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Multimodal bioimaging probes based on lanthanide doped Gd_2O_3 nanophosphors

Doan T. Kim Dung[1], Shoichiro Fukushima[1], Hirohiko Niioka[1], Masayoshi Ichimiya[1,2], Masaaki Ashida[1], Tsutomu Araki[1], Mamoru Hashimoto[1], Jun Miyake[1]

[1]Graduate School of Engineering Science, Osaka University,
[2]School of Engineering, The University of Shiga Prefecture
E-mail: dkdung@ bpe.es.osaka-u.ac.jp

1. Introduction

A variety of bioimaging techniques is regarded as indispensable tools for clinical diagnostics and scientific research. Each technique has its own merits and limitations in terms of spatial resolution, sensitivity, anatomical/functional information and depth. Hence, an interest in development of multimodal imaging, based on hardware or probes platform, is rapidly rising. The combination is expected to provide an comprehensive image incorporating molecular, functional and anatomical information.

Cathodoluminescent (CL) microscopy is the imaging technique with the most advantageous resolution limit [1]. Because the electron beam has much smaller wavelength than that of light, it is a very efficient technique for interpreting biological object at individual biomolecule level. By employing exogenous probes, such as lanthanide (Ln^{3+}) or diamond, CL imaging of a cell can be obtained. Ln-based are potential candidates for CL imaging due to their high luminescence, chromaticity and resistance to bleaching [1].

Recently, the emissions in near infrared (NIR) region under 980nm excitation are growing interest in biomedical applications due to the so called biological window [2]. In NIR range, the light has its maximum depth of penetration through biological tissue of several millimeters to centimeters in thickness [2, 3]. Upconversion Ln-based nanophosphors exhibited higher NIR–to–visible conversion efficiency in comparison to QDs or gold nanorods [4]. Moreover, Ln-based nanophosphors also emit luminescence in NIR region under NIR excitation. This is also very useful for deep tissue imaging.

Lanthanide elements are also well-known for their outstanding magnetic properties. Gadolinium with the highest magnetic spin is commonly applied as a T1 contrast agent for MR imaging (MRI). Gd_2O_3 host enables the option of opto-magnetic marker [2] by utilizing luminescence properties of the Ln^{3+}-dopants and their magnetic properties. Hereby, we develop multimodal imaging probes based on Gd_2O_3 particles: Gd_2O_3:Tm,Yb; Gd_2O_3:Ho,Yb and Gd_2O_3:Er,Yb. These particles are emissive under 980 nm or electron beam excitation synchronically with enhancement T1 contrast in MRI.

2. General Instructions

Homogenous precipitation (HP) to synthesize Ln^{3+} doped Gd_2O_3-based nanophosphors

Lanthanide-doped Gd_2O_3 were synthesized by HP method [5]. Precursors with 20-40 nm in size were obtained [Fig. 1]. The precursors were following calcinated at 900^0C in 3 hours.

Multimodal properties of Gd_2O_3-based nanophosphors

Multimodalities of synthesized nanophosphors were confirmed by CL, NIR luminescent, and MR properties. CL spectra and images of the nanophosphors were obtained with a field emission scanning electron microscope (FESEM; JEOL, JSM-6500F) and a CL measurement unit (HORIBA). Lanthanide doped nanophosphors emitted blue, green, and red luminescence and NIR emission in the range matches to the biological window of 800 nm – 1700 nm [Fig. 2]. MRI by BRUKER JH048806 indicated the contrast enhancement in T1 curves and T1-weight images.

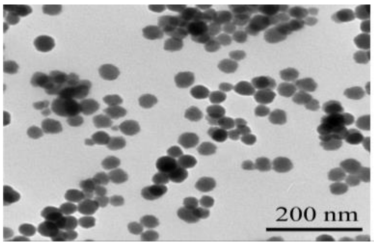

Fig. 1: TEM image of Gd_2O_3:Tm,Yb nanophosphors

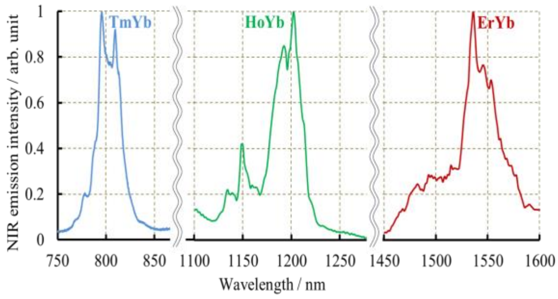

Fig. 2: NIR emission spectra of three kinds nanophosphors

3. Conclusions

Three kinds of Gd_2O_3-based nanophosphors were synthesized by homogenous precipitation method. Particles with size in range of 20-40 nm were produced. Three kinds of nanophosphors emitted green, red and blue color in visible and NIR range under 980 nm excitation. CL image and CL emission of nanophosphors were also confirmed. The brightness of T1-weight images indicated that Gd_2O_3 based nanophosphors have effects on contrast of MRI.

Acknowledgements

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