Knowledge Gaps & Potential New Directions

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Conflicts of Interest

Bracco Diagnostics: scientific advisory board, research support; Guerbet: scientific advisory board, consultant, research support; Philips Healthcare: consultant, research support.
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- **What are Gd retention rates/elimination rates with various GBCAs?**
  - What conditions influence elimination rates?
  - What are baseline urine levels? Over time?
  - Measure other Lanthanides/metals as controls for environmental exposure?

- **Postmortem tissue studies - human physiology; actual clinical conditions**
  - What are average background levels of Gd in various organs?
  - Validate observations from preclinical & *in vivo* studies
  - Speciation

- **Long term preclinical studies of various organs (Gd levels; histology; toxicity)**
  - Extended PK >>24 hours
  - Mimic young subject receiving many GBCA doses.
  - Within each organ/tissue: where is Gd depositing? Diffuse or focal? Intracellular/Extracellular?

- **Define vulnerable populations? Infants/children; conditions receiving multiple exposures; elderly?**
  - What are risks to development? To degenerative diseases in later life?
  - Are there special populations at increased risk in various organs: e.g. iron overload (liver, spleen, bone marrow); lead poisoning/heavy metal poisoning; bone mineralization disorders
  - Potential medication interactions resulting in supra-physiologic amounts of cations competing for transmetallation.
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Additional gaps - lessor priority

• Need sensitive, reproducible, non-invasive method for measuring Gd *in vivo*
  • Techniques: Xray fluorescence; Neutron activation analysis; other?

• Is chelation therapy needed? Best method?
  • Deferoxamine shown to reduce Gd liver levels - what is mechanism?

• Encourage collaborations across disciplines and areas of expertise
  • Identify centers of excellence for Gd measurement; speciation; EM
  • Centers with access to postmortem tissue collection