Adverse events surrounding the use of intravenous contrast media are widely encountered, primarily because the substances must be used in elevated concentrations to provide an adequate degree of contrast enhancement. The severity of adverse effects and the profile of preferentially-vulnerable patients must be determined to avoid subjecting such patients to unnecessary risks. This has not yet been done satisfactorily for many gadolinium based contrast-enhancing preparations.

A substance dispersed within the body fluids may injure tissue directly through chemical insult or osmotic damage. It can also injure organs selectively through occlusion, physico-chemical processes that impair the functioning of the organs or through destruction of viable cells within the organs. Immunologically-related injury mechanisms may prevail in situations where inflammation and tissue destruction result in the release of denatured tissue debris. Injuries can arise through occlusion of fluid paths and release of toxic entities derived in vivo from the contrast medium or its by-products.

MRI contrast agents with gadolinium owe their usefulness to the unique atomic structure of the element gadolinium. Yet gadolinium is a toxic substance with severe adverse effects. Thus, it is necessary to mask its aggressive nature by bonding the gadolinium ion to other atoms.

The stability of a contrast agent under conditions of use can vary. Temperature, environment, the presence of certain ions, pH and other factors influence the rate at which gadolinium may reappear in soluble toxic forms. Gadolinium-based contrast agents have a capacity to injure proportionally to the rate of increase of gadolinium from the bound form. Not all contrast agents have the same stability.

Gadolinium in ionic or as “free” ion is highly invasive, with a capacity to permeate organs and poorly irrigated tissue. Under some circumstance, it can remain in extracellular fluids for a sufficiently long time to induce severe pathological effects. Grossly, the ion is taken up preferentially by the liver and spleen. If the dwell time is sufficient, sclerotic side effects occur, specifically nephrogenic systemic fibrosis, a condition encountered in individuals with renal insufficiency subjected to gadolinium-based contrast agents. Further, ionic gadolinium is a powerful tissue irritant with inflammatory properties that promote tissue destruction and mineralization of tissue including skin and sites with ongoing tissue repair.

Individuals with a history of implant misadventure, chronic abscesses, radiation treatments and exposure to chemotherapeutic agents are subject to fluid accumulation and delayed excretion of fluids. The most common complications are the formation of a seroma, hematoma or abscess-like lesions with a limited ability to clear the uptake intravenously-administered substances. Implant users are also subject to long-term tissue repair, mainly in poorly vascularized areas. Such properties increase the retention time of intravenously-administered products. In the case of gadolinium-based contrast agents, the risks exceeds the possible benefits from improvement in diagnostic imaging, be it for MRI, radiodiagnostic or radiographic purposes.

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