertensive urgency
Facial edema without dyspnea	Isolated chest pain
Throat tightness or hoarseness without dyspnea	Vasovagal reaction that requires and is responsive to treatment
Wheezing / bronchospasm, mild or no hypoxia	



Reazioni al MdC



Severe

Severe reactions include:

Allergic-like	**Physiologic**
Diffuse edema, or facial edema with dyspnea	Vasovagal reaction resistant to treatment
Diffuse erythema with hypotension	Arrhythmia
Laryngeal edema with stridor and/or hypoxia	Convulsions, seizures
Wheezing / bronchospasm, significant hypoxia	Hypertensive emergency
Anaphylactic shock (hypotension + tachycardia)	

MdC e funzionalità renale

In un nuovo documento pubblicato sull'American Journal of Kidney Diseases (AJKD) e sul Journal of the American Society of Nephrology (JASN), una task force della National Kidney Foundation (NKF) e dell'American Society of Nephrology (ASN) ha delineato un nuovo approccio che non tiene conto della razza per diagnosticare la **malattia renale**.

JASN
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

A Unifying Approach for GFR Estimation: Recommendations of the NKF-ASN Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Disease
Cynthia Delgado, Mukta Baweja, Deidra Crews, Nwamaka Eneanya, Crystal Gadegbeku, Lesley Inker, Mallika Mendu, W. Greg Miller, Marva Moxey-Mims, Glenda Roberts, Wendy St. Peter, Curtis Warfield and Neil Powe
JASN September 2021, ASN.2021070988; DOI: https://doi.org/10.1681/ASN.2021070988

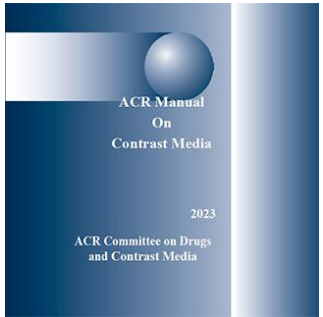
MdC e funzionalità renale

Nel rapporto la task Force NKF-ASN raccomanda l'adozione della nuova equazione della creatinina introdotta nel 2021 dalla Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI), che stima la funzione renale senza considerare la variabile della razza. La task force raccomanda anche un maggiore uso della **cistatina C** in combinazione con la **creatinina sierica** come valutazione di conferma della GFR o della funzione renale.

Settembre 2021

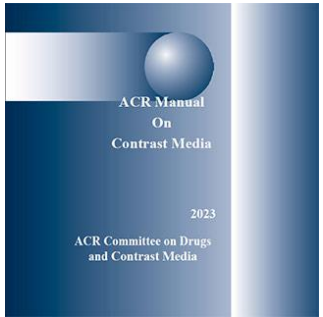
Misurazione della funzione renale nei bambini

La concentrazione sierica di creatinina riflette l'equilibrio tra la produzione e l'escrezione di creatinina. La creatinina è un prodotto di degradazione del muscolo scheletrico e il suo tasso di produzione è proporzionale alla massa muscolare. La massa muscolare dipende da una varietà di fattori, tra cui l'età del paziente, il sesso e il livello di attività fisica. Le normali concentrazioni di creatinina sierica, quindi, sono piuttosto variabili nei pazienti pediatrici, anche in presenza di funzionalità renale preservata. È importante riconoscere che le normali concentrazioni di creatinina adulta non possono essere applicate alla popolazione pediatrica. Le normali concentrazioni di creatinina sierica pediatrica aumentano con l'età, con i limiti superiori della norma sempre inferiori ai valori degli adulti. Anche le normali concentrazioni di creatinina sierica in base all'età possono variare leggermente da laboratorio a laboratorio.



Misurazione della funzione renale nei bambini

Ci sono problemi con l'utilizzo della concentrazione di creatinina sierica come unico marker della funzione renale. In primo luogo, un normale valore di creatinina sierica non significa che la funzione renale sia preservata. Ad esempio, un aumento della creatinina da 0,4 mg/dL a 0,8 mg/dL in un paziente di 10 anni sarebbe clinicamente significativo e suggerirebbe un certo grado di insufficienza renale, anche se entrambe le misurazioni potrebbero essere entro limiti accettabili per l'età del paziente. La concentrazione di creatinina sierica può non diventare anormale fino a quando la filtrazione glomerulare non è diminuita in modo sostanziale. In secondo luogo, potrebbero essere necessari diversi giorni nel contesto dell'insufficienza renale acuta prima che la concentrazione di creatinina sierica aumenti. Un paziente, quindi, può avere una funzionalità renale compromessa e una normale concentrazione di creatinina sierica.



MdC e bambini

Misurazione della funzione renale nei bambini

Un modo popolare con cui esprimere la funzione renale nei bambini è la **velocità di filtrazione glomerulare stimata** (**eGFR**). È importante notare che la formula utilizzata per calcolare l'eGFR pediatrico è diversa da quella utilizzata negli adulti. Il calcolo dell'eGFR nei bambini richiede la conoscenza della concentrazione e dell'altezza della creatinina sierica del paziente. Inoltre, deve essere noto il dosaggio utilizzato per misurare la concentrazione di creatinina sierica.

Calcolatrice GFR per bambini

Non esiste un modo perfetto per stimare il GFR nei bambini. Il National Kidney Disease Education Program, un'iniziativa del National Institutes of Health, fornisce un calcolatore online per scopi di stima e ha pubblicato le seguenti informazioni riguardanti la stima del GFR nei bambini.

https://www.niddk.nih.gov/

National Institute of Diabetes and Digestive and Kidney Diseases

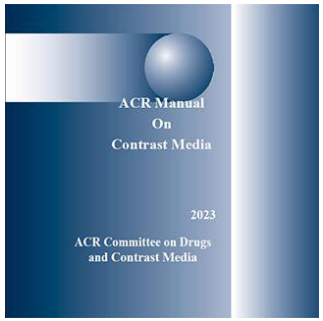
Misurazione della funzione renale nei bambini

Attualmente, la migliore equazione per stimare la velocità di filtrazione glomerulare dalla creatinina sierica nei bambini è **l'equazione Bedside Schwartz**. Questa formula è destinata all'uso con metodi di creatinina con calibrazione riconducibile alla spettroscopia di massa di diluizione isotopica (IDMS). L'uso dell'equazione originale di Schwartz (che non è più raccomandata) con un valore di creatinina sierica da un metodo con calibrazione riconducibile all'IDMS sovrastimerà la velocità di filtrazione glomerulare del 20-40%.

Equazione: Bedside Schwartz Equation

$$GFR\ (mL / min/1.73\ m_2) = (0.41 \times height) / serum\ creatinine$$

- Height in cm
- Serum creatinine in mg/dL



Misurazione della funzione renale nei bambini

Sebbene esistano altri metodi per stimare la velocità di filtrazione glomerulare (come la misurazione della cistatina C o lo studio della GFR di medicina nucleare), l'equazione Bedside Schwartz rimane la più facilmente disponibile e più facile da usare nei pazienti pediatrici.

MdC e bambini

Prevenzione della nefrotossicità indotta da mezzo di contrasto nei bambini a rischio

Agenti di contrasto IV a base di gadolinio.
Ci sono solo pochi studi pubblicati che affrontano le reazioni avverse ai mezzi di contrasto EV a base di gadolinio nei bambini. Le linee guida per l'uso EV di agenti di contrasto a base di gadolinio sono generalmente simili sia nella popolazione pediatrica che in quella adulta. Ci sono attualmente nove agenti di contrasto a base di gadolinio approvati per l'uso IV negli Stati Uniti. Questi agenti sono più comunemente usati off-label nei bambini poiché molti di questi agenti non sono approvati per l'uso in tutti i gruppi di età.

MdC e bambini

Prevenzione della nefrotossicità indotta da mezzo di contrasto nei bambini a rischio

Poiché non esistono linee guida basate sull'evidenza per la prevenzione della NSF nei bambini in particolare, raccomandiamo di seguire le linee guida degli adulti per identificare i pazienti a rischio e somministrare mezzi di contrasto a base di gadolinio in presenza di funzionalità renale compromessa. I bambini a rischio di insufficienza renale devono essere identificati (ad es., quelli con malattia renale medica nota [malattia renale cronica o danno renale acuto] o quelli con anomalie strutturali note del tratto renale/urinario) e sottoposti a screening per funzionalità renale compromessa. Come negli adulti, i mezzi di contrasto a base di gadolinio devono essere evitati in caso di insufficienza renale acuta o malattia renale cronica con eGFR <30 mL/min/1,73 m2.

MdC e bambini

Prevenzione della nefrotossicità indotta da mezzo di contrasto nei bambini a rischio

Sebbene non basati su prove specifiche, alcuni hanno suggerito di evitare gli agenti di gadolinio ad alto rischio nei bambini molto piccoli (ad esempio, neonati di età inferiore a 4 settimane). Sebbene fino ad oggi non sia stato segnalato alcun caso di NSF in un bambino molto piccolo, riteniamo che si debba usare cautela quando si somministrano questi agenti di contrasto, in particolare a neonati e lattanti prematuri a causa dell'immaturità renale e della potenziale velocità di filtrazione glomerulare inferiore a 30 ml / min/1,73 m^2. Come sempre, l'uso di mezzi di contrasto a base di gadolinio EV nei bambini di tutte le età dovrebbe essere giustificato e il beneficio della somministrazione dovrebbe superare i potenziali rischi.

Adult eGFR Calculators

National Institute of Diabetes and Digestive and Kidney Diseases

We are upgrading our adult eGFR calculators. Please use the National Kidney Foundation's eGFR calculator to estimate GFR in adults ages 18 and older.

For patients ages 18 to 25, we recommend using both the adult calculator and the pediatric 2021 Chronic Kidney Disease in Children under 25 (CKiD U25) calculator. Comparing the estimates from both calculators may provide a more informed assessment of kidney function for the patient.

https://www.kidney.org/professionals/kdoqi/gfr_calculator

NATIONAL KIDNEY FOUNDATION

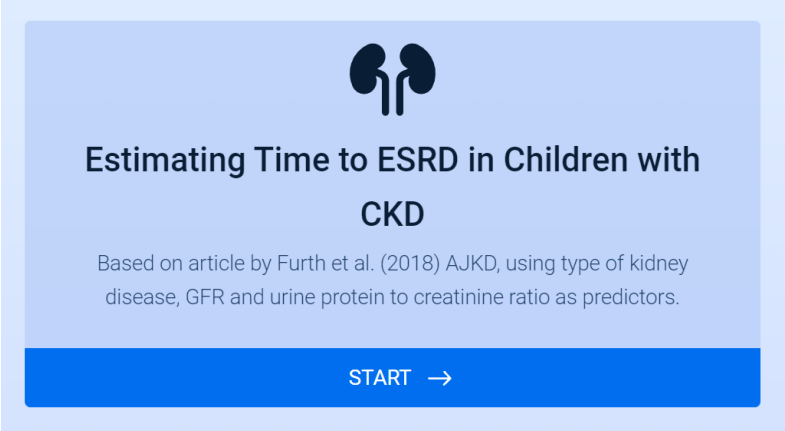
Pediatric eGFR Calculators

The 2021 CKiD U25 calculator is preferred for use in children, as it exhibits less bias across a broader age range than the 2009 CKiD "bedside" calculator.[2] The 2009 CKiD "bedside" calculator is older, but the equation is still commonly used in routine clinical practice.[3]

To estimate time to end-stage renal disease (ESRD) in children, use the Estimating Time to ESRD in Children with CKD calculator, developed using data from the NIDDK-funded CKiD study and the ESCAPE study.[4]

https://form.jotform.com/81565256783164

National Institute of Diabetes and Digestive and Kidney Diseases



National Institute of Diabetes and Digestive and Kidney Diseases

2021 CKiD U25 calculator

We are upgrading our pediatric eGFR calculator. Please use the NIDDK-funded CKiD U25 eGFR calculator ,[2] an interactive app developed by the hCode team, to calculate eGFR for children and young adults ages 1 to 25.

For patients ages 18 to 25, we recommend using both the pediatric 2021 CKiD U25 calculator and the adult calculator. Comparing the estimates from both calculators may provide a more informed assessment of kidney function for the patient.

https://ckid-gfrcalculator.shinyapps.io/eGFR/

National Institute of Diabetes and Digestive and Kidney Diseases

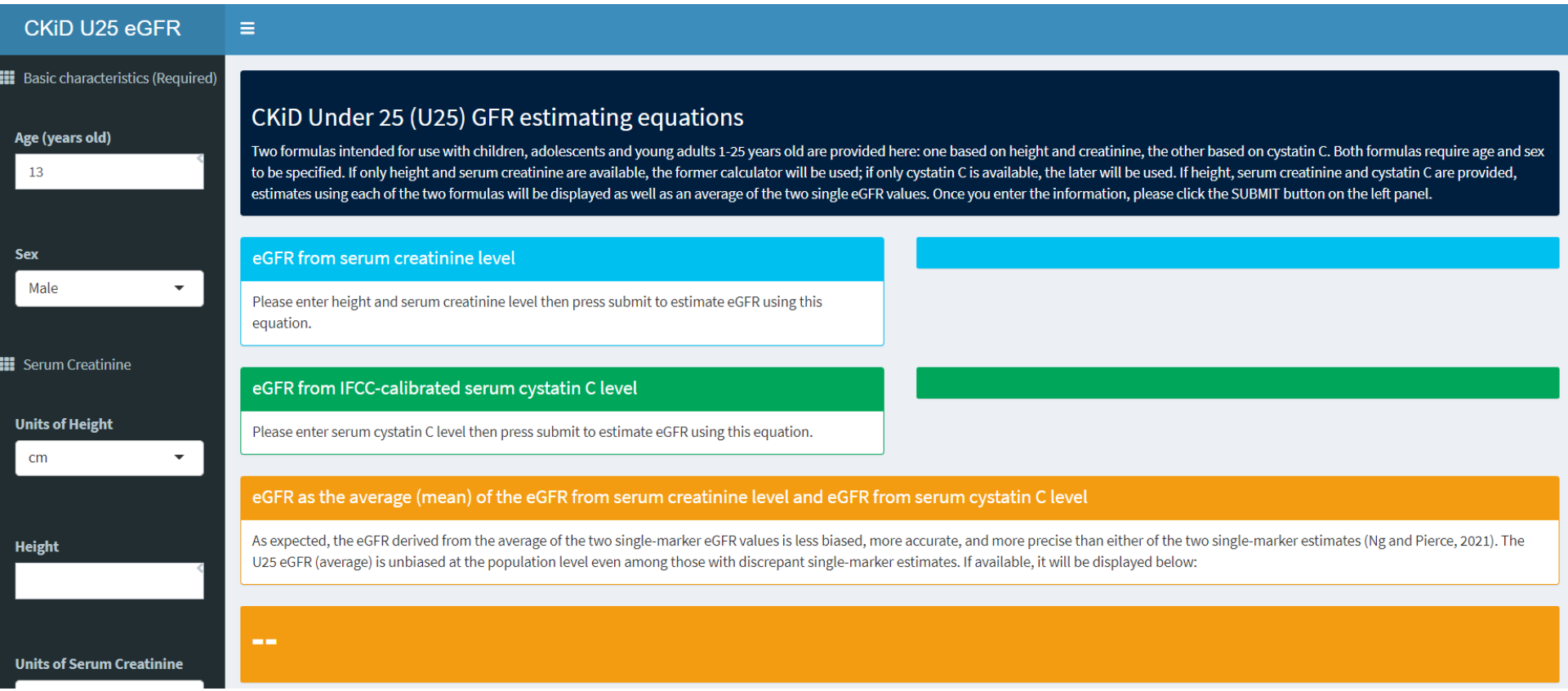


TABLE 2. eGFR Evaluation of Renal Function to Group I or Group III GBCA Administration

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

* If the new eGFR is to be obtained expressly for evaluation of suitability for administration of GBCA, obtaining the eGFR within 2 days of the MRI exam would avoid the situation where the new eGFR might be less than 45 and require another eGFR within two days of the MRI exam, as per the last line in the table.

Sicurezza e MdC

Table 2:

TREATMENT OF ACUTE REACTIONS TO CONTRAST MEDIA IN CHILDREN

Last updated: October 2020

- ❑ HIVES (Urticaria)
- ❑ Diffuse Erythema
- ❑ Bronchospasm
- ❑ Laryngeal edema
- ❑ Hypotension
- ❑ Unresponsive and Pulseless
- ❑ Pulmonary edema
- ❑ Seizures/convulsions
- ❑ Hypoglycemia
- ❑ Anxiety (panic attack)
- ❑ Reaction rebound prevention

Sicurezza e MdC

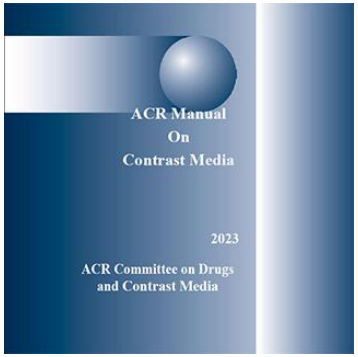
Table 3: MANAGEMENT OF ACUTE REACTIONS TO CONTRAST MEDIA IN ADULTS

Last updated: October 2020

- HIVES (Urticaria)
- Diffuse Erythema
- Bronchospasm
- Laryngeal edema
- Hypotension
- Hypertensive Crisis
- Pulmonary edema
- Seizures/convulsions
- Hypoglycemia
- Anxiety (panic attack)
- Reaction rebound prevention

Table 4:
EQUIPMENT FOR CONTRAST REACTION KITS IN RADIOLOGY
Last updated: January 2020

The following minimum equipment should be within or near any room in which contrast media is to be injected:



- Access to oxygen*
- Defibrillator or automated external defibrillator (AED)
- Blood pressure and pulse monitor
- Pulse oximeter
- Stethoscope

The following minimum medications should be within or near any room in which contrast media is to be injected:

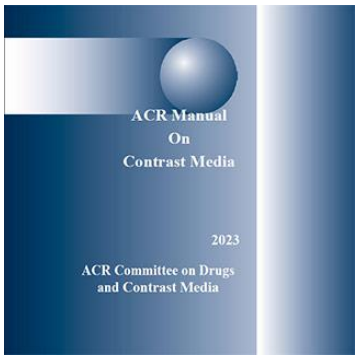
- Epinephrine IM 1mg/1mL (auto-injector or vials with needle and syringe for use)
- Inhaled short-acting beta-agonist (inhaler or nebulizer)
- Anti-histamine

Sicurezza e MdC

Table 4:
EQUIPMENT FOR CONTRAST REACTION KITS IN RADIOLOGY
Last updated: January 2020

The following discretionary medications and equipment may be considered for inclusion within or near any room in which contrast media is to be injected:

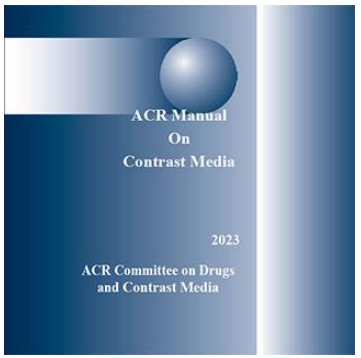
- Equipment
  - Suction: wall-mounted or portable; tubing and catheters
  - "Ambu®-type" bag-valve-mask device; masks in adult and pediatric sizes; protective barriers for mouth-to-mouth respiration optional if bag-valve-mask device is stocked
  - Normal saline (0.9%) and tubing
  - Syringes and IV cannulas: variety of sizes; tourniquets
  - Needle(s) for IM drug administration



Sicurezza e MdC

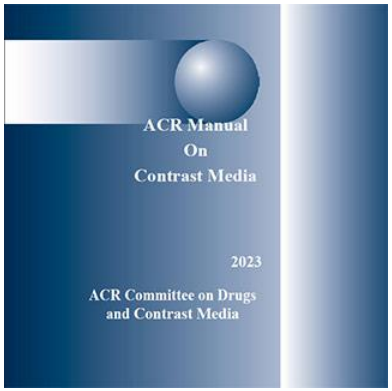
Table 4:
EQUIPMENT FOR CONTRAST REACTION KITS IN RADIOLOGY
Last updated: January 2020

- Medications
  - Epinephrine IV 1mg/10mL, 10-mL preloaded syringe
  - Atropine IV, 1mg/10mL, 10-mL preloaded syringe
  - Corticosteroid IV
  - Nitroglycerin sublingual, 0.4 mg tab
  - Aspirin per oral, 325 mg (for chest pain where myocardial ischemia is a consideration)
  - Lasix IV, 20–40 mg (for pulmonary edema)
  - Labetalol IV, 20 mg (for hypertensive emergency)
  - Dextrose IV, 50% 25g/50mL syringe (for hypoglycemia)



Gadolinium Pregnancy Screening Statement – 2022

It has been shown that some gadolinium-based contrast agents (GBCAs) **pass the placental barrier into the fetal circulation** of nonhuman primates. While multiple small sample size studies have not shown convincing evidence of adverse effects from fetal exposure to GBCAs, a 2016 retrospective study cited an increased risk of stillbirth/neonatal death as well as increased risk of rheumatologic, inflammatory, or infiltrative skin conditions in the offspring after GBCA exposure during pregnancy.



Gadolinium Pregnancy Screening Statement – 2022

The ACR Manual on Contrast Media and the ACR Manual on MR Safety is recommending avoidance of routine administration of GBCAs to pregnant patients. A decision to administer GBCAs to a pregnant woman should only be made when there is the potential for significant clinical benefit that outweighs the unknown risk of fetal exposure and should be the product of discussion that involves the referring provider and patient.

Gadolinium Pregnancy Screening Statement – 2022

The current standard of practice is to avoid routine GBCA administration during pregnancy due to the unknown risk of fetal exposure; and we recommend that imaging facilities have an established standardized system of screening in place that includes screening for unsuspected pregnancy prior to GBCA administration within existing institutional protocols that similarly screen patients prior to exposure to ionizing radiation and/or anesthesia. Protocols regarding pregnancy testing and reporting of results for pediatric patients and patients with legal guardians must be in accordance with local and state regulatory statutes.

Gadolinium Pregnancy Screening Statement – 2022

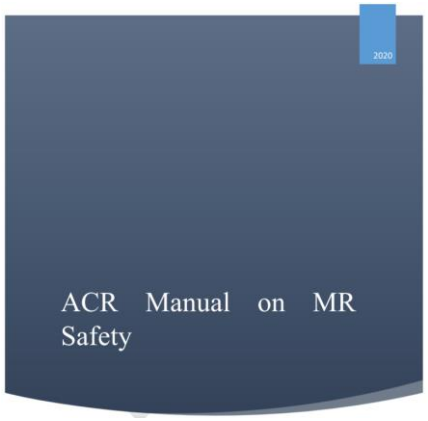
There is variability in the accuracy of pregnancy tests early in gestation, and at a minimum, testing will be falsely negative in the first two weeks of pregnancy. As such, there is no screening method that will be 100% effective in detection of unsuspected pregnancy. Regardless of which screening option is chosen, women of child-bearing age should be informed of the lack of certainty regarding risk of fetal GBCA exposure. An increased awareness of the issue by the patient may facilitate information sharing between patient and MRI staff regarding potential for pregnancy that would improve accuracy of screening. Any discussion with referring providers or patients acknowledging uncertain risks of GBCAs should always be coupled with an assessment of the known diagnostic benefits accrued from contrast-enhanced examinations on a per patient basis.

RM IN GRAVIDANZA

2023 MRI Safety: What the Radiologist Needs to Know

Pregnancy

"The vast majority of data today has failed to show that exposure to MR has deleterious effects on the developing fetus. Nevertheless, if pregnancy is established, the decision to proceed with a non-contrast MR study at 1.5 T should be based on the medical benefits weighed against unknown potential risk."



Pregnancy

"3-T MR examinations performed within normal operating mode for durations less than 30 minutes should be considered safe in pregnant patients. Ultimately, the decision to image a pregnant patient at 3-T should be based on local institutional policies, medical needs, and accessibility to 1.5-T versus 3-T MR scanners."

RM IN GRAVIDANZA

Pregnancy: GBCAs

"MR contrast agents should not be routinely administered to pregnant patients. Indeed, there is widespread consensus that avoiding gadolinium-based contrast agents (GBCAs) in pregnancy is prudent."

"The decision to administer an MR GBCA to pregnant patients should be accompanied by a well-documented and thoughtful risk-benefit analysis."

2023 MRI Safety: What the Radiologist Needs to Know

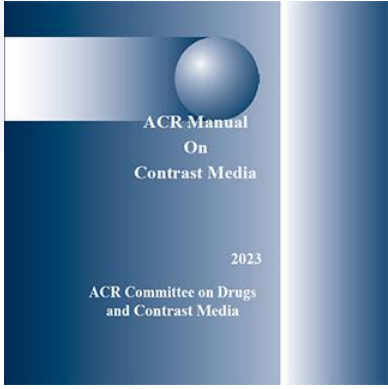
RM IN GRAVIDANZA

Pregnancy: GBCAs

"A recent publication highlighted an increased exposure level of first-trimester pregnancies to gadolinium, suggesting that increased screening and vigilance may be warranted when administering GBCAs to potentially pregnant patient populations."

Bird ST, Gelperin K, Sahin L, et al. First-trimester exposure to gadolinium-based contrast agents: a utilization study of 4.6 million U.S. pregnancies. Radiology. 2019;293(1):193–200

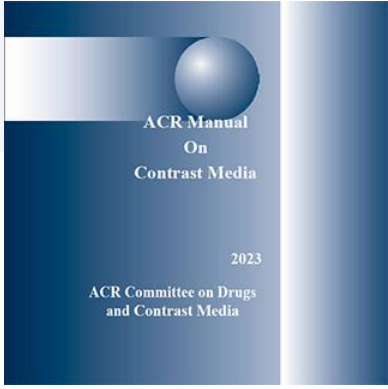
MdC e allattamento



ADMINISTRATION OF CONTRAST MEDIA TO WOMEN WHO ARE BREAST-FEEDING

Imaging studies requiring either iodinated or gadolinium-based contrast media are occasionally required in patients who are breast feeding. Both the patient and the patient's physician may have concerns regarding **potential toxicity to the infant** from contrast media that is excreted into the breast milk.

The literature on the excretion into breast milk of iodinated and gadolinium-based contrast media and the gastrointestinal absorption of these agents from breast milk is very limited; however, several studies have shown that the expected dose of contrast medium absorbed by an infant from ingested breast milk is extremely low.

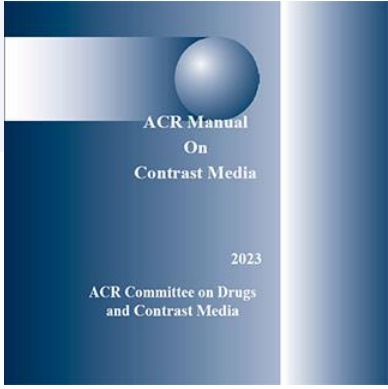


ADMINISTRATION OF CONTRAST MEDIA TO WOMEN WHO ARE BREAST-FEEDING

Iodinated X-ray Contrast Media (Ionic and Nonionic)

Background

The plasma **half-life** of intravenously administered iodinated contrast medium is approximately **2 hours**, with nearly 100% of the media cleared from the bloodstream in patients with normal renal function within 24 hours. Because of its low lipid solubility, less than 1% of the administered maternal dose of iodinated contrast medium is excreted into the breast milk in the first 24 hours [1,2]. In addition, less than 1% of the contrast medium ingested by the infant is absorbed from its gastrointestinal tract [3]. Therefore, the expected systemic dose absorbed by the infant from the breast milk is less than 0.01% of the intravascular dose given to the mother. This amount represents less than 1% of the recommended dose for an infant being prescribed iodinated contrast material related to an imaging study (usually 1.5 to 2 mL/kg).

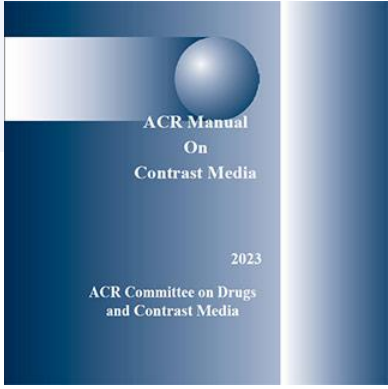


ADMINISTRATION OF CONTRAST MEDIA TO WOMEN WHO ARE BREAST-FEEDING

Iodinated X-ray Contrast Media (Ionic and Nonionic)

The potential risks to the infant include direct toxicity and allergic sensitization or reaction, which are theoretical concerns but have not been reported.

The likelihood of either direct toxic or allergic-like manifestations resulting from ingested iodinated contrast material in the infant is extremely low. As with other medications in milk, the taste of the milk may be altered if it contains contrast medium



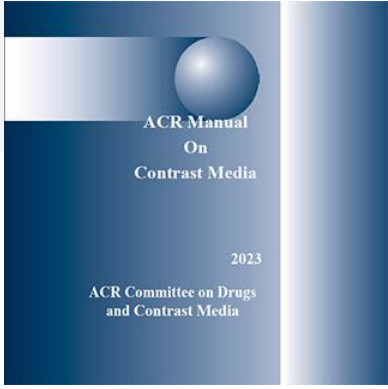
ADMINISTRATION OF CONTRAST MEDIA TO WOMEN WHO ARE BREAST-FEEDING

Iodinated X-ray Contrast Media (Ionic and Nonionic)

Recommendation

Because of the very small percentage of iodinated 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**.

Ultimately, an informed decision to temporarily stop breast-feeding should be left up to the mother after these facts are communicated. If the mother remains concerned about any potential ill effects to the infant, she may abstain from breast-feeding from the time of contrast administration for a period of 12 to 24 hours. **There is no value to stop breast-feeding beyond 24 hours**. The mother should be told to express and discard breast milk from both breasts during that period. In anticipation of this, she may wish to use a breast pump to obtain milk before the contrast-enhanced study to feed the infant during the 24-hour period following the examination.

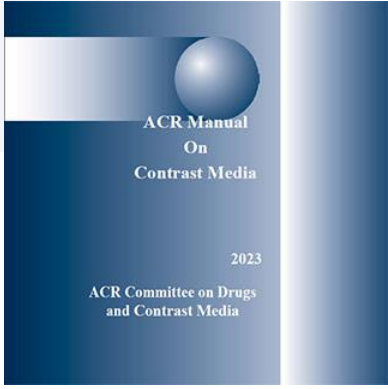


ADMINISTRATION OF CONTRAST MEDIA TO WOMEN WHO ARE BREAST-FEEDING

Gadolinium-Based Contrast Agents

Background

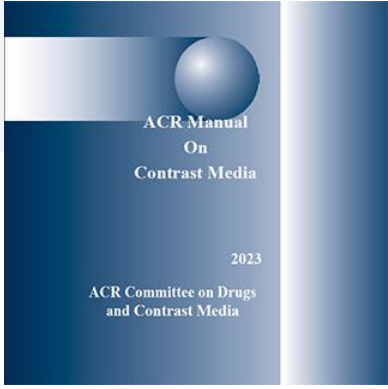
Like iodinated contrast media, gadolinium-based contrast media have a plasma **half-life** of approximately **2 hours** and are nearly completely cleared from the bloodstream in patients with normal renal function within 24 hours. Also similar to iodinated contrast media, gadolinium-based contrast media are excreted into the breast milk. It is likely that the overwhelming bulk of gadolinium excreted in the breast milk is in a stable and chelated form.



ADMINISTRATION OF CONTRAST MEDIA TO WOMEN WHO ARE BREAST-FEEDING

Gadolinium-Based Contrast Agents

Less than 0.04% of the intravascular dose given to the mother is excreted into the breast milk in the first 24 hours. Because less than 1% of the contrast medium ingested by the infant is absorbed from its gastrointestinal tract, **the expected systemic dose absorbed by the infant from the breast milk is less than 0.0004% of the intravascular dose given to the mother**. This ingested amount is far less than the permissible dose for intravenous use in neonates. The likelihood of an adverse effect from such a minute fraction of gadolinium chelate absorbed from breast milk is remote). However, **the potential risks to the infant include direct toxicity** (including toxicity from free gadolinium, because it is unknown how much, if any, of the gadolinium in breast milk is in the unchelated form) **and allergic sensitization or reaction**. These are theoretical concerns but none of these complications have been reported. As in the case with iodinated contrast medium, the taste of the milk may be altered if it contains a gadolinium-based contrast medium.



ADMINISTRATION OF CONTRAST MEDIA TO WOMEN WHO ARE BREAST-FEEDING

Gadolinium-Based Contrast Agents

Recommendation

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**.

Ultimately, an informed decision to temporarily stop breast-feeding should be left up to the mother after these facts are communicated. If the mother remains concerned about any potential ill effects to the infant, she may abstain from breast-feeding from the time of contrast administration for a period of 12 to 24 hours. There is no value to stop breast-feeding beyond 24 hours. The mother should be told to express and discard breast milk form both breast after contrast administration until breast feeding resumes. In anticipation of this, she may wish to use a breast pump to obtain milk before the contrast-enhanced study to feed the infant during the 24- hour period following the examination.

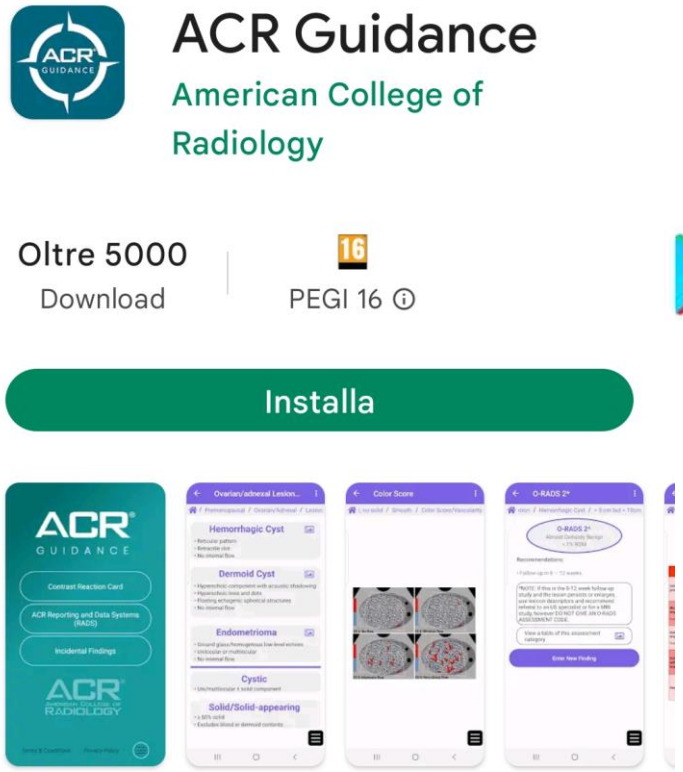
ACR APP

- The ACR® Guidance App provides interactive mobile access to select clinical guidance content from the ACR website. Download to access the ACR Contrast Reaction Cards, Reporting and Data Systems (RADS), and Incidental Findings (IF) content.

This app is intended for healthcare professionals such as radiologists, oncologists, referring physicians, and medical students who desire on the go reference materials from ACR. This app is not a medical device and should not be considered as one.

American College of Radiology

ACR APP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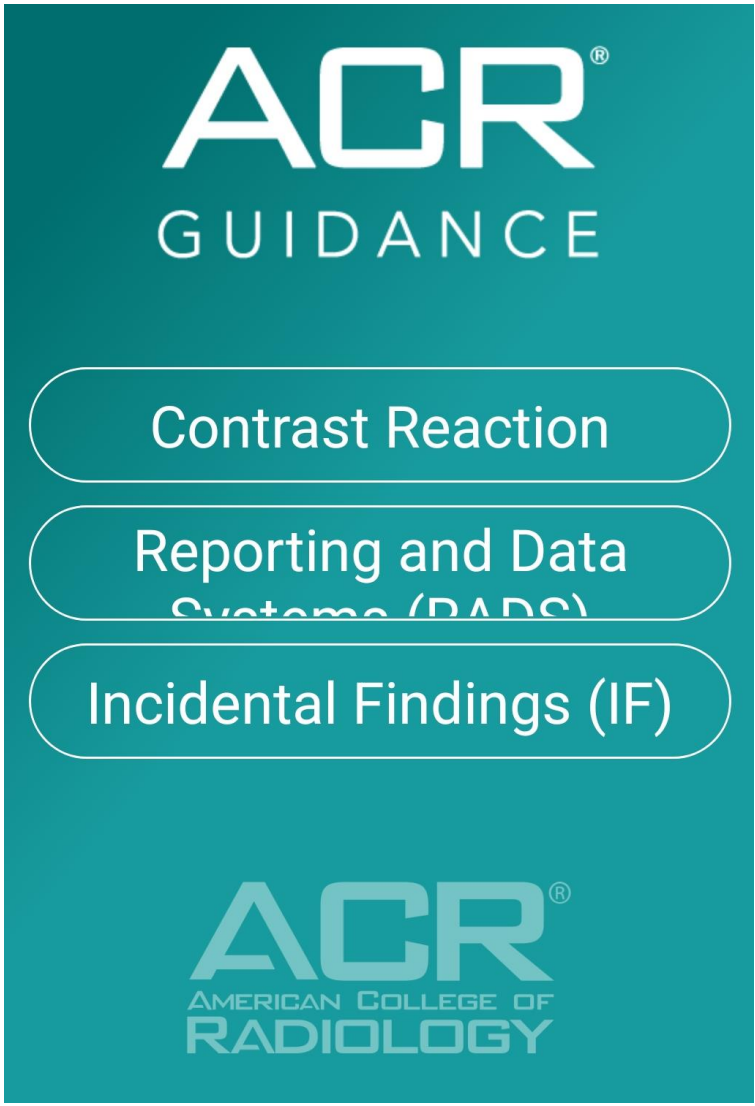
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GUIDANCE
Contrast Reaction
Reporting and Data
Incidental Findings (IF)
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CONTRAST REACTION CARD ADULT

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ADULT

CODE BLUE #:

EXAMPLE PREMEDICATION REGIMENS

Methylprednisolone 32 mg PO 12, 2 hrs prior +/- Benadryl 50 mg PO 1 hr prior.
OR
Prednisone 50 mg PO 13, 7, 1 hours prior
+/- Benadryl 50 mg PO 1 hr prior.
OR
Hydrocortisone 200 mg IV 5 hrs and 1 hr prior and Benadryl 50 mg IV 1 hr prior.
(urgent, NPO only, ER, inpatient)

CONTRAST EXTRAVASATION

Elevate arm (heart level), apply cool compress, remove rings. Observe. Consider surgical consultation for decreased perfusion, sensation, strength, active range of motion, or increasing pain.

Document reaction & monitor for return of symptoms post-treatment

HIVES/DIFFUSE ERYTHEMA

1. Observation; monitor vitals q 15 min. Preserve IV access.
2. If associated with hypotension or respiratory distress then considered **Anaphylaxis**:
   - O_2 6-10 L/min by face mask
   - IVF 0.9% NS wide open; elevate legs > 60°
   - Epinephrine 0.3 mL of 1mg/mL IM (or auto-injector) OR Epinephrine 1 mL of 1mg/10mL (0.1 mg/mL) IV with slow flush or IV fluids
   - **Call 911** or **CODE BLUE**
3. If *ONLY* skin findings but severe or progressive may consider Benadryl 50 mg PO, IM, IV but may cause or worsen hypotension.

CONTRAST REACTION CARD ADULT

HYPOTENSION WITH TACHYCARDIA (ANAPHYLAXIS)

1. Preserve IV access, monitor vitals q 15m
2. O_2 6-10 L/min by face mask
3. Elevate legs > 60°
4. IVF 0.9% NS wide open
5. Epinephrine 0.3 mL of 1mg/mL IM (or auto-injector) OR Epinephrine 1 mL of 1mg/10mL (0.1 mg/mL) IV with slow flush or IV fluids
6. **Call 911** or **CODE BLUE**

HYPOTENSION WITH BRADYCARDIA

1. Preserve IV access; monitor vitals
2. O_2 6-10 L/min by face mask
3. Elevate legs > 60°
4. IVF 0.9% NS wide open
5. Atropine 0.6-1.0 mg IV if refractory
6. **Consider calling 911** or **CODE BLUE**

ADULT

LARYNGEAL EDEMA (INSPIRATORY STRIDOR)

1. Preserve IV access, monitor vitals
2. O_2 6-10 L/ min by face mask
3. Epinephrine 0.3 mL of 1mg/ mL IM (or auto-injector) OR Epinephrine 1 mL of 1mg/10mL (0.1 mg/mL) IV with slow flush or IV fluids
4. **Call 911** or **CODE BLUE**

BRONCHOSPASM (EXPIRATORY WHEEZE)

1. Preserve IV access, monitor vitals
2. O_2 6-10 L/min by face mask
3. Beta-2 agonist inhaler 2 puffs; repeat x 3
4. If not responding or severe, then use Epinephrine 0.3 mL of 1mg/ mL IM (or auto-injector) OR Epinephrine 1 mL of 1mg/10mL (0.1 mg/mL) IV with slow flush or IV fluids
5. **Call 911** or **CODE BLUE**

www.acr.org/contrast

CONTRAST REACTION CARD PEDIATRIC

ACR® AMERICAN COLLEGE OF RADIOLOGY

PEDIATRIC

CODE BLUE #:

EXAMPLE PREMEDICATION REGIMENS

Prednisone 0.5-0.7 mg/kg PO (*Max 50 mg*) 13, 7 and 1 hr prior + Benadryl 1 mg/kg PO (*Max 50 mg*) 1 hr prior.
OR
Hydrocortisone 2 mg/kg IV (*Max 200 mg*) 5 hrs and 1 hr prior + Benadryl 1 mg/kg IV, IM, or PO (*Max 50 mg*) 1 hr prior.
(urgent, NPO only, ER, inpatient)

CONTRAST EXTRAVASATION

Elevate arm (heart level), apply cool compress, remove rings. Observe. Consider surgical consultation for decreased perfusion, sensation, strength, active range of motion, or increasing pain.

Document reaction & monitor for return of symptoms post-treatment

HIVES/DIFFUSE ERYTHEMA

1. Observation; monitor vitals q 15 min. Preserve IV access.
2. If associated with hypotension or respiratory distress then considered **Anaphylaxis:**
   - O_2 6-10 L/min by face mask
   - IVF 0.9% NS 10-20 mL/kg (max 500-1000 ml); elevate legs > 60°
   - Epinephrine IV or IM or Auto-injector
   - **Call 911** or **CODE BLUE**
3. If ONLY skin findings but severe or progressive, consider Benadryl PO, IM, IV 1 mg/kg (*max 50 mg*).

CONTRAST REACTION CARD PEDIATRIC

HYPOTENSION WITH TACHYCARDIA (ANAPHYLAXIS)

1. Preserve IV access, monitor vitals q15m
2. O_2 6-10 L/min by face mask
3. Elevate legs > 60°
4. IVF 0.9% NS 10-20 mL/kg (*Max 500-1000 mL*)
5. **Epinephrine IV, IM, or auto-injector***
6. **Call 911 or CODE BLUE**

HYPOTENSION WITH BRADYCARDIA

1. Preserve IV access; monitor vitals
2. O_2 6-10 L/min by face mask
3. Elevate legs > 60°
4. IVF 0.9% NS 10-20 mL/kg (*Max 500-1000 mL*)
5. If refractory, Atropine 0.02 mg/kg IV (*Max 1 mg infants/children and 2 mg adolescents*)
6. **Consider calling 911 or CODE BLUE**

PEDIATRIC

LARYNGEAL EDEMA (INSPIRATORY STRIDOR)

1. Preserve IV access, monitor vitals
2. O_2 6-10 L/ min by face mask
3. **Epinephrine IV, IM, or auto-injector***
4. **Call 911 or CODE BLUE**

BRONCHOSPASM (EXPIRATORY WHEEZE)

1. Preserve IV access, monitor vitals
2. O_2 6-10 L/min by face mask
3. Beta-2 agonist inhaler 2 puffs or nebulizer, can repeat x 3
4. If not responding or severe, add **Epinephrine IV, IM, or auto-injector***
5. **Call 911 or CODE BLUE**

*EPINEPHRINE DOSING - PEDIATRIC (can repeat q5-15 min)

IV 0.1 mL/kg of 1mg/10ml slowly into IVF (max 1 mL). **IM** 0.01 mL/kg of 1mg/mL (max 0.3 mL). If between **15-30 kg** use pediatric (Jr) auto-injector; if >30 kg use adult auto-injector; if **<15 kg** follow institutional guidelines

Reactions to CT contrast may also increase MRI contrast risk

AuntMinnie.com

February 22, 2022 -- Patients who have allergic reactions to iodinated contrast agents used in CT exams may also be at higher risk for allergic reactions from gadolinium-based contrast agents (GBCA) used with MRI, according to a study published February 22 in *Radiology*.

The findings highlight the need to carefully assess the contrast reaction history in patients undergoing MRI scans, said senior author Dr. Hye-Ryun Kang, PhD, of Seoul National University College of Medicine in South Korea, in a statement released by the RSNA.

"

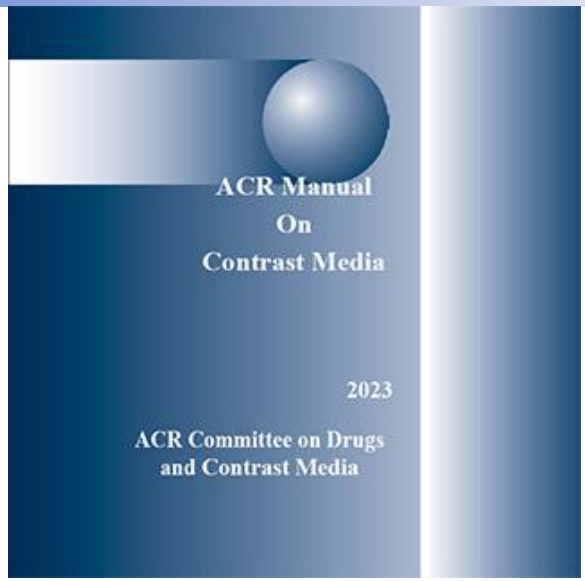
Reactions to CT contrast may also increase MRI contrast risk

AuntMinnie.com

"Traditionally, a history of iodinated contrast media hypersensitivity was not considered as a risk factor for hypersensitivity to GBCAs and vice versa, owing to the structural and compositional differences between the two," she said. "The results of our study challenge this idea."

GBCAs are commonly used with MRI exams, and although they are generally considered safe, their increased use has translated into higher rates of allergic reactions, wrote a team led by lead author Dr. Yoon Hae Ahn, also of Seoul National University.

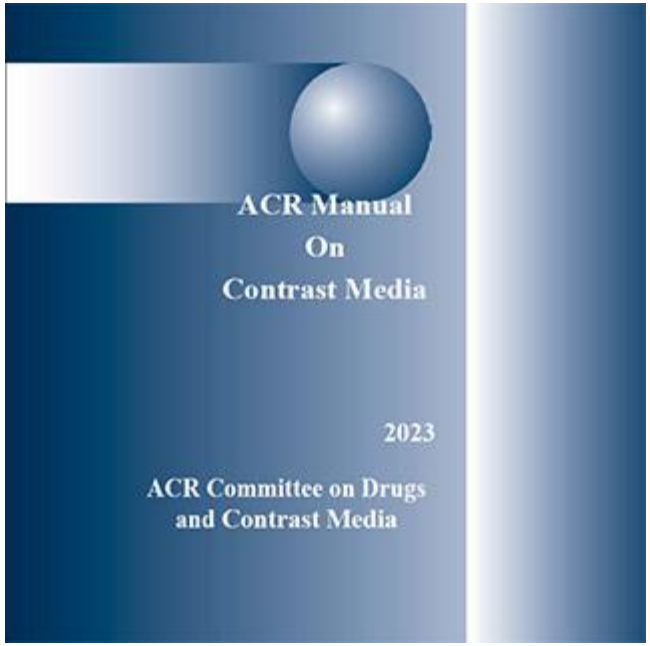
Sicurezza e MdC



There is no cross-reactivity between different classes of contrast medium. For example, a prior reaction to gadolinium-based contrast medium does not predict a future reaction to iodinated contrast medium, or vice versa, more than any other unrelated allergy.

Extravasation Bullet Points and Recommendations with Associated Strength of Evidence

- Extravasation of Contrast Media (Evidence Based Update) – 2022



Stravaso di MdC

Frequency

- 0.1-1.2% of CT injections result in extravasations.
- Most extravasations resolve without complication; severe extravasation injuries, including compartment syndrome (most common and skin ulceration / necrosis, are very rare (<<1% of extravasations)

Extravasation of Gadolinium Based Contrast Media

Extravasation of gadolinium-based contrast media is less common (i.e., approximately one-sixth as often) than iodinated contrast media. The difference is likely the due to much lower volumes of administered gadolinium-based contrast media for most clinical indications. Additionally, on a cc to cc basis, gadolinium-based contrast media may also have less toxicity than iodinated contrast agents.

Stravaso di MdC

Gadolinium-based contrast media

• Extravasation injuries after injection of gadolinium-based contrast media are much less common than those seen after injection of iodinated contrast material (i.e., approximately one-sixth as often), likely due, in part, to less toxicity and the low volumes of gadolinium-based contrast media that are injected.

Stravaso di MdC

Risks

- Extravasations and severe extravasation injuries are more common in patients who 1) are uncommunicative, 2) have altered circulation in the injected extremity, 3) have had radiation of the injected extremity, or 4) are injected in the hand, foot, or ankle.
- Extravasations are also more common in patients injected with more viscous contrast material.
- The risk of extravasation can be minimized by 1) using angiocatheters rather than butterfly needles, 2) performing meticulous intravenous catheter insertion technique (confirming intravenous location by aspirating blood through an inserted catheter and flushing the inserted catheter with a test injection), 3) and carefully securing an inserted catheter.

Stravaso di MdC

Evaluation and treatment

A health care provider should examine any patient in whom a contrast-media extravasation occurs; physical examination should include assessment of tenderness, swelling, erythema, paresthesia, active and passive range of finger motion, and perfusion

- There is no known effective treatment for contrast medium extravasation, although initial steps should include elevation of the affected extremity above the level or the heart, and use of cold or warm compresses. No medical interventions have been deemed helpful.
-

Stravaso di MdC

Evaluation and treatment

- Since severe extravasation injuries can develop slowly (up to hours after an extravasation), all discharged outpatients should be given clear instructions concerning where and when to seek additional medical care (including for worsening pain, development of paresthesia, diminished range of motion, and new skin ulceration or blistering).
- Surgical consultation should be obtained whenever there is concern for a severe extravasation injury; this can be suspected if the patient develops severe pain, progressive swelling or pain, decreased capillary refill, change in sensation, worsening active or passive range of motion in the elbow, wrist, or fingers, or skin ulceration or blistering; reliance on an extravasation volume threshold to trigger surgical consultation is not recommended.

Stravaso di MdC

I pazienti ambulatoriali che hanno subito uno **stravaso** con mezzo di contrasto devono essere dimessi dal reparto di radiologia solo dopo un periodo iniziale di osservazione, a condizione che il radiologo sia convinto che eventuali segni e sintomi inizialmente presenti siano migliorati o che non si siano sviluppati nuovi sintomi durante il periodo di osservazione. Al paziente devono essere fornite chiare istruzioni per cercare assistenza medica aggiuntiva per dolore intenso, dolore progressivo, intorpidimento o formicolio, ridotta mobilità (attiva o passiva), ulcerazione cutanea o altri sintomi neurologici o circolatori. Questo perché i sintomi iniziali di una grave sindrome compartimentale possono essere assenti o relativamente lievi (come limitati allo sviluppo di parestesie focali).

Stravaso di MdC

Power-injection through central venous catheters and peripherally inserted central catheters (PICCs)

- Contrast material can only be power-injected into central venous catheters or PICCs if these catheters have been certified for such use, with the flow-rate limit provided. All manufacturer recommendations should be followed.

Reazioni

Fatal Allergic Reaction to Gadolinium Contrast

Som N. Chalise [1], Elizabeth Palmer [1], Vikas Pathak [2]

1. Pulmonary and Critical Care, Riverside Health System, Newport News, USA 2. Pulmonary and Critical Care, Riverside Health System, Yorktown, USA

Corresponding author: Som N. Chalise, chalisesomnath@gmail.com

For the imaging study, the patient received intravenous (IV) 8mL of gadobutrol, a GBCA. All imaging studies were completed, and at the end of the procedure, she developed sudden-onset shortness of breath, chest heaviness, diaphoresis, diarrhea, nausea, and vomiting. She did not have any known history of previous gadolinium exposure. She was then transported to an urgent care where she was found to be hypoxic with oxygen saturations in the upper 70s. She was started on supplemental oxygen and given diphenhydramine 25 mg IV, dexamethasone 10 mg IV, famotidine 20 mg IV, and nebulized albuterol/ipratropium bromide. Shortly after her arrival, the patient was transferred to a full-service emergency department (ED). En route, she was given epinephrine 0.3 mg intramuscularly (IM) for hypotension.

Conclusions

Even though it is very rare to have an allergic reaction from an MRI contrast agent, if it happens, it may progress rapidly to severe anaphylaxis, DIC, and potentially death. The radiology department and the treating physician should be aware of this rare reaction and start the necessary management if the event occurs. More data is still needed in this area to determine the frequency of these reactions and if any common risk factors exist.

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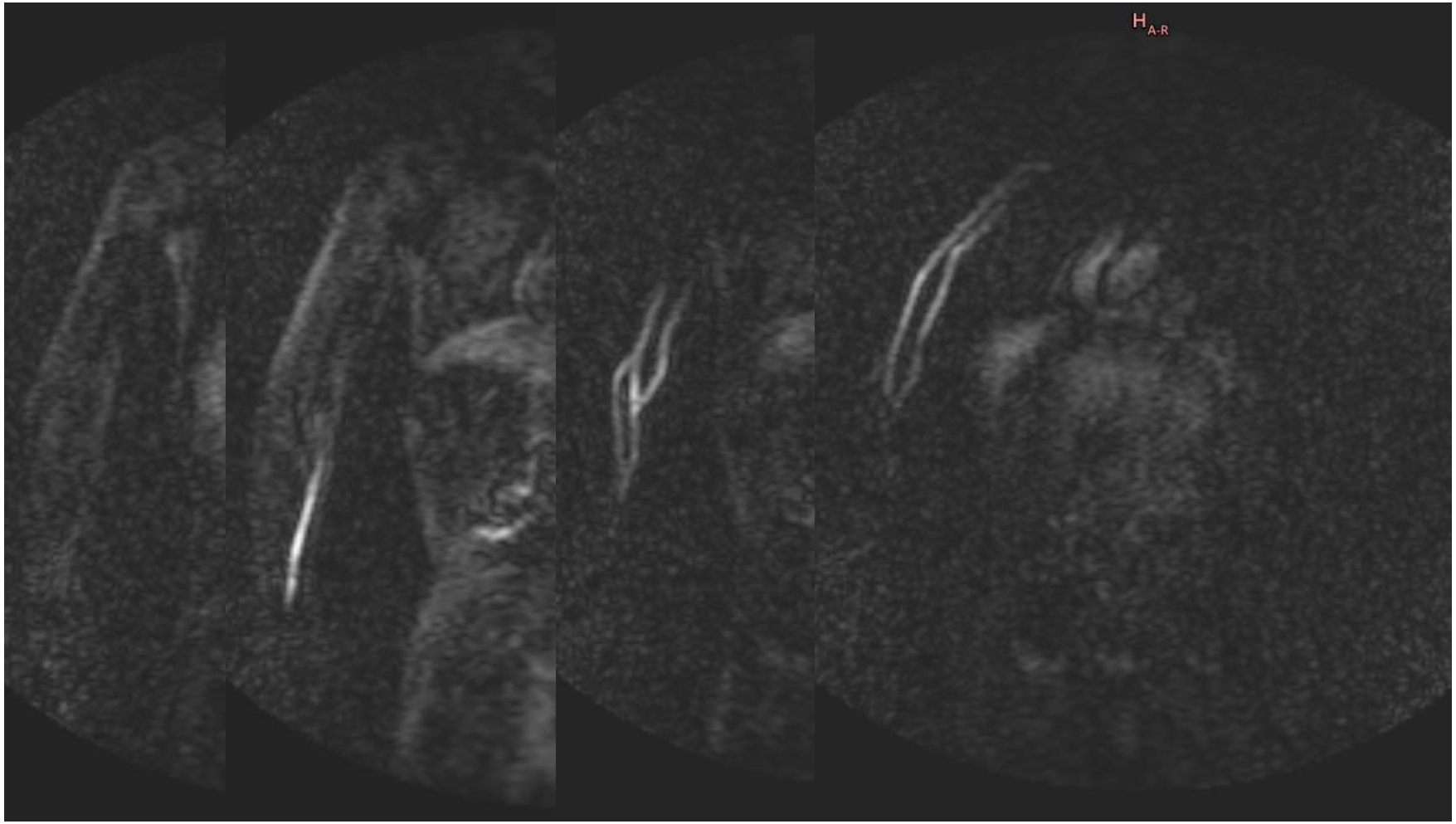

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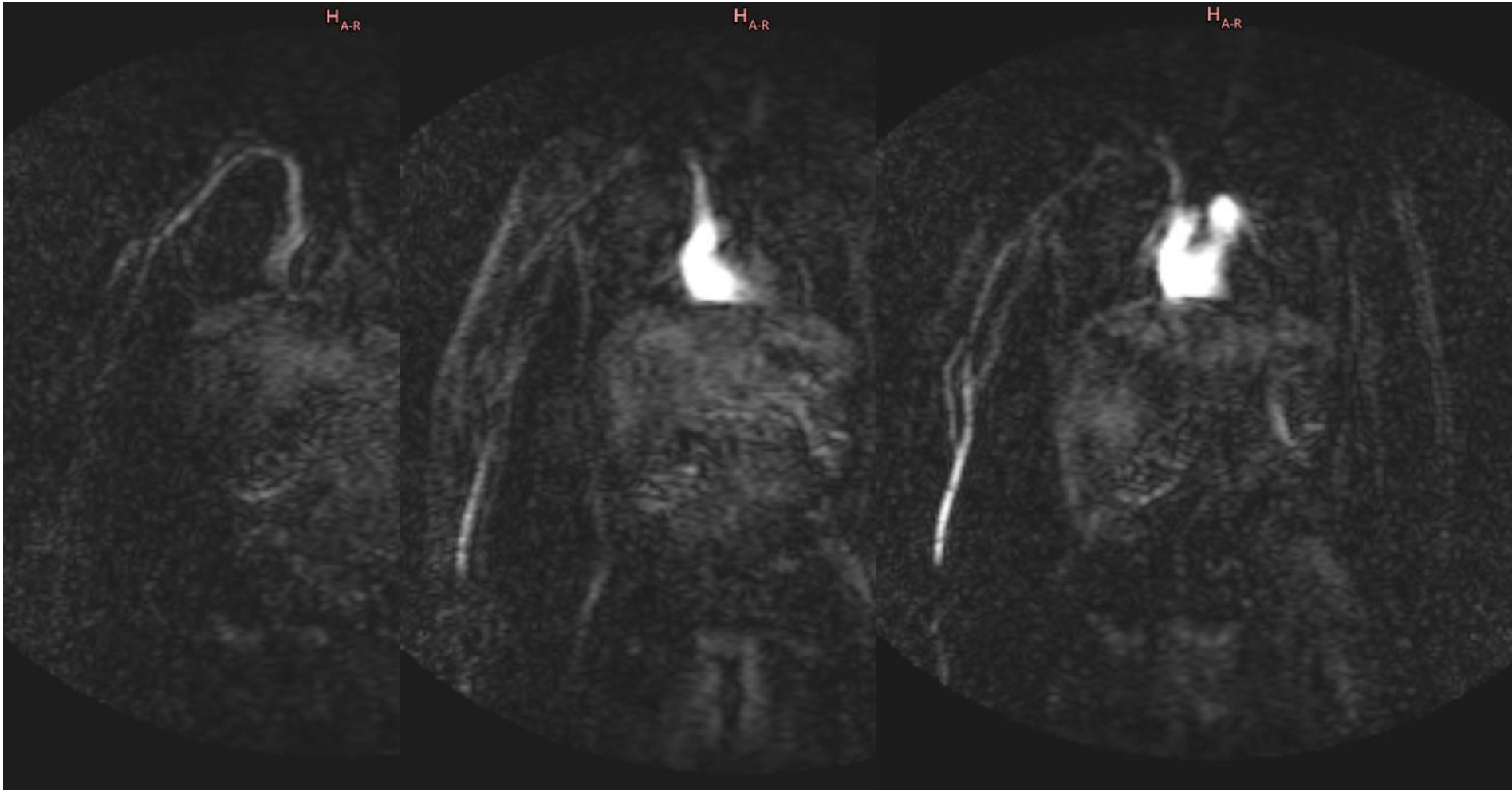

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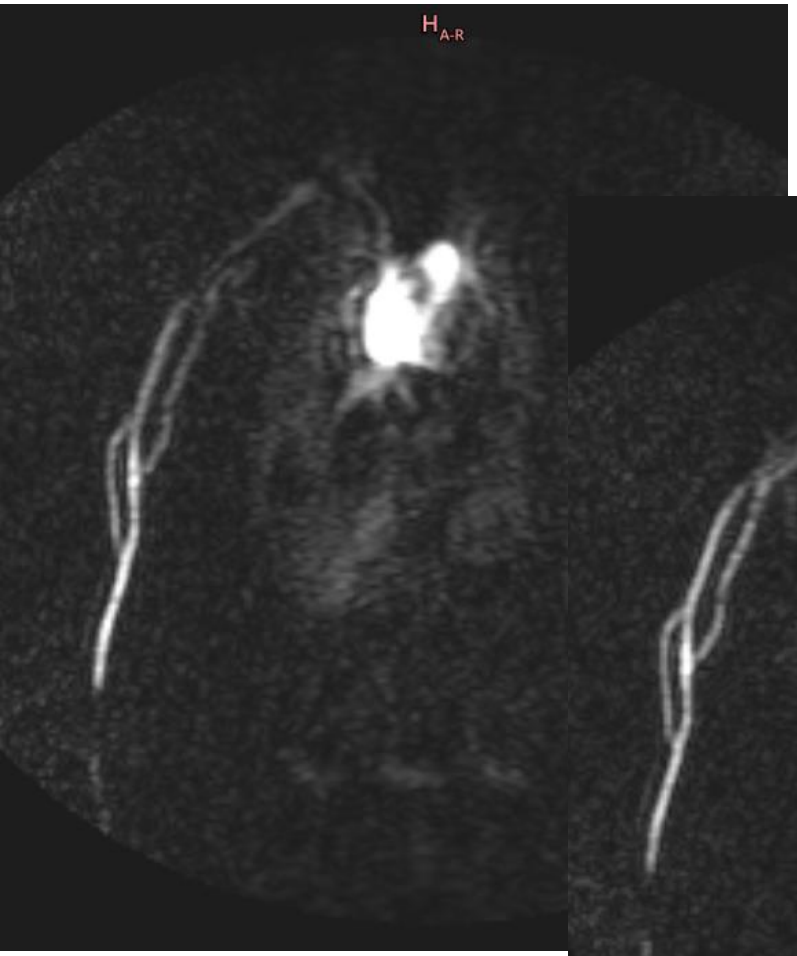

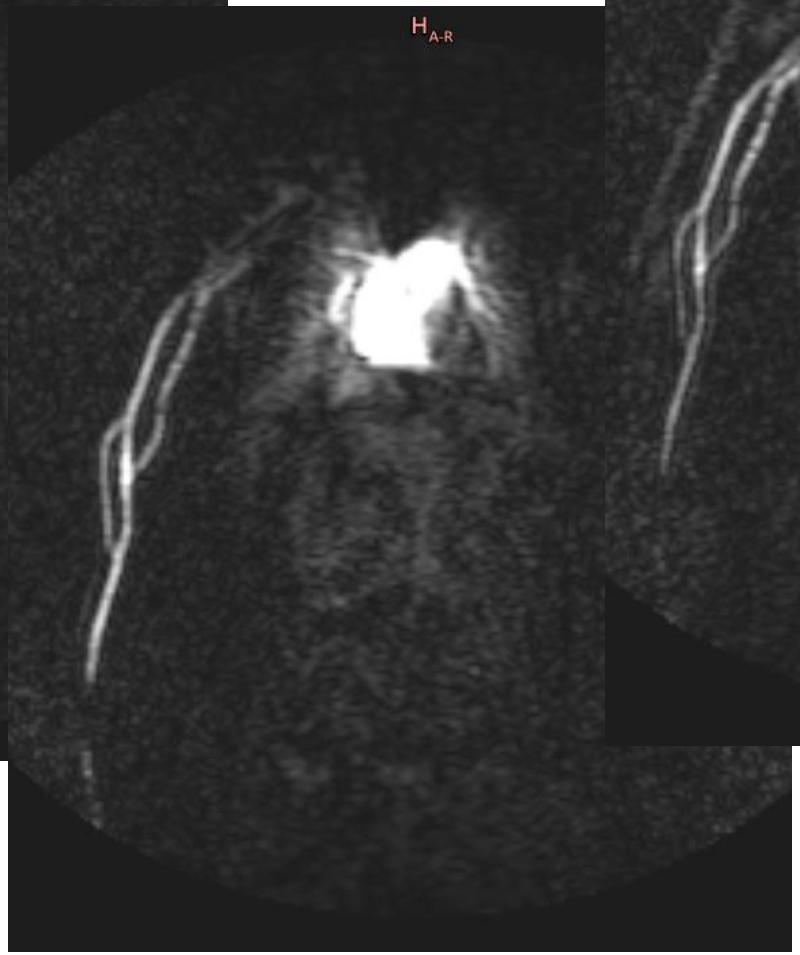

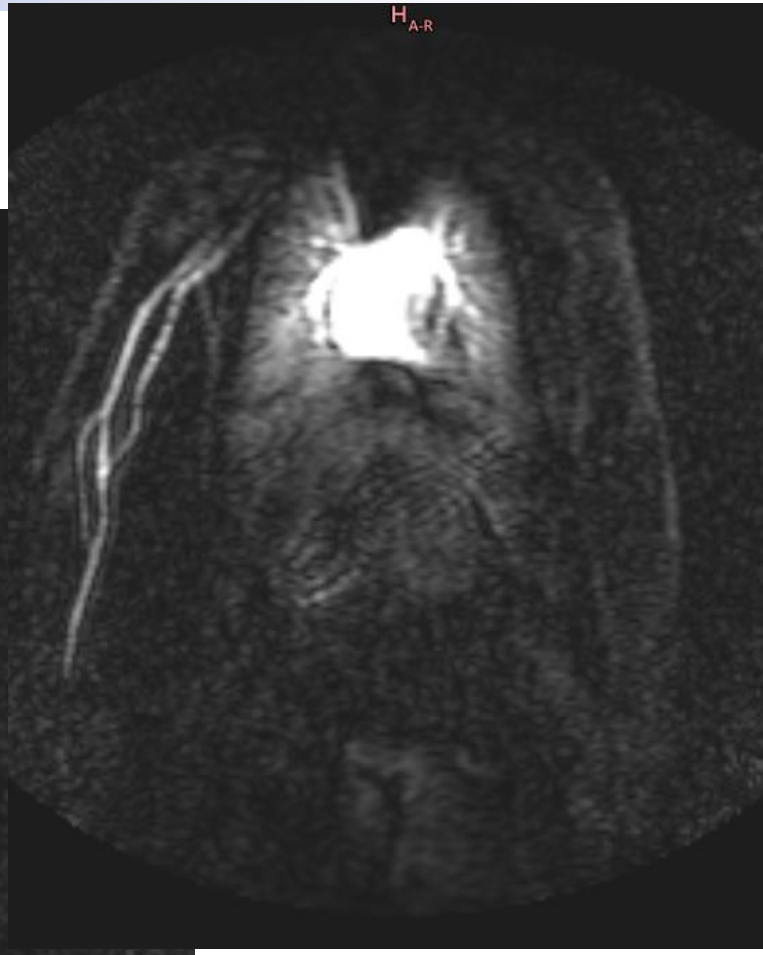

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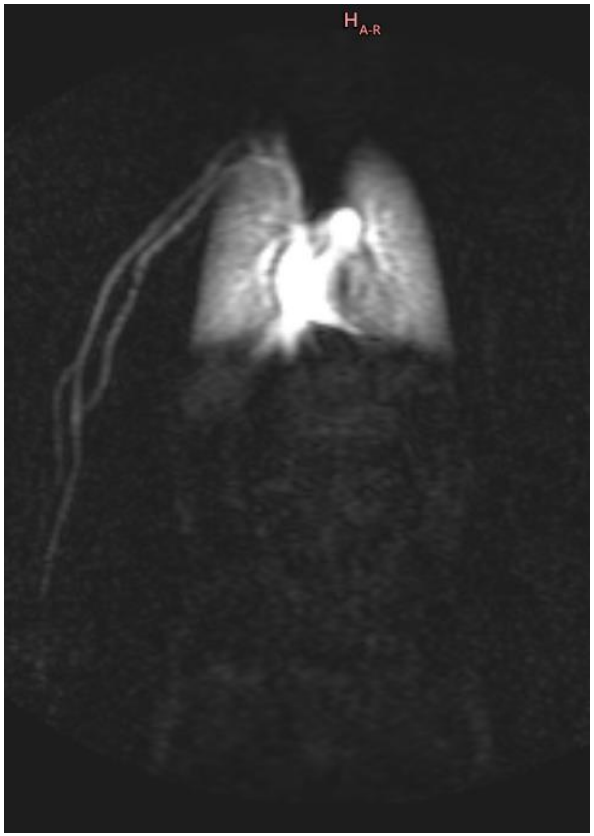

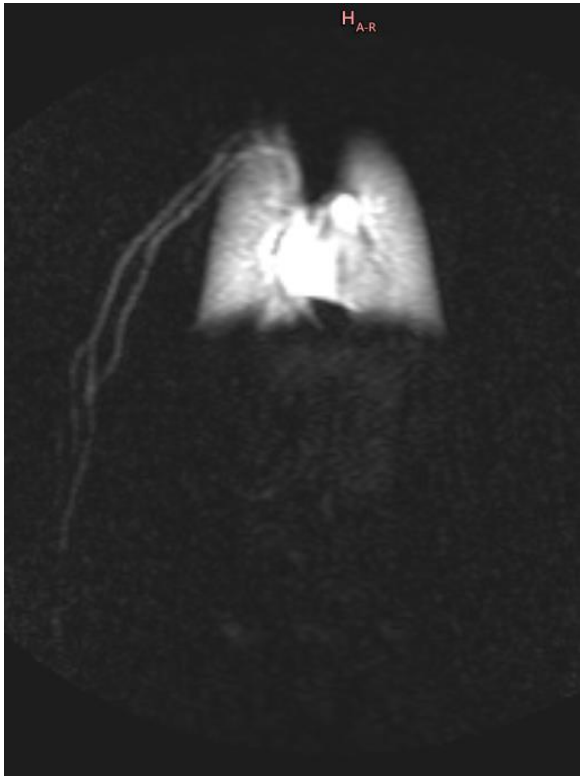

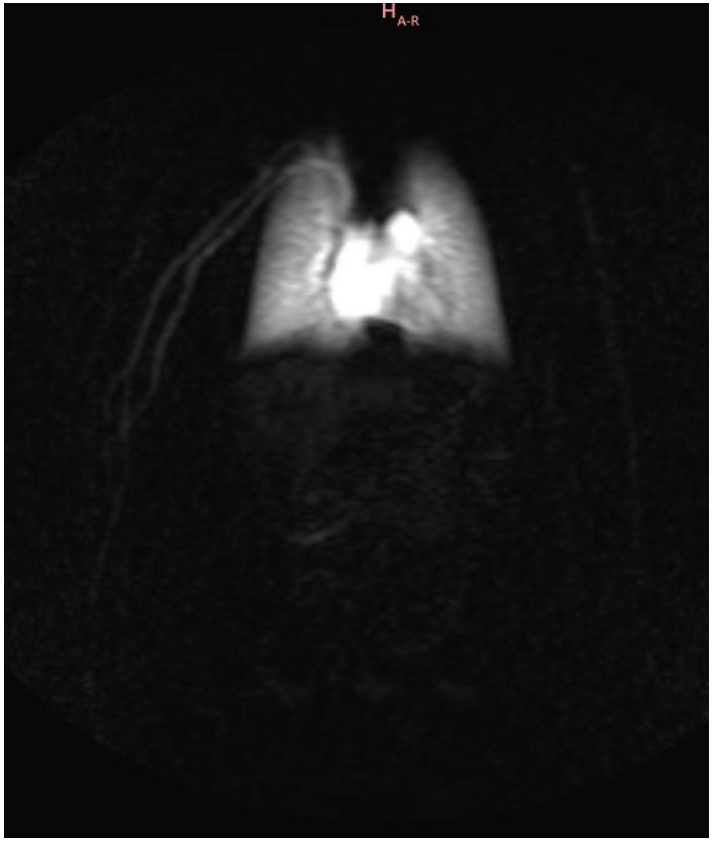

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