KNOWLEDGE GAPS & FUTURE DIRECTIONS

MATTHEW DAVENPORT MD

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

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- 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