

Application of Rare Earth Near-Infrared Fluorescence Spectroscopy in Biomedical Imaging

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ABSTRACT

Background: Traditional fluorescence imaging, such as fluorescence imaging in the visible light region, has some problems, such as shallow tissue penetration depth, easy scattering in living organisms, and strong autofluorescence interference. The phenomenon of spontaneous fluorescence scattering in biomedical imaging observation will interfere with the resolution of imaging and the detection of targeted targets is not accurate enough. In order to avoid the strong absorption of visible light in the living body, scattering phenomenon is observed. Rare earth near-infrared window has become the focus of research. Rare earth ions (such as Nd^{3+} , Yb^{3+} and Er^{3+}) have rich energy level transitions, can emit near-infrared light, and have long luminescence lifetime, narrow spectrum, and high stability, which are ideal near-infrared fluorescence probes. At the same time, near-infrared light (700-1700 nm) has less scattering and absorption in biological tissues, deeper penetration depth, and less autofluorescence interference, which is more suitable for biological imaging.

Methods: A comprehensive literature review is carried out, with emphasis on the spectrotunable characteristics of rare earth near infrared fluorescence spectroscopy. The absorption and scattering of near infrared light in living tissues are much smaller than that in visible light region. The fluorescence spectral curve is calculated and analyzed by imaging software to obtain a clear image with high resolution and high sensitivity.

Results: Fluorescence imaging technology is the use of optical detector to collect fluorescence probe light real-time imaging of a non-invasive imaging technique, with imaging speed, high sensitivity, high space-time resolution, the advantages of no radiation excitation and emission of light through the application of biological tissue organization in absorption, scattering and interference is autofluorescence fluorescence imaging resolution is the main factor and tissue penetration depth. Compared with visible (400-700 nm) and near-infrared I (700-1000 nm) fluorescence imaging, biological tissues have weaker absorption and scattering of near-infrared II (1000-1700 nm) light and lower autofluorescence. Therefore, Near-infrared region 2 fluorescence imaging has been favored by people due to its deeper tissue penetration ability and higher imaging signal-to-noise ratio.

Conclusion: There are advantages and challenges in near-infrared fluorescence spectroscopy medical imaging technology at home and abroad. Due to the late start of near-infrared fluorescence spectroscopy biomedical imaging technology in China, compared with foreign technology maturity and innovation ability at the technical level, it needs to be improved. However, in China, it has broad prospects in market expansion and interdisciplinary cooperation. In the future, along with the advance of technology and international cooperation to strengthen, near-infrared fluorescence spectrum of medical imaging technology will be more widely used on a global scale.

Keywords: Rare Earth Luminescence; Biomedical Imaging; Nanoprobes

Introduction

In recent years, with the rapid development of biomedical imaging technology, rare earth near-infrared fluorescence spectroscopy has received extensive attention as an emerging imaging method (Wang Shaowei, et al. [1]). Compared with the traditional optical imaging, the near-infrared fluorescence imaging can achieve high sensitivity, high resolution and high signal-to-noise ratio of imaging, the tumor diagnosis, small molecule in vivo detection, biological sensors and immune analysis, and other fields has a broad application prospect (Xue Toshiba, et al. [2]). Short wavelength visible light (380-760 nm) is easily absorbed and scattered when penetrating biological tissues, so it can only meet the requirements of in vitro diagnosis and biological imaging at the cellular level (Roy C, et al. [3]). Compared with visible light or ultraviolet light, near infrared (NIR, 700 ~ 1700nm) can be more deeply through biological tissue, make it very suitable for deep in vivo imaging (Ji A, et al. [4]). Therefore, the transformation of rare earth luminescence near infrared region of the window, can be used as a biological tissue is relatively "transparency" of the optical window (Dong S, et al. [5]).

There are medical imaging technology has:

1. Fluorescence microscope
2. Fluorescence endoscope
3. Fluorescence tomography
4. Fluorescence spectrum analysis of living
5. Fluorescence imaging system
6. Fluorescence correlation spectroscopy (FCS)
7. Super resolution fluorescence imaging
8. Fluorescence resonance energy transfer (FRET)
9. Fluorescent marker flow cytometry (Feng S, et al. [6]).

Application of Fluorescence Imaging in Clinical Practice

1. **Cancer Diagnosis:** the use of fluorescently labelled antibodies or probes to achieve early detection and surgical navigation of tumors.
2. **Cardiovascular Disease Diagnosis:** by fluorescence labelling blood vessels and heart tissue, evaluate the structure and function.
3. **Diagnosis of Infectious Diseases:** the use of fluorescently labelled pathogens to achieve rapid detection and localization.

Application of Fluorescence Imaging in Drug Research and Development Drug Distribution and Metabolism Research

To study the distribution and metabolism of drug molecules in

vivo by fluorescently labelling them. Efficacy evaluation: The use of fluorescently labelled cells or tissues to evaluate the therapeutic effect of a drug.

Application of Fluorescence Imaging in Biological Research Cellular and Molecular Features Research

By fluorescence labelling cells and molecules, studies its function and interaction. Gene expression studies: use fluorescent reporter gene, real-time monitoring of gene expression and regulation. Through these biomedical effect's detection cannot meet the requirements of medical imaging to the deeper internal layers of biological tissues with high resolution and high sensitivity (Zhang X, et al. [7]). Therefore, near-infrared fluorescence imaging technology has special spectral bands near infrared region 1 (NIR, 700 ~ 1700 nm) and near infrared region 2 (NIR, 700 ~ 1700 nm). These two bands of light have weak absorption, scattering and lower autofluorescence in biological tissues, especially the 1000nm-1700 nm near-infrared second region fluorescence, which has deeper tissue penetration ability and higher imaging signal-to-noise ratio (Yang S, et al. [8]).

Research Objectives

This research seeks to fulfil the following objectives: Through the fluorescence spectra of rare earth doped nanocrystals analysis combined with the existing image processing technology to design high resolution, high sensitivity of biomedical imaging solutions, thereby provide more effective tool for disease diagnosis, and treatment (Qiu Q, et al. [9]).

The Research Content

Preparation of Fluorescent Probe Materials: Try all kinds of wet chemical methods, explore the structure of product, size, morphology and surface physical and chemical properties of effective control of path and the experimental conditions, the preparation of high dispersibility and crystallinity of nanocrystals.

Structure and the Luminescent Properties of Fluorescent Probe Materials Research: Proposed by various imaging technology and spectral characterization and analysis of the material micro-structure, crystal phase purity, size and morphology, and through a variety of steady-state/time-resolved spectroscopy methods such as spectrum, fluorescence dynamics, quantum efficiency, temperature spectrum and so on further study of the main factors influencing the luminous material process and luminous performance.

Fluorescent Probe Image Sensing Properties of Nanocrystalline Materials Research: To study the relationship between the fluorescence intensity of the nanocrystal probe and the clarity of in vivo imaging, and the relationship between the measurement range and sensitivity of rare earth materials as fluorescent probes.

Methodology

The general framework of rare earth near-infrared fluorescence spectroscopy in biomedical imaging research mainly includes the following key steps and components:

Synthesis and Characterization of Rare Earth Fluorescent Materials

One of the key factors in this study is to select suitable rare earth elements, including Pr^{3+} , Nd^{3+} , Ho^{3+} , Er^{3+} , Tm^{3+} and their compounds, which have unique near-infrared fluorescence characteristics. Because of its emission wavelength at 1000 nm to 1700 nm spectral range, is a rare earth doped nanoparticles under transfer luminescence probe that is commonly used in luminescent centers. We usually adopt chemical synthesis method (such as water hot method, sol-gel method, etc.) preparation of nanoparticles or rare earth complexes. Using X-ray diffraction (XRD), transmission electron microscope (TEM) and fluorescence spectrometer technology on physical and chemical properties of the materials were characterized. Design and optimization of fluorescence probe Surface modification (such as ligand exchange, polymer coating, etc.) can improve the biocompatibility and targeting of the materials.

Data Analysis and Image Processing

Fluorescence imaging system was used to collect image data. Through image processing software for collected image analysis and processing, extract useful biomedical information.

Biosafety Assessment

The cytotoxicity of rare earth fluorescent probes to cells was evaluated by MTT assay, flow cytometry and other methods. The fluorescent probes were injected into mice for a long time and the activity and vital signs of mice were observed regularly.

Literature Review

At the end of the 20th century, scientists began to explore rare-earth doped nanomaterials. Most rare-earth ion-doped nanoparticles have narrow absorption and emission spectra, and at first attention was paid to their upconversion luminescence properties from longer infrared to shorter wavelength (Yang R, et al. [10]). However, short-wavelength visible light (400-700 nm) is easily absorbed and scattered when passing through biological tissues, so it can only meet the requirements of in vitro diagnosis and biological imaging at the cellular level (Pan Y, et al. [11]). Compared with visible or ultraviolet light, near-infrared light (NIR, 700-1700 nm) can penetrate biological tissues more deeply, making it well suited for deep in vivo imaging. Therefore, the near-infrared window of the down-conversion luminescence of rare earth, as a relatively "transparent" optical window of biological tissues, has a deeper tissue penetration ability and higher imaging signal-to-noise ratio due to the weak absorption and scat-

tering of biological tissues and lower autofluorescence, especially in the 1000nm-1700 nm near-infrared two-region fluorescence (Chen M, et al. [12]). In 2021, the method of doping Ce^{3+} and Zn^{2+} in Er-doped fluorescent probes to regulate their internal energy transfer process has also been confirmed to be an effective strategy to improve³⁺ the fluorescence intensity of Er^{3+} in the near infrared second region by the team of Hongjie Zhang and Yinghui Wang from Changchun Institute of Applied Chemistry, Chinese Academy of Sciences. By using the single-atom layer continuous growth method, the team of Fan Zhang from Fudan University realized the precise regulation of the core-shell structure of the rare earth near-infrared probe at the subnanometer scale, and significantly improved the luminescence efficiency and stability of the rare earth near-infrared probe. In 2024, Lu Shan, Chen Xueyuan and other researchers from the Fujian Institute of Structure of Matter, Chinese Academy of Sciences developed a new rare earth nano-optical diagnosis and treatment material, which realized non-invasive optical diagnosis and treatment in a mouse model of pulmonary infection. The research of the above teams has laid the foundation for the application of rare earth near-infrared fluorescence spectroscopy in biomedical imaging of this project.

Results

Rare-earth NIR fluorescence spectroscopy is widely used in biological imaging, covering multiple levels from cell to vivo. In cellular imaging, rare earth NIR fluorescent probes can be used for cell labelling, tracing, and physiological process monitoring. Its long fluorescence lifetime properties can be used for time-resolved imaging to effectively eliminate the interference of background fluorescence. In tissue imaging, rare earth near-infrared fluorescent probes can be used for tumor detection, vascular imaging and neuroimaging. The deep penetration of NIR light gives this technique a unique advantage in 3D imaging of tissues. In live imaging, rare earth near-infrared fluorescent probes can be used for real-time and dynamic imaging of small animal models, providing important tools for disease diagnosis and drug development.

Discussion

In recent years, rare earth near-infrared fluorescence spectroscopy biomedical imaging technology has triggered a wide range of discussions in the medical field, mainly focusing on the following aspects:

Technical Advantages - High Sensitivity and Resolution

Rare earth near-infrared fluorescent probes have excellent optical properties and can achieve high-resolution imaging in deep tissues, contributing to early disease diagnosis.

Low Background Interference: The scattering and absorption of near-infrared light in biological tissues is low, which can reduce background noise and improve the clarity of imaging.

Versatility: Rare earth elements (such as europium, terbium, ytterbium, etc.) have a rich energy level structure, which can achieve multi-mode imaging (such as fluorescence, magnetic resonance imaging, etc.) by designing different probes.

Cancer Diagnosis: Rare earth near-infrared fluorescent probes can be used for the detection of tumor markers and the accurate definition of tumor boundaries, providing support for surgical navigation.

Cardiovascular Diseases: Imaging techniques are used to observe vascular structure and hemodynamics to assist in the diagnosis of diseases such as atherosclerosis.

Neurological Diseases: Used to study the pathological mechanisms of brain diseases (such as Alzheimer's disease) and track neural activity.

Drug Delivery and Efficacy Evaluation: Combined with fluorescence imaging, real-time monitoring of drug distribution and metabolic processes in the body.

Biosafety: Although rare earth materials perform well in imaging, their long-term biocompatibility and potential toxicity still require further study.

Cost and Accessibility: The high cost of extraction and processing of rare earth materials limits their widespread clinical use.

Technical Standardization: The current lack of uniform imaging standards and probe design specifications affects the promotion of technology and clinical.

Conclusion & Recommendations

Fluorescence imaging technology is the use of optical detector to collect fluorescence probe light real-time imaging of a non-invasive imaging technique, with imaging speed, high sensitivity, high space-time resolution, the advantages of no radiation excitation and emission of light through the application of biological tissue organization in absorption, scattering and interference is autofluorescence fluorescence imaging resolution is the main factor and tissue penetration depth. Compared with visible (400-700 nm) and near-infrared I (700-1 000 nm) fluorescence imaging, biological tissues have weaker absorption and scattering of near-infrared II (1 000-1 700 nm) light and lower autofluorescence. Therefore, Near-infrared region 2 fluorescence imaging has been favored by people due to its deeper tissue penetration ability and higher imaging signal-to-noise ratio. There are still some technical bottlenecks in the stability, imaging resolution and signal-to-noise ratio of fluorescent probes in China.

Future Directions

1. The development of new fluorescent probes and the research of multimodal imaging technology should be strengthened.
2. Strive for technological breakthroughs in super-resolution imaging, single molecule detection and in vivo imaging.
3. Strengthen the cross-disciplinary and multi-field cooperation to promote the diversified development of near-infrared fluorescence spectroscopy imaging technology.

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