

86 Contrast Media: Gd Chelates with Extracellular Distribution

The gadolinium (Gd) chelates are the dominant class of contrast media for MRI. They are clear, colorless fluids, formulated without bacteriostatic additives for intravenous administration. The standard dose (excluding use in MR angiography) is 0.1 mmol/kg, which corresponds to 15 mL for a 75-kg patient (with all agents except one formulated at a concentration of 0.5 molar). The distribution of the agents is to the extracellular space.

Lesion enhancement occurs by one of two mechanisms: disruption of the blood-brain barrier (for intraaxial brain lesions) and lesion vascularity. The gadolinium ion is strongly paramagnetic, leading to a reduction in both T1 and T2, which is visualized on T1-weighted images as an increase in signal intensity. In **Figure 86.1**, thin-section T1-weighted images are illustrated at the level of the internal auditory canal, revealing a soft tissue mass (a vestibular schwannoma) on the right precontrast (**Fig. 86.1A**), which demonstrates prominent enhancement postcontrast (white arrow, **Fig. 86.1B**). Enhancement of normal vascular structures includes the nasal turbinates (black arrow, **Fig. 86.1B**) and choroid plexus, easily recognized markers of postcontrast scans. Clinically, contrast enhancement is used both for improved lesion detection and characterization. Contrast injection is routinely performed in the question of neoplastic disease, infection, and vascular abnormalities, with broad overall indications. In recent years, the field of contrast-enhanced MR angiography has developed as an additional major application of the gadolinium chelates.

The word chelate comes from the Greek root *chelos*, meaning “claw.” The safety basis of the gadolinium chelates rests with the ability of the chelate to hold extremely

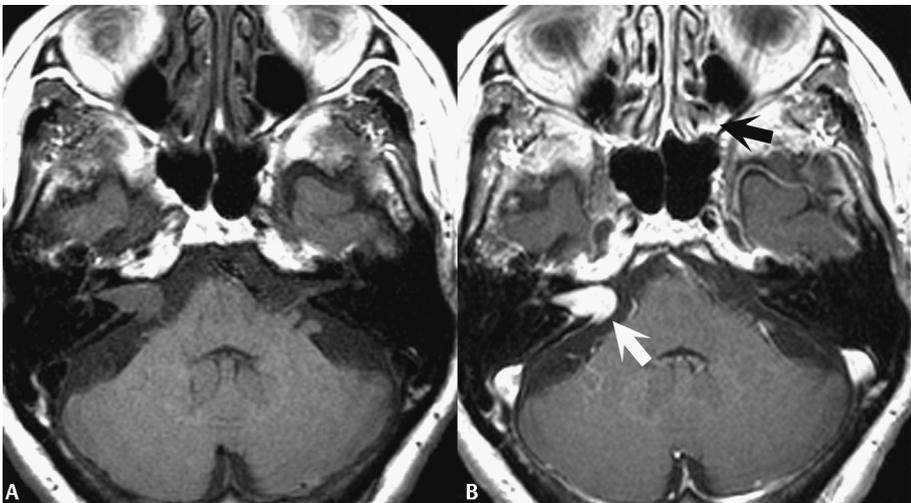


Fig. 86.1

tightly the gadolinium ion and ensure near 100% excretion. Gadolinium is a heavy metal, a member of the transition elements (atomic number 64), and as such is extremely toxic in elemental form (Gd^{3+}). The gadolinium chelates are 100% renally excreted, with the exception of two agents with combined renal and hepatobiliary excretion (MultiHance and Primovist).

The gadolinium chelates currently available for clinical use can be differentiated on the basis of charge (ionic or nonionic), structure (linear or cyclic), and stability. Given that the gadolinium ion carries a +3 charge, if the ligand, for example, is HP-DO3A (that for ProHance, with a charge of -3), the metal chelate itself will carry a net charge of zero, and thus be nonionic. In the U.S. market, considering only the gadolinium chelates with 100% renal excretion, there are three nonionic agents (ProHance, Omniscan, and Optimark) and one ionic agent (Magnevist). The structure of the chelate can be linear or macrocyclic (ring-like), with the cyclic chelates demonstrating higher in vivo stability and thus an improved safety margin. ProHance is the only macrocyclic chelate available in the United States. Internationally, two other extracellular gadolinium chelates are in widespread use, both macrocyclic: Dotarem (ionic) and Gadovist (nonionic).

The identification of nephrogenic systemic fibrosis (NSF) in 1997 and the subsequent, although delayed, recognition of its cause has led to a reassessment of gadolinium chelate use in MRI. NSF is an uncommon but serious acquired systemic disorder affecting patients with severe renal insufficiency, now known to be due to gadolinium chelate administration. Limb contractures and pain are prominent features, with the disease fatal in a small percentage of cases. Development of the disease is due to gadolinium chelate dissociation, with deposition of the free metal, and is thus related to chelate stability, dose, and cumulative (lifetime) dose. The vast majority of documented cases have occurred after Omniscan injection, although a substantial number of cases have also been documented after injection of Optimark or Magnevist. Early in 2007, the use of Omniscan (and subsequently Magnevist) was banned in patients with an estimated glomerular filtration rate (GFR) less than $30 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$ by European authorities. Cautious use of the macrocyclic agents, with high thermodynamic and kinetic stability, is believed acceptable even in chronic kidney disease (CKD)4 and CKD5 (< 30 and $< 15 \text{ mL min}^{-1} 1.73 \text{ m}^{-2}$ GFR) patients. In terms of incidence of the disease, this has been reported to be as high as 18% in CKD5 (dialysis) patients when given Omniscan.

Contrary to an often-used marketing/sales approach, the gadolinium chelates cannot be differentiated on the basis of common major reactions. All share the same safety profile in this regard, with nausea reported in 1.5% and urticaria in 0.5% of all injections. Health care personnel should be aware of the potential (although rare) for severe anaphylactoid reactions, with treatment identical to that for an iodinated contrast reaction. Patients with asthma, prominent allergies, or known drug sensitivities (including allergy to iodinated contrast media) are at increased risk for a severe anaphylactoid reaction.