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Presenter Information

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Multi-systemic heart, kidney, and liver disease induced by gadolinium-based contrast treatment

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Introduction: Gadolinium-based contrast agents have revolutionized clinical imaging. Conversely, there is growing concern of the overall safety of these agents. Once administered there is long-term retention of gadolinium in tissues. The long-term biologic impact of gadolinium retention is of monumental concern to patients and drug-regulating administrations. **Methods:** Our research team was the first to establish a rodent model of iatrogenic systemic fibrosis using chimeric mice. Wild-type C57/BL6 mice were randomized by sex and weight into contrast treatment (2.5 mmol/kg intraperitoneally, 20 doses over 4 weeks) or untreated groups. Ultrasound (Vevo 3100, FujiFilm VisualSonics) was performed several days-post final contrast treatment. Animals were perfused with formalin. Fixed tissues were prepared for magnetic resonance imaging (Bruker, 7.0T 40 cm bore MR scanner) or analyzed histologically and with electron microscopy (Hitachi HT7700, AMT 16-megapixel digital camera). Samples for the latter were further examined using scanning/transmission electron microscopy equipped with energy-dispersive x-ray spectroscopy (Jeol 2010F FASTEM with Oxford Analytical EDS). **Results:** *Gadolinium-based contrast agents induced intracellular nanostructure formation in the kidney along with acute tubular and mitochondrial damage.* Elemental analysis of these nanostructures by energy-dispersive X-ray spectroscopy revealed that these electron-dense structures were rich in gadolinium. Furthermore, exposure to gadolinium induced liver steatosis. Treatment groups paradoxically demonstrated increases in several functional cardiac parameters, particularly cardiac outputs. MRI analysis further illustrates gadolinium retention in the renal cortex of treatment groups. **Conclusions:** Exposure to gadolinium-based contrast agents leads to gadolinium retention in the form of electron-dense nanostructures. Gadolinium-based contrast agent treatment **induces multi-systemic** heart, kidney and liver disease.