

Shakour Philip Simon, Verma Kriti

GADOLINIUM: CONTRAST FOR MAGNETIC RESONANCE IMAGING OR ETIOLOGICAL FACTOR OF THE PATHOLOGICAL PROCESS

Tutor: associate professor Pereverzeva E.V.

*Department of Pathological Physiology,
Belorussian State Medical University, Minsk*

Gadolinium (Gd^{3+})-based magnetic resonance imaging (MRI) contrasts have been used since 1988 and significantly improve the quality of diagnosis. About 40% of MRI scans in the world use Gd^{3+} contrast agents. The Gd^{3+} administered to patients for research is several tens of tons per year.

Gadolinium is able to influence the spin-lattice T1 relaxation time of protons during MRI. Reducing the T1 relaxation time eventually allows for the so-called positive contrast - to enhance the light areas in the resulting images.

Free Gd^{3+} ions are toxic. Therefore, their toxicity should be eliminated by combining metal atoms with reliable chemical "insulators" that quickly and completely remove Gd^{3+} from the body. Linear Gd^{3+} compounds with chelates, and later cyclic ones, were such "insulators". Linear Gd^{3+} contrasts have been used in clinical practice and in scientific research to study the physiological processes of the brain.

Gradually, data has been accumulated that cast doubt on the absolute safety of the contrasts used for MRI. The first data from 2014 were indirect – they indicated signal amplification on T1-weighted MRI images of the dentate nucleus, globus pallidus of the brain in patients who had been repeatedly subjected to MRI examinations. In addition, cases of systemic fibrosis have been reported, an aggressive disease involving both the skin and internal organs; it was believed that this was possible only in patients with renal insufficiency.

The broad scientific discussion on this topic touches on many points; Gd^{3+} penetration into the brain bypassing blood brain barrier through cerebrospinal fluid. the insufficient resistance of linear Gd^{3+} compounds, which leads to its release from chelates into the bloodstream and body tissues. Rodent studies regarding Gd^{3+} accumulation confirming the possibility of damage. Even some studies that found that 50% of breast cancer cases were not detected on MRI scans with Gadolinium Based Contrast Agents.

Skeptics argued that the doses used in the studies on rodents are inconsistent with those used in clinical practice. In addition, the evidence for the association of neurodegenerative diseases with the effects of Gd^{3+} was not convincing. It was claimed that usually damage to the dentate nucleus and globus pallidus gave specific symptoms that did not develop in any of the studies.

The problem nevertheless exists. In 2017, the Mayo Clinic reported direct confirmation of the detection of Gd^{3+} in the brains of deceased children after undergoing MRI with Gd^{3+} ; specifically the dentate nucleus and pons. This suggests that Gd^{3+} accumulation does not depend on changing BBB permeability due to aging. Furthermore, Gd^{3+} is detected in the adult brain several years after MRI. Gd^{3+} dechelates and combines with phosphorus and forms nano particles accumulations leading to nano toxicity.

According to the principles of pathological physiology, accumulation of Gd^{3+} in the brain or other vital organs leads to cell and tissue damage, which will manifest itself.

The consensus was as follows: usage of cyclic Gd^{3+} contrasts instead of linear ones were recommended in Europe. The food and drug administration (FDA) did not recommend the abandonment of linear contrasts, but recommended restrictions for children, pregnant women, and patients with severe inflammation. In Russia, research is being conducted in order to create a fundamentally new and safer class of Gd^{3+} contrasts.