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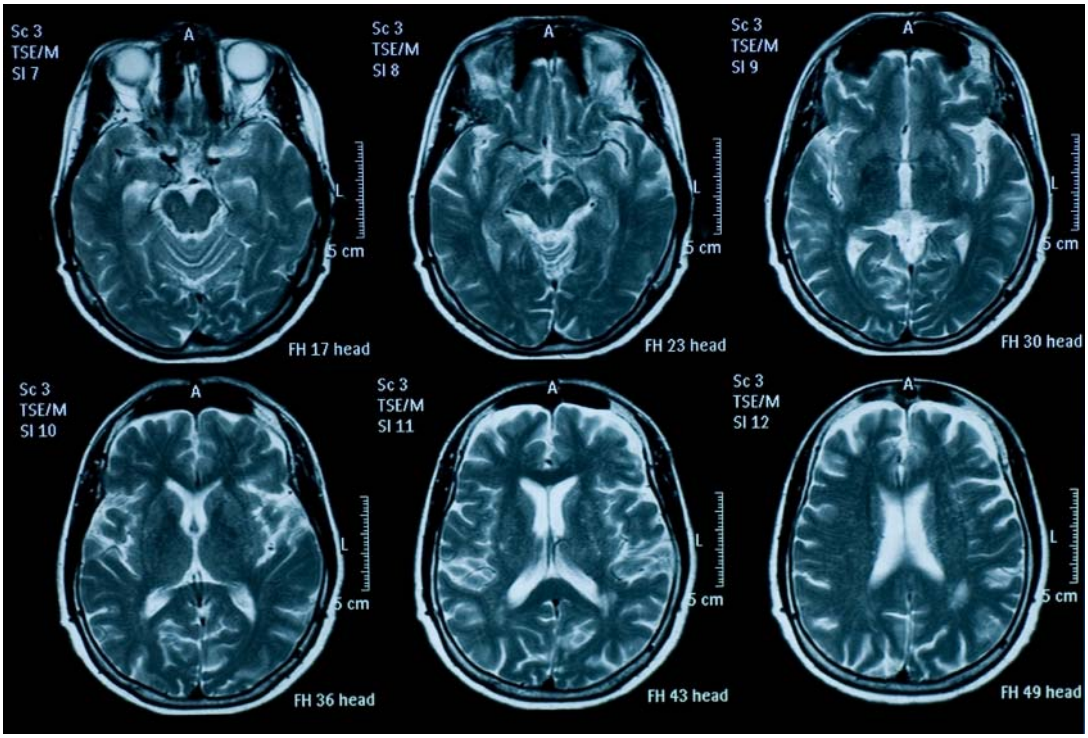
PARACEST-Based Contrast Agents

For MR imaging of labile ferrous iron

Elevated iron levels have been identified in a variety of neurologic disorders, including Parkinson's, Huntington's, Alzheimer's, Friedreich's ataxia and multiple sclerosis. It has been hypothesized that excess iron may play a role in the progressive deterioration observed in patients suffering from those diseases. Current MRI techniques (e.g. magnetic susceptibility imaging, and T_2 and T_1 weighted MR images) used to detect excess iron deposits rely on differences of bulk water proton relaxivity. Unfortunately, these techniques suffer from the presence of artifacts, thereby complicating clinical interpretation. More direct imaging methods are needed that would specifically image iron and only iron in tissue. A UB chemist has developed a series of ligands that represent an entirely new class of contrast agents that respond only upon sequestering endogenous iron in cells, making it possible to image Fe(II) and only Fe(II) within a sea of metal ions and other cellular components. These PARACEST-based contrast agents appear to be useful tools for monitoring excess iron levels in tissue and may facilitate the tracking and treatment (e.g. chelating agents, CNS drugs, etc.) of diseases involving aberrant iron levels. Additionally, their development as clinical tools would provide a much-needed alternative to lanthanide contrast agents (e.g. gadolinium), which can be problematic for patients with compromised renal function.



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OVERVIEW

Abnormally high non-heme iron levels such as those seen in neurologic disorders such as Parkinson's and Alzheimer's are considered toxic and may contribute to the progressive deterioration seen in patients suffering from such diseases. In addition, brain microbleeds, which have been attributed as a contributor toward dementia and Alzheimer's, also lead to the deposition of iron in brain tissue.

Current MRI techniques used to detect and monitor excess iron in the body rely on indirect measures: differences of bulk water proton relaxivity in tissues that contain excess iron; thus, they are hampered by artifacts from other structures such as areas of calcification that can complicate clinical interpretation. As a result, there exists a need for direct imaging methods and compositions that would specifically image iron and only iron in tissue. The development of such tools for monitoring excess iron levels in tissue would greatly facilitate the study, monitoring and treatment of these diseases.

INVENTION(S)

A UB chemist has developed a series of small hydrophobic PARACEST-based agents that appear ideally suited for molecular imaging applications.

Like other PARACEST agents, the paramagnetic complexes formed when these ligands sequester endogenous iron result in a shift in the exchangeable proton resonances far from the bulk water proton resonance to reduce interference from the magnetization transfer effects that give rise to the broad water peak observed in tissue. Further, they are highly sensitive to oxidation state, spin state and coordination geometry of the iron cation. These ligands have been designed to image Fe(II) and only Fe(II) despite being present in an environment rich with metal ions and other cellular components.

The promise of these agents being able to serve as clinical tools to study, diagnose and monitor diseases involving excess iron is enhanced by the fact that they have been modeled after compounds developed as iron overload drugs, which already possess optimal and/or desirable properties:

- Membrane permeability and facile passage into cellular compartments for binding to iron pools
- Low toxicity
- Ability to cross the blood brain barrier

Additional information is available under STOR's Confidential Disclosure Agreement (CDA). If interested, please request a CDA from the Contact Person listed below.

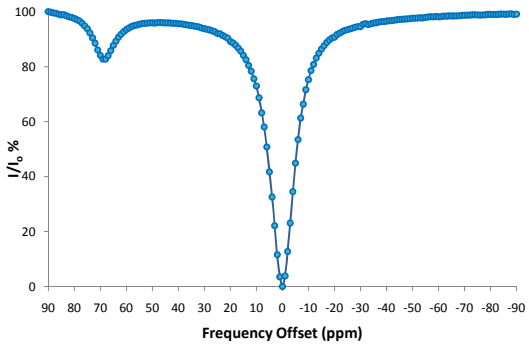

Figure 1. CEST spectrum of Fe(II) complex at pH 7.3, 37 °C, 100 mM NaCl, 20 mM Hepes buffer, B_1 = 1900 Hz, 3 s. The dip at about 70 ppm is attributed to the chemical exchange saturation transfer of the amide protons of the complex with water.

APPLICATIONS and MARKETS

- Research
- Diagnostic Imaging and Thermometry
- Clinical and Therapeutic Monitoring

PRIMARY INVENTOR(S)

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Professor

PUBLICATIONS

No publications to date

PATENT STATUS

Patents pending

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