What is new in contrast enhanced MRI

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To improve sensitivity and specificity of MRI as well as for the introduction of new functional or physiologic MRI methods, the use of contrast media (CM) techniques is mandatory. The standard dose of contrast media for most MRI applications is 0.1 mmol/Kg body weight, through it is proved that higher doses can improve lesion detection. Contrast-enhanced MRI helps distinguish tumor growth from other pathological processes and in depicting signs of tumor response to therapy, such as change in tumor size, morphology and degree of contrast material enhancement.

In the recent past new and advanced techniques like perfusion imaging and contrast enhanced-MRI provided new insights to the pathophysiology of various diseases. Perfusion MRI, is recognized as an important means of assessing esp. tumor grading, planning treatment strategies, follow up, treatment failure, recurrence etc. Dynamic contrast-enhanced MRI (DCE-MRI) is also now widely used for the same purpose.

In the presented overview the various properties of currently available CM, their dosage, field dependencies and their benefits also will be discussed in details with special reference to the new high relaxivity or highly concentrated contrast agents.

Gd-diethylenetriamine pentaacetic acid (DTPA) [Magnevist; Berlex; Wayne; NJ] was the first contrast agent available, but now several new agents are available in the market with varied properties and search is still on for more. The currently available agents are classified as below; the different dose schedules and strategies are also discussed herein (Figure 1-2).

One differentiate between paramagnetic contrast media and superparamagnetic contrast agents.

In the group of paramagnetic contrast media there are three new concepts which will be addressed in the first presentation of this course:

High dosage contrast agents, represented by the agent Gadovist®, a weak protein interaction with higher relaxivity, represented by the agent MultiHance®, and high relaxivity protein binding contrast agents, represented by the agent Vasovist®.

Gadobutrol, Gadovist®, is the first approved 1 molar MR contrast agent and has been well established for CNS imaging. The advantages of the high molarity, are the short applyable bolus which gives substantial advantages for perfusion MR imaging and MR angiography. There are several studies available that showed superiority of that agent in patients with MS or brain tumor imaging.

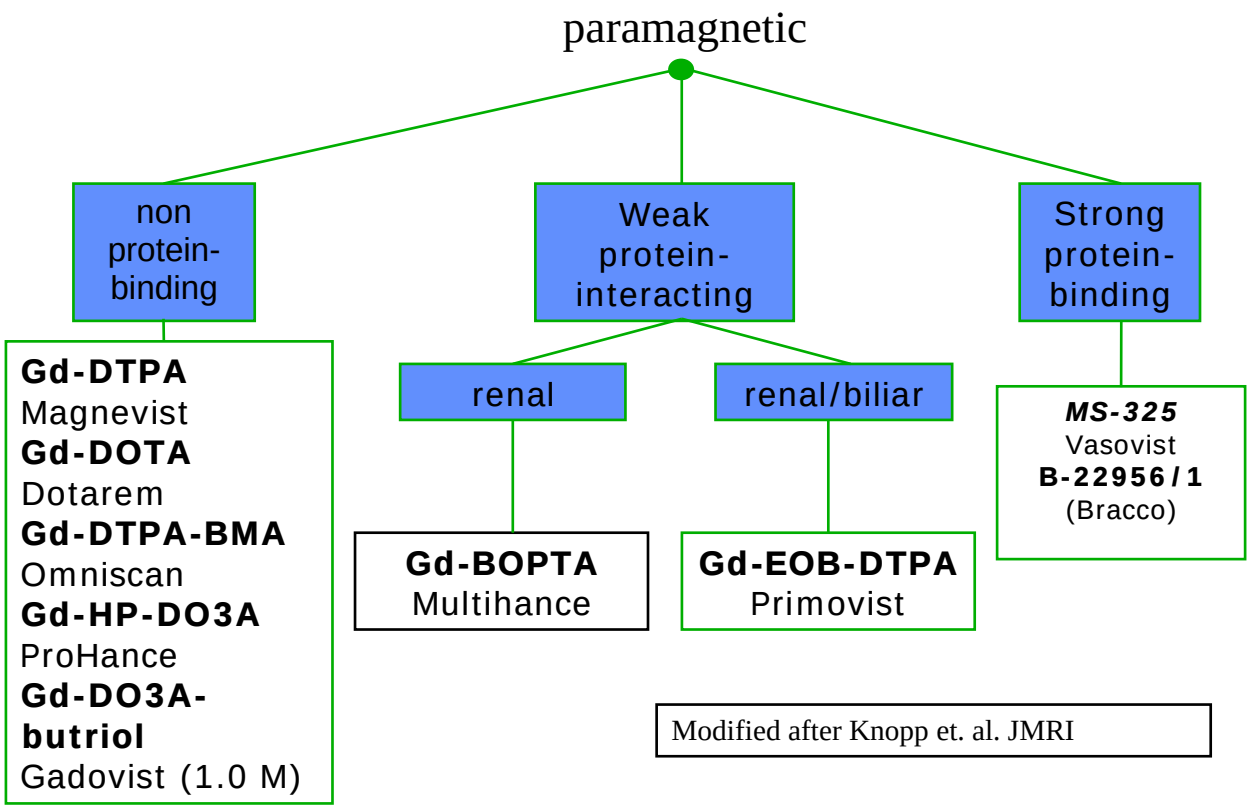
Gadovosveset trisodium, Vasovist ® is the first approved blood pool contrast agent for MRI. The concept of blood-pool contrast agents for use in MRA was introduced to overcome many of the above-mentioned limitations of conventional contrast agents. The first available intravascular contrast agent is gadofosveset trisodium, a gadolinium-based agent that enables high-resolution imaging of the carotid vessel walls and yields morphological and functional information with a single injection.
The optimum dose, clinical efficacy, and safety of gadofosveset trisodium have been evaluated in two Phase II and four multicentre, Phase III clinical trials. The optimum dose was found to be 0.03 mmol/kg and an injection time of 2–3 ml/s is recommended for first-pass imaging. The Phase III trials showed that the overall accuracy of gadofosveset trisodium-enhanced MRA was similar to that of catheter-based DSA. Gadofosveset trisodium binds reversibly and non-covalently to albumin, with a half-life of approximately 15 hours; this provides higher relaxivity and an extended imaging time compared with other contrast agents. The relaxivity (20 mHz) of gadofosveset trisodium measured in human plasma or ex vivo samples from rabbits and monkeys is approximately six to ten times greater that that of gadolinium diethylenetriaminepentaacetic acid. Because gadofosveset trisodium remains in the blood vessels in the steady state for longer than extravascular agents, this allows an imaging window of 30–60 minutes and makes possible not only first-pass but also steady-state imaging. Thus,

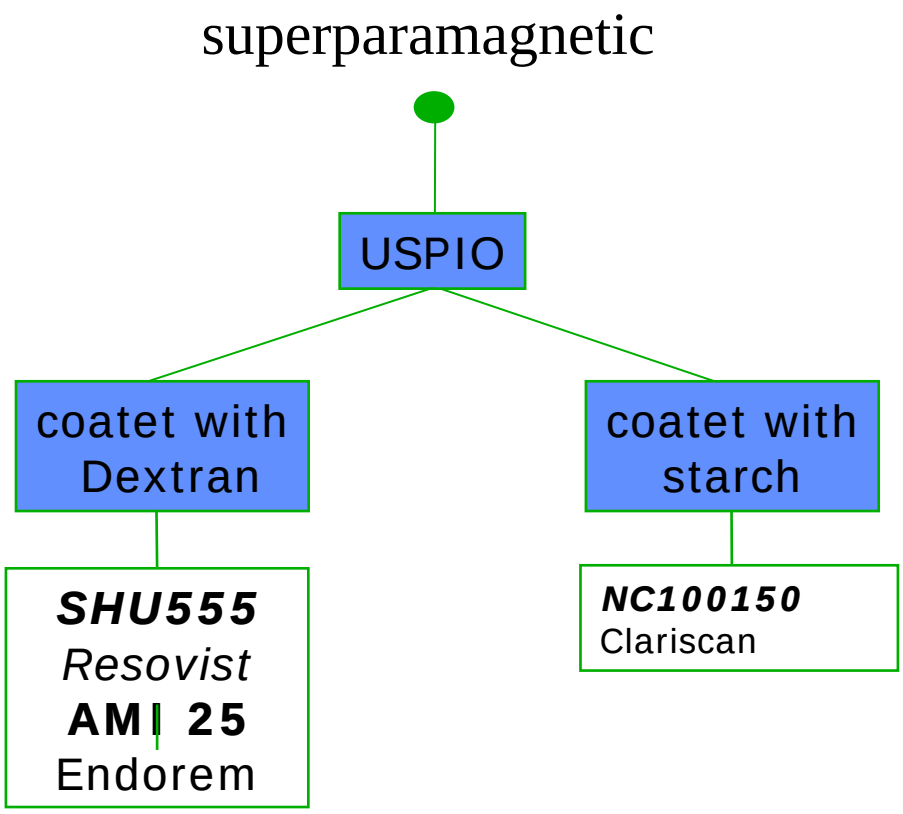
there is the potential to integrate the different diagnostic requirements of morphological and functional imaging in one comprehensive scan, with only one injection of contrast agent.

Gadobenate dimeglumine (Gd-BOPTA, MultiHance®) is a gadolinium-based MR contrast agent which differs from other available gadolinium contrast agents in possessing roughly two-fold higher T1 relaxivity *in vivo* due to weak and transient interactions with serum albumin. Numerous clinical trials have been conducted with doses up to 0.3 mmol/kg bodyweight to determine whether this high relaxivity offers advantages over other agents for MR imaging of the CNS. Clinical evaluation of the signal enhancement properties of MultiHance indicate that this agent possesses the potential for improving contrast enhancement relative to other agents, which may lead to better visualization of lesions and improved sensitivity for detection of CNS pathologies.

Although the higher relaxivity of MultiHance confers substantial benefits for MR imaging of the CNS, no major modifications to standard T1-weighted post-contrast pulse sequences are required. Like other gadolinium based MR contrast agents, MultiHance is an extracellular fluid space (ECF) agent. This means that after injection MultiHance distributes to the ECF where it shortens the T1 and T2 relaxation times of tissues in which the contrast agent accumulates. It is this effect that causes the visible contrast enhancement seen on contrast-enhanced MR images. In essence, MultiHance can be used just like other MR contrast agents, but will produce more signal enhancement at the same dose.

Figures 1-2


paramagnetic
non protein-binding
Weak protein-interacting
Strong protein-binding
Gd-DTPA
Magnevist
Gd-DOTA
Dotarem
Gd-DTPA-BMA
Omniscan
Gd-HP-DO3A
ProHance
Gd-DO3A-butriol
Gadovist (1.0 M)
renal
renal/biliar
MS-325
Vasovist
B-22956/1
(Bracco)
Gd-BOPTA
Multihance
Gd-EOB-DTPA
Primovist
Modified after Knopp et. al. JMRI



Modified after Knopp et. al. JMRI