The Gadonanotubes: a new paradigm in low-field MR Imaging

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Introduction: Magnetic Resonance Imaging (MRI) is one of the versatile non-invasive modalities widely used for diagnostic imaging. There are 60 million MRI scans performed annually, however, their potential is not completely realized owing to the high cost associated with superconducting magnets in current high-field clinical instruments. In addition, the greater field strength of the magnet in high-field instruments (>1.5 T) makes imaging difficult for patients with metal implants. Lack of portability, coupled with the heating associated with the higher field strengths, also precludes the use of MRI in some surgical procedures. Though low-field MRI instruments have the advantages of very low cost and portability, their low signal-to-noise ratio (SNR), low gradient strength with slow gradient slew rate and longer T_1 hinders their application. We present here a new class of contrast agent, the gadonanotubes, which shows very high relaxivity at very low field strengths. This presents a new paradigm for low-field molecular imaging. Herein, we analyze the efficiency of the gadonanotubes at 15 mT using specialized instrumentation capable of animal imaging at the National Cancer Institute (NCI) of the National Institute of Health (NIH), Bethesda, Maryland.

Methods:

Sample Preparation:

Full-length single-walled nanotubes (SWNTs) were cut into ultra-short single-walled carbon nanotubes (US-tubes) by fluorination followed by pyrolysis at 1000 °C in an inert atmosphere[1]. These US-tubes were then loaded with gadolinium ions as described elsewhere[2] to yield the gadonanotubes (Fig.1). The absence of externally-adhered gadolinium ions were confirmed by chelation studies and Inductively-coupled Plasma (ICP) measurements. The gadonanotubes were dispersed in a biocompatible pluronic F-108 surfactant (0.17 wt%) for the Phantom studies.

In Vitro Phantom Studies at 15 mT:

The MRI experiments were performed on a custom-built scanner (Philips Research Laboratories, Hamburg, Germany) with a human whole-body magnet. The resonator assembly was tuned to 625 kHz and consisted of a transmit saddle coil and a solenoidal receiver coil with a bandwidth of 80 kHz. A Gradient echo sequence was used to calculate the r_1 efficiency with TR= 120 ms, TE=25 ms with a slice thickness of 10mm. The phantom assembly is presented in Fig.2a and signal enhancement phantom images in Fig.2b.

Results:

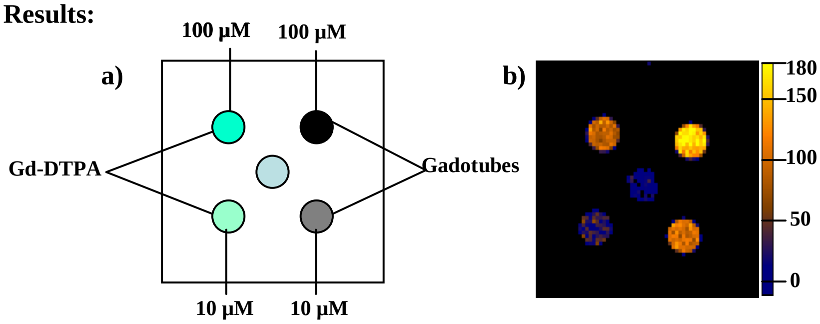

Fig.2. Phantom assembly & Phantom Images

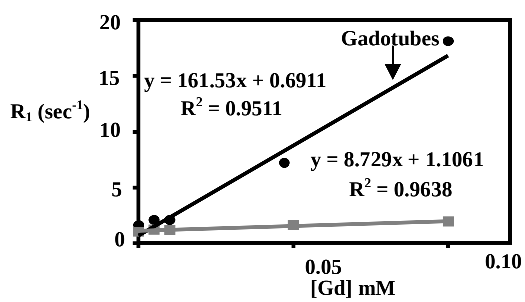

Fig.3. R_1 vs [Gd] plot

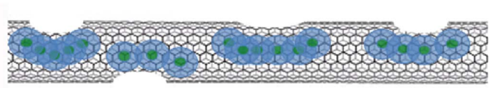

Fig1. Schematic representation of gadonanotubes

Discussion and Conclusions:

Relaxivity at 15 mT for gadonanotubes (162 $mM^{-1}s^{-1}$) is about 20 times higher than that of commercially available Gd-DTPA (~ 8.8 $mM^{-1}s^{-1}$) as shown in Fig.3. Even better relaxivities (~600 $mM^{-1}s^{-1}$) could be obtained by using optimized pulse sequences which are currently restricted due to instrumental limitations. With their superior efficiency, the gadonanotubes could overcome the difficulties associated with low-field imaging such as low resolution and longer T_1. Our initial studies (data not given at present) suggest that the gadonanotubes can internally label cells efficiently without toxicity, thus presenting a new paradigm for low-field *in vivo* molecular imaging and cell trafficking studies.

References:

1. Z. Gu *et al*., *Nano Lett.* **2002,** *2*(9), 1009-1013
2. Sitharaman, B. *et al*. *Chem. Commun.* **2005**, 3915-3917