Specialty area: *Molecular & Cellular Imaging: From Bench to the Bed*

Highlights

- Contrast agents play key roles in Molecular and Cellular Imaging
- Biological effects of a contrast agent can be dependent on many variables such as chemical, size, dose, route of delivery
- Toxicity of a contrast agent may be subtle, may occur long after exposure, challenging and expensive to fully establish by individual research laboratories
- Understanding what each toxicity assay is measuring guides subsequent physicochemical modifications to reduce toxicity.

Title: Toxicity

Target Audience: This information will benefit researchers and clinicians who develop and use molecular and cellular imaging contrast agents.

Objectives: Following this lecture, attendees will be able to identify particular assays for determining toxicity for a variety of different classes of molecular and cellular imaging contrast agents. Further, researchers will be cognizant of the potential effects of multiple variables on toxicity, such as chemical species, size of the construct or nanoparticle, dose at the organism and cellular level, and route of delivery both to the organism and to the cell.

Purpose: Measuring the toxic effects of contrast agents is a key step in the fabrication and characterization scheme. Understanding which assays to perform, as well as proper interpretation of the results, is key.

Methods: Molecular and cellular imaging contrast agents comprise a wide variety of chemical species and forms. Gadolinium and other lanthanides are used mostly as small chelates, but have also been commonly used within nanoparticles, both chelated and as a metal oxide. Iron is most commonly used as iron oxide, either as a nanoparticle or microparticle. Both synthetic and natural biocompatible nanoparticle formulations have been employed. Manganese has mostly been used as manganese chloride but has recently found use as manganese oxide. A variety of non-metallic biologically based materials have been developed as agents, such as proteins and small molecules. Each agent has the potential for unique toxic effects, despite some being comprised of the same chemical entity.

Results and Discussion: Toxicity is the degree to which a substance can damage an organism. While viability, both cellular and organism is a critical first check of a new contrast agent, more intricate toxicity measurements are required to determine the biological effects of an agent. These include measurements on altered genetics, metabolism, protein expression, cellular functions, migrational capability and long term fate. These experiments can be expensive and performed multiple ways.

Conclusion: Measurement of toxicity is critical in the characterization of novel contrast agents. This lecture will give examples of some assays commonly used and will emphasize the challenges in interpretation of results.