





# Gadolinium Deposition: What We Know and Don't Know, A Research Roadmap Workshop

**No Evidence of Harm!** 

What is GDD?

What is GAP?

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	Patient #
=	Hospital
6	Country
PATIEN	Diagnosis
2	Treatment
	Comorbidities
	Age at first GBCA injection
	Age at first enhanced MR scan
⋖	Progressive #eMRI scan
GBCA	GBCA type (unconfounded)
ច	GBCA type (confounded)
	Number injections
	Total GBCA Volume recorded
	B0 (Tesla)
	Vendor
	Coil
	Coil channels
	Gradient strenght
	SE or GRE
•	2DFT or 3DFT
MR SETUP	TR (ms)
<u> </u>	TE (ms)
S 2	Flip angle
¥	TI (ms)
_	Slice thk (2D)
	Slab thickness (3D)
	Voxel volume
	FOV
	Matrix
	NEX/averages
	Receiver bandwidth
	DN to Pons Ratio First scan
ES	DN to Pons Ratio Last scan
≅	T1 relaxometry
ร	
Sa	
Ξ	
MR MEASURES	
Σ	



#### **Conflicts of Interest**

Bayer Healthcare-Speaker Agreement.



## Dose-Dependent Effects (chronic exposure)?

Long-Term Retention and Gd<sup>+++</sup> Deposition

Cumulative amount of deposited gadolinium

To reach a threshold for toxicity (if any)

Increased Risk at threshold dose

Time Challenges the hypotheses

Predictable effect

If any: rare events of patients with symptoms after very high cumulative doses

### **Exposure Effects** (idiosyncratic reaction)?

No Gd<sup>+++</sup> Deposition

No threshold dose (in clinical range)

Gadolinium/GBCA - Drug Interactions

Gadolinium/GBCA - Protein binding

Gadolinium/GBCA and Immune system

Unpredictable effect

If any: rare events of patients with symptoms after exposure to GBCA (immune sensitization is theoretically possible)

Big data to increase epidemiological signal to noise ratio



#### **OPPORTUNITIES:**

Identifications of vulnerable patients

Differences between GBCA molecules? Large datasets with unconfounded exposure and clinical / imaging outcome

Body symptoms/signs in CNS disease patients

Neurological symptoms/signs in NON-CNS disease patients

Gadolinium tissue topographic distribution (intra / extracellular in brain, skin, bone, liver etc.) – biosamples –

Ionic		Non-ionic
Linear	HO Gd-TPA (Magnevist)	H.C.N. G.J.C.P.A.BMA (Compiscan)
	GG-BOPTA GG-EOB-DTPA (MultiMANCE)	H,C,O,E,O,E,O,E,O,E,O,E,O,E,O,E,O,E,O,E,O
Macrocyclic	Gd-DOTA (Dotarem)	Gd-BT-DOJA (Gadovist)
		Gd-HP-DOJA (ProHANCE)



#### **PITFALLS:**

Data validation among centers, institutions, national registries

Systematic Errors

Disease-Related Effects introduced by the pathological processes and treatments (especially in the scenario of long-term dose-dependent effects of gadolinium deposition)



## International and European Gadolinium Retention Evaluation Consortia

**I-GREC & E-GREC** 





Repository: T1 and T2

mapping

NON-CNS

DATABASE standardised protocol

Executive

unctions Test

Demograph

Registry

Clinical

Data

Repository

- → Multi-center MR image repository
- → Demographic registry
- ♦ Bio-banking repository
- ♦ International Database for Big data mining
- Gateway to resource utilization
- ♦ Scientific consultation of Regulatory agencies
- Source of Clinical Guidelines

www.igrec.net



Chelates Registry

Biospecimen

Samples