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1/T1 NMRD Profile For Protein Binding of Gd-EOB-DTPA: The Detailed Analysis

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Purpose: The new hepatobiliary MRI contrast agent, Gd-EOB-DTPA, exhibits non-covalent binding to proteins. One key effect of binding is the development of enhancement in proton relaxivity. This many-fold increase in relaxivity is understood in terms of slower rotational motion of metal chelates upon binding. The aims of this study are: to assess the effect of non-covalent protein binding on the overall 1/T1 NMRD profile, and to determine the relative contributions from the various mechanisms responsible for proton relaxation.

Materials and Method: 1/T1 NMRD data were obtained on an IBM field cycling relaxometer operating at proton Larmor frequencies from 0.02 MHz to 50 MHz. The data were then fitted by a non-linear least square fitting algorithm. Human Serum Albumin (5, 10, 15% by weight) doped with Gd-EOB-DTPA in concentrations ranging from 0.5 to 2.5 mM was used. The 1/T1 NMRD profile simulations were performed using multidimensional minimization programs based on the simplex method for the following computational model

$$[1/T1](\text{observed}) = [1/T1](\text{bound}) + [1/T1](\text{unbound}) + [1/T1](\text{HSA})$$

Results: The best fit with the two-population model reveals that only 20% of 1 mM Gd-EOB-DTPA in 5% HSA appears to bind to HSA and 40% is bound in 10% HSA. For bound contrast agent, the inner sphere contribution shows that the relaxation enhancement is similar to that of covalently bound complexes, due to slower rotational motion. Other mechanism important for the interpretation of the 1/T1 NMRD profiles of non-covalently bound protein-agent complexes are the outer sphere and the protein contributions.

Conclusion: The T1 relaxivity of Gd-EOB-DTPA in case of protein binding results from the sum of three contributions. The dominant one is slowed rotational motion. The outer sphere and the protein contribution could not be neglected.