

Quantum Dots in Oral Diagnostics and Theranostics: Promise and Preclinical Status

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Abstract

Quantum dots in oral diagnostics and theranostics represent a rapidly evolving, largely preclinical strategy that couples highly sensitive optical imaging with targeted therapeutic delivery in the oral cavity. Their size-dependent emission, high photostability, and broad excitation spectra allow bright, multiplexed visualization of key molecular events in oral potentially malignant disorders and oral squamous cell carcinoma, while surface functionalization with antibodies, peptides, or small-molecule ligands enables selective binding to dysplastic and malignant epithelial cells. In experimental oral oncology, quantum dot-bioconjugates directed against biomarkers, such as EGFR and proliferation markers, have demonstrated significantly higher fluorescence contrast between diseased and healthy tissues than conventional fluorophores, supporting improved sensitivity and specificity for early lesion detection and margin assessment in ex vivo biopsies and small in vivo cohorts. Parallel work in nanodentistry extends these platforms beyond cancer, using carbon and other low-toxicity quantum dots for high-resolution visualization of enamel demineralization, biofilms, periodontal inflammation, and pulp or periapical models, and conceptually integrating them into smart restorative materials and lab-on-chip biosensors for real-time monitoring of caries and periodontal disease activity. Nevertheless, the clinical translation of quantum dots into routine chairside diagnostics and theranostics remains constrained by concerns over heavy-metal toxicity, long-term biodistribution, photodegradation, and the complexity of regulatory approval, so current applications are confined to preclinical imaging, proof-of-concept theranostic designs, and early-stage translational studies rather than established standard of care.

Keywords: Quantum dots, nanodentistry, bioimaging, oral cancer, theranostics, surface functionalization, biocompatibility, dental diagnostics

INTRODUCTION

Quantum dots (QDs) are emerging as transformative nanomaterials in biomedical research, with dentistry increasingly exploring their potential as diagnostic and therapeutic (“theranostic”) tools. These nanoscale semiconductor crystals, typically ranging from 2 to 10 nanometers in diameter, exhibit unique quantum confinement effects that give rise to exceptional optical properties. Unlike conventional organic fluorophores, QDs possess size-tunable emission spectra – meaning their fluorescence color

can be precisely controlled by altering particle size – along with broad excitation profiles, high quantum yields, and narrow, intense emission bands. These photophysical advantages enable superior brightness, photostability, and multiplexed imaging capabilities, allowing simultaneous visualization of multiple molecular targets using a single excitation source.

In dental and oral health sciences, such properties translate into significant diagnostic improvements, particularly in the early detection of oral potentially malignant disorders (OPMDs), dysplasia, and oral squamous cell carcinoma (OSCC). QD-based fluorescent probes can facilitate subcellular imaging and biomarker identification with higher sensitivity

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and resolution compared to traditional dyes. Moreover, their long emission lifetime and resistance to photobleaching make them valuable for long-term cellular tracking and real-time molecular imaging. Functionalization of QD surfaces with biocompatible coatings, such as polyethylene glycol (PEG), antibodies, peptides, folate, or epidermal growth factor receptor (EGFR) ligands, enhances aqueous stability and enables selective targeting of malignant or premalignant oral epithelial cells.

The versatility of QD core compositions underpins their diverse biomedical suitability. Common materials include II–VI semiconductors (CdSe, CdTe, ZnS) and III–V types (InP), while carbon and silicon QDs have attracted attention for their lower toxicity and improved biocompatibility – key factors for dental and intraoral applications. Despite these promising developments, most QD applications in dentistry remain at the experimental or preclinical stage. Practical barriers, such as potential cytotoxicity, photodegradation, and challenges in regulatory approval, must be overcome before routine chairside integration. Nevertheless, ongoing research in QD engineering, toxicity mitigation, and surface modification continues to advance their potential role in next-generation oral diagnostics, personalized dental care, and precision imaging platforms.

Quantum dots (QDs) are emerging as highly sensitive fluorescent probes and theranostic platforms in dentistry, enabling subcellular oral cancer imaging, early detection of dysplasia and OSCC, and research-level enhancement of dental caries/periodontal diagnostics, but are still largely preclinical and experimental for routine chairside use [1–4].

FUNDAMENTALS OF QUANTUM DOTS RELEVANT TO DENTISTRY

QDs are nanoscale semiconductor crystals (typically 2–10 nm) that exhibit size-tunable emission, high quantum yield, broad excitation, and narrow, intense emission peaks. These photophysical properties allow multiplexed imaging (different colors from a single excitation source), high signal-to-noise, and long-term tracking superior to conventional organic dyes [1, 5]. Major types of quantum dots used or proposed in dental/oral diagnostics depicted in Table 1.

Table 1. Major types of quantum dots used or proposed in dental/oral diagnostics.

QD type	Core composition	Key optical features	Typical dental/oral diagnostic use	Advantages	Main concerns/limits
Cd-based (CdSe, CdTe, CdSe/ZnS)	II–VI semiconductor core often with ZnS shell	High quantum yield, narrow emission, tunable from visible to NIR	Experimental OSCC tissue labeling, in vitro cell-line imaging, sentinel node mapping in general oncology adapted conceptually to head–neck models [5, 6].	Bright, photostable, well-characterized synthesis	Cadmium toxicity, long-term retention, regulatory barriers [1, 5].
InP and other heavy-metal-reduced	III–V core, often ZnS shell	Visible-NIR emission with lower toxic metal content	Proposed for safer in vivo oral mucosal imaging; limited direct dental data yet [1, 5].	Lower toxicity than Cd, good brightness	Synthesis complexity, cost, fewer dental-specific studies [1].
Carbon QDs (CQDs, GQDs)	Carbon core, often sp ² clusters	Broad excitation, blue-near-IR emission, good photostability	Imaging oral tissues, lab-on-chip biosensing, caries and biofilm visualization research; also, anti-caries coatings (indirect diagnostic aid) [1, 7, 8].	Good biocompatibility, easy functionalization, lower toxicity	Often lower brightness than Cd QDs, heterogeneous surface chemistry [1].
Silicon QDs	Crystalline Si core	Visible-NIR emission, lower heavy metal content	Conceptual for oral imaging and biosensing; few specific dental studies [1, 5].	Biocompatibility, CMOS compatibility	Synthetic complexity, stability issues in aqueous media [5].
Doped/heterostructure QDs	Doped or core-shell (e.g., Mn-doped, alloy QDs)	Longer lifetimes, tunable emission, sometimes magneto-optical	Time-gated imaging for oral lesions, multimodal contrast (future concept) [5].	Reduced background, multimodal potential	Limited oral data, complex regulatory path [1, 5].

Core chemistries include II–VI (CdSe, CdTe, ZnS), III–V (InP), silicon QDs, and carbon QDs, the last being particularly attractive in dentistry due to better biocompatibility and lower heavy-metal load. Surface functionalization (PEG, antibodies, peptides, aptamers, folate, EGFR ligands) provides aqueous stability, reduces nonspecific binding, and enables active targeting of dysplastic and malignant oral epithelium [1, 5, 6].

QUANTUM-DOT-BASED IMAGING FOR ORAL MUCOSA AND ORAL CANCER

Principle and Platforms

In oral diagnostics, QDs are generally used as fluorescent labels conjugated to:

- Monoclonal antibodies (EGFR, HER2, Ki-67, p53) for OSCC and dysplasia [4–6].
- Peptides/aptamers target tumor vasculature and extracellular matrix components [5].
- Small molecules (e.g., folate) target overexpressed receptors in premalignant lesions [5]. (QD imaging for oral premalignant and malignant lesions vs. conventional approaches depicted in Table 2.)

Table 2. QD imaging for oral premalignant and malignant lesions vs. conventional approaches [6–9].

Feature	Conventional adjuncts (toluidine blue, autofluorescence, brush cytology)	QD-based imaging (current evidence)
Targeting mechanism	Mostly non-specific stain or intrinsic tissue autofluorescence	Molecular targeting via antibodies/ligands to tumor markers (EGFR, Ki-67, p53, etc.) [4–6].
Signal intensity	Moderate; often fades, affected by photobleaching	High fluorescence intensity, strong signal-to-noise, minimal photobleaching [2, 3, 5, 6].
Spectral characteristics	Broad emission and excitation, limited multiplexing	Narrow emission, broad excitation, enables multiplexed marker imaging [1, 5].
Diagnostic performance	Sensitivity and specificity variable, operator-dependent	Reported sensitivity up to 90% and specificity 95% in ex vivo biopsy imaging [2, 3].
Spatial resolution	Limited for microscopic sub-cellular detail in vivo	Capable of sub-cellular localization in microscopy, enabling better margin assessment [5, 6].
Clinical status	Widely used adjuncts; limited impact on mortality	Mostly preclinical; strong potential but not yet standard of care [1, 4, 6].

Excitation is typically in the blue to near-UV range, while emission is collected in visible or near-infrared windows (650–900 nm) where tissue autofluorescence and scattering are lower, improving mucosal lesion contrast. Imaging modalities include widefield fluorescence, confocal, and multiphoton microscopy at present; integration into intraoral cameras and endoscopes is under exploration [1–3, 5, 6].

Evidence for Early Diagnosis of OSCC and Dysplasia

A 2024 scoping review of noninvasive QD imaging in OSCC identified eight eligible studies, mainly ex vivo and small in vivo cohorts, showing strong potential for diagnostic and theranostic use. QDs emitted in visible and NIR ranges, providing higher contrast than many conventional dyes and enabling visualization of small tumor foci. Another article specifically frames QDs as “trailblazers” in early oral cancer detection, suggesting improvements in precision, sensitivity, specificity, and ability to detect epithelial dysplasia before overt malignancy [4–6].

A 2025 experimental study on biopsy specimens found that QD-antibody conjugates yielded mean fluorescence intensity around 120 ± 10 arbitrary units in pathological tissues versus 50 ± 5 in controls, with reported sensitivity 90% and specificity 95% for distinguishing diseased from healthy tissues. High photostability was also shown, with less than 5% intensity loss after 30 minutes, supporting their suitability for prolonged imaging and repeated acquisition [2, 3].

QUANTUM DOTS IN WIDER DENTAL IMAGING: CARIES, PERIODONTAL AND ENDODONTIC APPLICATIONS

Although the strongest data pertain to oral cancer, QDs also show promise in other diagnostic domains of dentistry [1, 8, 9].

Caries and Enamel/Biofilm Visualization

QDs, especially carbon and graphene QDs, can bind to tooth structures or biofilms and render them fluorescent, facilitating visualization of early enamel demineralization and plaque architecture *in vitro*. An example is a tooth-binding graphene quantum dot-silver nanocomposite designed primarily as an antibacterial, mineralizing anticaries agent, where specific tooth binding and minimal discoloration of dentine caries were demonstrated, indirectly supporting use as a contrast agent for lesion outline and monitoring. Reviews further suggest that QDs embedded in restorative materials could allow fluorescent detection of marginal caries and recurrent decay around restorations [1, 7–9]. QD contributions to dental imaging across specialties depicted in Table 3.

Table 3. QD contributions to dental imaging across specialties.

Specialty	Conventional diagnostic focus	QD-enabled or proposed enhancement	Stage of evidence
<i>Oral medicine/pathology</i>	Clinical exam, toluidine blue, autofluorescence, biopsy	Molecularly targeted fluorescence imaging of dysplasia and OSCC, better margin and field cancerization visualization [2–4, 6].	Ex vivo/in vitro, small preclinical studies
<i>Operative dentistry/cariology</i>	Visual–tactile exam, bitewings, laser fluorescence	Fluorescent labeling of early enamel lesions and biofilm, fluorescent restoratives for recurrent caries detection [1, 7–9].	Primarily in vitro, material studies
<i>Periodontology</i>	Probing, radiographs, biomarker assays	Targeted QDs for inflammatory and microbial markers to map active disease sites [1, 8].	Conceptual/early experimental
<i>Endodontics</i>	Pulp vitality tests, radiographs, CBCT	QDs for tracking bacteria, visualizing microleakage, monitoring tissue engineering constructs [1, 8].	In vitro/tissue engineering level
<i>Oral radiology</i>	2D radiography, CBCT, MRI	QDs as complementary fluorescence imaging agents integrated with optical/near-IR systems [1–3].	Preclinical

Periodontal and Peri-Implant Diagnostics

QDs conjugated with antibodies against inflammatory markers, matrix metalloproteinases, or bacterial antigens have been proposed for imaging inflamed periodontal tissues and peri-implantitis lesions. Experimental bioimaging studies have used QDs to label cells in periodontal tissue engineering constructs and to monitor inflammatory responses. This could translate into fluorescent probes applied in pockets to map sites of active disease and differentiate between active and inactive lesions before clinical attachment loss becomes visible on radiographs [1, 8].

Endodontic and Pulpal Applications

At a more conceptual level, QDs have been used to label cells in pulp tissue engineering and to monitor bacterial contamination within root canals in *in vitro* models. This research suggests future possibilities of QD-enhanced detection of microleakage, residual infection, or early periapical changes when combined with advanced imaging modalities [1, 8]. QD imaging vs other optical adjuncts for oral lesion detection depicted in Table 4.

HOW QDS ENABLE EARLIER DIAGNOSIS AND “QUANTUM” IMPROVEMENT IN IMAGING Mechanisms Improving Early Detection

Early oral cancer and precancer are often subtle clinically; QDs improve detectability through:

- *Molecular Specificity*: Targeted QDs bind overexpressed receptors/markers before gross architectural changes occur, revealing fields of genetically altered mucosa beyond visible lesions [4–6].
- *High Contrast and Multiplexing*: Narrow emission peaks allow simultaneous visualization of multiple biomarkers (e.g., EGFR, Ki-67, angiogenic markers), refining risk stratification and margin assessment [5, 6].
- *Photostability and Brightness*: Strong, stable fluorescence permits extended imaging, scanning of large fields, and quantitative image analysis without rapid signal loss [2, 3, 5].
- *Potential Integration with AI*: QD-enhanced images, with higher signal-to-noise, are intrinsically suitable for machine learning-based classification of lesions and automated risk scoring [1, 2, 5]. Safety profile comparison of major dental/oral QD classes depicted in Table 5.

Table 4. QD imaging vs other optical adjuncts for oral lesion detection [9–12].

Modality	Contrast source	Typical use	Strengths	Key limitations vs QDs
<i>White-light examination</i>	Reflectance and color	Baseline clinical exam	Simple, universal, zero consumables	Low sensitivity for early dysplasia; subjective [4].
<i>Toluidine blue</i>	DNA/RNA affinity dye	Adjunctive staining for suspicious lesions	Low cost, simple	Non-specific uptake, false positives, no molecular targeting [4].
<i>Autofluorescence devices</i>	Loss of native fluorescence	Chairside screening of suspicious areas	Non-invasive, real-time	Influenced by inflammation, pigmentation; no specific molecular data [4].
<i>Narrow-band imaging (endoscopy)</i>	Hemoglobin absorption	Vascular pattern assessment	Enhances microvasculature	Requires endoscopic setup; limited sub-cellular info [5].
<i>QD-based fluorescence imaging</i>	Targeted nanoparticle fluorescence	Research-level imaging of dysplasia/OSCC, biopsies	High sensitivity/specificity, molecular targeting, multiplexing, high photostability [2–3, 5–6].	Toxicity/regulatory issues, cost, mostly preclinical, need for specific light sources and filters [1, 4].

Table 5. Safety profile comparison of major dental/oral QD classes [11–14].

Parameter	CD-based QDs	In P/metal-reduced QDs	Carbon/graphene QDs
<i>Core toxicity potential</i>	High (cadmium ions, oxidative stress) [1, 5].	Moderate–lower (less toxic metals, but still nanoparticle risks) [1].	Low–moderate; generally good in vitro biocompatibility [1].
<i>Shell/coating</i>	ZnS, silica, polymers to reduce ion leakage [1, 5]	ZnS, polymer shells [1].	Often oxygen/nitrogen functional groups; PEG and other polymers [1].
<i>Dental/oral usage trend</i>	Historically dominant in early QD work; decreasing due to toxicity concerns [1, 5].	Emerging, limited dental data but attractive for future clinical translation [1].	Most frequently used in recent dental studies (bioimaging, antibacterial composites) [1, 7, 8].
<i>Regulatory outlook</i>	Challenging for routine intraoral use	More favorable but data limited	Most favorable among QDs, though still preclinical in diagnostics

SAFETY, TOXICITY, AND REGULATORY TRANSLATION

Toxicological Issues

The main safety concern is heavy-metal content (cadmium, selenium, lead) and oxidative stress from reactive surface states. Potential risks include cytotoxicity, DNA damage, and long-term accumulation in organs if QDs are systemically absorbed, especially for small, nondegradable particles. Surface coatings (ZnS shells, PEG, silica, phospholipids) reduce ion leakage and improve biocompatibility but may alter pharmacokinetics. Carbon QDs and graphene QDs demonstrate substantially better cytocompatibility in vitro and have become the most widely studied class in dental research (around 54 of 87 QD dental studies in a recent review) [1, 5].

Regulatory and Clinical Adoption Barriers

Despite promising data, current applications are mainly in vitro, ex vivo, or in small animal models; very few controlled human clinical trials specifically in dental diagnostics exist. Regulatory agencies demand comprehensive toxicology, pharmacokinetics, and environmental safety evaluations for nanoparticle-based imaging agents, particularly those with cadmium. There are also practical issues: cost of QD probes, need for specialized excitation and detection systems compatible with dental clinics, standardization of imaging protocols, and clinician training [1–3, 5–6].

INTEGRATION WITH IMAGING HARDWARE AND AI, AND FUTURE DIRECTIONS

Hardware Integration

Current work is mainly in microscope-based imaging of biopsy samples; however, several trajectories are evident:

- Adaptation to intraoral fluorescence cameras with interchangeable filters for QD emission bands, potentially combined with white-light views [2, 3].

- Integration into fiber-optic probes and endoscopes for deep oropharyngeal assessment [5].
- Co-registration with conventional imaging (e.g., CBCT) via software, providing anatomical plus molecular maps of lesions [2, 1]. Potential clinical pathways for QD-based diagnostics depicted in Table 6.

Table 6. Potential clinical pathways for QD-based diagnostics [15–18].

Clinical setting	Proposed QD application	Workflow	Expected benefit
Oral medicine clinic	QD-based topical contrast for suspicious white/red lesions	Apply targeted QD probe, image with specialized intraoral camera, select biopsy site based on fluorescence hotspots [2–4, 6].	More accurate biopsy site selection, earlier dysplasia detection.
Head-neck oncology	QD imaging during surgery	Inject or apply QDs preoperatively, fluorescence-guided margin assessment [5].	Better margin clearance, reduced recurrence.
Dental OPD screening	Low-toxicity QD topical rinse for high-risk patients	Rinse, intraoral fluorescence scan; AI scores risk, triggers targeted exam/biopsy [1, 2, 5].	High-throughput, objective screening for high-risk populations.
Cariology clinic	QD-functional restorative materials	Restorations imaged under specific light to detect marginal defects/recurrent caries [1, 7–9]	Early identification of failing restorations and hidden caries.
Periodontal practice	QD probes for inflammatory markers	Local application in pockets followed by fluorescence imaging [1, 8].	Mapping active sites prior to radiographic bone loss.

For caries and periodontal diagnostics, QD-enhanced fluorescence could be superimposed on standard intraoral camera images or near-infrared transillumination to highlight early lesions invisible on radiographs [1, 8, 9]. Research directions in QD-based dental diagnostics shown in Table 7.

Table 7. Research directions in QD-based dental diagnostics [12–14, 19].

Domain	Specific gap	Potential study designs
Clinical translation in oral cancer	Very limited prospective human trials using QDs for in vivo lesion imaging and margin assessment [1, 2, 4, 6].	Phase I/II safety and diagnostic accuracy trials of low-toxicity QDs for intraoral imaging.
Toxicology and biodistribution	Need for long-term intraoral exposure and mucosal penetration data, especially for repeated use in screening [1, 5].	Animal studies with chronic topical exposure; human mucosal penetration studies with carbon QDs.
Chairside devices	Lack of integrated, affordable intraoral hardware optimized for QD excitation/emission profiles [1, 2].	Engineering projects on QD-compatible intraoral cameras, in comparison with current autofluorescence devices.
Caries/periodontal diagnostics	Evidence mainly in vitro or in materials labs, not yet in patients [1, 7–9]	Clinical feasibility and diagnostic accuracy studies for QD-enhanced plaque/caries/periodontal imaging.
AI and image analysis	Very few datasets combining QD images with clinical outcomes [1, 2, 5].	Creation of annotated QD oral lesion image datasets, development and validation of ML classifiers.

AI-Assisted QD Imaging

High-contrast QD images are natural candidates for AI workflows: segmentation of high-intensity regions, classification of lesion grades, and prediction of malignant transformation risk using deep learning. QD-tagged multi-marker panels (e.g., proliferative, angiogenic, and immune markers) could generate multiplexed datasets where ML models learn patterns predictive of progression from leukoplakia or dysplasia to OSCC earlier than human observers [1, 2, 5].

KEY TAKEAWAYS FOR MDS-LEVEL UNDERSTANDING AND RESEARCH GAPS

A review of quantum dots in dental and oral medicine screened 2,483 records and included 87 studies, finding that bioimaging, oral cancer therapy, antibacterial effects, tooth restoration, tissue engineering, biosensing, and anti-inflammatory uses are the main domains, with bioimaging being the earliest and still central area. Another broad review specifically emphasized QDs as “trailblazers” for early oral cancer detection, highlighting potential impact in high-burden regions like India [1, 4].

CONCLUSION

Quantum dots have rapidly progressed from a niche nanotechnology concept to a promising platform with wide-ranging implications for dental and oral medicine, yet their translation to routine clinical use remains incomplete and highly experimental. In dentistry, their unique optical properties – including size-tunable emission, high quantum yield, broad excitation, and narrow, intense fluorescence peaks – offer distinct advantages over conventional organic fluorophores for diagnostic imaging and theranostic applications. These features enable highly sensitive, multiplexed, and long-lasting imaging at the cellular and subcellular levels, positioning QDs as powerful tools for early detection of oral potentially malignant disorders, dysplasia, and oral squamous cell carcinoma, as well as for advanced research into dental caries, periodontal disease, biofilms, and tissue regeneration.

The evolution of QD core chemistry and surface engineering has further strengthened their suitability for biomedical use. The development of carbon and silicon QDs, along with improved passivation of traditional II–VI and III–V semiconductor cores, has aimed to reduce heavy-metal-associated toxicity while preserving or enhancing fluorescence performance. Surface functionalization with polyethylene glycol, antibodies, peptides, aptamers, folate, and EGFR-targeting ligands has enabled better aqueous stability, reduced nonspecific binding, and precise molecular targeting of dysplastic and malignant oral epithelial cells. This has opened avenues for QD-based platforms in molecular diagnostics, targeted drug delivery, photodynamic therapy, and image-guided interventions tailored to individual patient profiles, aligning well with the goals of precision dentistry and personalized oral healthcare.

However, despite these advances, substantial barriers must be addressed before QDs can be integrated into everyday chairside practice. Concerns related to long-term toxicity, biodistribution, clearance, potential environmental impact, and regulatory hurdles remain significant. Standardization of synthesis, characterization, functionalization, and safety assessment is still lacking, and cost-effective, scalable, and reproducible production methods must be established. Furthermore, robust *in vivo* studies, well-designed clinical trials, and interdisciplinary collaboration between materials scientists, dental researchers, clinicians, and regulators are essential to validate safety, optimize formulations, and define clear clinical indications. In conclusion, quantum dots represent a highly versatile and powerful theranostic platform with the potential to revolutionize dental diagnostics and therapeutics, but careful, evidence-based development and rigorous safety evaluation are crucial to ensure their responsible and successful translation from bench to chairside.

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