

The assessment of gadolinium in post mortem tissue and special considerations in pediatrics

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Conflicts of Interest

Guerbet: scientific advisory board, consultant, research support.

1. Knowledge Gap: Comprehensive Tissue Databank

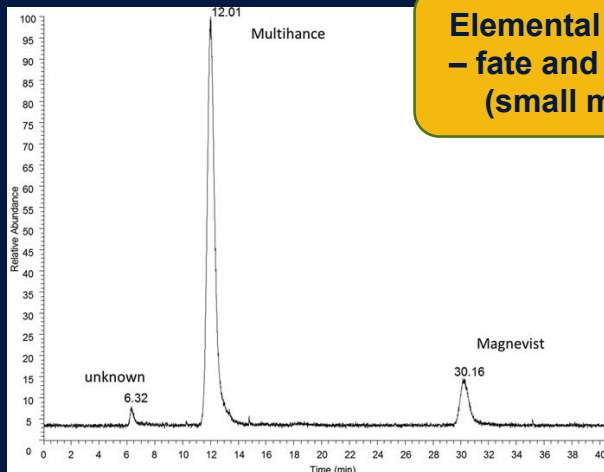
(all agents, timing, dose, tissue types, human and animal)

National Institute of Standards and Technology



NIST Biorepository

- Cryogenic Storage (-150 °C) for sample stability/security
- Standardized protocols for collection, processing and archival of samples; including chain of custody and tissue access policies
- 24/7 computerized monitoring of freezers/room conditions
- Specimen tracking and freezer inventory database
- ISO Certified Clean Rooms



Elemental Speciation
– fate and form of Gd
(small molecule)

Total Gd Determination
– Yes / No

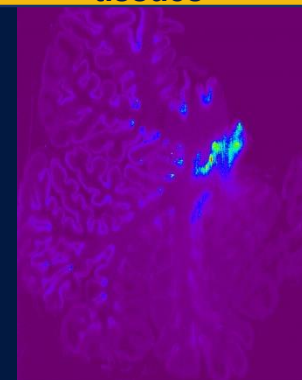
Metalomics – fate and form of Gd
(macromolecule)

Protein Function

Analytical Core Capabilities

- High resolution ICP-MS
- Laser ablation ICP-MS
- LC-ICP-MS
- High resolution MS

Elemental Imaging - distribution of Gd bioaccumulation in tissues



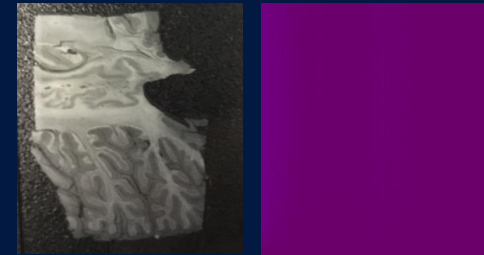
Gadolinium Quantification, Distribution, and Speciation

Case #1

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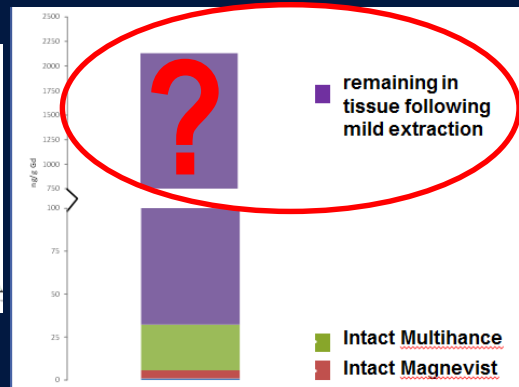
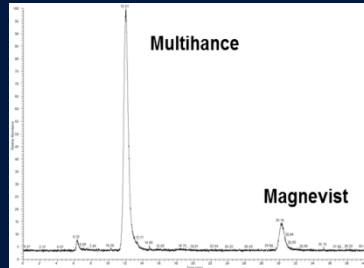
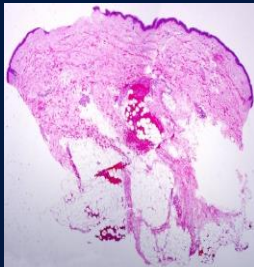
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Case #2



Control – below LOD (0.075 ug/g)

¹⁵⁷Gd



Case #3

A patient with dx GBM underwent 61 MRI scans over 11 years from age 19 until 30 with multiple contrast agents: gadobenate dimeglumine, gadopentetate dimeglumine (Magnevist), gadodiamide (Omniscan), and gadoteridol.

2. Knowledge Gap: Vulnerability of Pediatric Patients

- Vulnerability of the Pediatric Brain
 - The developing pediatric brain is known to be sensitive to metals and other man-made chemicals in very small amounts (lead toxic threshold of 10 µg/dL)¹
- Active skeletal formation
 - Fusion of secondary ossification centers of the human femur 11-18 years females; 14-19 years males²
 - 23 X higher levels in bone than brain³



Age 6 after 22 doses of GBCA

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	<input type="checkbox"/>	Recruiting	Gadolinium Retention in Human Bone Tissue in Pediatric Patients	<ul style="list-style-type: none"> • Gadolinium • MultiHance • Dotarem • (and 2 more...) 	<ul style="list-style-type: none"> • Drug: Pre-operative MRI with Dotarem • Drug: Pre-operative MRI with MultiHance • Procedure: Surgery 	<ul style="list-style-type: none"> • Medical University of South Carolina Charleston, South Carolina, United States



- Neonatal Renal Function Immaturity
 - Normal term newborn mean GFR = 39 mL/min/1.73 m² (range 11-15)⁴
- Gadolinium MRI at any time during pregnancy is associated with an increased risk of **rheumatological, inflammatory, or infiltrative skin conditions** and for **stillbirth or neonatal death**.⁵

¹Stein J, et al. *J Dev Behav Pediatr.* 2002;23:S13-22.
²Zoetis T, et al. *Birth Defects Research (Part B).* 2003;68:86-110.
³Murata, et al. *Invest Radiol.* 2016;51(7):447-453
⁴Cooper, S., "The Harriet Lane Handbook, Chapter 19 Nephrology"; 2012, p484.
⁵Ray JG, et al. *JAMA.* 2016;316(9):952-961.