INDUSTRY-UNIVERSITY
COOPERATION FOUNDATION
YONSEI UNIVERSITY

Title (Name of Technology)

Magnetic Resonance Imaging Contrast Comprising Zinc-containing Magnetic Metal Oxide Nanoparticles

Executive Summary

Dr. Jinwoo Cheon, a professor of Yonsei University, has developed novel magnetic resonance imaging contrast agents (hereinafter referred to as 'the agents') that are very interesting in terms of sensitivity, efficacy, stability and commercializing potential.

The nanoparticle based imaging contrast agent prepared following prior arts, commercially available contrast agents such as Feridex and Resovist, and conventional iron oxide nanoparticles have relatively low magnetic moment and poor MR contrast effect. Thus it has been pointed out that they have reduced sensitivity in the MRI diagnosis of cancer or other diseases.

The Industry-University Cooperation Foundation Yonsei University, a Technology Licensing Organization in Yonsei University, intends to enter into a technology transfer or licensing transaction with regard to the agents. Terms of the transaction are not set, and interested parties may further discuss the details if they wish to enter into an agreement

② Industry Sector: 1. Academic/Research (Diagnostic) 2. Diagnostic (MRI Contrast agent), 8. Non-profit org./Government (universities)

③ Therapeutic Target: 11. Hospital and Surgery (All of diseases)

④ Development phase: early stage

⑤ Type of business relationship sought (including licensing availability): development collaboration, or non-exclusive or exclusive licensing agreement

■ IP Owner Summary

Industry-University Cooperation Foundation Yonsei University

▫ TLO in Yonsei University

■ Personal Description of Researcher

▫ **Name**

Jinwoo Cheon, Ph.D

▫ **Present Position**

Professor

Department of Chemistry,

College of Science,

Yonsei University

▫ **Lab address**

Department of Chemistry,

College of Science,

Yonsei University, Seoul, Korea

Key Technology Highlights

□ Enhanced Magnetic Moment and Excellent MRI Contrast Effect

Zinc containing metal oxide magnetic nanoparticles have improved magnetic moment and enhanced MRI contrast effect as compared to normal metal oxide nanoparticles without zinc.

□ Safety for Toxicity and Biocompatibility

As compared with the conventional MRI contrast agent, even a small amount can provide an effect of enhancing the signals to a desired level. Accordingly, they can be used as a contrast agent having lower biological toxicity and side-effects than conventional materials.

□ Veriaty of the Agents Usage

The water-soluble zinc-containing metal oxide nanoparticles can be also coupled to other diagnostic probes and used as a double- or multiple-diagnostic probe. The MRI contrast agents may be applied to single photon emission computer tomography (SPECT), a positron emission tomography (PET), computed tomography (CT) and the optical imaging and the spectroscopy.

Technology Overview

- **Technology Platform**

The core technology of Yonsei University is to provide a promising MRI contrast agent that includes zinc-containing water-soluble metal oxide nanoparticles and has an improved contrast effect.

Background and unmet needs: The nanoparticle based imaging contrast agent prepared following prior arts, commercially available contrast agents such as Feridex and Resovist, and conventional iron oxide nanoparticles have relatively low magnetic moment and poor MR contrast effect.

The way to resolve these problems is developing MR contrast agents comprising magnetic nanoparticles with enhanced magnetic moment. To achieve the purpose of increasing the magnetic moment, controlling the composition of metal oxide nanoparticles can be one method (Ittrich et al, *Rofo* 2005, /*77*, 1151; Shultz et al, J. *Magn. Magn, Mater*. 2007, *311*, 464; Lee et al, *Nat. Med.* 2007, *13*, 95). It has been tried adding various metal dopants to iron oxide nanoparticle.

However, most of possible metallic dopants (*e.g*. Co, Ni, Mg, Ba, etc) do not increase magnetic moment and, in some cases, even reduce it after the addition (*e.g*. Co, Ni, Mg, Ba) (Valdes-Solis et al, *Nanotechnology* 2007, 18, 145603).

Discovery and Achievements: MR contrast agents of Yonsei University has been developed on the basis of ideas that development of a new metal oxide having more improved magnetic moment is very important in maximizing the MR contrast effect.

The zinc-containing metal oxide nanoparticles are nanoparticles in which zinc atoms/ions are added to the metal oxide nanoparticle. The zinc-containing metal oxide nanoparticles have the excellent magnetic moment and T2 MRI contrast enhancement effect, the high colloidal stability in an aqueous solution, and the low cytotoxicity due to the enhanced bio-compatibility. In addition, they are easily conjugated to a material having a biological activity or a chemical activity to satisfy the optimum condition as the MRI contrast agent.

The zinc-containing metal oxide nano-particles have a chemical formula of:

(a) $Zn_aM_{b-a}O_c$

(0<a<8, 0<b<16, 0<c<8, 0<a/(b-a)<10, and M is a magnetic metal atom or an

alloy thereof); or

(b) $Zn_dM_{e-d}\ M'_fO_g$

(0<d<8, 0<e<16, 0<f<16, 0<g<8, 0<d/{(e-d)+f}<10,

M is a magnetic metal atom or an alloy thereof; and M' is an element selected from the group consisting of Group 1 elements, Group 2 elements, Group 12 elements, Group 13 elements, Group 14 elements, Group 15 elements, transition metal elements, lanthanide elements, and actinide elements).

FIG 1 (A) An transmission electron microscopic (TEM) image of zinc containing ferrite nanoparticle and (B) a high resolution TEM and its fast Fourier transform image.

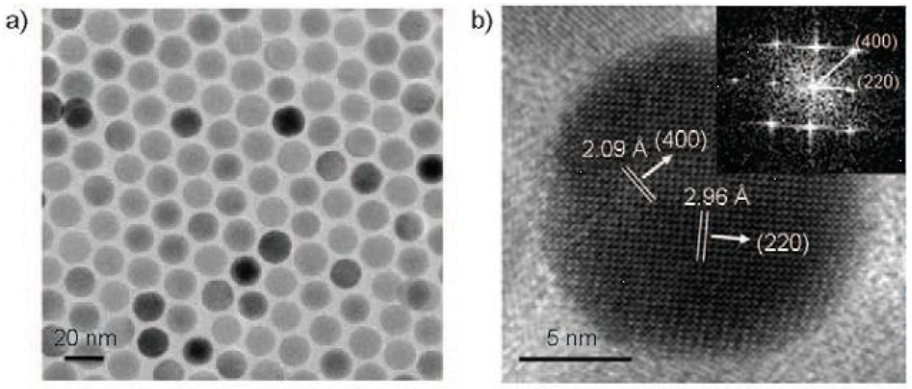
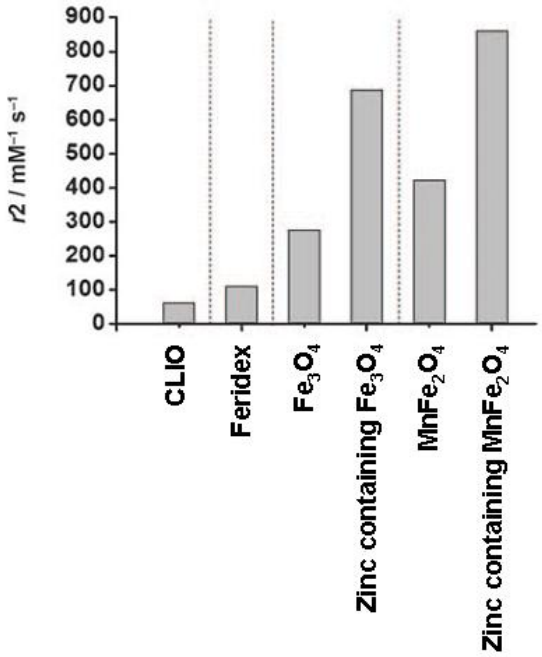


FIG 2 Comparison of T2 contrast effect of nanoparticles (r2; T2 relaxivity coefficient), showing that Zn containing nanoparticles have significantly enhanced MRI contrast effects compared to conventional iron oxide nanoparticles.



Key Features and Advantages:

(1) Enhanced Magnetic Moment and Excellent MRI Contrast Effect

Zinc containing metal oxide magnetic nanoparticles have improved magnetic moment and enhanced MRI contrast effect as compared to normal metal oxide nanoparticles without zinc.

(2) Safety for Toxicity and Biocompatibility

As compared with the conventional MRI contrast agent, even a small amount can provide an effect of enhancing the signals to a desired level. Accordingly, they can be used as a contrast agent having lower biological toxicity and side-effects than conventional materials.

(3) Veriaty of the Agents Usage

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Patents and Publications

Yonsei has filed application with four international countries, Patent Cooperation Treaty (PCT) and Korea regrading novel magnetic resonance imaging contrast agents.

TABLE. List of Patents for Novel Magnetic Resonance Imaging Contrast Agents

Country	Appln. No.	Status	Description
Korea	2008-0033719	Published	Magnetic Resonance Imaging Contrast Agents Comprising Zinc-Containing Magnetic Metal Oxide Nanoparticles
PCT	PCT/KR2008/002050	Published	Magnetic Resonance Imaging Contrast Agents Comprising Zinc-Containing Magnetic Metal Oxide Nanoparticles
USA	12/527,482	Published	Magnetic Resonance Imaging Contrast Agents Comprising Zinc-Containing Magnetic Metal Oxide Nanoparticles
EPO	08741295.3	Published	Magnetic Resonance Imaging Contrast Agents Comprising Zinc-Containing Magnetic Metal Oxide Nanoparticles
China	200880000852.3	Published	Magnetic Resonance Imaging Contrast Agents Comprising Zinc-Containing Magnetic Metal Oxide Nanoparticles
Japan		Published	Magnetic Resonance Imaging Contrast Agents Comprising Zinc-Containing Magnetic Metal Oxide Nanoparticles

Prof. Cheon is one of the most active researcheres in Korea and published his research accomplishments in various journals. The representative publications are summarized as follows:

1. **Critical Enhancements of MRI Contrast and Hyperthermic Effects by Dopant-Controlled Magnetic Nanoparticles,** *Angew. Chem. Int. Ed.* **2009**, *48*, pp1234.

2. **Synergistically Integrated Nanoparticles as Multimodal Probes for Nanobiotechnology,** *Accounts Chem. Res.* **2008**, *41*, pp1630.

3. **Two-Dimensional SnS2 Nanoplates with Extraordinary High Discharge Capacity for Lithium Ion Batteries**, *Adv. Mater.* **2008**, *20*, pp4269.

4. **Chemical Design of Nanoparticle Probes for High-Performance Magnetic Resonance Imaging,** *Angew. Chem. Int. Ed.* **2008**, *47*, pp5122.

5. **Nanoparticle assisted magnetic resonance imaging of the early reversible stages of amyloid β self-assembly**, *Chem. Commun.* **2008**, pp2197.

6. **Nanoscaling Laws of Magnetic Nanoparticles and Their Applicabilities in Biomedical Sciences**, *Accounts Chem. Res.* **2008**, *41*, pp179.

7. **Noninvasive Remote-Controlled Release of Drug Molecules in Vitro Using Magnetic Actuation of Mechanized Nanoparticles,** *J. Am. Chem. Soc.* **2010**, *132*, pp10623.

Nano-scaling Laws of Magnetic Nanoparticles" *Acc. Chem. Res.* **2008**, *41*, pp179.

8. **Artificially Engineered Magnetic Nanocrystals for Ultra-Sensitive Molecular Imaging,** *Nature Med.* **2007**, *13*, pp95.

9. Magnetic Superlattices and Their Nanoscale Phase Transition Effects, *Proc. Natl. Acad. Sci. USA* **2006**, *103*, pp3023.

10. **Shape Control of Semiconductor and Metal Oxide Nanocrystals Through Nonhydrolytic Colloidal Routes,** *Angew. Chem. Int. Ed.* **2006**, *45*, pp3414.