Long-term retention of Gadolinium in the skin of rodents following the administration of Gadolinium based contrast agents

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Purpose:

Several recent publications suggest a role for Gadolinium based contrast agents (GBCAs) as a possible trigger for Nephrogenic Systemic Fibrosis (NSF). The aim of the study was to evaluate the possible long-term retention of Gadolinium (Gd) in the skin of rodents following administration of different GBCAs.

Methods and Materials:

Gd-concentration in the skin was measured after application of linear non-ionic (Omniscan® and OptiMARK®); linear ionic (Magnevist®); macro-cyclic GBCAs (Gadovist®, ProHance® and Dotarem®) in Han-Wistar rats. The GBCAs were injected *i.v.* once daily at a dose of 2.5 mmol Gd/kg for 5 consecutive days. The Gd-concentration in skin biopsies was determined at various time points (up to 250 days *p.i.*) by ICP-MS.

Results:

Regarding the Gd-concentration in the skin, we observed statically significant differences between the different GBCAs classes. For linear non-ionic compounds, accumulation during the injection period (5 days) and high Gd-concentration were maintained over time in the skin (up to 250 days). For the linear ionic compounds, a relatively lower Gd retention was observed over time in the skin. Beginning 40 days after the last injection, the Gd values in the skin observed after application of all macro-cyclic compounds were in the same range as observed in saline treated and in untreated animals.

Conclusion:

We observed a correlation between the complex stability of GBCAs and the amount of residual Gd in the skin up to several months after application of GBCAs. No long-term retention of Gd in the skin could be detected after application of macro-cyclic GBCAs.