Gadolinium toxicity
Knowledge gaps, prioritization of research roadmap

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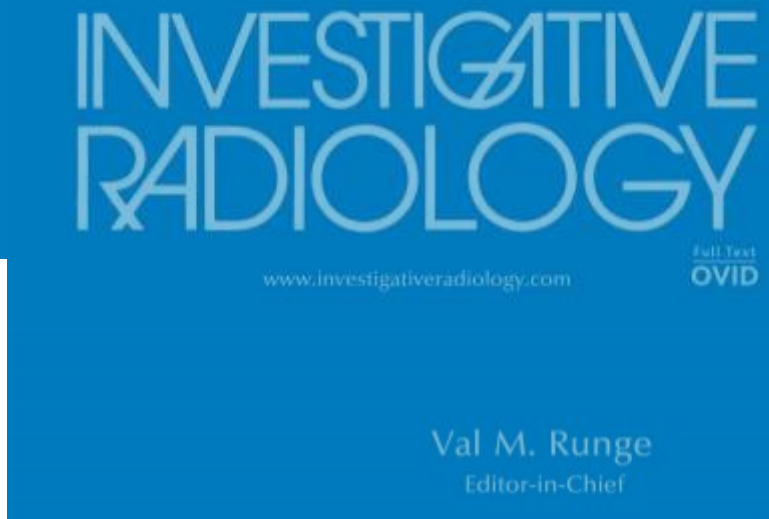

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Conflicts of Interest

Has been involved in gadolinium-related research since 1982; in the current year, 2018, is principal investigator for two small research grants to his department in Bern Switzerland, <= 10,000 Euro each, one from Guerbet and one from Bayer; will also receive honoraria in 2018 for presentations at the CMR meeting in Barcelona and the ECR meeting in Vienna during industry-sponsored (Bayer) symposia.

Discussion and Knowledge Gaps

- need to re-evaluate aspects of nonclinical studies
  - Exposure/toxicity relationship of GBCAs particularly for chronic exposure
  - CNS safety in juvenile and adult animals
- filling the gaps from nonclinical perspectives
  - Animal models: species; prenatal, juvenile, adult
  - Study protocol standardization: dose, dose multiples, dose timing, dose frequency, observational batteries, timing of evaluations, assay methodologies (Gd)

Discussion and Knowledge Gaps 2

- dissociation of Gd may result in unknown number of intermediate metabolites, the toxicology of which has not been evaluated
- could there be any resultant organo-metallic compounds formed?
- what concentration of Gd deposits of what diameter(s) result in a certain observed MRI signal?

Discussion and Knowledge Gaps 3

- how does one define gadolinium toxicity?
- are symptoms of gadolinium toxicity reproducible?
- is dechelation required to produce symptoms?
- what are the stabilities of the gadolinium chelates at lysosomal pH?