Method of Preparing Macromolecular Contrast Agents and Uses Thereof

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Technology

- Problem → Macromolecular MR contrast agents are:
  - difficult to characterize;
  - results are complex mixtures;
  - unstable Gd(III) complexes;
  - less than expected molar relaxivity.
- Stage of research → pre-clinical *in vivo*
- Patent Status – Filed 2009
- Recent Publication:
  - Nwe, K., et al., Bioconjugate Chem. 2009, **20**, 1412-1418.
- Related Patent:
  - Gansow, O. A., Brechbiel, M. B., Magerstadt, M. A.: Complexes of Functionalized Tetraazacyclododecane Chelates with Bismuth, Lead, Yttrium, Actinium, or Lanthanide Metal Ions. U.S. Patent 5,428,154

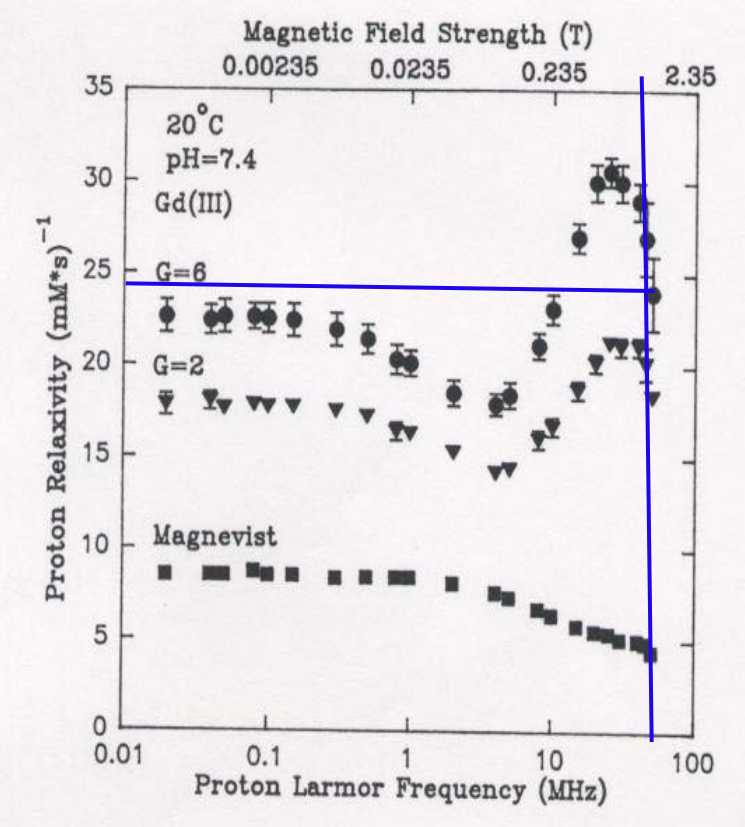
Technology Applications

- Areas in which the technology can be applied
  - All macromolecular Gd(III) MR contrast agents
  - All macromolecular Gd(III) MR contrast agents that are combined with other imaging modalities.
  - Impacts LMW Gd(III) MR contrast agents
- Why is it important? Why is it different?
  - Simplifies characterization concerns → Reproducible chemistry
  - Eliminates toxicity concerns → kinetically inert complex
  - Enhances molar relaxivity → decreases required injected dose
- Validation
  - *In vivo* animal imaging
  - Proper formation of Gd(III) complexes

Commercial Applications

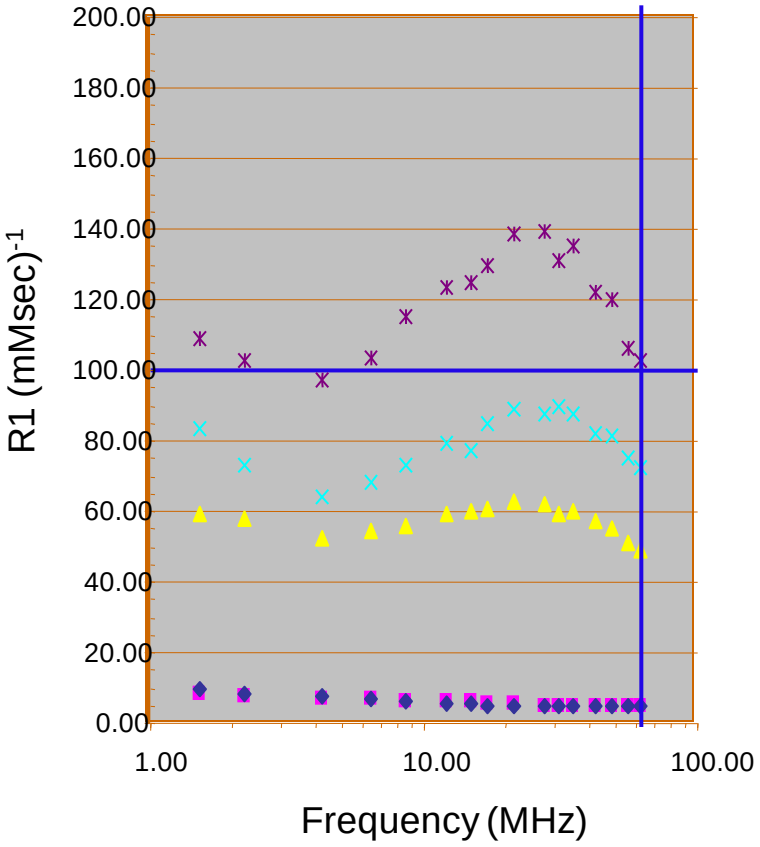
- MRI contrast agents with greatly improved homogeneity and stability
- Greater molar relaxivity, allows using much less of the agent than previously required to acquire comparable or better images

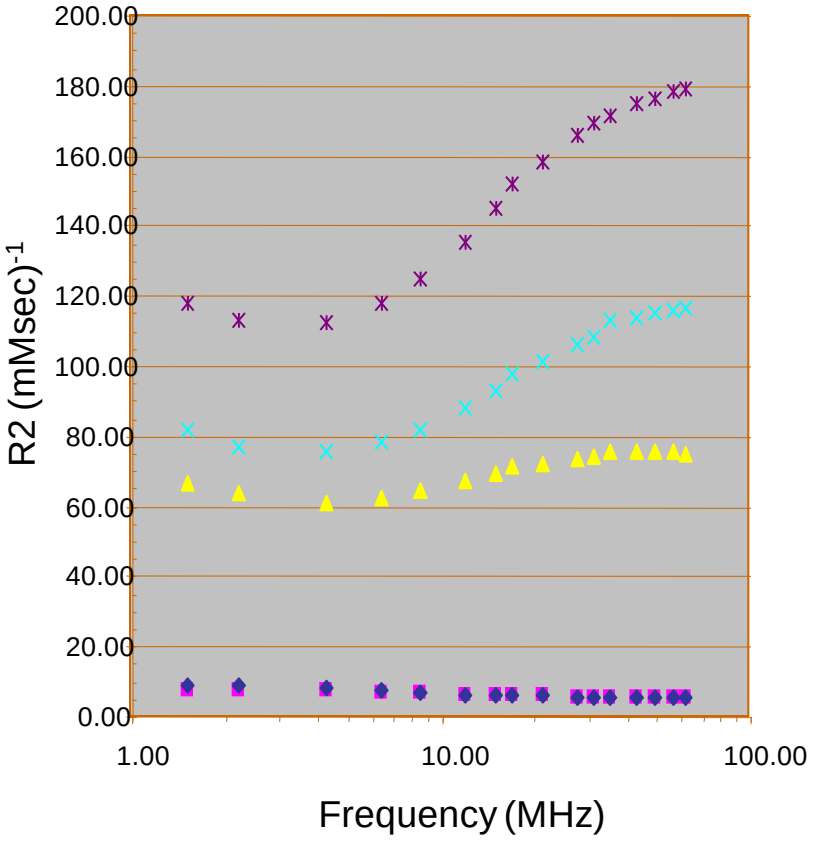
Dendrimer–based gadolinium chelates exhibit large proton relaxation enhancements



Weiner, Brechbiel, Brothers, Magin, Gansow, Tomalia, Lauterbur, *Mag. Res. Med*. 1994, **31**, 1-8.

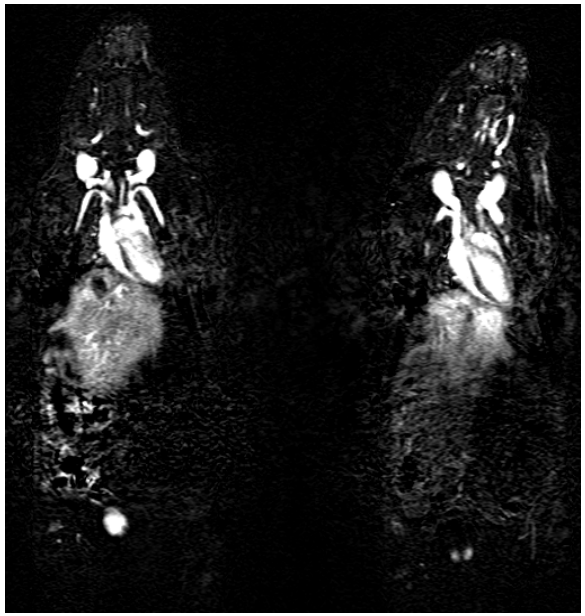
Dendrimer –based using pre-formed *C*-DOTA chelated Gd^{+3} exhibit Larger proton relaxation enhancements!

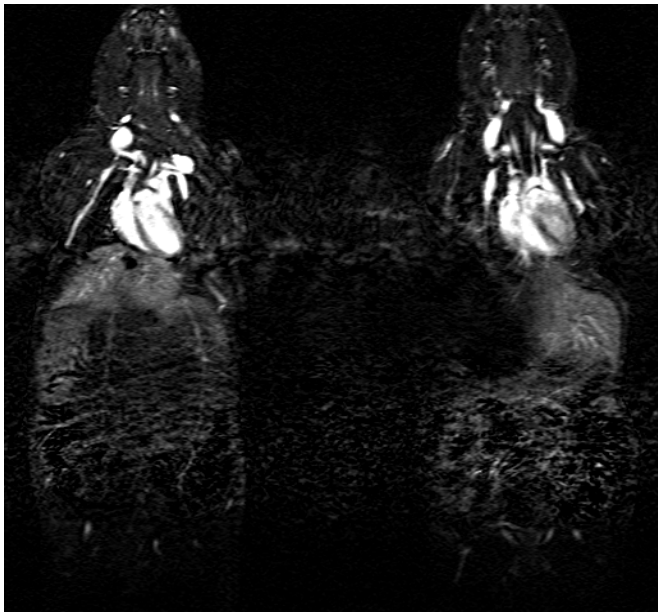




Magnevist Prohance G4 (DOTA[Gd]) G5 (DOTA[Gd]) G6 (DOTA[Gd])

In vivo imaging – pre-Gd^{+3} incorporation DTPA vs. *C*-DOTA





G4-(1B4M-DTPA-Gd)$_{30}$

G4-(*C*-DOTA-Gd)$_{28}$

Collaboration Opportunities

- Licensing and/or CRADA opportunities
  - Future research → actively targeted agents
  - What would you want out of a collaboration?
    - Novel targets & targeting vectors w/ corresponding animal models
    - Access to imaging instrumentation
  - Available for licensing? → YES!

Contact Information

- For further information contact:
  - Licensing:

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