

A Review on Quantum Dots and Their Bioimaging Applications

Deepanjali¹, Naisergik Deepika Khanna^{2,*}

Abstract

Quantum dots are nanoscale semiconductor crystals engineered to emit highly intense, photo-stable luminescence with quantum yields reaching 90%. Structurally, they are synthesized as single-substance core types, hetero-structured core-shell architectures for enhanced stability, or blended alloys. They are further categorized by synthesis and functional traits into colloidal, magnetic, and highly fluorescent varieties, alongside specialized silicon and eco-friendly carbon-based variants derived from organic waste. Due to their exceptional optoelectronic properties, they are highly effective in photocatalysis, solar energy conversion, and high-definition displays. In biomedical applications, these nanocrystals advance cellular imaging by facilitating single-molecule tracking, deep-tissue penetration, and targeted organelle visualization. Furthermore, they can be engineered for stimuli-responsive fluorescence and self-illuminating mechanisms to optimize drug delivery and diagnostics. Despite their immense potential, quantum dots face limitations, including structural instability, manufacturing difficulties, and environmental degradation under UV light or moisture. Crucially, toxicity from heavy metals – like cadmium – poses a major challenge, driving current research toward safer cadmium-free alternatives and protective coatings to ensure biocompatibility.

Keywords: Quantum dots, classification, synthesis, functionalization, toxicity, bioimaging applications

INTRODUCTION

The emergence of quantum dots (QDs) represents a transformative milestone in nanotechnology, evolving from a theoretical physics discovery in the early 1980s into a cornerstone of modern biomedical engineering. These ultra-small semiconductor nanocrystals, typically measuring between 2 and 10 nanometers, exhibit a unique phenomenon known as quantum confinement. Unlike bulk materials, the optical and electronic properties of quantum dots are governed by their physical size; by simply altering the diameter of the crystal, researchers can tune their light emission across the entire visible and near-infrared spectrum. This precise tunability, combined with an extraordinary resistance to photobleaching and high brightness, has positioned quantum dots as superior alternatives to traditional organic dyes and fluorescent proteins in the field of bioimaging.

*Author for Correspondence

Naisergik Deepika Khanna

E-mail: naisergikdeepikakhanna@gmail.com

¹Student, Department of Chemistry, NSCBM Government College, Hamirpur, Himachal Pradesh, India

²Assistant Professor, Department of Chemistry, NSCBM Government College, Hamirpur, Himachal Pradesh, India

Received Date: June 02, 2026

Accepted Date: June 05, 2026

Published Date: June 05, 2026

Citation: Deepanjali, Naisergik Deepika Khanna. A Review on Quantum Dots and Their Bioimaging Applications. Journal of Nanoscience, Nanoengineering & Applications. 2026; 16(2): 44–60p.

In the current scientific landscape, the relevance of quantum dots is underscored by their ability to facilitate multiplexed imaging (the simultaneous tracking of multiple biological pathways within a single cell using a single excitation source). As we move through 2026, the focus has shifted toward the Near-Infrared II (NIR-II) window, where these dots allow for high-resolution, deep-tissue visualization that was previously impossible with standard fluorophores. This capability is critical for non-invasive cancer detection and real-time monitoring of drug delivery systems.

However, the path to widespread clinical application is hindered by a significant dual-sided problem. Many of the most efficient quantum dots are traditionally composed of heavy metals, like cadmium or lead, raising persistent concerns regarding long-term toxicity and metabolic degradation within the human body. Furthermore, achieving the necessary water solubility for biological environments often increases their hydrodynamic size, which can lead to unwanted accumulation in the liver and spleen rather than efficient renal clearance. Consequently, the primary challenge in the field today lies in developing “green,” cadmium-free quantum dots that maintain peak brightness and stability while ensuring total biocompatibility for humans.

LITERATURE REVIEW

Quantum dots (QDs) have emerged as the most formidable rivals to traditional organic fluorophores in the field of biomedical imaging over the last decade. These semiconductor nanocrystals, typically ranging from 2 to 10 nanometers in size, exhibit unique quantum confinement effects where their band gap energy and thus their emission color are precisely tunable by adjusting their size and composition. In the past five to ten years, research has shifted significantly from the visible spectrum toward the Near-Infrared II (NIR-II, 1000–1700 nm) window. This “second biological window” is a milestone in bioimaging because it experiences dramatically reduced tissue scattering, absorption, and autofluorescence compared to visible light, enabling high-resolution imaging at centimeter-scale depths. Recent studies have demonstrated that NIR-II QDs, such as Ag₂S, Ag₂Se, and PbS, can provide real-time, non-invasive visualization of intricate vascular networks, organ perfusion, and even the metabolic pathways of tumors in small animal models with unprecedented clarity.

A comparative analysis between QDs and conventional organic dyes (like fluorescein or rhodamine) highlights why QDs are often superior for long-term tracking. QDs possess 10 to 100 times higher brightness and a remarkable resistance to photobleaching, allowing for continuous observation over hours or days without signal degradation. Unlike organic dyes, which have narrow absorption and broad, asymmetric emission spectra with “red tails,” QDs feature broad absorption spectra and narrow, symmetric emission peaks. This allows for multiplexing, where a single light source can simultaneously excite multiple colors of QDs to track different cellular components at once. Furthermore, the large Stokes shift of QDs (the gap between excitation and emission wavelengths) effectively eliminates background noise, significantly enhancing the signal-to-noise ratio in complex biological environments.

Despite these advantages, critical research gaps persist that prevent the widespread clinical translation of QDs. The primary concern is long-term toxicity; traditional high-performance QDs often contain heavy metals like Cadmium (Cd) or Lead (Pb). While “core-shell” architectures (e.g., CdSe/ZnS) and PEGylation improve biocompatibility, the potential for heavy metal leaching over months remains a barrier for human use. Consequently, there is an urgent research focus on “green” or heavy-metal-free alternatives like Carbon Dots (CDs), Graphene QDs (GQDs), and Silicon QDs. Another significant gap is the protein corona effect, where serum proteins spontaneously coat QDs upon entering the bloodstream, altering their size and potentially masking their targeting ligands. Current research is struggling to standardize the surface chemistry needed to ensure predictable biodistribution and renal clearance, as many QDs still accumulate in the liver and spleen for extended periods. Future efforts are now directed toward theragnostic QD probes that can simultaneously deliver drugs and provide diagnostic imaging while ensuring they can be safely cleared from the body.

The history of quantum dots (QDs) is a classic scientific journey that began with theoretical predictions in the 1930s and culminated in the 2023 Nobel Prize in Chemistry. It is the story of how three scientists transformed mathematical curiosity into a multi-billion-dollar industry. The core discovery is that the electronic and optical properties of nanocrystals (ranging roughly 1–11 nanometers) are determined by their size rather than their material composition. Smaller dots emit blue light; larger dots emit red. As particles shrink to the nanoscale, electrons are forced into tighter, discrete energy levels. This phenomenon is known as quantum confinement. In 1993, Bawendi revolutionized the field by introducing a method to produce almost perfectly sized, high-quality colloidal quantum dots, making them useful for commercial applications.

Classification of Quantum Dots

Quantum dots are classified into various types based on composition, structure, type of material used, and type of technique used for synthesis [1].

Based on Their Composition and Structure

Core-Type Quantum Dots

Core-type quantum dots (Figure 1(a)) are nanoscale semiconductor crystals, typically measuring 2 to 10 nanometers in diameter, composed of a single metallic chalcogenide substance such as cadmium telluride (CdTe) or lead sulphide (PbS). At this scale, quantum confinement effects alter their electrical and optical properties relative to bulk materials, enabling size-tunable photoluminescence. Consequently, smaller nanocrystals emit shorter wavelengths (blue light) due to a wider energy bandgap, while larger crystals emit longer wavelengths (red light). Characterized by high extinction coefficients and extended photoluminescence lifetimes, these dots deliver high color purity and brightness, making them exceptionally well-suited for advanced optoelectronic devices and biomedical imaging applications [2].

Core-Shell Type Quantum Dots

Core-shell type quantum dots are hetero structured nanocrystals consisting of an inner semiconductor core enclosed within an outer shell composed of a different semiconductor material (Figure 1(b)). This architectural design significantly enhances chemical stability and photoluminescence efficiency by isolating the core from environmental oxidation and degradation. Synthesized via high-temperature organic reactions or aqueous precipitation, these methods allow for precise control over dimensions and composition, directly tuning their optoelectronic properties. Structurally, the shell passivates surface defects and confines excitons to the core, which drastically minimizes non-radiative recombination losses and maximizes the photoluminescence quantum yield. Consequently, these nanocrystals feature narrow, high-intensity emission peaks ideal for high-purity color output, alongside a broadened absorption spectrum that enhances their efficacy in photovoltaic systems and biological imaging [3].

Alloyed Type Quantum Dots

Alloyed quantum dots are multi-component nanocrystals typically synthesized via high-temperature thermal decomposition or wet chemical methods, which allow for precise control over particle dimensions and elemental stoichiometry (Figure 1(c)). The chosen synthesis pathway heavily dictates the final optoelectronic properties and structural stability of the nanocrystals. These dots are commonly fabricated by blending II–VI and III–V semiconductor groups such as cadmium selenide (CdSe), zinc sulphide (ZnS), and indium phosphide (InP). By gradiently mixing these materials, alloying effectively minimizes lattice strain and suppresses non-radiative recombination pathways. This structural optimization significantly enhances the photoluminescence quantum yield, resulting in highly efficient light emission [4].

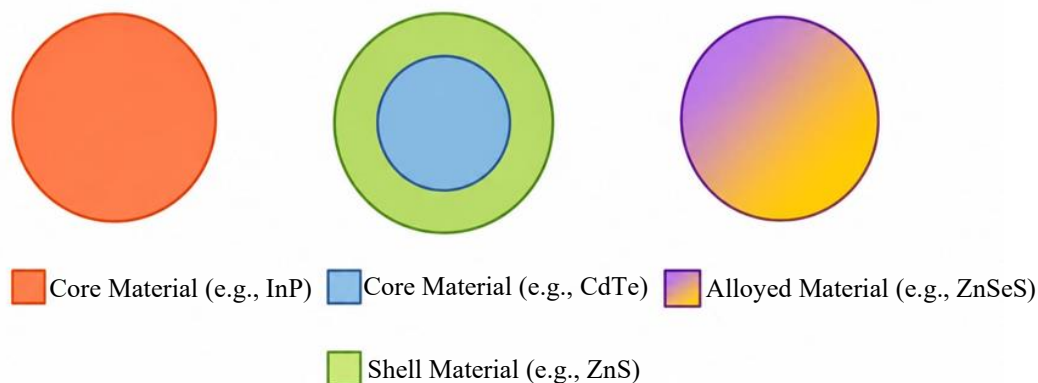


Figure 1. (a) Core type QD, (b) Core-shell type QD, and (C) alloyed type QD.

Based on the Material Used***Semiconductor-Based Quantum Dot***

Semiconductor quantum dots (QDs) are described as nanosized semiconductor crystals typically ranging from 2 to 10 nanometers in diameter. Their most defining characteristic is quantum confinement, a phenomenon where the physical size of the particle is smaller than the Bohr exciton radius. This allows the dots to exhibit unique optical and electrical features that differ significantly from their bulk material counterparts. A key property emphasized in literature is size-tunability. High-quality quantum dots can achieve a photoluminescence quantum yield (QY) of up to 90%, making them exceptionally efficient light emitters.

Research categorizes these materials into various structures to optimize performance. Core-type QDs consist of a single semiconductor substance, while core-shell QDs feature a secondary semiconductor layer that protects the core from degradation and increases light efficiency. Recent advancements also highlight alloyed QDs, which use mixed materials to reduce internal losses and improve stability [1–4].

Examples of semiconductor-based quantum dots include:

- *Cadmium Selenide*: A widely researched core material known for its bright and pure color output, often used in high-end displays.
- *Silicon Quantum Dots*: These are composed mostly of silicon and are valued for their low toxicity and high light yield (up to 90%), making them ideal for biological imaging.
- *Indium Phosphide*: Frequently used as an environmentally friendly, “cadmium-free” alternative in consumer electronics like QLED TVs.
- *Perovskite Quantum Dots*: They have a defect-tolerant structure. A newer class of materials recognized for exceptional color purity and high defect tolerance, useful for next-generation solar cells and LEDs. They are highly efficient light emitters, reaching a quantum yield of 80%.
- *Lead Sulphide*: These are specifically effective for applications requiring near-infrared light absorption and emission such as night-vision technology.

Carbon Quantum Dot

Carbon Quantum Dots (CQDs) are zero-dimensional carbon nanoparticles, typically under 10 nm in size, that have revolutionized the field of sustainable nanotechnology. According to recent research, their special power lies in their unique tunable photoluminescence, where they emit different colors based on their size and surface chemistry, a phenomenon driven by the quantum confinement effect. Unlike traditional semiconductor dots that rely on toxic heavy metals, CQDs are intrinsically biocompatible and non-toxic, making them safe for medical use.

Recent studies highlight their incredible efficiency; specifically, heteroatom doping (using nitrogen or boron) can push photoluminescence quantum yields to nearly 99%. Their primary advantage is versatility; they are currently being engineered for targeted drug delivery, heavy metal detection in water, and even high-moisture retention for cosmetic applications like lipsticks. Because they can be synthesized from organic “green” sources like fruit peels or biowaste, they offer a low-cost, eco-friendly alternative for next-generation bioimaging and optoelectronic displays [5].

Carbon Quantum Dots Are Classified into

- *Graphene Quantum Dots (GQDs)*: Crystalline, disk-like fragments of graphene (sp^2 hybridized) that exhibit strong quantum effects and high conductivity.
- *Carbon Nanodots (CNDs)*: Spherical, mostly amorphous structures with high oxygen content, often used as non-toxic fluorescent probes.
- *Carbonized Polymer Dots (CPDs)*: A hybrid structure featuring a carbonized core surrounded by dense polymer chains, gaining power through crosslink-enhanced emission to achieve long decay lifetimes for sensing dissolved oxygen.

Based on the Technique to Synthesise

Colloidal Quantum Dots (CQDs)

The energy bandgap of colloidal quantum dots (CQDs) can be engineered by modulating their physical dimensions and elemental composition, enabling precise control over their optical absorption and emission spectra (Figure 2(a)). These nanocrystals are fabricated through advanced methodologies that allow for strict stoichiometric and morphologic regulation, including the hot-injection method, solvothermal synthesis, and ligand-assisted reprecipitation (LARP). This spectral tunability extends across the visible and near-infrared (NIR) wavelengths. Furthermore, CQDs can achieve photoluminescence quantum yields of up to 80%, rendering them highly efficient emitters for solid-state lighting and display technologies. They typically exhibit a narrow full-width at half maximum (FWHM), which ensures exceptional color purity necessary for high-definition light-emitting diodes. Crucially, many CQDs are synthesized from non-toxic precursors, offering a biocompatible alternative that significantly mitigates the cytotoxicity risks associated with conventional heavy-metal-based quantum dots [6].

Magnetic Quantum Dots (MQDs)

Magnetic quantum dots (MQDs) are nanoscale semiconductor particles that uniquely couple quantum confinement effects with distinct magnetic properties (Figure 2(b)). These multifunctional nanocrystals are typically synthesized via advanced methodologies, such as colloidal synthesis, laser ablation, solvothermal, or hydrothermal processes, which allow for structural regulation. MQDs predominantly exhibit superparamagnetic behavior, meaning they possess strong magnetization when exposed to an external magnetic field but retain zero remanent magnetization once the field is removed. This magnetic responsiveness can be precisely tuned by modifying the nanocrystals' size, morphology, and surface chemistry. Crucially, the ability to engineer their surface characteristics facilitates functionalization with specific biomolecules or polymers, significantly enhancing their efficacy in targeted drug delivery systems and advanced biomedical imaging [7].

Fluorescent Quantum Dots

Fluorescent quantum dots are semiconductor nanocrystals that have attracted significant attention in biomedical imaging, optical sensing, and targeted therapeutics due to their exceptional photophysical properties (Figure 2(c)). These nanocrystals exhibit high photoluminescence quantum yields, enabling the generation of intense optical signals upon excitation. Because of quantum confinement effects, their emission wavelengths can be precisely tuned by modulating the nanocrystal diameter, yielding a broad spectral range that spans from visible blue to the NIR region, a feature highly advantageous for multiplexed detection assays [8, 9].

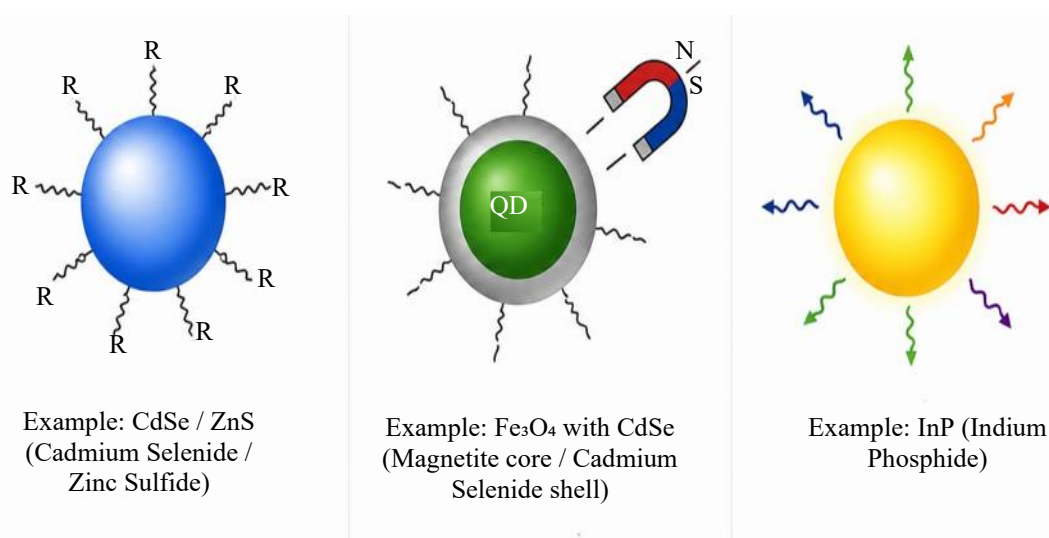


Figure 2. (a) Colloidal QD, (b) Magnetic QD, and (c) Fluorescent QD.

SYNTHESIS OF QUANTUM DOTS

The synthesis of quantum dots (QDs) is generally categorized into two fundamental approaches based on starting material: Top–Down and Bottom–Up [10–14].

Top–Down Methods (Physical/Chemical Breakdown)

The top–down approach is essentially a subtractive manufacturing process (Figure 3(a)). It starts with a macroscopic bulk material (like a chunk of silicon or a graphite rod) and uses physical, chemical, or thermal energy to break it down into nanometer-sized particles.

Mechanical Milling (High-Energy Ball Milling)

High-energy ball milling is a mechanical process that shrinks bulk materials like metal or graphite into nanocrystalline powders. By rotating or vibrating a sealed vial at high speeds, heavy steel or ceramic balls repeatedly crash into the material with massive kinetic energy. These intense impacts create shear stresses that first flatten particles into thin flakes, which then fuse through cold welding. As the material continues to harden and become brittle, it eventually fractures and shatters into millions of nanoscale pieces, effectively reducing the size from millimeters to nanometers through a continuous cycle of breaking and rebuilding.

Laser Ablation

Laser ablation is a high-tech top–down method that uses a focused, high-powered pulsed laser to convert solid targets, like silver or silicon, submerged in liquid, into exceptionally clean nanoparticles. When the laser strikes, it vaporizes a tiny spot of the solid into a super-heated plasma plume of ions. This hot cloud expands rapidly, sending a shockwave through the surrounding liquid before being instantly chilled by the cold environment. This rapid quenching forces the vaporized atoms to cluster together, forming tiny, spherical nanospheres that remain suspended in the liquid, making them perfect for advanced energy storage research despite the low production volume.

Chemical Etching

Chemical etching is a top–down synthesis method that creates quantum dots by using a chemical acid bath to shrink larger crystals. In this process, a solid semiconductor is dipped into a strong etchant solution that reacts with and dissolves surface atoms. By precisely controlling the chemical strength and immersion time, the outer layers are eaten away until the material is refined into perfect nanoscale particles, effectively reducing bulk chunks into quantum-sized dots without building them from scratch.

Bottom–Up Methods (Chemical Synthesis)

This method builds nanomaterials from the ground up, starting with individual atoms or molecules (Figure 3(b)). It is like an architect building a house brick-by-brick to create a precise structure. Key features of this method are high precision for creating perfect shapes like dots, wires, or tubes, pure quality to produce very clean materials with almost no flaws, and easy changes, which can tune the final shape just by adjusting the temperature. These features are the industry standard for bioimaging applications because they allow for precise tuning of the QD size (and thus color) through chemical kinetics.

Colloidal Synthesis (Hot-Injection Method)

Colloidal synthesis is a liquid-phase Bottom–Up approach where chemically grown nanocrystals are suspended in a solvent. It is widely considered the most effective way to produce high-quality quantum dots (0D nanostructures) with precise size control. This mechanism describes the colloidal synthesis of quantum dots, which progresses through three sequential phases governed by precursor concentration. Initially, nucleation occurs when precursor chemicals are rapidly injected into a high-temperature solvent, decomposing into reactive monomers. Once these monomers reach critical supersaturation, they spontaneously aggregate to form the initial crystalline seeds, or nuclei. Following this burst of nucleation, the monomer concentration drops below the threshold required to form new seeds, initiating

the growth stage. During this phase, remaining monomers deposit directly onto the existing nuclei, with the final nanocrystal size determined by modulating temperature and reaction time. Finally, stabilization is achieved through surface functionalization, where capping agents or surface ligands bind to the outer layer of the quantum dots. This protective organic shell introduces steric or electrostatic hindrance, preventing particle aggregation and ensuring long-term colloidal stability.

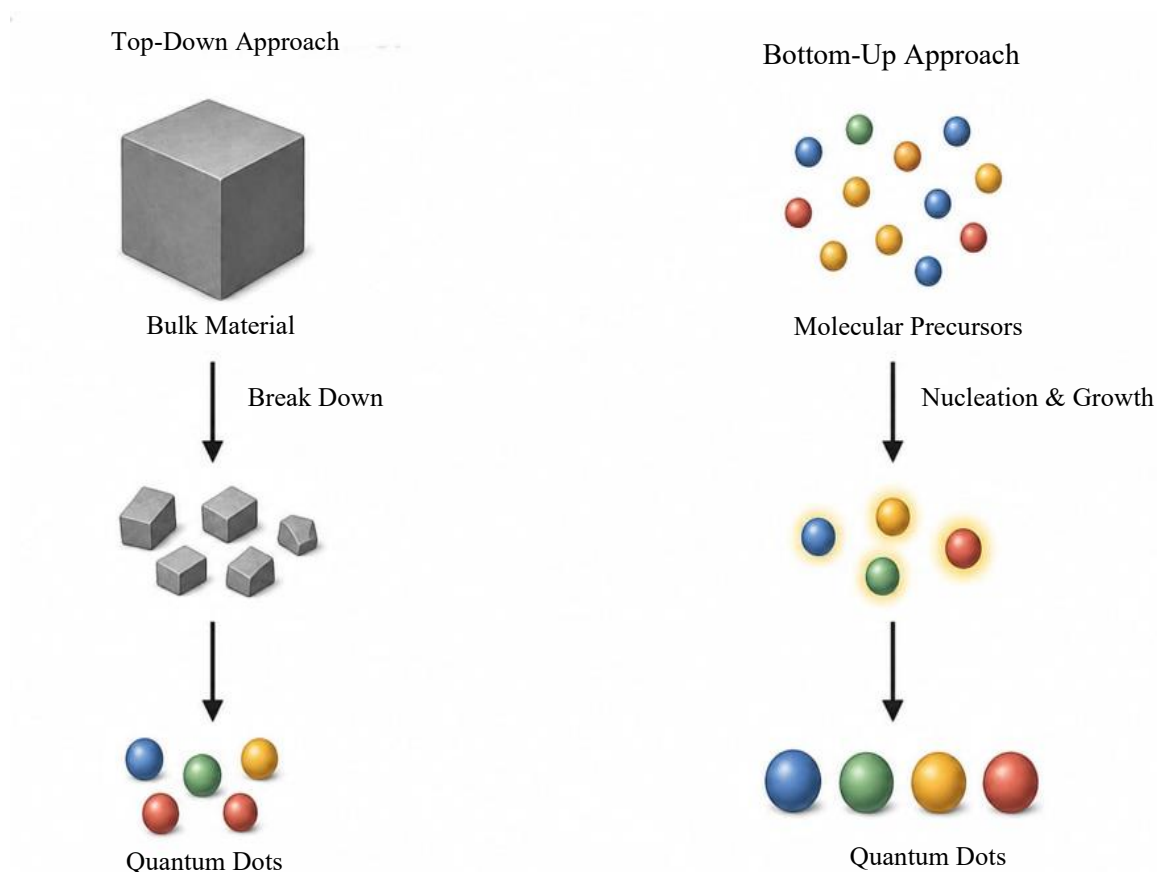


Figure 3. (a) Top–down approach and (b) bottom–up approach.

Hydrothermal and Solvothermal Synthesis

This method uses a pressure cooker approach, just as giant crystals grow deep inside the earth, scientists use this extreme heat and pressure to force atoms to bond into perfect nanocrystals. It is the Gold Standard for making battery materials like metal oxides. Precursors are placed in a sealed autoclave (a Teflon-lined stainless-steel container) with a solvent (water for hydrothermal, organic solvent for solvothermal).

This synthesis method relies on elevated pressure and temperature to enhance precursor solubility, promoting the development of highly pure crystals at temperatures well below those required for the hot-injection technique. The process begins by dissolving metal salts in water at room temperature, where they remain unreactive. This solution is then sealed inside a specialized, airtight steel reaction vessel known as an autoclave and heated in an oven to temperatures ranging from 100°C to 250°C. Because the system is completely sealed, the internal pressure increases dramatically, creating supercritical fluid conditions that make the water highly reactive. Under this intense environment, the mobilized metal atoms frequently collide and bond to initiate nucleation. These newly formed nuclei continuously accumulate atoms to undergo controlled crystal growth, ultimately assembling into intricate nanostructures, such as nanoflowers, depending on the total reaction duration. This method is often used for green synthesis of Carbon Quantum Dots using precursors like citric acid or glucose.

Sol-Gel Synthesis

Sol-Gel is a Soft Chemistry Bottom-Up strategy that builds solid Quantum Dots from a liquid at room temperature. Like making jelly, it transforms a liquid Sol (atomic precursors) into a solid Gel (3D network), ensuring molecular-level mixing for ultra-pure materials.

The sol-gel process begins with sol preparation, where metal precursors – such as salts or alkoxides – are dissolved in a solvent like water or alcohol. Next, hydrolysis occurs as water is introduced to generate reactive hydroxyl groups within the solution. These reactive species then undergo a condensation reaction, linking together while releasing water or alcohol byproducts to form a continuous, three-dimensional solid skeleton that spans the container, known as the gel. During the subsequent aging phase, the gel is left to rest, allowing the interconnected network to strengthen and thicken. The trapped liquid is then removed during the drying stage; oven drying produces a dense xerogel, while supercritical drying yields a highly porous, lightweight aerogel. Finally, the material undergoes calcination, a high-temperature heating process that eliminates remaining impurities and optimizes the final crystalline structure.

Chemical Vapor Deposition

This method turns a chemical into a gas, blow it over a hot surface, and let it settle down to build nanostructures atom-by-atom. The chemical vapor deposition process begins with gas injection, where source gases containing the material precursors are introduced into a heated furnace. Through thermal decomposition, intense temperatures reaching up to 1100°C break the gas molecules apart to liberate the individual atoms. These free atoms undergo adsorption as they deposit onto a flat substrate surface. During the surface reaction and growth phase, the atoms migrate across the substrate to stable bonding sites, clustering together to form zero-dimensional quantum dots rather than continuous layers, wires, or tubes. By precisely regulating the gas flow, this growth can be terminated while the structures remain at the nanoscale. Finally, during the exhaust phase, any unreacted gases are evacuated from the system, leaving behind ultra-pure nanocrystals.

FUNCTIONALIZATION OF QUANTUM DOTS

Functionalization refers to the surface modification of an already created quantum dot to change its properties such as stability, solubility, or biological targeting abilities. Scientists are improving Quantum Dots (QDs) by controlling their size and shape. They use “top-down,” “bottom-up,” or biological methods to build them. To use QDs safely in medicine, researchers must make them water-soluble and “body-friendly” (biocompatible) through special coatings so they can target specific cells without causing harm [15, 16].

Preparation of Water-Soluble QDs

Since Quantum Dots (QDs) are often made in oil-like (organic) liquids, they start water-repellent (Figure 4(a)). To use them in the human body, which is mostly water, scientists use two main “makeover” strategies:

The Protective Coat (Encapsulation)

This method wraps the QDs in a special shell that is “water-loving” on the outside and “oil-loving” on the inside. Scientists use tiny fat bubbles (liposomes), glass-like coatings (silica), or plastics (polymers). This shell makes them safe for the body and allows scientists to attach “hooks” to target specific areas like cancer cells.

The Part Swap (Ligand Exchange)

Instead of adding a coat, this method swaps the original water-repellent molecules (Hydrophobic molecules) on the QD surface for new, water-friendly one's, hydrophilic ones (like PEG or Mercaptoacetic acid). Scientists soak the QDs in a solution of new molecules until they naturally switch places. By using multi-dentate ligands, the connection will be much stronger and safer in molecules.

Both methods ensure the dots stay bright and stable while being safe enough for medical use.

Biomolecular Conjugation

To make Quantum Dots (QDs) useful in medicine, scientists must attach them to biological molecules like proteins or DNA. This process, called biomolecular conjugation, allows the dots to “recognize” and stick to specific targets like cancer cells (Figure 4(b)). Here are the common ways scientists “hook” these molecules together:

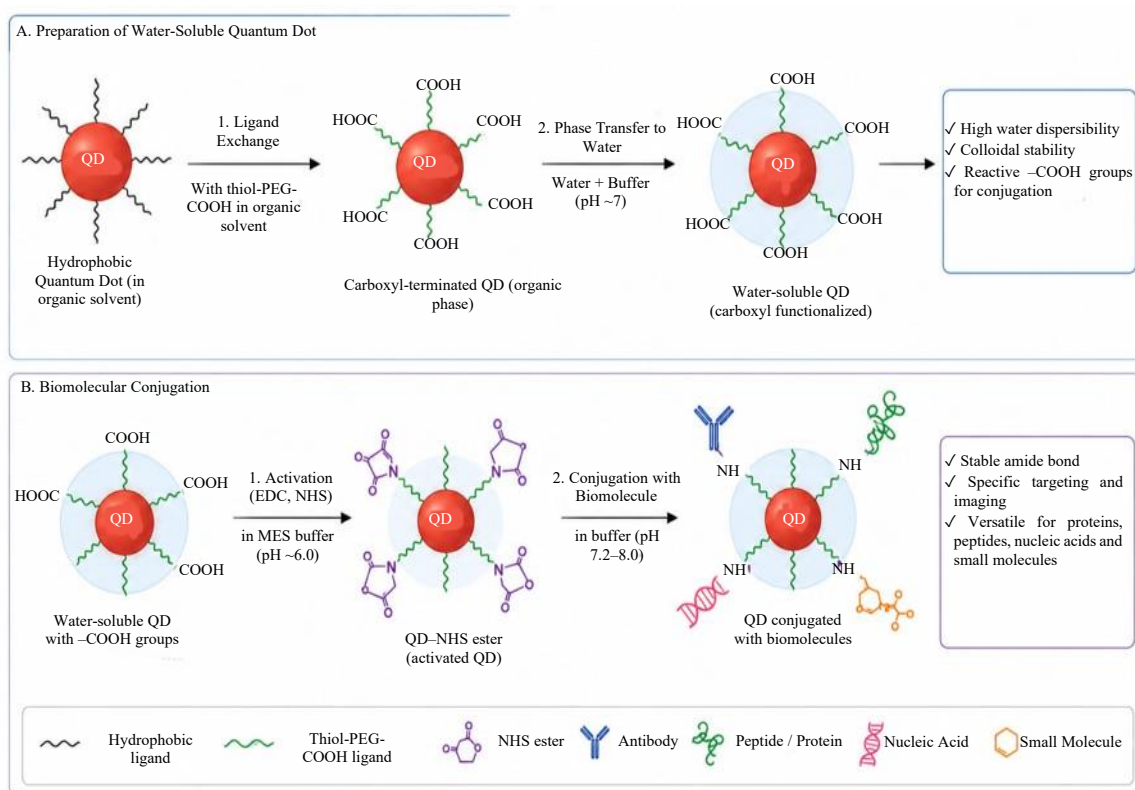


Figure 4. Functionalization of QD, (a) Preparation of Water –Soluble Quantum Dot and (b) Biomolecular Conjugation.

Simple Attachment (Physical Adsorption)

Think of this like static electricity. Molecules stick to the QD surface naturally. It’s easy but not very precise, and molecules can fall off or face the wrong way.

Chemical Superglue (Covalent Conjugation)

Now that the dot is in the water, it needs a target (like a cancer cell)

Covalent Conjugation (EDC/NHS Coupling)

This is the most precise way to “glue” an antibody to a QD.

- **Step 1 (EDC):** The EDC molecule reacts with the -COOH on the QD surface to “activate” it.
- **Step 2 (NHS):** NHS is added to make that connection more stable, creating an NHS-ester.
- **Final Step:** When an Antibody (the Y-shaped molecule) comes near, its amine group (-NH₂) attacks the NHS-ester. This forms a permanent chemical bond (an amide bond), locking the antibody onto the QD.

Natural Attraction (Metal-Affinity & Ligand-Receptor)

- **Metal-Affinity:** Certain protein tags (like Histidine) naturally “grip” the metal shell of the QD. It’s fast and very stable.

- *Ligand-Receptor*: Uses famous biological pairs that fit together like a lock and key such as Biotin and Streptavidin.

Advanced Methods (Click Chemistry & Virus Cages)

- *Click Chemistry*: A high-speed, “snap-together” reaction that is incredibly efficient and selective.
- *Virus Encapsulation*: Scientists hide the QD inside a hollow virus shell. This makes the dot look “natural” to the body, allowing it to hitch a ride and track how viruses move through cells.

TOXICITY OF QUANTUM DOTS

The toxicity of quantum dots (QDs) is a complex subject because their “poisonous” nature isn’t just about what they are made of, but how they interact with biological systems at the nanoscale [17].

Here is an explanation of the primary factors driving QD toxicity:

Compositional Toxicity (Heavy Metals)

Most traditional quantum dots (like CdSe or CdTe) contain heavy metals. Toxicity often occurs when these dots degrade inside a cell, releasing free metal ions. These cadmium ions can bind to tiger-like proteins in the mitochondria, disrupting cellular respiration and leading to cell death. Studies have shown that the release of these ions is the primary cause of acute cytotoxicity in unprotected core QDs. To mitigate this, researchers developed core-shell structures (e.g., CdSe/ZnS) to trap the toxic core.

Oxidative Stress (ROS Generation)

Even if the heavy metals stay trapped, QDs can kill cells through Reactive Oxygen Species (ROS). Due to their specialized electron properties, QDs can transfer energy to nearby oxygen molecules, creating free radicals. These radicals attack the cell membrane, proteins, and DNA (a process called oxidative stress). This often leads to inflammation or apoptosis (programmed cell death).

Size and Bioaccumulation

We know that QDs are so small (typically 2–10 nm), so the body has a hard time getting rid of them. Once injected, QDs tend to migrate to the liver, spleen, and kidneys. If the body cannot clear them via the renal system (kidneys), they stay in these organs for long periods, potentially leading to chronic inflammation.

BIOIMAGING APPLICATIONS FOR QDS

Bioimaging applications of QDs (Figure 5) are generally categorized into three distinct domains: in vivo Bioimaging, in vitro Bioimaging, and biosensing and detection [17–19].

In Vivo Bioimaging

In vivo imaging refers to the visualization of biological processes within a living, intact organism. The most significant research milestone between 2016 and 2026 has been the move toward the NIR-II Window.

- *Deep Tissue Vascular Imaging*: Traditional imaging struggles with light scattering. Research in 2021 (Frontiers in Chemistry) and subsequent updates in 2026 demonstrate that Silver Sulphide QDs emitting in the 1000–1700 nm range can visualize deep blood vessels in the brain and limbs with sub-millimeter clarity through skin and bone. This allows for non-invasive vascular mapping with a resolution of a few micrometers at depths of up to 10 mm. Scientists now use this for real-time monitoring of blood-flow dynamics in the brain and hindlimbs without removing skin or using ionizing X-rays.
- *Image-Guided Surgery (IGS)*: Clinical trials in 2025 have used QDs to “light up” tumor margins. Surgeons use NIR-sensitive cameras to identify cancerous tissue in real-time during an operation, ensuring total tumor removal while saving healthy nerves.

- *Lymphatic System Mapping*: By tracking how QDs drain into “sentinel” lymph nodes, surgeons can identify exactly which nodes to remove, sparing healthy tissue.
- *Deep-Brain Imaging*: Using Graphene or Silicon-based QDs with multiphoton microscopy, researchers can penetrate the blood–brain barrier to visualize neural circuits and Alzheimer’s plaque progression.
- *Theragnostic (Cargo Tracking)*: QDs act as a “GPS” for gene therapy, allowing doctors to see exactly when a CRISPR-loaded nanoparticle reaches its target organ before the gene editing process begins.

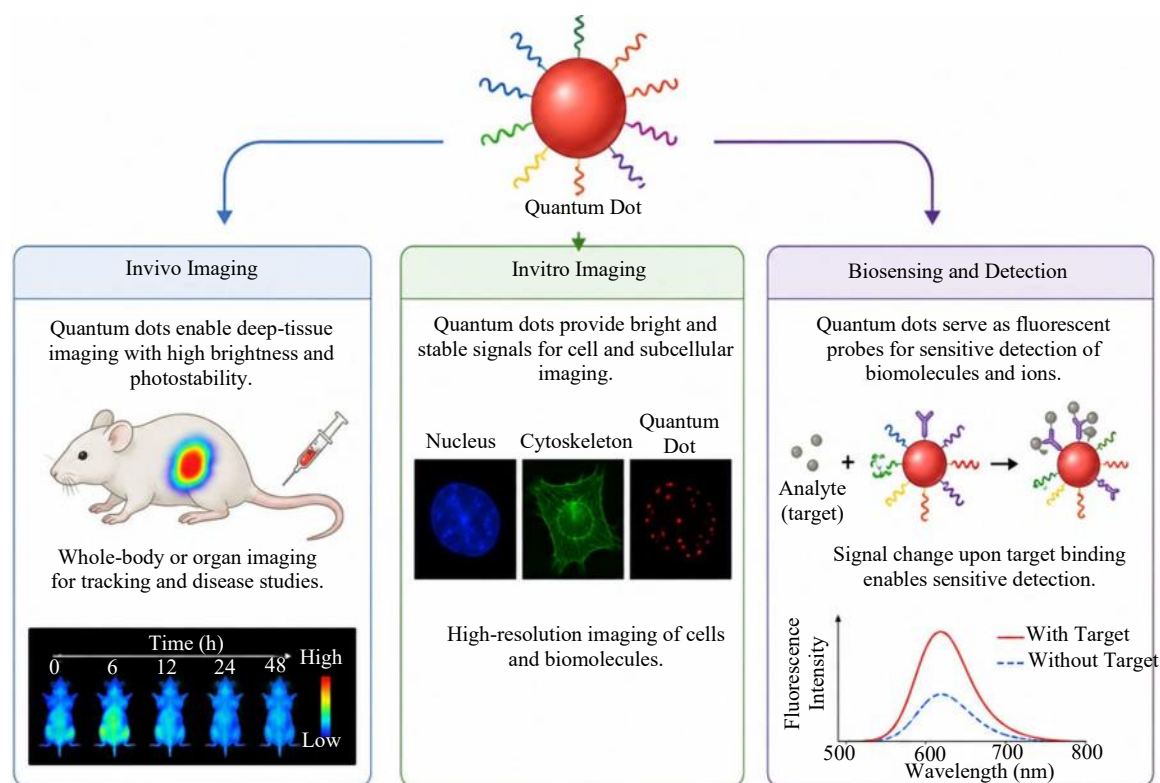


Figure 5. Bioimaging applications of quantum dot.

In Vitro Bioimaging (Cellular Level)

In vitro imaging involves using QDs to study biological processes in controlled environments outside a living organism such as in cell cultures or tissue slices.

- *Single-Protein Monitoring*: Researchers attach a single QD to a single membrane protein (e.g., a neurotransmitter receptor). This allows them to watch the lateral diffusion of proteins across the cell membrane, which is critical for understanding how brain cells communicate.
- *Live-Cell Organelle Dynamics*: Using “Green” Carbon QDs (CQDs), scientists can observe the real-time movement of mitochondria and lysosomes for several days without causing phototoxicity (cell death from light).
- *High-Content Screening (HCS)*: Because QDs are incredibly bright, machines can automatically scan thousands of cells to see how new drug candidates affect organelle shapes and structures.
- *Intracellular Sensing*: Modern “dual-emitting” QDs act as microscopic thermometers or pH meters, where one color stays constant as a reference while the other changes based on the cell’s internal environment.

Biosensing and Detection

This field uses QDs as “smart switches” to detect specific pathogens or toxins. This application uses QDs as “active sensors” that change their signal in response to a specific biological trigger.

- *Liquid Biopsy*: QDs can detect circulating tumor DNA (ctDNA) in a single drop of blood, potentially catching cancer recurrence months before a physical tumor appears.
- *FRET-Based Molecular Beacons*: Fluorescence Resonance Energy Transfer (FRET) allows QDs to act as switches. These sensors are off by default. When a specific virus (like COVID-19) binds to them, the QD turns on, providing an instant diagnostic signal. A QD is paired with a quencher. When a specific target (like a glucose molecule or a specific DNA sequence) is present, it breaks the bond, and the QD suddenly begins to glow.
- *Wearable Sweat Sensors*: Graphene Quantum Dots (GQDs) have been integrated into wearable sensors (like smartwatches) to detect glucose or lactic acid in sweat. So these are used in monitoring diabetic patients non-invasively.
- *Environmental & Pathogen Detection*: QDs are used in lab-on-a-chip devices to detect waterborne pathogens or heavy metal toxins. Their high surface-area-to-volume ratio allows for the detection of even a few parts per billion (ppb).

ADVANTAGES AND DISADVANTAGES OF QDS

Advantages of Quantum Dots

Here are the specific advantages of quantum dots in bioimaging and diagnostics:

- Quantum dots possess a unique size-tunable emission property where the color of light they emit can be shifted across the entire spectrum from ultraviolet to the near-infrared region simply by modifying the physical diameter of the nanocrystal during synthesis.
- They exhibit exceptional photostability, meaning they are highly resistant to photobleaching; unlike traditional organic dyes that fade within seconds under a microscope, quantum dots can glow for hours or days, enabling the long-term tracking of cellular processes.
- These nanocrystals feature broad absorption coupled with narrow emission, allowing a single light source to excite multiple colors of dots simultaneously without the resulting signals overlapping, which is a massive advantage for multiplexed diagnostic testing.
- Quantum dots offer extreme brightness due to their high molar extinction coefficients and quantum yields, providing a signal-to-noise ratio that allows for the detection of single molecules or rare cancer biomarkers that would otherwise be invisible.
- Advanced engineering has enabled deep-tissue penetration via the NIR-II window, where quantum dots emitting in the 1000–1700 nm range can bypass the scattering effects of skin and bone to provide high-resolution images of internal organs in living subjects.

Disadvantages of Quantum Dots

The primary disadvantages of quantum dots include:

- Many of the most effective quantum dots are made from heavy metals, specifically cadmium (e.g., CdSe). This poses a major risk. They can be highly toxic to living organisms, which limits their use in human medical applications. Their production and disposal require extremely careful handling to avoid ecological damage.
- Compared to traditional organic fluorophores, QDs are relatively bulky. This makes it harder for them to diffuse across cellular membranes, often requiring complex delivery methods that can cause cell injury.
- Producing high-quality QDs (especially those emitting blue light) requires precise, difficult-to-control conditions. This complexity leads to high production costs and makes it hard to scale up manufacturing. It is difficult to maintain perfectly uniform sizes. Minor variations in size result in different emission wavelengths, complicating multiplexing (using multiple colors at once).
- Their performance is highly sensitive to external factors. Changes in pH levels, ionic strength, or the presence of specific chemicals in their surroundings can negatively impact their stability and fluorescence.

RECENT ADVANCES IN QUANTUM DOT AND ITS BIOIMAGING APPLICATIONS

Latest Research Findings

Recent research papers from the last decade, particularly those published between 2023 and 2026, demonstrate a significant transition toward “green” and high-performance quantum dots (QDs) for clinical diagnostics. A primary finding involves the emergence of Carbon Quantum Dots (CQDs) synthesized from biowaste, such as garlic peels or banana skins, which have largely superseded cadmium-based dots due to their intrinsic biocompatibility and low systemic toxicity. These materials are now being used for real-time intracellular imaging and stem cell tracking without the risk of heavy-metal leaching.

Another critical breakthrough is the expansion into the NIR-II biological window (1000–1700 nm). Research indicates that Indium Phosphide (InP) and Silver-based QDs emitting in this range offer unprecedented deep-tissue penetration and high spatial resolution by minimizing light scattering and tissue autofluorescence. This has enabled non-invasive mapping of the brain vasculature and early detection of metastatic clusters in lymph nodes.

Furthermore, the shift toward targeted theragnostics has turned QDs into multifunctional agents. Findings show that QDs functionalized with specific ligands, such as folic acid or antibodies, can selectively target cancer cells for both diagnostic “glowing” and the delivery of chemotherapeutic cargo like doxorubicin. This dual-mode capability allows for real-time monitoring of drug release and therapeutic efficacy. Finally, recent studies highlight advances in renal clearance, where surface-passivated QDs are engineered to be small enough to be excreted safely through the kidneys, addressing the long-standing concern of nanoparticle accumulation in the liver.

Case Studies

Recent research into quantum dots (QDs) for bioimaging highlights their superior photostability and brightness compared to traditional organic dyes.

Targeted in Vivo Pancreatic Cancer Detection Using Perovskite Scintillators

A prominent challenge in deep tissue bioimaging is the autofluorescence and scattering that occur when using visible light on thick biological specimens. To overcome this, a case study explored using cesium lead bromide (CsPbBr₃) perovskite quantum dot scintillators for high-resolution in vivo X-ray imaging. In this study, the perovskite quantum dots were double encapsulated in protective silicon dioxide (SiO₂) layers and bioconjugated with specific antibodies targeting pancreatic cancer cell biomarkers. When tested in animal models, these engineered QDs successfully bound to pancreatic tumors, converting low-dose X-ray excitation into high-contrast luminescence. This allowed researchers to clearly delineate, and image tumor margins buried deep within thick tissue structures where conventional optical probes fail [20].

Dual-Modality Tumor Diagnostics with Gadolinium-Doped Carbon Dots

Combining multiple imaging techniques into a single nanostructure, known as multimodal imaging, enables clinicians to gather complementary diagnostic data simultaneously. Recent research evaluated the efficacy of Gadolinium-doped carbon dots (Gd-CD) derived via green engineering as a dual-modality probe for fluorescence and magnetic resonance imaging (MRI). The carbon-based core provided highly efficient, tunable visible photoluminescence for micro-level cellular tracking, while the incorporated gadolinium ions delivered strong T₁ contrast enhancement for macro-level MRI scanning. Case models demonstrated excellent biocompatibility and low systemic toxicity, validating (Gd-CDs) as highly stable, safe alternative probes for tracking tumor masses across both optical and magnetic imaging platforms [20].

Multifunctional Gold Quantum Dot

Au-QDs are often classified as ultra small gold nanoclusters (Au-NCs) as breakthrough probes emitting in the second biological window (NIR-II, 1000–1700 nm) for deep-tissue cancer diagnostics.

Researchers investigated how these biocompatible, photostable Au-NCs track intracellular microenvironments within fibroblasts and macrophages. By engineered tracking of core-ligand alterations, the study successfully monitored live cell internalization and localized tumor signatures in real time with zero tissue autofluorescence. These are being developed as theragnostic agents, probes that can simultaneously perform diagnostic imaging and deliver targeted drug payloads. Unlike metal alloys, gold is chemically inert, preventing heavy-metal leaching in the body. It is mainly used in targeted drug delivery and cellular labelling in oncology and cardiology [21].

Antibody-Conjugated QDs for Prostate Cancer Targeting

A case study involving antibody-conjugated QDs showed that these probes can effectively target human prostate cancer in nude mice. The results indicated that the probes accumulate at tumor sites through both antibody binding to specific biomarkers and the enhanced permeability and retention effect, allowing for multicolor fluorescence imaging of cancer cells in vivo [22].

Silver-Based (Ag_2S) QDs for Surgical Navigation

Research published in early 2026 highlights Silver-based quantum dots as a stable, non-toxic alternative for real-time angiography. They provide ultra-high spatial resolution ($\approx 40 \mu\text{m}$), which is essential for tracking the tiny blood vessels that feed tumors. Application of this QD is High-resolution surgical navigation and monitoring of drug distribution in vivo [23].

CHALLENGES, MITIGATION STRATEGIES, AND FUTURE PERSPECTIVES

Challenges and Mitigation Strategies

While Quantum Dots (QDs) are revolutionary, their transition from laboratory research to clinical and industrial applications has been met with significant hurdles. Research has focused heavily on finding mitigation strategies to make these nanocrystals safer, more stable, and more reliable.

Toxicity of Heavy Metal Cores

The most critical challenge for medical use is that many high-performance QDs (like CdSe or PbS) contain toxic heavy metals.

- *The Challenge:* If the outer shell of a QD degrades, it can release Cadmium or Lead ions, causing DNA damage and cell death.
- *Mitigation Strategy: Core-Shell Engineering:* Developing thick, multi-layer shells (e.g., CdSe/ZnS/Silica) that act as a chemical “vault” to prevent ion leaching.
- *Elemental Substitution:* Shifting to naturally non-toxic materials, such as Indium Phosphide (InP), Silicon, or Carbon Quantum Dots (CQDs), synthesized from organic waste like citrus peels
- *Fluorescence Blinking:* QDs often toggle randomly between a bright and dark state, which interferes with precise data collection.
- *The Challenge:* Blinking makes it difficult to track single molecules continuously or to use QDs in quantum computing, where a steady stream of photons is required.
- *Mitigation Strategy: Alloyed Grading:* Creating a graded interface between the core and the shell rather than a sharp boundary. This smooth transition prevents the electron traps that cause blinking.
- *Chemical Additives:* Bathing QDs in antioxidant solutions (like vitamin C derivatives) to plug surface defects that cause the dark state.

Long-Term Bioaccumulation

Because QDs are inorganic, the human body does not have a natural way to break them down.

- *The Challenge:* Larger QDs accumulate in the liver and spleen, leading to concerns about chronic inflammation over many years.
- *Mitigation Strategy: Renal-Clearable Designs:* Engineering QDs to have a hydrodynamic diameter of less than 5.5 nm. This size is small enough to bypass the liver and be filtered directly by the kidneys and excreted in urine.

- *Biodegradable Coatings*: Using specialized polymers that eventually break apart, allowing the tiny inorganic core to be cleared more easily.

Non-Specific Binding (Background Noise)

QDs are sticky and often cling to healthy tissue instead of just the intended target.

- *The Challenge*: This creates high background noise in images, making it hard to distinguish a small tumor from healthy cells.
- *Mitigation Strategy: PEGylation*: Coating the QDs with Polyethylene Glycol (PEG), which creates a “stealth” layer that prevents the dot from sticking to unintended proteins.
- *Zwitterionic Ligands*: Using molecules that have both positive and negative charges to create a neutral surface, drastically reducing off-target sticking.

Environmental and Regulatory Barriers

Strict international regulations (like RoHS) limit the use of hazardous materials in consumer electronics and medicine.

- *The Challenge*: The high cost of meeting these regulations and the difficulty of large-scale, uniform production.
- *Mitigation Strategy: Microfluidic Synthesis*: Moving from batch cooking to automated microfluidic chips. This allows for continuous, highly reproducible production with 99% uniformity, reducing waste and cost.

Future Perspective

The future of quantum dots (QDs) is centered on environmental sustainability, high-resolution optoelectronics, and next-generation quantum computing. A major shift is occurring toward cadmium-free alternatives, such as Indium Phosphide (InP) and Carbon QDs, to meet strict global safety regulations while maintaining high photoluminescence quantum yields.

In the display industry, the integration of QD-OLED technology is expected to dominate, providing unprecedented color accuracy and energy efficiency for μ -LEDs and flexible electronics.

The future of quantum dot (QD) bioimaging is shifting toward NIR-II imaging (1000–1700 nm) and cadmium-free formulations to ensure deep-tissue penetration and clinical safety. Research suggests that Ag₂S and carbon-based QDs will dominate due to their low toxicity and superior signal-to-noise ratios. Furthermore, some research highlights the potential of intelligent QD probes for real-time surgical guidance and theragnostics, where imaging and drug delivery occur simultaneously. These advancements, supported by recent market analysis, aim to transition QDs from laboratory tools to standard clinical diagnostics for early-stage cancer detection.

CONCLUSION

The study of quantum dots (QDs) has evolved from a complex physics concept into a vital tool for modern medicine. Unlike traditional dyes, these tiny crystals can be “tuned” to glow in specific colors simply by changing their size. They are also much tougher, meaning they don’t fade away quickly during medical exams. This has transformed bioimaging, allowing doctors to see deep inside the body with high-resolution, multi-colored views that help track single molecules or detect early-stage cancer.

The real power of this research lies in theragnostics, creating particles that can both find a disease and treat it at the same time. This is a huge step forward for precision surgery and targeted therapy. However, a major hurdle remains: many common QDs contain heavy metals, like cadmium, which can be toxic to the body and the environment.

Looking ahead, the focus is shifting toward greener alternatives. Researchers are now developing carbon-based dots and graphene versions that are much safer for human use. The next phase of work

involves using artificial intelligence to analyse the glowing signals more accurately and designing better coatings so the body can flush the particles out safely after use. By balancing their incredible brightness with higher safety standards, quantum dots are set to make real-time, molecular-level checkups a standard part of healthcare.

REFERENCES

1. Mirnajafizadeh F, Stride JA. A brief review on core/shell quantum dots. *SDRP J Nanotechnol Mater Sci.* 2020;2(1):121–126.
2. Remya VR, Prajitha V, George JS, Jibin KP, Thomas S. Quantum dots: A brief introduction. In: *Nanoscale Processing*. Elsevier; 2021. p. 181–196.
3. AbouElhamd RA, Al-Sallal KA, Hassan A. Review of core/shell quantum dots technology integrated into building's glazing. *Energies.* 2019;12(6):1058.
4. Sahu J, Prusty D, Mansingh S, Parida K. A review on alloyed quantum dots and their applications as photocatalysts. *Int J Hydrogen Energy.* 2023;48(75):29097–29118.
5. Singh I, Arora R, Dhiman H, Pahwa R. Carbon quantum dots: Synthesis, characterization and biomedical applications. *Turk J Pharm Sci.* 2018;15:219–230.
6. Meng L, Xu Q, Zhang J, Wang X. Colloidal quantum dot materials for next-generation near-infrared optoelectronics. *Chem Commun.* 2024;60:1072–1088.
7. Akbarzadeh A, Samiei M, Davaran S. Magnetic nanoparticles: Preparation, physical properties, and applications in biomedicine. *Nanoscale Res Lett.* 2012;7:144.
8. Gaurav A, Jain A, Tripathi SK. Review on fluorescent carbon/graphene quantum dots: Promising material for energy storage and next-generation light-emitting diodes. *Materials.* 2022;15(22):7888.
9. Wang Z, Yao B, Xiao Y, Tian X, Wang Y. Fluorescent quantum dots and its composites for highly sensitive detection of heavy metal ions and pesticide residues: A review. *Chemosensors.* 2023;11(7):405.
10. Murray CB, Norris DJ, Bawendi MG. Synthesis and characterization of nearly monodisperse CdE (E = sulfur, selenium, tellurium) semiconductor nanocrystallites. *J Am Chem Soc.* 1993;115.
11. Singh I, Arora R, Dhiman H, Pahwa R. Carbon quantum dots: Synthesis, characterization and biomedical applications. *Turk J Pharm Sci.* 2018;15:219–230.
12. Sofia M, Mariya A, Aleksandr V. Silicon quantum dots: Synthesis, encapsulation, and application in light emitting diodes. *Front Chem.* 2020;8:7.
13. Anikin KV, Melnik NN, Simakin AV, Shafeev GA, Voronov VV, Vitukhnovsky AG. Formation of ZnSe and CdS quantum dots via laser ablation in liquids. *Chemical physics letters.* 2002 Dec 10;366(3-4):357-60.
14. Huang Z, Ren L. Large scale synthesis of carbon dots and their applications: A review. *Molecules.* 2025;30:774.
15. Vibhute A, Patil T, Gambhir R, Tiwari AP. Fluorescent carbon quantum dots: Synthesis methods, functionalization and biomedical applications. *Appl Surf Sci Adv.* 2022;11:100311.
16. Karakoti AS, Shukla R, Shanker R, Singh S. Surface functionalization of quantum dots for biological applications. *Adv Colloid Interface Sci.* 2015;215:28–45.
17. Gidwani B, Sahu V, Shukla SS, Pandey R, Joshi V, Jain VK, et al. Quantum dots: Prospectives, toxicity, advances and applications. *J Drug Deliv Sci Technol.* 2021;61:102308.
18. Avirup P, Patra PP. A review on quantum dots (QDs) and their biomedical applications. *4open.* 2023;6(1).
19. Chinnathambi S, Shirahata N. Recent advances on fluorescent biomarkers of near-infrared quantum dots for in vitro and in vivo imaging. *Sci Technol Adv Mater.* 2019;20:337–355. doi: 10.1080/14686996.2019.1590731.
20. Le N, Kim K. Current advances in the biomedical applications of quantum dots: Promises and challenges. *Int J Mol Sci.* 2023;24(16):12682.
21. Jindal S, Jindal S. Applications of gold nanoparticle, quantum dot and magnetic nanoparticle. *J Biomed Nanotechnol Phys Rep.* 2025:44–52.

22. Pang J. Research progress on the biological applications of Ag-based quantum dots: Targeted antibody conjugation for prostate-specific antigens. *Appl Phys.* 2026;16(5):447–455.
23. Wang J, Huang Z, Wu Y, Jiang X, Ji Y, Braeckmans K, Wang M, Wang L, Chen WR, Xia Y, Tang Z. Long-term in vivo immune tracking nanoplatfrom based on Ag₂S quantum dots for the photothermal immunotherapy of breast cancer. *BMC biology.* 2025 Apr 28;23(1):111.