

# NOVEL BIORESORBABLE MAGNETIC CONTRAST AGENT NANOCERAMICS

I. Kuriashkin<sup>1</sup>, L. Lee<sup>1</sup>, R. Haggerty<sup>2</sup>, W. Kriven<sup>2</sup>

<sup>1</sup>Veterinary Clinical Medicine Department, University of Illinois at Urbana-Champaign, Urbana, Illinois, United States, <sup>2</sup>Materials Science and Engineering Department, University of Illinois at Urbana-Champaign, Urbana, Illinois, United States

## Introduction

Nanoceramic particles, such as layered double hydroxides (LDHs), have possible applications to become drug delivery carriers. Bimolecules and drugs can be intercalated into LDHs, displacing the interlayer anions. A new ceramic contrast reagent for MRI, (Gd<sup>3+</sup>-DTPA)<sup>2-</sup> intercalated LDHs, have been developed and verified by confocal microscopy, EPR and MRI. When endosomes bring LDH particles into mammalian cells via endocytosis, lysosomes become active and digest the LDH shells. Then the intercalated biomolecules, such as MRI contrast agents or chemotherapeutic drugs, will be released into cell's cytoplasm to carry out desired functions. The phenomenon of LDH particles penetrating through the cell membranes has been verified by the fluorescent microscopy (Fig 2).

## EPR verification

The successful synthesis of Gd-DTPA intercalated LDH was accomplished by synthesizing [Mg<sub>3</sub>Al(OH)<sub>8</sub>](OH)<sup>-</sup>nH<sub>2</sub>O, denoted as "MgAl-OH-LDH". The XRD patterns (Cu-K $\alpha$ ) of the MgAl-CO<sub>3</sub>-LDH (a), calcined LDH (b), MgAl-OH-LDH (c), and MgAl-Gd-DTPA-LDH (d) convey that the molecular plane of Gd-DTPA complex is horizontally-oriented along the hydroxide basal plane.

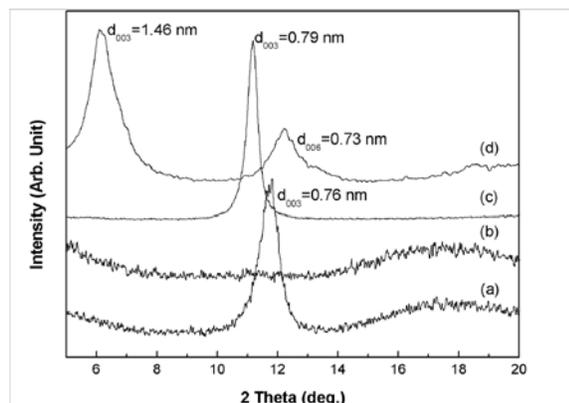


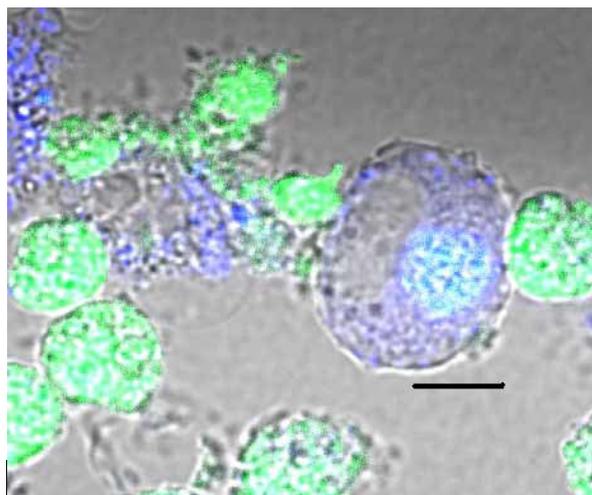
Fig. 1. XRD patterns (Cu-K $\alpha$ ) of the MgAl-CO<sub>3</sub>-LDH (a), calcined LDH (b), MgAl-OH-LDH (c), and MgAl-Gd-DTPA-LDH (d).

## MRI Experiments

The rate of LDH particles absorption by NIH/3T3 cells (on cell culture) as well as the rate of the LDH-Gd-DTPA intracellular metabolism is currently being investigated using 1 Tesla MR (Siemens Impact) imaging system. The relaxivity of Gd-containing LDH compounds is yet to be determined.

## Confocal Microscopy

FITC-intercalated LDH particles ([Mg<sub>2</sub>Al(OH)<sub>6</sub>](FITC)<sub>1/2</sub>) and LysoTracker<sup>®</sup> Red DND-99 (L-7528) fluorescent agents are incubated with Chinese hamster ovarian cells (NIH/3T3, GIBCO cat. 11619-012) for about 30 minutes. The LysoTracker becomes fluorescent only when lysosomes are active. In this confocal microscopy, both lysosomes and FITC are fluorescent within the cell, proving the efficacy of LDHs as drug carriers and the relationship between lysosomal activation and release of intercalated fluorescein-5-isothiocyanate (FITC).



and blue 50 nM LysoTracker both emit fluorescence at the same time in some cells. Black