

## Anomalous Behavior of Lanthanide Chelates at 7T

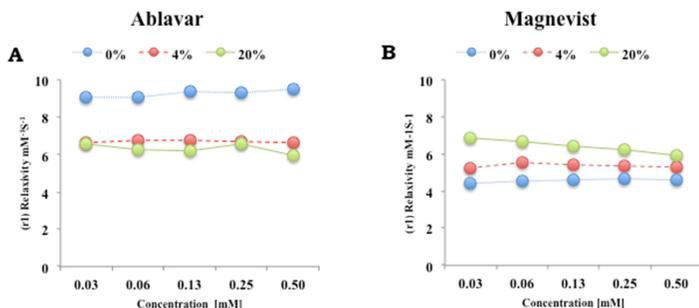
Talaignair N Venkatraman<sup>1</sup> and Christopher D Lascola<sup>2</sup>

<sup>1</sup>Radiology, Duke University Medical Center, Durham, NC, United States, <sup>2</sup>Radiology, Duke University Medical Center, Durham, NC, United States

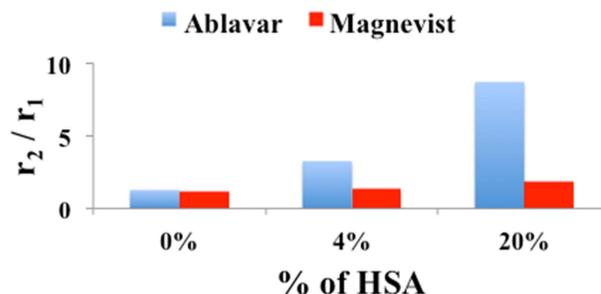
**Purpose / Introduction:** Clinical 7T MR imaging is a rapidly emergent modality, yet the behavior of common lanthanide chelates at higher field strengths remains poorly characterized. Classic contrast agents such as Gd-DTPA, as well as more recent approved compounds such as Gadofost, have been characterized primarily at lower field strengths [1, 2]. Although historical studies have revealed unexpected and sometimes paradoxical relaxation properties of lanthanide chelates at higher fields, only limited data exists on the behavior of these more recently approved contrast agents at 7T [3]. In this study, we investigated both longitudinal and transverse relaxivities of Magnevist and Ablavar at clinically relevant concentrations in the presence and absence of human serum albumin (HSA) at 7.0T. These data reveal paradoxical behavior of Gadofost in the presence of protein at higher field strength. The importance of measuring both  $r_1$  and  $r_2$  relaxivities at high field is also discussed.

**Materials and Methods: Phantoms:** Magnevist<sup>®</sup> (Bayer Pharma), Ablavar<sup>®</sup> (Lantheus Medical Imaging), were diluted with 1xPBS and transferred to 1.5CC vials over the range of 500 $\mu$ M, 125 $\mu$ M, 62.5 $\mu$ M, 32.3 $\mu$ M. For Human Serum Albumin (HSA) phantoms, a stock of HSA 25% (Talecris BioTherapeutics) was diluted with 1xPBS to 4% and 20%. **MRI Measurements:** All experiments were carried out using a Bruker Biospec Bruker 70/30 7T MRI scanner (Billerica, MA, USA) with quadrature volume coil set up. All phantoms were scanned at 20°C. The  $T_1$  experiments were performed using saturation-recovery sequence with the following parameters: Matrix Size 256  $\times$  256, FOV = 6  $\times$  6 and TE = 9.5ms, TR = 60, 300, 750, 1500, 4000 and 8000 msec. The  $T_2$  experiments were performed with the following parameters. FOV = 6  $\times$  6, Matrix Size 256  $\times$  256; TR = 2400 ms; TE = 20, 40, 60, 80, 100, 120, 140 and 160 msec.  $T_1$  &  $T_2$  maps were post-processed using Paravision 5.1 (Bruker, Billerica, MA, USA).

**Results and Discussion:** Figure 1A and 1B are plots of molar relaxivity at different concentrations for Ablavar and Magnevist. Both these compounds show steady relaxivity over the concentration range studied with and without HSA. The  $r_1$  and  $r_2$  relaxivities of 0% (1x PBS) are 4.7  $\text{mM}^{-1}\text{sec}^{-1}$  and 5.7  $\text{mM}^{-1}\text{sec}^{-1}$ . The  $r_1$  &  $r_2$  relaxivities in 4% and 20% HSA are 5.3  $\text{mM}^{-1}\text{sec}^{-1}$  & 7.1  $\text{mM}^{-1}\text{sec}^{-1}$  and 5.9 & 10.8  $\text{mM}^{-1}\text{sec}^{-1}$  (Table. 1). The ratio  $r_2/r_1$  increased from 1.2 (0% ) to 1.8 (20%). In the case of Ablavar,  $r_1$  decreased from 9.5  $\text{mM}^{-1}\text{sec}^{-1}$  (at 0%) to 6.0  $\text{mM}^{-1}\text{sec}^{-1}$  (at 20%) with HSA, whereas  $r_2$  increased with % of HSA. Figure 2 shows  $r_2/r_1$  for Magnevist and Ablavar at 0%, 4% and 20% HSA. For Magnevist  $r_2/r_1$  remains unchanged over a wide range of HSA, while for Ablavar there is a quadratic increase  $[-0.0077x^2 + 0.53x + 1.3; R^2 = 1]$  observed. The changes in  $r_2/r_1$  reflect weak and strong protein binding of these compounds, respectively.



**Figure 1:** Plot of  $r_1$  relaxivity at different concentrations ranging from 32  $\mu$ M to 500  $\mu$ M for Ablavar [A] and Magnevist [B] in (1xPBS) 0%, 4% and 20% HSA at 20°C using 7.0T



**Figure 2:** Bar graph of ratio of relaxivities  $r_2/r_1$  with varying % of HSA for Ablavar (■) and Magnevist (■) at 20°C using 7.0T.

**Table-1: Longitudinal ( $r_1$ ) and Transverse ( $r_2$ ) relaxivities [ $\text{mM}^{-1}\text{Sec}^{-1}$ ] of different contrast agents in 0%, 4% and 20% HSA**

Compound	0% HSA			4% HSA			20% HSA		
	$r_1$	$r_2$	$r_2/r_1$	$r_1$	$r_2$	$r_2/r_1$	$r_1$	$r_2$	$r_2/r_1$
Magnevist <sup>®</sup>	4.66	5.67	1.21	5.34	7.14	1.33	5.92	10.79	1.82
Ablavar <sup>®</sup>	9.47	11.98	1.27	6.6	21.5	3.25	5.98	51.94	8.69

All the values are calculated from linear fit of Relaxation rates ( $1/T_1$  &  $1/T_2$ ) [ $\text{Sec}^{-1}$ ] with the concentration of Contrast Agents [mM]

**Conclusions:**  $r_1$  relaxivity of Ablavar at higher field strength shows paradoxical behavior in the presence of HSA as compared to lower field strength data, but nonetheless pronounced  $r_2$  effects. Thus, behavior of a lanthanide chelate at one field strength is not necessarily predictive of behavior at another. These data also emphasize the importance of examining both  $r_1$  and  $r_2$  relaxation properties of various lanthanide contrast agents in tandem, given that changes in these parameters do not necessarily occur in lockstep with each other at different field strengths.

**References:** [1] Laurent S *et al* Contrast Media and Molecular Imaging 2006;1:128-137. [2] Lauffer RB *et al* 1998;207(2):529-538. [3] Noebauer-Huhmann IM *et al* Invest. Radiol 2010;45(9):554-558.