

## LANTHANIDES AS LOW TEMPERATURE RELAXATION SWITCHES

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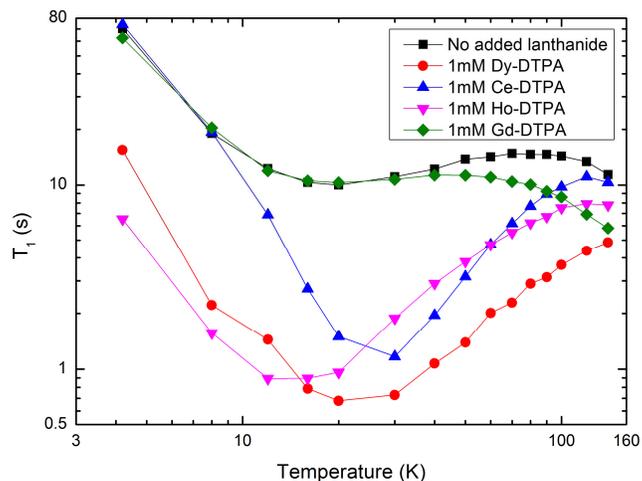
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**Introduction** We report a series of longitudinal relaxation studies designed to evaluate the effectiveness of certain lanthanides as low temperature relaxation agents. This could be of value in the context of 'brute-force' polarization, i.e. polarization by exposure to high magnetic field and low temperature (high ratios of B/T). This technique has been hindered by the extremely long T1 values found at very high values of B/T. It is also desirable to have reasonably long survival times for the polarization on returning to room temperature. Dysprosium and holmium might provide a practical solution to the problem because at room temperature they display weak relaxivity as a result of their very short electron spin relaxation times (which determine the correlation time of the electron-nucleus interaction), whereas at low temperatures their electron spin relaxation times become comparable to the nuclear Larmor period which leads to a reduction in nuclear T1 values.

**Purpose** Our goal was to achieve high polarizations of nuclei such as <sup>13</sup>C and <sup>15</sup>N with a view to using pre-polarized <sup>13</sup>C- or <sup>15</sup>N-labelled agents to probe tissue metabolism *in vivo*. Here, we place much of our focus on the relaxation conferred to bulk (primarily solvent) protons. The reason for this is that we have recently shown (1) that polarization can be transferred from the solvent protons to other more slowly relaxing nuclei (for example <sup>13</sup>C or <sup>31</sup>P nuclei) by low-field thermal mixing, a technique that equilibrates spin temperatures. We can therefore use the solvent relaxation properties and polarization as a surrogate indicator of the polarization that we might be able to achieve for our target nuclei of interest.

**Methods** We performed a series of <sup>1</sup>H T1 measurements on samples containing lanthanides including dysprosium and holmium. Solutions of the lanthanide chloride or DTPA chelate were made in a water/glycerol solvent. The <sup>1</sup>H T1 times were measured at 4-200K at 2T and below 4K at a range of fields.

**Results** The figure shows <sup>1</sup>H T1 values as a function of temperature for a pure 50:50 water/glycerol solution, and for the solution following the addition of lanthanide-DTPA chelates. At the low temperatures holmium and dysprosium are very much more effective relaxation agents than gadolinium, which displays very little relaxation enhancement at temperatures below 40K. The maximum contribution to relaxation can be expected to occur when the correlation time that characterizes the electron-nucleus interaction is the inverse of the nuclear resonance angular frequency, i.e.  $\sim 2 \times 10^{-9}$ s in these experiments. The maximum is at approximately 10K for Ho-DTPA, 20K for Dy-DTPA and 30K for Ce-DTPA, while the maximum for Gd-DTPA is evidently well above 100K. Below 4 K we are able to achieve absolute proton polarizations of about 2%. However, we find that T1 varies approximately as  $(B/T)^n$  where  $n \sim 3-4$  and tends to become very long below 0.5K for fields of a few tesla and above. The high proton polarization can be transferred to other spin species such as <sup>13</sup>C and <sup>31</sup>P by low-field thermal mixing (1).



**Discussion and conclusions** Dysprosium-DTPA and holmium-DTPA offer scope for acting as relaxation switches, in the sense of enhancing relaxation at low temperatures without causing undue enhancement of relaxation on returning to room temperature. With the aid of these agents, brute-force polarization could provide a very simple and rapid method of achieving a several hundred-fold enhancement of polarization compared with values obtained at room temperature and 3T. However, the effectiveness of these agents is limited at very high values of B/T.

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### References

(1). Gadian DG, Panesar KS, Perez Linde AJ, Horsewill AJ, Köckenberger W, and Owers-Bradley JR (2012). Phys. Chem. Chem. Phys. 14:5397-5402.