The Effects of Rotational Correlation Time of Paramagnetic Contrast Agents On Relaxation Enhancement: Partial Binding to Macromolecules

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Purpose: To evaluate the effect of rotational correlation time (τ_R) and the possible related changes of other parameters, τ_M, τ_s, and τ_v of gadolinium (Gd) chelate on T1 relaxation enhancement in the model system of partial binding of MR agents to macromolecules. This model system is very important for the development of highly efficient MR agent and for the understanding of detailed relaxation mechanism of tissue-specific MR agents such as Gd-EOB-DTPA.

Materials and Method: The NMRD (Nuclear Magnetic Relaxation Dispersion) profiles were simulated from 0.02 MHz to 800 MHz proton Larmor frequency for different values of rotational correlation times based on Solomon-Bloembergen equation for inner-sphere relaxation enhancement. To include both the unbound agents (pool A) and the agents bound to macromolecules (pool B), the relaxivity was divided by contribution from unbound pool and bound pool. The rotational correlation time for pool A was fixed at the value of 0.1 ns, which is a typical value for low molecular weight complexes such as Gd-DTPA in solution and τ_R for pool B was changed from 0.1 ns to 20 ns to allow the slower rotation by binding to macromolecule. The fractional factor (f) was also adjusted from 0 to 1.0 to simulate different binding ratios to macromolecule. Since the binding of Gd-chelate to macromolecule can alter the electronic environment of Gd ion and also the degree of bulk water access to hydration site of Gd-chelate, the effects of these parameters were also included.

Results: The result shows that low field profiles, ranged from 0.02 to 40 MHz, are dominated by contribution from bound pool, which is bound to macromolecule regardless of binding ratios. In addition, as more Gd-chelate bound to macromolecule, sharp increase of relaxivity at higher field occurs. The NMRD profiles for different values of τ_s show the enormous increase of low field profile whereas relaxivity at high field is not affected by τ_s. On the other hand, the change in τ_v does not affect low field profile but strongly influences on both inflection field and the maximum relaxivity value. The results shows a parabolic dependence of relaxivity on τ_M.

Conclusion: Binding of Gd-chelate to a macromolecule causes slower rotational tumbling of Gd-chelate and would result in relaxation enhancement, especially in clinical imaging field. However, binding to macromolecule can change water enchange rate (τ_M) and electronic relaxation time (T1e) via structural deformation of electron environment and the access of bulk water to hydration site of metal-chelate. The clinical utilities of Gd-chelate bound to macromolecule are the less dose requirement, the tissue specificity, and the better perfusion and intravascular agents.