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Research Paper

Optimization of Optical Excitation of Upconversion Nanoparticles for Rapid Microscopy and Deeper Tissue Imaging with Higher Quantum Yield

Qiuqiang Zhan[1,2], Sailing He[1,2,3,✉], Jun Qian[2], Hao Cheng[2], Fuhong Cai[2]

1. ZJU-SCNU Joint Research Center of Photonics, Centre for Optical and Electromagnetic Research, South China Academy of Advanced Optoelectronics, South China Normal University (SCNU), 510006 Guangzhou, P. R. China.
2. Centre for Optical and Electromagnetic Research, JORCEP, Zhejiang Provincial Key Laboratory for Sensing Technologies, Zijingang campus, Zhejiang University (ZJU), 310058 Hangzhou, P. R. China.
3. Department of Electromagnetic Engineering, Royal Institute of Technology, 10044 Stockholm, Sweden.

✉ Corresponding author: sailing@jorcep.org.

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Abstract

Relatively low quantum yield (QY), time-consuming scanning and strong absorption of light in tissue are some of the issues present in the development of upconversion nanoparticles (UCNPs) for biomedical applications. In this paper we systematically optimize several aspects of optical excitation of UCNPs to improve their applicability in bioimaging and biotherapy. A novel multi-photon evanescent wave (EW) excitation modality is proposed for UCNP-based microscopy. The scanning-free, ultrahigh contrast and high spatiotemporal resolution method could simultaneously track a few particles in a large area with a speed of up to 350 frames per second. The HeLa cancer cell membrane imaging was successfully performed using $NaYF_4$: 20% Yb^{3+}/2% Er^{3+} targeting nanoparticles. Studies with different tissues were made to illustrate the impact of optical property parameters on the deep imaging ability of 920-nm band excitation. In the experiments a semiconductor laser with a 920 nm wavelength was used to excite UCNPs in tissue phantom at five depths. Our experimental and computational results have shown that in UCNP-based diffusion optical imaging with 920-nm laser excitation could lead to larger imaging depth range compared to traditional 974-nm excitation in a wide dynamic range of tissue species. As the QY is power density dependent, a pulsed laser is proposed to improve the QY of UCNPs. This proposal is promising in drastically increasing the imaging depth and efficiency of photodynamic therapy.

Key words: upconverting, total internal reflection, pulsed excitation, deep imaging, quantum yield.

Introduction

Upconverting nanoparticles (UCNPs) constitute a novel type of contrast agent with interesting and unique properties for luminescence bio-imaging[1]. Superior to organic dyes and quantum dots (QDs), UCNPs enable autofluoresence-free imaging under near-infrared excitation[2]. The research topic of *UCNPs* has become popular for biomedical applications, particularly optical bioimaging. UCNPs exhibit practically no autofluorescence, no photobleaching, no blinking, large anti-Stokes shifts, sharp emission band, deep detection ability and a high spatial resolution[3, 4]. In recent years, UCNPs have therefore attracted much attention in the biophotonics area. They have widely been employed in *in vitro* microscopy[5-7], small animal imaging[8, 9], diffusion optical tomography[10], multimodal animal imaging[11, 12], high sensitivity biosens-