Use of gadolinium contrast agents for pediatric neuroimaging

and gadolinium retention: to stain or not to stain

Several recent reports have documented gadolinium retention ("stain") in the globus pallidus and dentate nuclei of the cerebellum both inferred by MR imaging and mass spectroscopy of autopsied tissues. Gadolinium deposits have also been documented within the cerebellar perivascular glial cells. However, to date there are no reports of neuronal damage or inflammatory reactions to the retained gadolinium nor have there been reports of neurologic dysfunction related to damage to the globus pallidus and dentate nuclei such as problems with fine motor movements, ataxia, dysarthria, and extrapyramidal dysfunction.

The gadolinium staining appears to occur after exposure to both linear and macrocyclic gadolinium contrast agents even with normal renal function and is presumed to reflect dechelation of gadolinium from the chelate, with binding of the free gadolinium to tissue. Gadolinium likely has the capacity to bind in sites normally occupied by calcium, and as such has the theoretical potential to disrupt physiology. The thermodynamic and kinetic stability of the gadolinium-chelate is measured in vitro, however the entire in vivo milieu, e.g. the presence of other ions that facilitate transmetalation, remains incompletely understood. The macrocyclic agents demonstrate higher in vitro stability then the linear agents, and this bears out in current in vivo observations. Using T1 hyperintensity of deep grey matter structures on nonenhanced images as an indicator of gadolinium staining, the linear contrast agents Omniscan (Gadodiamide) and Magnevist (Gadopentetate) appear to be associated with more gadolinium staining than the macrocyclic agents, Prohance and Dotarem (Gadoterate). Similar results have been found with pathologic studies. Of note is that higher gadolinium levels have been found in bone then in the brain, the circulation of which is unknown.

The jury is still out with regards to the clinical significance of gadolinium staining in the brain, however as providers of care to children, we have an obligation to protect them from known and potential causes of harm. As such, the recommendations about the use of all gadolinium agents is – if there is not a clear clinical indication to give the gadolinium agent, don’t. The ordering physician should provide justification for the use of gadolinium agents if they are insisting on their administration by the radiologist. A preferable approach is that gadolinium agents are given at the discretion of the radiologist and the order for MRI indicates as such. This will entail changes in practice in many hospitals and imaging centers and may slow through put of patients in MRI until the culture of routine administration of gadolinium contrast agents is changed.

Murata N¹, Gonzalez-Cuyar LF, Murata K, Fligner C, Dills R, Hippe D, Maravilla KR. Macrocyclic and Other Non-Group 1 Gadolinium Contrast Agents Deposit Low Levels of Gadolinium in Brain and Bone Tissue: Preliminary Results From 9 Patients With Normal Renal Function. Invest Radiol. 2016 Feb 8. [Epub ahead of print]

Errante Y¹, Cirimele V, Mallio CA, Di Lazzaro V, Zobel BB, Quattrocchi CC. Progressive increase of T1 signal intensity of the dentate nucleus on unenhanced magnetic resonance images is associated with cumulative doses of intravenously administered gadodiamide in patients with normal renal function, suggesting dechelation. Invest Radiol. 2014 Oct;49(10):685-90.