# In Vitro Relaxivities Studies of Gadolinium Carbon Nanotubes at 0.2T

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## Introduction

The r1 relaxivities of Gadolinium loaded ultra-short single wall carbon nanotube (Gadonanotubes) at 0.2T has been shown to be about 40 times stronger than existing clinically available gadolinium chelates, Magnevist (Gd-DTPA) as shown by previous NMRD studies (1-3). However, the performance of these agents at low field MR imaging has not been evaluated. Low field MRI systems are usually associated with low signal-to-noise ratio, reduced $T_1$, low gradient strength with slow gradient slew rate, and is usually consists of a permanent magnet to provide the static magnetic field. The large field inhomogeneity and eddy current effects from the permanent magnet may impact the practical $T_1$ relaxivity enhancement in Gadonanotubes MR imaging. In this paper, we present r1/r2 relaxivities of Gadonanotubes with different surfactant coatings at 0.2T using in vitro phantom imaging characterization and the results would be compared to Magnvist Gd-DTPA.

## Methods

Phantom Samples Preparation

The $Gd^{3+}$@US-tubes (Gadonanotubes) were synthesized according to previous publication (1). Ultra-short single walled carbon nanotubes (US-tubes, 20-50nm in length and 1.0nm in diameter) were soaked in aqueous $Gd^{3+}$ solution followed by sonication. The $Gd^{3+}$-loaded US-tubes were then washed extensively with HPLC grade water to ensure the absence of external $Gd^{3+}$ ions. The Gadonanotubes as produced were dispersed in 1.0% Pluronic F-108 (biocompatible surfactant) solution for the relaxivity studies. The natural form of Gadonanotubes is in bundled form due to the hydrophobic nature of nanotubes. Portion of US-tubes were reduced using $Na^0$/THF to yield individual US-tubes (4). These individual nanotubes were loaded with $Gd^{3+}$ in the same way as above. 10 mg of these nanotubes were dispersed in 1.0% solution of pluronic F-108 and used for relaxivity studies. Another 10 mg of these gadonanotubes were refluxed with Carboxy dextran (MW 10K) solution to yield dextran-coated individual gadonanotubes.

Three Gadonanotube phantoms were prepared. They are a) Individual Gadonanotube at 0.083 mM Gd concentration in 1.0% Pluronic F-108 solution (Individual Gadonanotube), b) Bundled Gadonanotube at 0.104 mM Gd concentration in pluronic solution (Bundled Gadonanotube), and c) Individual Gadonanotube at 0.039 mM Gd concentration with dextran coating (GadoDex). These Gadonanotube phantoms were tested against d) 20mM Gd Magnevist phantom diluted with physiological saline. All the solution phantoms were cylindrical in shape with 1cm diameter and 1cm height with the cylinder axis perpendicular to the main magnetic field.

In Vitro Phantom Studies at 0.2T

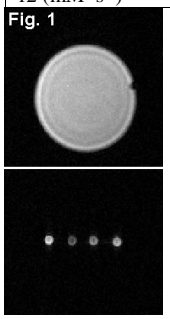
All the in vitro MRI experiments were conducted using GE 0.2T Profile MRI system (General Electric, Milwaukee, WI). The system control console was replaced by a Tecmag Apollo console (Tecmag, Houston, TX). The phantoms were arranged from left to right: Individual Gadonanotube, Magnevist, Bundled Gadonanotube and GadoDex as shown in Fig. 1. A standard quality assurance ball-shaped phantom from the manufacturer was used to ensure proper shimming. A 10mm single slice image covering all the phantoms was obtained for each TR/TE for relaxivity calculation. Care was taken to ensure all the phantoms are aligned properly. Gradient-echo sequence was used to image all the phantoms to study their r1 relaxivities with TE=6ms, TR=200ms, 150ms, 100ms, 50ms, 25ms and 18ms. Circular ROIs were defined for each phantom to measure the mean image intensity. Background noise effect was removed by subtracting the mean phantom image intensity with mean image noise. A non-linear fitting module in Matlab (Mathworks, Natick, MA) was used to fit the $T_1$ of each phantom based on the signal form $S=S_0*(1-\exp(-TR/T_1))$. Similar imaging experiments were conducted to evaluate the r2 relaxivities of the phantoms by Hahn spin-echo sequence with TR=1000ms, TE=6.5ms, 7ms, 8ms, 10ms, 20ms, 25ms, 50ms, and 100ms. $T_2$ of each phantom were obtained by linear fitting $\log(S)=\log(S_0)-TE/T_2$.

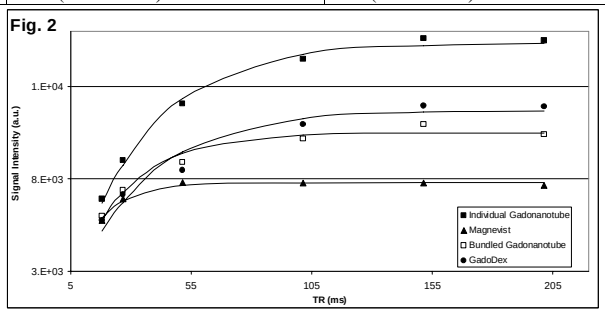
## Results

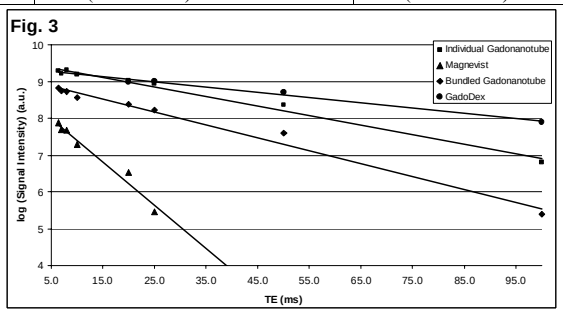
In the r1 relaxivity experiment, the fitted signal intensity curves for each phantom are shown in Fig. 2. Gadonanotubes phantoms have a high r1 relaxivity at about 380 $mM^{-1}s^{-1}$. and GadoDex can be as high as 810 $mM^{-1}s^{-1}$. In the r2 relaxivity analysis, the log signal intensity of the phantoms were plotted against TE as shown in Fig. 3. The r2 relaxivities of all the Gadonanotubes phantoms are around 300 $mM^{-1}s^{-1}$. The r1/r2 relaxivities results are summarized in Table 1.

**Table 1** r1 and r2 relaxivities of Gadonanotubes and Magnevist

| | **Individual Gadonanotube** | **Magnevist** | **Bundled Gadonanotube** | **GadoDex** |
|---|---|---|---|---|
| r1 ($mM^{-1}s^{-1}$) | 377 (95% CI [336 431]) | 3.8 (95% CI [3.4 4.4]) | 421 (95% CI [340 552]) | 814 (95% CI [601 1254]) |
| r2 ($mM^{-1}s^{-1}$) | 289 ($R^2$=0.9877) | 5.8 ($R^2$=0.9668) | 317 ($R^2$=0.9854) | 313 ($R^2$=0.9862) |




## Discussion and Conclusion

The r1 relaxivity of Gadonanotubes at 0.2T is higher than 350 $mM^{-1}s^{-1}$, which is higher than previously report NMRD analysis (1). Gadonanotubes has a strong r1 relaxivity which is about 70x-100x larger than Magnevist in typical MR imaging experiment at 0.2T. The r2 relaxivity of all Gadonanotubes are similar and is at about 50x higher than Magnevist. Current studies justify the in vivo development of Gadonanotubes as a generic MR contrast agent, in which the high contrast relaxivity will improve the detection sensitivity commonly associated with low field MRI in applications such as tumor patients with metal implants or orthopedic applications in sports medicine.

## Reference

1) Sitharaman B, Kissell KR, et al. Chem Commun (Camb). 2005;(31):3915-7.
2) B. Sitharaman and L. J. Wilson. Intl J of Nanomedicine. 2006;(1): 291-295.
3) E. Toth, R. D. Bolskar, et al. J. Am. Chem. Soc. 2005;(127): 799-805.
4) Ashcroft, J.M, Hartman, K. B, et al. Nanotechnology 2006, 17, (20), 5033-5037