Synthesis and Properties of Gadolinium Iodate Nanoparticles as a MRI/CT Contrast Agnet

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Introduction

The present work deals with bimodal imaging agent which emerges as new and efficient imaging techniques in clinical applications. D-glucuronic acid surface-coated ultra-small gadolinium iodate ($Gd(IO_3)_3$ nanoparticles have been synthesized and well characterized. The nanoparticles were found to be monodisperse and spherical, with an average diameter (d) of 3-5 nm. The relaxivity was measured to be r_1 of 54.55 s^{-1} mM^{-1} and r_2 of 65.60 s^{-1} mM^{-1}, which is much larger than those of Gd(III)-chelates. It may be used for both MRI contrast agent and CT contrast agent. Finally, we took *in vivo* T_1 MR images and CT images of a rat with a brain tumor by using D-glucuronic acid coated ultrasmall gadolinium iodate nanoparticles. We observed a clear contrast enhancement in MR images and CT images of the tumor after injection of nanocolloid.

Material and Methods

For the synthesis of D-glucuronic acid coated ultrasmall gadolinium iodate nanoparticles, 1 mmol of Gd(III) ion precursor ($GdCl_3.xH_2O$) was dissolved in 10 mL distilled water and 1mmol of D-glucuronic acid was added into the reaction mixture. It was heated at 80 °C and magnetically stirred. In a separate beaker, 3 mmol potassium iodate was dissolved in 10 mL distilled water. This aqueous potassium iodate solution was injected slowly into the flask. The reaction was continued for 30 minutes at this temperature. The reaction flask was allowed to cool at room temperature, and the precipitate was washed with distilled water to remove potassium ions, uncoated ligand, free chloride ions etc. This procedure was repeated three times. Finally, the solution was stored for few days and the top transparent solution was decanted. The first half of the nanocolloid was dried on air to make powder sample and remaining half part was used to prepare finely dispersed nanocolloid for MRI-Phantom experiment. For this purpose, sodium citrate (2 mmol) was added to 40 mL of nanocolloid to increase the colloidal stability of the D-glucuronic acid coated ultrasmall gadolinium iodate nanoparticles in solution. However, potential measurement showed that the colloidal stability only slightly increased after the addition of sodium citrate. This solution was used as a sample solution for both relaxivity and *in vivo* T_1 MR image measurements.

Results and Discussion

The longitudinal (T_1) and transverse (T_2) relaxation times were measured at various solutions of different Gd(III) ion concentrations. The r_1 and r_2 were then estimated to be 54.55 and 65.60 s^{-1} mM^{-1} from the slopes of the $1/T_1$ ($=R_1$) and $1/T_2$ ($=R_2$) plots *versus* Gd(III) ion concentration, respectively (fig.1a). The r_2/r_1 ratio is estimated to be 1.20. The R_1 and R_2 map images were also measured (fig. 1b and 1c). They show a clear dose-dependent color change which is due to increase of the relaxation with increasing Gd(III) ion dose. This suggests a high sensitivity of ultrasmall gadolinium iodate nanoparticles as T_1 MRI contrast agent. In general, the r_1 should be as large as possible, and the r_2/r_1 ratio should be as close to 1 as possible in order for a chemical to be used as a highly sensitive T_1 MRI contrast agent.

In addition, the prepared nanoparticles showed excellent contrast enhancement compared to commercially available 'Ultravist' having comparable concentration range. From figure 2, it is revealed that 42.4 mM gadolinium iodate enhancement is brighter than ultravist with comparable Gd(III) ion concentration. The hounsfield coefficient is estimated to be 1015 HU at 42.4mM Gd(III) ion concentration while ultravist possesses only 306 HU for its 50 mM concentration. This evidence showed its efficiency for T_1 MR images-Phantom imaging experiment. Furthermore, it is expected that the D-glucuronic acid coated ultrasmall gadolinium iodate nanoparticle will be extremely valuable for target specific cancer detection, which we plan to do in the near future.

Conclusion

Paramagnetic ultrasmall gadolinium iodate ($Gd(IO_3)_3$) nanoparticles with particle diameters (d) of 3-5 nm were synthesized and characterized. A large longitudinal relaxivity (r_1) of water proton of 54.55 s^{-1} mM^{-1} was estimated. This large r_1 is discussed in terms of the huge surface to volume ratio (S/V) of the ultrasmall gadolinium oxide nanoparticles coupled with the cooperative induction of surface Gd(III) ions for the longitudinal relaxation of a water proton. The resulting data suggest that the paramagnetic ultrasmall gadolinium oxide nanoparticles can be used as an advanced T_1 MRI contrast agent. Also a large houndsfield coefficient of X-ray absorption i.e. 1015 HU was recorded which is desired for phantom imaging experiment. Hence, ultrasmall gadolinium iodate ($Gd(IO_3)_3$) nanoparticles can be used as a dual imaging probe.

Figure 1. (a) Plots of the R_1 and R_2 as a function of Gd(III) ion concentration. Slopes provide the r_1 and r_2. (b) R_1 and (c) R_2 map images as a function of Gd(III) ion concentration.

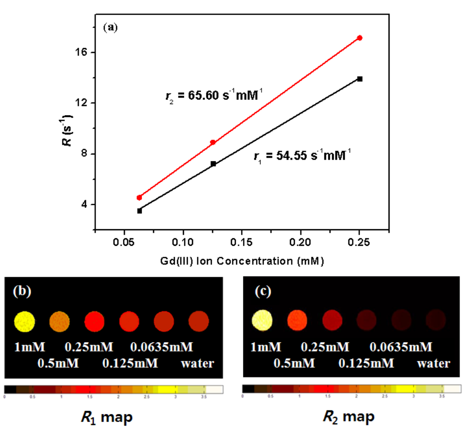

Figure 2. (a) Houndsfield coefficient of Ultravist and ($Gd(IO_3)_3$) nanoparticles at 80kV. (b) *In vitro* CT Phantom images of Ultravist and ($Gd(IO_3)_3$) nanoparticles.

(a)

No.	name	HU
1	Ultravist 10mM	48
2	Ultravist 20mM	111
3	Ultravist 30mM	167
4	Ultravist 50mM	306
5	Ultravist 100mM	505
6	Ultravist 250mM	1218
7	Ultravist 500mM	2397
8	$Gd(IO_3)_3$ 10mM	228
9	$Gd(IO_3)_3$ 42.4mM	1015
10	Distilled water	0