GADOLINIUM (GD): THE TOXIC CONTRAST INGREDIENT

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What is Gadolinium?

Gadolinium is a rare earth ion with paramagnetic properties that is toxic when introduced to the bloodstream by itself[2]. It is an essential catalyst of gadolinium-based contrast agents, which are administered prior to many MRI studies[1].

Is it dangerous?

One possible, but very uncommon adverse reaction would be "Gadolinium Deposition Disease[7]," where gadolinium leaks into the bloodstream, causing transmetallation[A] in cells.
*It is estimated that only about 1% or less gadolinium may be retained in the bone following a gadolinium contrast study[3].

Symptoms of gadolinium retention:

Nausea, vomiting, diarrhea, weakness, hives, itchy eyes, Nephrogenic System Firbosis (NSF), and more.[B]
*Because of the lack of evidence linking these symptoms with gadolinium retention, many healthcare personnel do not recognize the disease as such[6].

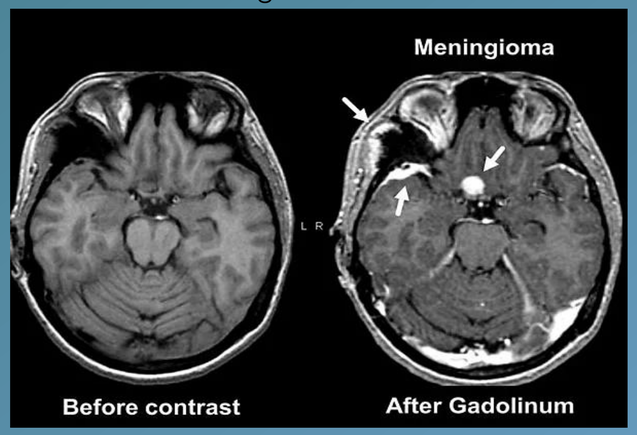

Image 1. MRI scan of the brain, looking at a meningioma both with, and without a gadolinium-based contrast agent[9].

How does it work?

Gadolinium is first chelated[C] then enters the body either orally or intravenously[1,3]. Because gadolinium has seven (7) unpaired electrons, it is considered to be an excellent paramagnetic agent[2,3]. Once the contrast media enters the bloodstream, the paramagnetic properties of gadolinium will cause the protons in water molecules to rearrange themselves to repel due to increased magnetism[10]. This causes a decreased T1 relaxation rate[D,5,8], which increases the intensity of the signal, allowing us to better visualize the necessary anatomy[8].

There are 9 marketed gadolinium-enriched contrast agents, which are approved for the MRI exams explained in table 1[3].

Exam	Purpose of Exam
Whole body MRI	Health overview; Can detect tumors, arthritis, aneurysms, inflammation, and stenosis.
Cranial and spinal tomography	Can detect masses, extents of injuries, malformation of vessels, anomalies, and herniations.
Myocardial perfusion	Will show the flow of blood through the heart muscle.
Renal transplant functional MRI	Will show flow and function of kidneys following a kidney transplant.
Osteoarticular pathologies	Will detect certain bone conditions such as osteoporosis, rickets, Paget's disease, osteoarthritis, osteomyelitis, and osteomalacia.

Table 1. Exams that use gadolinium-based contrast agents, and the purpose of each.
*Note: there are many more benefits to each of these exams; only a few are listed.

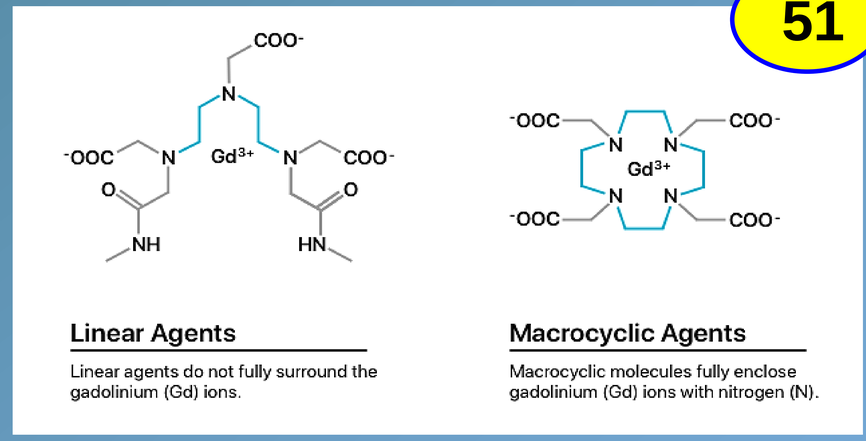

Image 2. Diagram of structural components of linear and macrocyclic chelating agents[7].

How is toxic gadolinium neutralized?

In order for gadolinium to be safely introduced to the bloodstream, it must be chelated by a ligand, or macromolecule such as a polyethylene glycol derivative[5]. The macromolecule can protect the gadolinium in one of two configurations: linear or macrocyclic (refer to the diagrams in image 2)[7]. Linear agents do not surround the gadolinium, but rather wrap itself around the ion and hold it closely, similar to the way a cobra will wrap itself around its prey. Due to this formation, it is fairly easy for certain elements in the macromolecule to dissociate and pair with other metals such as zinc[7]. If this were the case, the gadolinium would no longer be held to the macromolecule as tightly, allowing the possibility for gadolinium to leak into the blood vessels. In a macrocyclic configuration, the gadolinium is held in the middle and the macromolecule encases the ion similar to the way a clam shell will hold a pearl inside. Macrocyclic agents will have a much harder time dissociating due to their many bonds, therefore the gadolinium is held together much tighter[7]. Because of this, macrocyclic agents have the preferred configuration to use in gadolinium-based contrast MRI studies.

Term	Definition/ Explanation
A. Transmetallation[3]	Instance in which a molecule such as carbon dissociates itself from gadolinium and bonds with a different metal, such as zinc
B. NSF[1]	Nephrogenic systemic fibrosis; Occurs in patients with decreased kidney function. Thickening and scarring of connective tissue, subcutaneous tissue, skeletal muscle, and possibly internal organ muscles and tissues if the fibrosis becomes systemic
C. Chelated[1]	Gadolinium is bound with macromolecules in a linear or macrocyclic configuration in order to prevent the gadolinium from leaking into the vessels
D. T1 Relaxation Rate[8]	Time it takes for proteins in water molecules to go from an excited state, back to a relaxed state

Table 2. Definitions and/ or explanations of superscripted terms throughout the slide.

Conclusion

Although gadolinium is toxic in the human body, when bound with a macromolecule, it's an invaluable tool to use when administering a contrast MRI study[1,3]. As seen in image 1, the difference in the ability to see the meningioma and surrounding vessels with contrast is outstanding compared to the MRI image that was taken without contrast[9]. Due to lack of research, it cannot be proven that gadolinium retention does in fact cause gadolinium deposition disease. Therefore, it is logical to believe that the use of gadolinium-based contrast agents should not be halted, but rather encouraged for patients who need these studies done[6]. Certain conditions such as poor renal function could be a contraindication to the use of gadolinium[1,2,5], but for a majority of cases, the chelated contrast media has proven to be safe to use.

References

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