KNOWLEDGE GAPS & FUTURE DIRECTIONS

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CONFLICTS OF INTEREST

Royalties from Wolters Kluwer.
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• We lack controlled studies demonstrating evidence of clinical manifestations from gadolinium retention
• Sufficiently large studies demonstrating absence of clinical harm are few, retrospective, and targeted to a few diseases
• Efforts to treat patients who believe their symptoms are caused by gadolinium retention are experimental and uncontrolled
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- If there is a clinical manifestation from gadolinium retention, it is unclear whether:
  - The risk varies by GBCM or by GBCM class
  - The risk is dose dependent
  - Any dose-dependent threshold is crossed in clinical use
  - The manifestation is acute or delayed in onset
If clinical harm from gadolinium retention is present but rare, it is unclear what risk is acceptable.

- We will never prove a negative
- So what level of risk should our studies be powered to detect?
FUTURE DIRECTIONS

• Establish a threshold of tolerable harm to enable studies to be appropriately powered to detect it
• Identify likely manifestations of gadolinium retention using best available surrogates (preclinical data, other metals, distribution)
• Encourage unbiased multi-vendor and NIH collaboration to fund necessary research
FUTURE DIRECTIONS

• Analyze pre-existing large prospectively accrued databases on aging or neurological diseases that include cognitive testing
• Initiate prospective phase IV studies analyzing subclinical and delayed manifestations targeted to plausible symptomatology
• Encourage double-blind controlled studies in willing patients who believe they have been affected by gadolinium retention