The Luigi Sacconi Memorial Lecture in Chemistry 2026

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"Programming Gd(III) Coordination Chemistry to Image the Molecular Hallmarks of Aging"

Monday, September 7th, 2026
5:00 p.m.
Room 25, Blocco Aule, Polo Scientifico, Università di Firenze
Sesto Fiorentino

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Programming Gd(III) Coordination Chemistry to Image the Molecular Hallmarks of Aging

Aging is accompanied by progressive molecular and cellular changes that drive tissue dysfunction and age-associated disease. Magnetic resonance imaging (MRI), despite its extraordinary clinical reach, remains largely dependent on passive contrast agents that report anatomy rather than biochemical function. Our laboratory has developed a chemically programmable platform of enzyme-responsive Gd(III)-based MR contrast agents that transform specific molecular activity into detectable MR signal through rational control of coordination chemistry. These probes are engineered so that enzymatic activation modulates inner-sphere hydration (q), rotational correlation time (τR), and biological retention, converting molecular recognition events into measurable T_1 enhancement.[1,2]

We have applied this strategy to cellular senescence, a central hallmark of aging and a major contributor to musculoskeletal disorders including osteoarthritis. Currently, no clinically available imaging methods directly assess the biodistribution or efficacy of emerging gene and senolytic therapies in senescent tissues.[3]

Our β-galactosidase-responsive probes enable direct MR visualization of senescent cell populations in vivo, providing spatiotemporal information on disease progression and therapeutic response in the central nervous system, peripheral nervous system, and musculoskeletal tissues.

The modular architecture—combining responsive triggers, self-immolative linkers, and programmable Gd(III) coordination environments—provides a generalizable framework that can be extended to additional hallmarks of aging by *reprogramming* the molecular recognition element. These studies illustrate how responsive coordination chemistry can move MRI beyond structural imaging toward direct visualization of dynamic biochemical function in living systems.

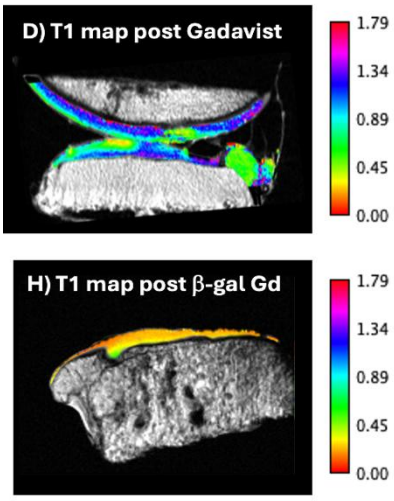

Figure 1. Top: Human osteoarthritis joints exposed to a commercial MR contrast agent (Gadavist), where senescent cells are not detected. **Bottom:** A bioresponsive MR agent that is enzymatically activated by the presence of senescent cells.

1. Daldrup-Link HE., et., al., Skeletal Radiol. 2024, 53, 1879-1887.
2. Nernekli K, et. al., njp imaging, 2025, 3, 18-22.
3. Tang JH, et. al., Biocon. Chem. 2026, 37545-552.

Thomas J. Meade *is the Eileen M. Foell Professor of Cancer Research and the Charles Deering McCormick Professor of Teaching Excellence at Northwestern University, where he holds joint appointments in Chemistry, Molecular Biosciences, Neurobiology, and Radiology. He earned his M.S. in Biochemistry and Ph.D. in Inorganic Chem. followed by an NIH fellow at Harvard Medical School and a postdoc appointment at the California Institute of Technology. His research lies at the interface of coordination chemistry and biology, with a focus on molecular imaging, transcription factor inhibition, and the development of electronic biosensors for DNA & protein detection. He has authored over 350 peer-reviewed publications, holds 109 U.S. patents, and is the founder of five biotech companies.*