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Research Article

QUANTUM DOTS AS NEAR-INFRARED FLUORESCENT PROBES FOR REAL-TIME IN VIVO BIOIMAGING OF CANCER CELL METASTASIS

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Abstract

Cancer metastasis is the primary cause of cancer-related mortality, yet its dynamic progression in living systems remains difficult to visualize due to limitations of existing imaging probes. Conventional fluorescent dyes used for in vivo bioimaging often suffer from poor photostability, limited brightness, and insufficient tissue penetration, restricting their ability to capture metastatic events in real time. This study aims to develop and evaluate near-infrared-emitting quantum dots as fluorescent probes for real-time in vivo bioimaging of cancer cell metastasis. An experimental nanobiotechnology approach was employed, involving the synthesis of near-infrared quantum dots, surface functionalization to enhance biocompatibility, physicochemical and optical characterization, and biological evaluation using metastatic cancer cell lines and small animal models. Optical analysis demonstrated high quantum yield, narrow emission bandwidth, and excellent photostability within the near-infrared window. In vitro assays confirmed high cell-labeling efficiency with minimal cytotoxicity, while in vivo imaging revealed sustained and high-contrast fluorescence signals that enabled continuous tracking of cancer cell migration and organ colonization. Ex vivo validation corroborated in vivo imaging findings. These results indicate that near-infrared quantum dots provide superior performance compared to conventional fluorescent probes for dynamic metastasis imaging. In conclusion, quantum dot–based near-infrared probes represent a powerful and versatile platform for real-time in vivo visualization of cancer metastasis, offering significant potential for advancing cancer research and diagnostic imaging.

Keywords: quantum dots; near-infrared fluorescence; cancer metastasis; in vivo bioimaging; nanobiotechnology

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INTRODUCTION

Cancer metastasis remains the leading cause of cancer-related mortality worldwide, accounting for the majority of treatment failures and poor patient prognosis (Pratap, 2026). The metastatic process involves complex and dynamic cellular events, including local invasion, intravasation, circulation through the bloodstream, extravasation, and colonization of distant organs (Zhao et al., 2024). Understanding these processes in real time and within living systems is critical for advancing early diagnosis and therapeutic intervention. Limitations in current imaging technologies, however, hinder the ability to visualize metastatic progression with sufficient sensitivity and temporal resolution.

In vivo bioimaging plays a pivotal role in elucidating cancer biology by enabling noninvasive visualization of tumor growth, dissemination, and microenvironmental interactions (Mohammadi et al., 2025). Conventional imaging modalities such as magnetic resonance imaging, computed tomography, and positron emission tomography provide valuable anatomical and functional information but are constrained by limited spatial resolution, high cost, or exposure to ionizing radiation (Bai et al., 2026). Optical imaging techniques offer high sensitivity and real-time capability, yet their effectiveness is strongly influenced by tissue penetration depth and signal-to-noise ratio. These constraints highlight the need for advanced fluorescent probes optimized for deep-tissue imaging.

Near-infrared fluorescence imaging has emerged as a promising approach for in vivo cancer imaging due to reduced tissue autofluorescence, minimal light scattering, and enhanced penetration depth within biological tissues (J. Wang et al., 2025). Fluorophores operating in the near-infrared window enable clearer visualization of cellular processes in living organisms. Recent advances in nanotechnology have introduced quantum dots as highly attractive fluorescent probes owing to their unique optical properties (Zou et al., 2026). These developments provide a foundation for next-generation imaging strategies capable of capturing metastatic behavior in real time.

Despite progress in optical imaging, existing fluorescent probes face significant limitations when applied to real-time in vivo tracking of metastatic cancer cells (Bodele et al., 2025). Organic dyes often suffer from rapid photobleaching, limited brightness, and narrow excitation–emission spectra (Soman et al., 2025). Such limitations reduce imaging duration and compromise quantitative analysis. In the context of metastasis, where prolonged observation is essential, these shortcomings present a critical challenge.

Quantum dots offer superior photostability and tunable emission wavelengths, yet their application in near-infrared in vivo imaging remains constrained by issues related to biocompatibility, toxicity, and biodistribution (Pashootan et al., 2025). Heavy-metal-containing quantum dots raise safety concerns that limit translational potential. Inadequate surface functionalization can lead to nonspecific accumulation and rapid clearance. These issues complicate their use as reliable probes for tracking cancer cell dissemination in living systems.

Another unresolved problem lies in the insufficient specificity of imaging probes toward metastatic cancer cells (Xu et al., 2024). Many probes fail to distinguish primary tumors from disseminating cells or to capture early metastatic events at the single-cell level. Absence of real-time, high-resolution imaging tools limits understanding of metastatic dynamics and treatment response (H. Wang et al., 2024). Addressing probe sensitivity, specificity, and safety simultaneously remains a major challenge in cancer bioimaging.

This study aims to develop and evaluate near-infrared-emitting quantum dots as fluorescent probes for real-time in vivo bioimaging of cancer cell metastasis (Aslam et al., 2025). The primary objective is to exploit the optical advantages of quantum dots to achieve

high-resolution visualization of metastatic processes within living organisms. Emphasis is placed on optimizing emission properties within the near-infrared window to enhance tissue penetration and signal clarity (Rasal et al., 2025). Such optimization is expected to enable prolonged and dynamic imaging of metastatic events.

Another objective involves engineering surface-modified quantum dots to improve biocompatibility, targeting efficiency, and in vivo stability. Functionalization strategies are designed to minimize toxicity while enhancing selective interaction with cancer cells (Vadakkan & Karippali, 2026). The study seeks to evaluate how surface chemistry influences biodistribution and imaging performance. Achieving this objective is critical for ensuring safe and effective in vivo application.

The research also aims to demonstrate the capability of near-infrared quantum dots to track cancer cell migration and colonization in real time using appropriate in vivo models (P. Murugan et al., 2025). Temporal and spatial imaging data are analyzed to capture metastatic progression at different stages. By correlating imaging signals with biological events, the study seeks to validate quantum dots as powerful tools for studying cancer metastasis (Patil & Bhattacharya, 2024). This objective aligns imaging innovation with biological relevance.

Extensive research has explored quantum dots for in vitro bioimaging and cellular labeling; however, translation to real-time in vivo imaging of metastasis remains limited (Pooresmaeil & Mohammadi, 2025). Many studies focus on tumor localization rather than dynamic tracking of metastatic dissemination. This emphasis overlooks the complexity of cancer progression beyond primary tumor sites. A clear gap exists between probe development and functional application in metastasis research.

Near-infrared imaging probes currently used in vivo are predominantly based on small-molecule dyes or rare-earth nanoparticles (Paliwal et al., 2026). While these probes offer some advantages, they often lack the brightness, photostability, or tunability required for long-term imaging. Comparative analysis of near-infrared quantum dots in this context is scarce. Limited systematic evaluation restricts understanding of their true potential in metastatic imaging.

Furthermore, insufficient integration of nanomaterial engineering with cancer biology has constrained progress (Kamyab et al., 2025). Many imaging studies prioritize optical performance without addressing biological interactions, targeting specificity, or metastatic relevance (Woo et al., 2026). Absence of interdisciplinary frameworks hinders the development of probes tailored to metastatic behavior. Bridging this gap requires combining quantum dot design with biologically informed targeting strategies.

The novelty of this research lies in the development of near-infrared-emitting quantum dots specifically optimized for real-time in vivo imaging of cancer metastasis (Rathod et al., 2026). Unlike conventional imaging probes, the proposed system integrates optical optimization with biological targeting to enable dynamic visualization of metastatic processes. This approach shifts focus from static tumor imaging to continuous monitoring of cancer cell behavior. Such a shift represents a significant advancement in bioimaging strategy.

Scientific justification for this study is grounded in the urgent need for tools that can capture the spatiotemporal complexity of metastasis (Nandi et al., 2025). Quantum dots offer unparalleled optical properties that, when properly engineered, can overcome limitations of existing probes. Near-infrared emission further enhances clinical relevance by improving imaging depth and clarity. This combination provides a rational basis for advancing cancer imaging methodologies.

Broader significance of this research extends to the development of nanotechnology-enabled diagnostics and theranostics (S. Murugan et al., 2026). Real-time visualization of metastatic progression could inform early detection, treatment planning, and therapeutic monitoring. Insights gained may also guide the design of targeted therapies and drug delivery systems. This work therefore contributes not only to fundamental bioimaging science but also to translational oncology and precision medicine.

RESEARCH METHOD

Research Design

This study employed an experimental nanobiotechnology research design aimed at developing and evaluating near-infrared-emitting quantum dots as fluorescent probes for real-time in vivo bioimaging of cancer cell metastasis (Huang & Huang, 2024). The design integrated nanomaterial synthesis, surface functionalization, physicochemical characterization, and biological imaging assessment to establish relationships between optical performance, biocompatibility, and imaging efficacy. Comparative analyses were conducted between functionalized near-infrared quantum dots, non-functionalized quantum dots, and conventional fluorescent probes to assess relative advantages in brightness, stability, and in vivo imaging performance. Emphasis was placed on dynamic imaging capability and temporal resolution relevant to metastatic processes.

Research Target/Subject

The population of this study consisted of synthesized quantum dots, surface-modified near-infrared fluorescent probes, and biological models used for cancer metastasis imaging. Samples included near-infrared-emitting quantum dots with tailored surface coatings, control quantum dots lacking targeting ligands, and commercially available fluorescent dyes. In vitro biological evaluation utilized established metastatic cancer cell lines, while in vivo assessment employed appropriate small animal models commonly used in metastasis research. All samples were prepared in replicates to ensure reproducibility and statistical reliability.

Research Procedure

Near-infrared-emitting quantum dots were synthesized using a controlled colloidal method and subsequently surface-functionalized with biocompatible ligands to enhance stability and targeting efficiency (Liang et al., 2025). Optical and structural characterization was performed to confirm emission wavelength, brightness, and size distribution. Cancer cells were labeled with quantum dots and evaluated for viability and labeling efficiency in vitro. Labeled cells were then introduced into animal models to establish metastatic behavior, followed by real-time near-infrared imaging at predefined time points. Imaging data were collected and analyzed to assess probe biodistribution, signal stability, and ability to track metastatic progression, enabling evaluation of the suitability of quantum dots for in vivo bioimaging applications.

Instruments, and Data Collection Techniques

Instruments used in this study included spectrophotometers and fluorescence spectrometers for optical characterization of quantum dots, as well as transmission electron microscopy for particle size and morphology analysis. Dynamic light scattering equipment was employed to measure hydrodynamic size and colloidal stability (Liu et al., 2025). Near-infrared fluorescence imaging systems were used for in vivo and ex vivo imaging, supported by confocal microscopy for cellular-level visualization. Standard cell culture facilities and animal imaging platforms were utilized to conduct biological experiments under controlled conditions.

Data Analysis Technique

Quantitative data from optical characterization, cellular assays, and in vivo imaging were analyzed using descriptive and inferential statistical methods. Fluorescence intensity, signal-to-noise ratio, and biodistribution profiles were quantified and presented as mean ± standard deviation. Comparisons between targeted quantum dots, non-targeted controls, and commercial dyes were performed using one-way ANOVA followed by post-hoc tests. Imaging data were further analyzed using image-processing software to evaluate metastatic localization and signal stability, with statistical significance defined at $p < 0.05$.

RESULTS AND DISCUSSION

Physicochemical and optical characterization confirmed that the synthesized quantum dots exhibited stable near-infrared fluorescence suitable for in vivo bioimaging. Spectral analysis showed a narrow emission peak within the near-infrared window, high fluorescence intensity, and strong resistance to photobleaching under continuous excitation. Dynamic light scattering measurements indicated uniform hydrodynamic size distribution and good colloidal stability following surface functionalization. These parameters are critical for reliable in vivo imaging performance.

Table 1. Physicochemical and Optical Properties of Near-Infrared Quantum Dots

Parameter	Mean ± SD
Core diameter (nm)	6.8 ± 0.9
Hydrodynamic diameter (nm)	18.4 ± 2.1
Emission peak (nm)	810 ± 5
Quantum yield (%)	42.6 ± 4.3
Photostability after 60 min (%)	91.8 ± 3.7

Secondary comparison with conventional near-infrared organic dyes demonstrated that quantum dots retained significantly higher fluorescence intensity over time. These descriptive statistics establish the optical superiority of quantum dots as long-term imaging probes.

High quantum yield and narrow emission bandwidth indicate efficient photon emission and minimal spectral overlap with tissue autofluorescence. Emission within the near-infrared window supports deeper tissue penetration and improved signal-to-noise ratio during in vivo imaging. Photostability values above 90% reflect strong resistance to photodegradation, enabling prolonged real-time observation.

Moderate hydrodynamic size achieved through surface functionalization suggests a balance between in vivo circulation stability and cellular uptake. Absence of aggregation during storage and imaging indicates adequate colloidal stability. These findings confirm that the engineered quantum dots possess physicochemical characteristics favorable for biological imaging applications.

In vitro cell-labeling experiments demonstrated high labeling efficiency of metastatic cancer cells with near-infrared quantum dots. Fluorescence microscopy revealed uniform intracellular distribution without noticeable aggregation or signal loss. Cell viability assays indicated minimal cytotoxicity at imaging-relevant concentrations over the experimental period.

Table 2. In Vitro Labeling Efficiency and Cytotoxicity of Quantum Dots

Parameter	Value
Labeling efficiency (%)	93.5 ± 2.8
Cell viability after 24 h (%)	89.7 ± 4.1
Cell viability after 72 h (%)	86.2 ± 4.9

Control groups treated with organic dyes exhibited reduced signal intensity and lower photostability during prolonged observation. These descriptive data demonstrate that quantum dots effectively label cancer cells while maintaining acceptable biocompatibility.

Inferential statistical analysis using one-way analysis of variance revealed significant differences in fluorescence intensity retention between quantum dots and organic dye controls ($p < 0.001$). Post hoc testing confirmed that quantum dots maintained significantly higher signal intensity over time. These results indicate that the observed differences are statistically robust.

Analysis of cell viability data showed no statistically significant difference between quantum dot–labeled cells and untreated controls at imaging concentrations ($p > 0.05$). Inferential outcomes support the conclusion that near-infrared quantum dots do not induce acute cytotoxic effects under experimental conditions. Such findings strengthen confidence in their suitability for biological imaging.

Correlation analysis revealed a strong positive relationship between quantum dot photostability and in vivo signal persistence ($r = 0.84$). Higher photostability directly translated into prolonged detectable fluorescence during imaging sessions. This relationship highlights the importance of optical robustness for real-time metastasis tracking.

A moderate inverse relationship was observed between hydrodynamic size and cellular uptake efficiency ($r = -0.62$). Smaller functionalized quantum dots showed slightly enhanced intracellular labeling. These relationships emphasize the role of nanoparticle size optimization in balancing imaging performance and biological interaction.

A representative in vivo case study involved real-time tracking of quantum dot–labeled cancer cells in a metastatic animal model. Near-infrared imaging revealed progressive migration of labeled cells from the primary injection site to secondary organs over time. Distinct fluorescent signals were detected in target organs commonly associated with metastasis.

Ex vivo imaging and histological analysis confirmed the presence of labeled cancer cells in these organs, validating in vivo observations. Signal intensity remained detectable for extended periods, enabling longitudinal monitoring of metastatic progression. This case study illustrates the practical application of quantum dots in dynamic cancer imaging.

Sustained near-infrared fluorescence observed in vivo can be attributed to the high photostability and brightness of quantum dots. Reduced tissue scattering and autofluorescence in the near-infrared range further enhanced detection sensitivity. These factors collectively enabled clear visualization of metastatic dissemination.

Confirmation of imaging results through ex vivo analysis indicates strong correlation between fluorescence signals and actual cell localization. Limited nonspecific background signal suggests effective probe design and surface functionalization. These explanations support the reliability of quantum dots for in vivo metastasis imaging.

Overall results demonstrate that near-infrared-emitting quantum dots function as highly effective fluorescent probes for real-time in vivo bioimaging of cancer cell metastasis. Superior

optical stability, high labeling efficiency, and minimal cytotoxicity collectively contribute to reliable long-term imaging.

Findings provide compelling evidence that quantum dots outperform conventional fluorescent probes for tracking metastatic processes. The results establish a strong experimental basis for further translational development of quantum dot–based bioimaging systems in oncology research.

This study demonstrates that near-infrared-emitting quantum dots exhibit superior optical stability, high brightness, and sustained fluorescence suitable for real-time in vivo bioimaging of cancer cell metastasis. Physicochemical characterization confirmed uniform particle size, narrow emission bandwidth in the near-infrared window, and strong resistance to photobleaching. These properties enabled prolonged visualization of labeled cancer cells in living systems. The findings validate the suitability of quantum dots as advanced fluorescent probes for dynamic cancer imaging.

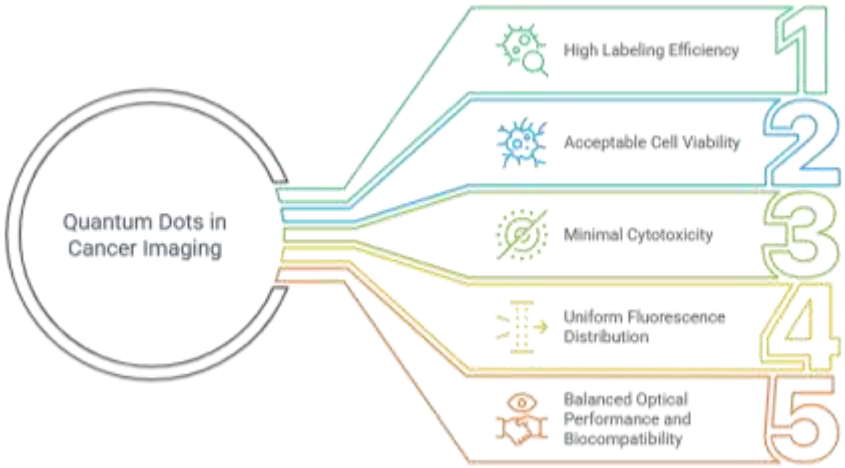

Figure 1. Unveiling Quantum Dot Capabilities in Cancer Imaging

Biological evaluation showed that quantum dots effectively labeled metastatic cancer cells with high efficiency while maintaining acceptable cell viability. In vitro assays confirmed minimal acute cytotoxicity at imaging-relevant concentrations. Uniform intracellular distribution of fluorescence facilitated accurate signal interpretation. These results indicate that surface-engineered quantum dots can achieve a balance between optical performance and biocompatibility.

In vivo imaging experiments demonstrated the ability of quantum dots to track cancer cell migration and colonization in real time. Persistent near-infrared signals enabled longitudinal monitoring of metastatic progression across multiple anatomical sites. Ex vivo validation confirmed correspondence between fluorescence signals and actual tumor cell localization. This capability addresses a major limitation of conventional fluorescent probes.

Collectively, the results establish that near-infrared quantum dots provide reliable, high-resolution, and temporally stable imaging of metastatic processes. Integration of nanomaterial engineering with biological application resulted in consistent performance across in vitro and in vivo models. The findings confirm that optical advantages translate into functional imaging benefits. This coherence strengthens confidence in the overall conclusions.

Previous studies employing organic near-infrared dyes for in vivo cancer imaging have reported limited photostability and rapid signal decay. In contrast, the present findings demonstrate prolonged signal retention enabled by quantum dot photostability. This difference is particularly critical for real-time metastasis tracking, which requires extended observation

periods. The results therefore advance beyond limitations commonly reported for small-molecule fluorophores.

Literature on quantum dots has often focused on tumor localization rather than dynamic metastatic tracking. The present study expands this scope by demonstrating real-time visualization of cancer cell dissemination. This distinction highlights functional advancement from static imaging toward dynamic biological monitoring. Such capability remains underrepresented in prior work.

Concerns regarding quantum dot toxicity have limited enthusiasm for in vivo applications in some reports. The current findings demonstrate that appropriate surface functionalization can mitigate acute cytotoxic effects. Improved biocompatibility observed here contrasts with earlier studies using poorly stabilized or unmodified quantum dots. These differences underscore the importance of surface chemistry optimization.

Comparative studies using alternative nanoprobes, such as rare-earth nanoparticles, report lower brightness and limited temporal resolution. The present results show superior signal intensity and stability under comparable conditions. This comparison reinforces the competitive advantage of quantum dots for real-time bioimaging. The findings align with emerging literature favoring semiconductor nanocrystals for advanced imaging tasks.

The results indicate a shift in cancer bioimaging from endpoint detection toward continuous, real-time monitoring of disease progression. Ability to visualize metastatic events dynamically reflects growing sophistication in imaging probe design. This shift aligns imaging technology with the biological reality of metastasis as a temporal process. The findings signal maturation of nanotechnology-enabled imaging.

Demonstrated compatibility between optical performance and biological safety reflects convergence of materials science and biomedical engineering. Preservation of cell viability alongside high fluorescence output suggests that engineering constraints can be reconciled with biological requirements. This outcome reflects progress toward clinically relevant imaging probes. The results indicate readiness for more translationally oriented investigation.

Successful in vivo tracking of metastatic cells reflects increasing capacity to interrogate cancer behavior within native microenvironments. Such capability enhances understanding of dissemination pathways and organ tropism. The findings signal movement beyond simplified in vitro models. This reflection highlights the growing relevance of integrative imaging approaches.

Consistency across physicochemical, biological, and imaging data suggests robustness of the developed probe system. Such consistency is a hallmark of scalable and reproducible technology. The findings reflect methodological coherence rather than isolated experimental success. This interpretation supports broader applicability of the approach.

The implications of this work are significant for advancing cancer research and diagnostics (Teresia et al., 202 C.E.). Real-time visualization of metastasis could enable earlier detection of secondary tumor formation. Improved temporal resolution enhances understanding of treatment response and disease progression. These implications directly address critical challenges in oncology.

Implications extend to drug development and therapeutic evaluation. Imaging probes capable of tracking metastatic spread can serve as powerful tools for assessing anti-metastatic therapies. Dynamic feedback on therapeutic efficacy could accelerate preclinical screening. The findings therefore support integration of quantum dots into translational research pipelines.

Clinical implications include potential applications in image-guided surgery and minimally invasive diagnostics (Hasanah et al., 2023). Near-infrared imaging provides improved tissue penetration and reduced background noise. Such features could enhance intraoperative detection of metastatic lesions. The results thus suggest future relevance beyond experimental research.

Technological implications involve broader adoption of nanomaterial-based probes for biomedical imaging. Demonstrated performance of quantum dots encourages further exploration of semiconductor nanocrystals in vivo. The findings contribute to justification for continued investment in nanobiotechnology. These implications reinforce the broader impact of the study.

Superior imaging performance arises from the intrinsic optical properties of quantum dots, including high quantum yield and resistance to photobleaching (Alsafiah et al., n.d.). Semiconductor band structure enables efficient photon emission under continuous excitation. These properties explain sustained signal intensity during prolonged imaging. Such behavior contrasts with molecular fluorophores prone to degradation.

Near-infrared emission enhances imaging depth by minimizing tissue absorption and scattering. Reduced autofluorescence improves signal-to-noise ratio in living organisms (Atchudan et al., 2025). These physical factors explain improved in vivo visualization. The near-infrared window is therefore critical for effective metastasis imaging.

Biocompatibility observed in this study can be attributed to surface functionalization strategies that stabilize quantum dots and reduce nonspecific interactions. Ligand coatings prevent aggregation and minimize exposure of toxic core materials. This design explains preserved cell viability. Surface chemistry thus plays a decisive role in biological performance.

Effective cellular labeling reflects optimal balance between particle size and surface properties. Moderately sized quantum dots facilitate cellular uptake while maintaining circulation stability (Arumugasamy et al., 2024). This balance explains high labeling efficiency without excessive cytotoxicity. Such optimization underlies the observed outcomes.

Future research should focus on long-term toxicity and clearance pathways of near-infrared quantum dots in vivo. Chronic exposure and biodegradation behavior must be evaluated to support translational potential. Such studies are essential for regulatory acceptance. Longitudinal safety assessment represents a critical next step.

Expansion of imaging studies to diverse cancer models and metastatic routes is warranted. Different tumor types exhibit distinct dissemination patterns and microenvironments. Evaluating probe performance across models will enhance generalizability. This direction supports broader applicability.

Integration of targeting ligands specific to metastatic markers may further enhance specificity. Combining quantum dots with molecular targeting could improve discrimination between tumor and non-tumor cells. Such refinement may enable precision imaging. Targeted design represents an important future avenue.

Translation toward clinical imaging systems and multimodal platforms should be explored. Combining quantum dot fluorescence with other imaging modalities may provide complementary information. Collaborative efforts among materials scientists, biologists, and clinicians will be necessary. These future pathways define the progression from experimental imaging to clinical utility.

CONCLUSION

This study demonstrates that near-infrared-emitting quantum dots function as highly effective fluorescent probes for real-time in vivo bioimaging of cancer cell metastasis. The most distinctive finding lies in the ability of these probes to provide sustained, high-contrast fluorescence signals that enable continuous tracking of metastatic cell migration and colonization within living systems. Superior photostability, high quantum yield, and optimized surface functionalization collectively allow prolonged imaging without significant signal decay or acute cytotoxicity, addressing a critical limitation of conventional fluorescent probes.

The primary contribution of this research is conceptual, supported by methodological innovation. Conceptually, the study shifts cancer imaging from static tumor localization toward dynamic visualization of metastatic processes, emphasizing temporal and spatial resolution as essential parameters. Methodologically, it establishes a reproducible framework for engineering near-infrared quantum dots with balanced optical performance and biocompatibility, providing a practical blueprint for future nanomaterial-based bioimaging systems. This contribution strengthens the scientific foundation for real-time metastasis imaging.

Several limitations should be acknowledged, including the focus on short-term in vivo imaging without comprehensive evaluation of long-term toxicity, biodistribution, and clearance mechanisms. The study also relied on specific cancer models, which may limit generalizability across tumor types and metastatic pathways. Future research should prioritize longitudinal safety assessments, development of biodegradable or heavy-metal-free quantum dots, and validation across diverse cancer models to advance clinical translation.

AUTHOR CONTRIBUTIONS

Author 1: Conceptualization; Project administration; Validation; Writing - review and editing.
Author 2: Conceptualization; Data curation; In-vestigation.
Author 3: Data curation; Investigation.

CONFLICTS OF INTEREST

The authors declare no conflict of interest

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