# Water-soluble MnO nanocolloid for a molecular T1 MR imaging: A facile one-pot synthesis, in vivo T1 MR images, and account for relaxivities

**E. Lee[1], J. Park[1], W. Xu[1], K. Kattel[1], H. Kim[1], and G. Lee[1]**
[1]Department of Chemistry, Kyungpook National University, Daegu, Gyeongsangbuk-do, Korea, Republic of

## Introduction

We report the synthesis of water-soluble MnO nanocolloid with a monodisperse core particle diameter ($d$) ranging from 2 to 3 nm. The magnetic nanocolloids with $d$ in this size range will be very useful as $T_1$ MRI contrast agents because first of all, they can be easily excreted through kidneys because of their small sizes, which is an essential requirement for clinical application, and because they can have high $r_1$ relaxivities due to their high surface to volume ratio ($P$), as observed in the $Gd_2O_3$ nanocolloid. This is because only the surface metal ions in a nanoparticle are mainly active for the longitudinal water proton relaxation. In the case of the $Gd_2O_3$ nanocolloid, the optimal $d$ for the maximal $r_1$ relaxivity was found to be between 1.0 and 2.5 nm. This is opposite to a $T_2$ MRI contrast agent, which has a somewhat large $d$. This is because the magnetic moment ($M$) which induces the $r_2$ relaxivity rapidly decreases with decreasing the $d$. For this reason, the $T_2$ MRI contrast agent such as the superparamagnetic iron oxide (SPIO) nanocolloid at least has a $d$ value greater than 5 nm and thus is used only as a liverspecific $T_2$ MRI contrast agent.

## Material and Methods

10 mmol of $MnCl_2.4H_2O$ and 30 mL of triethylene glycol were added to a 100 mL three-necked flask and the mixture was magnetically stirred at room temperature under $N_2$ gas flow. Separately, 20 mmol of NaOH was dissolved in 10 mL of solvent. The latter solution was slowly added to the former solution through a syringe after the precursor was completely dissolved in the solvent. The reaction temperature was raised to 200 °C and kept at that temperature for 6 hours. The reaction temperature was lowered to 140 °C and then, 10 mmol of D-glucuronic acid was added to the reaction solution. The reaction continued for more 24 hours. The reaction solution was cooled to room temperature and then, transferred to a 1 L beaker. The solvent, unreacted coating ligand, unreacted Mn(II), and Cl- ions were removed from the reaction solution by washing it with distilled water three times. To do this, we added 500 mL of distilled water to the reaction solution, and then magnetically stirred it for ~30 min. The reaction solution was kept for a week or so until the MnO nanocolloid was settled down to the bottom of the solution. The top transparent solution was decanted. This procedure was repeated three times. Half of the MnO nanocolloid was dispersed in distilled water to prepare a MRI solution. The remaining half was dried in air to prepare a powder sample for characterizations.

## Results and Discussion

From DLS particle size analyzer, the average diameter of the MnO nanocolloid was estimated to be 5 nm. The data from SQUID magnetometer suggest that the MnO nanoparticle was nearly paramagnetic down to 3 K and showed a high magnetic moment of ~90 emu/g at $T$ = 5 K and $H$ = 5 T, which mainly arises from surface Mn(II) ions with $S$ = 5/2 as well as a decent $P$ (≈ 0.35) of the MnO nanoparticle. For these reasons, a high $r_1$ relaxivity of 7.02 $s^{-1}$ $mM^{-1}$ was observed. This value is higher than those of the clinically used metal ion chelated MRI contrast agents. The observed $r_2$ relaxivity of 47.97 $s^{-1}$ $mM^{-1}$ is likely due to a tiny $M$ of the MnO nanoparticle arising from incomplete spin cancellation of antiferromagnetic spins of its inside Mn(II) ions. *In vivo* testing of an MRI solution showed high contrast $T_1$ MR images, proving that the MnO nanocolloid functions as a sensitive $T_1$ MRI contrast agent.

## Conclusion

High contrast in vivo $T_1$ MR images were obtained for various organs, showing the capability of the MnO nanocolloid as a sensitive $T_1$ MRI contrast agent. The suggested three key-parameters which control the $r_1$ and $r_2$ relaxivities of nanocolloids (i.e., the $S$ value of a metal ion, the spin structure, and the surface to volume ratio of a nanoparticle) successfully accounted for the observed $r_1$ and $r_2$ relaxivities of the MnO nanocolloid.

Figure 1.
(a-c) HRTEM images of the MnO nanocolloid at different magnifications.

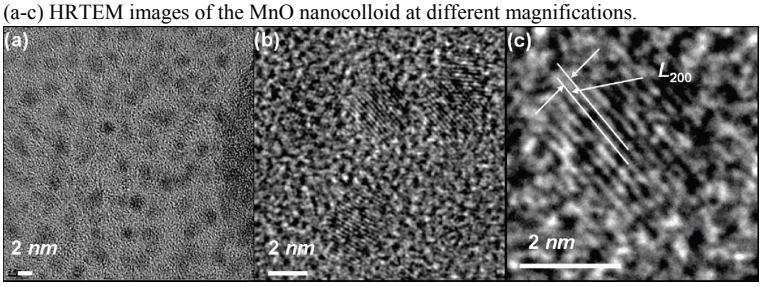


Figure 2.
A series of 1.5 T in vivo $T_1$ MR images of a mouse with time a after injection of a MRI solution into a mouse tail vein.

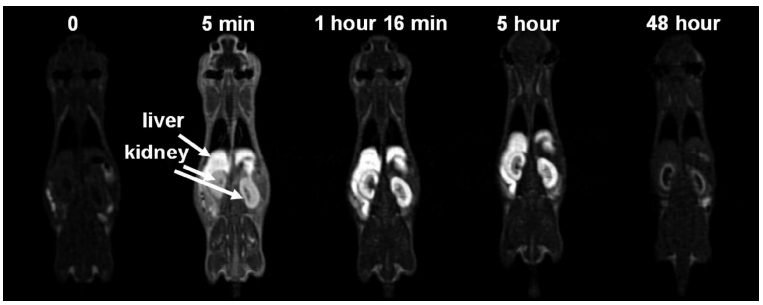


Figure 3.
MR signal intensity variations with time in both liver and kidneys after injection of a MRI solution into a mouse tail vein.

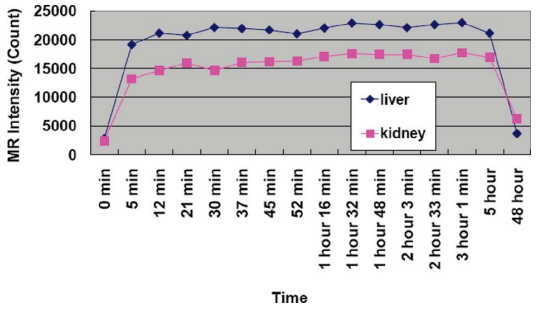


Figure 4.
(a) $R_1$ and (b) $R_2$ map images of MRI solutions as function of Mn concentration.