

Review

Machine-Learning-Assisted Micro-CT and Multimodal Imaging for Osseointegration Assessment of Zirconia Ceramic Implants: Linking Processing, Microstructure, and *In-Vivo* Performance

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Abstract

The transition from titanium to zirconia implants represents a paradigm shift in restorative dentistry, driven by aesthetic demands, biocompatibility concerns, and the need for enhanced long-term stability. This review critically evaluates the processing-microstructure-performance nexus of zirconia ceramics, emphasizing how sintering parameters, phase stability, and surface modifications collectively determine mechanical reliability and biological integration. The unique phenomenon of transformation toughening provides zirconia with competitive strength, yet susceptibility to low-temperature degradation, underscoring the importance of microstructural control and compositionally tailored systems such as ATZ and Ce-TZP composites. *In vivo* evidence reveals a heterogeneous landscape of survival rates, shaped by implant design and clinical application, highlighting both the promise and limitations of current systems. To address the shortcomings of conventional 2D histomorphometry, this review surveys the rise of high-resolution, non-destructive micro-computed tomography (micro-CT) and its integration with multimodal tools like Raman spectroscopy and nanoindentation for quantitative and qualitative assessment of osseointegration. The application of machine learning, particularly deep learning architectures such as U-Net and ResNet, is explored as a transformative solution for automated segmentation, morphometric analysis, and predictive modeling of clinical outcomes, with explainable AI (XAI) offering interpretability and trust. Finally, the convergence of advanced imaging and AI-enabled analytics is discussed within the framework of personalized medicine, where patient-specific digital twins may enable virtual testing and optimization of implant strategies. Collectively, these developments chart a pathway toward predictive, data-driven implantology and position zirconia as a viable and evolving alternative to titanium.

Keywords: Transformation toughening, low-temperature degradation, osseointegration assessment, deep learning, digital twin

I. Introduction

For over four decades, titanium and its alloys have been regarded as the undisputed gold standard in dental implantology, a status earned through a vast body of clinical evidence demonstrating excellent biocompatibility, robust mechanical properties, and a predictable capacity for osseointegration¹. The formation of a stable, passive titanium dioxide (TiO₂) layer upon exposure to physiological environments renders the material largely inert, facilitating a direct structural and functional connection with living bone. This long and successful clinical track record has underpinned the high predictability of implant-supported prostheses, transforming the field

of restorative dentistry. However, despite this success, a growing body of research and clinical observation has brought to light certain limitations that challenge the universality of titanium as the ideal implant material. A primary concern is aesthetic in nature. In patients with a thin gingival biotype or in cases of subsequent soft-tissue recession, the metallic gray hue of the implant can become visible through the peri-implant mucosa, creating an undesirable discoloration that compromises the final aesthetic outcome, particularly in the anterior maxilla^{2,3}. Beyond aesthetics, while exceedingly rare, documented cases of allergic or hypersensitivity reactions to titanium or its alloying elements (such as aluminum and vanadium in Ti-6Al-4V) have been reported, manifesting as local inflammation or even systemic effects⁴. Furthermore, the oral cavity presents a complex and corrosive environment.

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Under certain conditions, such as low pH or the presence of fluoride ions, the protective oxide layer on titanium can be compromised, leading to the release of metallic ions into the surrounding tissues^{5–7}. This phenomenon, while often subclinical, is hypothesized to contribute to a low-grade, chronic inflammatory response that may, in susceptible individuals, increase the risk of long-term complications like peri-implantitis⁸.

These challenges, coupled with a rising patient demand for metal-free restorative solutions, have catalyzed the search for viable alternatives. In response to the limitations of titanium, the field of dental materials has turned to high-strength ceramics, with yttria-stabilized tetragonal zirconia polycrystal (Y-TZP) emerging as the most promising candidate for endosseous implants. First introduced for medical applications in the late 1960s and later refined for dentistry, zirconia offers a compelling combination of material properties that directly address the primary drawbacks of titanium. Its inherent tooth-like white color provides a significant aesthetic advantage, eliminating the risk of gingival discoloration and acceding to patient demand for metal-free restorations^{2,3}. Moreover, the discourse surrounding zirconia reflects a fundamental evolution in the philosophy of biomaterial design. While titanium's success is rooted in its "bio-inertness," zirconia is increasingly characterized by its potential for active, favorable bio-integration. Studies have demonstrated that zirconia surfaces can promote the proliferation of human gingival fibroblasts more effectively than titanium, potentially leading to a superior soft-tissue seal^{9,10}; and *in vitro* work often shows reduced bacterial adhesion/biofilm formation on zirconia compared with titanium¹¹, although cytokine profiles *in vivo* may be comparable in healthy conditions¹². Furthermore, several preclinical studies and meta-analyses report bone-to-implant contact (BIC) for roughened/modified zirconia surfaces that is comparable to, and under certain treatments approaches favorable relative to, sandblasted/acid-etched titanium controls^{13,14}.

Despite its promising properties, the clinical translation of zirconia implants has been marked by a heterogeneous landscape of outcomes, with reports ranging from excellent long-term survival to premature failures. Recent systematic reviews/meta-analyses indicate high 10-year cumulative survival but emphasize variability related to design (one- vs two-piece), surface treatment, and narrow-diameter fracture susceptibility^{3,15}. This variability underscores a critical gap in understanding: the intricate, multiscale relationship that connects the initial processing of the ceramic material to its final microstructure, and how this microstructure dictates its *in-vivo* performance and osseointegration. The long-term success of a zirconia implant is not an inherent property of the material itself but is a direct consequence of highly controlled manufacturing processes that balance competing demands for mechanical toughness, resistance to low-temperature degradation (LTD), translucency, and surface bioactivity^{16,17}. A schematic comparison between titanium and zirconia implants is presented in

Fig. 1, highlighting their respective clinical limitations and advantages. While titanium is associated with a grayish hue, possible ion release, and bioinert osseointegration, zirconia offers a tooth-colored aesthetic, reduced bacterial affinity, and the potential for active biological modulation with enhanced bone-to-implant contact.

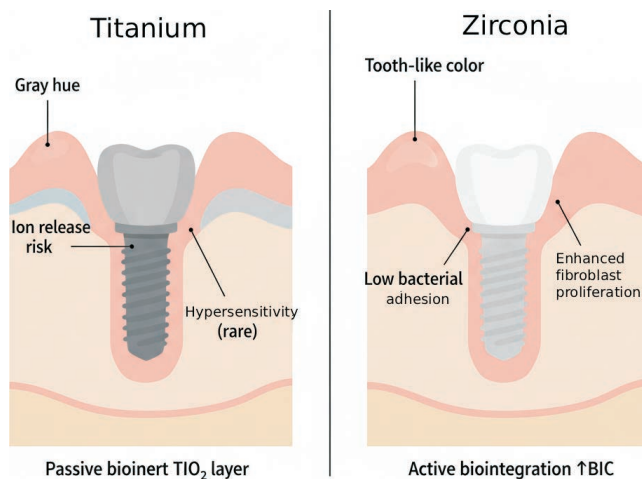


Fig. 1: Comparative schematic of titanium and zirconia dental implants.

This review posits that a robust and predictive understanding of this processing-microstructure-performance linkage can only be achieved through the synergistic application of advanced characterization techniques and powerful analytical tools. This review does not attempt to provide an exhaustive narrative of all zirconia biomaterials or all imaging/AI techniques. Rather, our central research question is: How can advances in zirconia processing be quantitatively linked to *in-vivo* osseointegration outcomes through micro-CT-centered multimodal imaging and machine-learning analysis? We delimit scope to endosseous zirconia implant systems and focus on the processing→microstructure→performance pathway, emphasizing: (i) where zirconia differs from titanium in clinical behavior; (ii) how three-dimensional micro-CT and correlative modalities capture peri-implant bone architecture and quality; and (iii) how ML models translate these imaging features into automated measurements and predictive outcomes.

This manuscript provides a critical, cross-disciplinary synthesis of the literature, adopting the methodology of a narrative review. To build a comprehensive foundation for this analysis, a literature survey was conducted using the Scopus, PubMed, and Web of Science databases. The search period primarily focused on publications from 2005 to 2024 to capture the evolution of modern zirconia systems and the recent rise of applied machine learning. The search strategy employed a combination of keywords and their variants, which were grouped into three main conceptual pillars:

1. Material Science: "zirconia," "Y-TZP," "dental implants," "processing," "sintering," "low-temperature degradation," "transformation toughening," and "surface modification."

2. Imaging and Assessment: “osseointegration,” “micro-CT,” “histomorphometry,” “multimodal imaging,” “nanoindentation,” and “Raman spectroscopy.”
3. Computational Analysis: “machine learning,” “deep learning,” “convolutional neural network (CNN),” “U-Net,” and “digital twin.”

Peer-reviewed original research articles, systematic reviews, and meta-analyses published in the English language were considered. The initial selection of articles was screened for relevance to the core theme of the processing-microstructure-performance nexus for zirconia dental implants. Subsequently, the literature was evaluated and curated based on methodological rigor, relevance to advanced imaging techniques (specifically micro-CT), and the application of computational models for analysis or prediction. This narrative methodology was deliberately chosen to effectively bridge the distinct domains of ceramic engineering, preclinical biological assessment, and data science, rather than to exhaustively catalog all clinical survival studies.

II. Zirconia Ceramic Implants: A Critical Appraisal of Material Properties and Performance

The successful application of zirconia in implant dentistry is predicated on a deep understanding of its unique material science. Unlike ductile metals, ceramics are brittle materials whose performance is exquisitely sensitive to their processing history and resulting microstructure. This section critically examines the fundamental properties of dental zirconia, the profound influence of manufacturing and surface treatments, and the complex landscape of its *in-vivo* clinical performance.

(1) The material science of Y-TZP: polymorphism and transformation toughening

ZrO₂ is a polymorphic material, meaning it can exist in different crystal structures depending on temperature. At room temperature, pure zirconia is stable in a monoclinic (m) phase. Upon heating, it transforms to a tetragonal (t) phase at approximately 1170 °C and subsequently to a cubic (c) phase at ~2370 °C; the reverse cooling induces the t→m transition with a volumetric expansion of roughly 3–5% that would otherwise generate catastrophic stresses and cracking^{18,19}. To harness the superior mechanical properties of the tetragonal phase, stabilizing oxides such as Y₂O₃ are added – typically ~3 mol% in dental grades (3Y-TZP) – so that a fine-grained tetragonal microstructure can be retained metastably at room temperature after sintering²⁰.

This metastability underpins the classic phenomenon of transformation toughening. When a crack tries to propagate, the high tensile field at the crack tip can trigger local t→m transformation of metastable grains; the associated 3–5% transformation dilatation generates a compressive shielding zone that resists further crack advance^{21,22}. Quantitatively, well-processed 3Y-TZP used in dentistry typically exhibits flexural strength in the order of 900–1200 MPa and fracture toughness in the 4–6 MPa·√m range – values that are exceptional among oxide ceramics and trace directly to stress-assisted transformability of sub-micrometer grains^{20,23}. At the same

time, the elastic modulus for Y-TZP is ~190–210 GPa, nearly double that of Ti implants (~110 GPa), which has implications for load transfer and mismatch in compliance at the bone-implant interface¹⁸. Importantly, the grain size window governs transformability: when the average grain size drops below ~0.3 μm, tetragonal grains become too stable to transform and toughness falls; conversely, excessive grain growth (> ~0.5–0.8 μm in many processing routes) increases transformability but can compromise translucency and aging resistance²⁴.

From a processing-microstructure perspective, the balance is delicate. Speed-sintering or prolonged high-temperature holds can alter phase assemblage and grain size, shifting the stability of t-ZrO₂ and thereby the magnitude of stress-induced transformation toughening; hydrothermal environments (e.g., autoclave-like conditions) can accelerate near-surface t→m transformation (“LTD”), especially when cubic-rich or yttria-depleted regions exist, progressively roughening the surface and diminishing strength if not controlled^{18,19,25}. These kinetic realities explain why apparently similar 3Y-TZP formulations may diverge in R-curve behavior, LTD resistance, and translucency once processing histories differ²⁴. This metastability is the key to zirconia’s exceptional mechanical properties, enabling a phenomenon known as “transformation toughening”. When a crack attempts to propagate through the 3Y-TZP material, the high tensile stress field concentrated at the crack tip provides the energy needed to trigger the localized transformation of metastable tetragonal grains into the more stable monoclinic phase (Fig. 2). This t→m transformation, with its associated volume expansion, creates a zone of compressive stress that effectively clamps down on the crack, hindering its further propagation and thereby imparting high fracture toughness to the material. This intrinsic toughening mechanism gives 3Y-TZP flexural strength and fracture toughness values that are far superior to other dental ceramics and comparable in many respects to titanium alloys, earning it the moniker “ceramic steel”. A comparison of the key properties of 3Y-TZP and titanium is provided in Table 1.

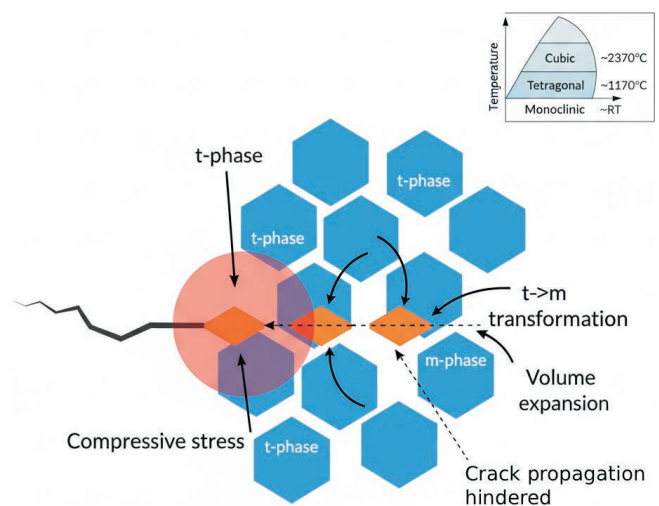


Fig. 2: Schematic illustration of the transformation toughening mechanism in 3Y-TZP.

Table 1: Comparative properties of zirconia and titanium dental implants.

Property Category	Parameter	Titanium (Ti-6Al-4V)	Zirconia (3Y-TZP)
Mechanical	Flexural Strength (MPa)	~ 800–1100	900–1200
	Fracture Toughness (MPa·m ^{1/2})	High (ductile)	9–10 (brittle)
	Young's Modulus (GPa)	~ 110	~ 210
Physical	Color	Grayish metal	Tooth-like white
	Corrosion Resistance	Good (forms oxide layer)	Excellent (inert oxide)
Biological	Biocompatibility	Excellent	Excellent
	Allergenicity	Rare but possible	Hypoallergenic
	Plaque Affinity	Moderate	Low
Clinical	Design Flexibility	High (one- and two-piece)	Limited (mainly one-piece)
	Long-term Data	Extensive (> 40 years)	Limited (< 20 years)

(2) *The processing-microstructure-property nexus*

The final clinical performance of a zirconia implant is not guaranteed by its chemical composition alone; it is critically determined by the manufacturing process, which establishes a direct and immutable link between processing parameters, the resulting microstructure, and the final material properties. This nexus is the source of both zirconia's potential and its variability²⁰.

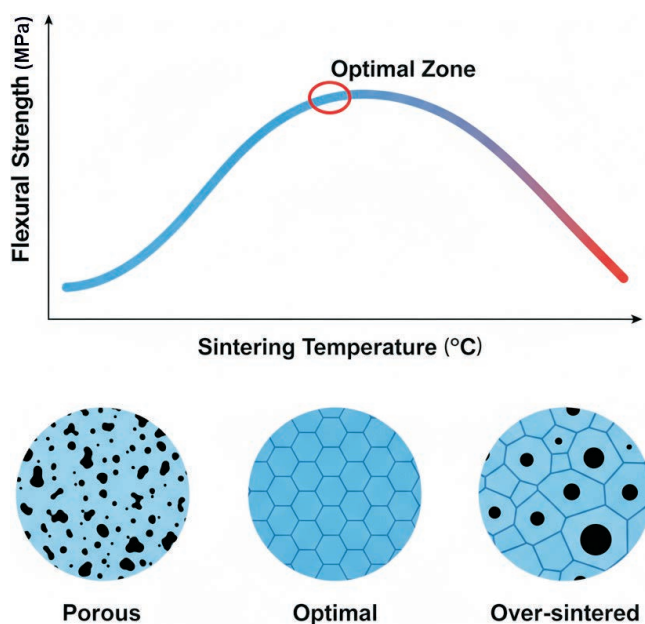


Fig. 3: Effect of sintering temperature on the flexural strength of zirconia.

(a) *Sintering and its dominant influence*

The most critical step in processing zirconia is sintering, where a porous, “green” body machined from a pre-sintered block is heated to high temperatures (typically 1350 °C to 1600 °C) to achieve full densification. The sintering parameters – namely the peak temperature, the duration (or dwell time) at that temperature, and the heating/cooling rates – exert dominant control over the final microstructure^{26,27}. Generally, higher sintering

temperatures and longer dwell times promote greater densification and lead to an increase in the average grain size. As shown in **Fig. 3**, flexural strength tends to increase with temperature up to a certain point as densification progresses; however, beyond an optimum window, exaggerated grain growth (and Ostwald ripening of residual pores) can reduce strength and homogeneity²⁷. Recent studies also show that non-conventional “speed” sintering schedules can raise strength when time-temperature profiles are carefully optimized for the specific zirconia grade²⁸. Manufacturers therefore provide powder-specific sintering protocols to balance density, grain size and strength; deviations can markedly affect reliability.

(b) *The double-edged sword of LTD*

The same thermodynamic metastability that enables transformation toughening also renders zirconia susceptible to low-temperature degradation (LTD, “aging”). In the presence of water or water vapor – even at physiological temperature (≈ 37 °C) – the metastable tetragonal phase can spontaneously transform to monoclinic over time²⁹. Transformation usually initiates at the surface and propagates inward, producing volume-change-induced microcracks, surface roughening, and progressive loss of mechanical properties²⁵. The LTD kinetics are highly sensitive to microstructure and processing history. Three main factors are critical: stabilizer content, residual stresses introduced by machining/surface treatments, and especially grain size. Larger grains markedly accelerate LTD, whereas finer microstructures are more resistant³⁰. Surface treatments (e.g., grinding, sandblasting) alter near-surface residual stresses and monoclinic content, thereby modulating aging behavior; carefully executed polishing/grinding can induce beneficial compressive stresses, while aggressive abrasion can be deleterious. Porous or roughened surfaces may age faster because of increased water access and stress concentration³¹. Importantly for implants, LTD interacts with cyclic loading and can impact fatigue reliability in aqueous conditions³².

(c) *Mitigating LTD: material and processing strategies*

To enhance long-term stability, microstructural control is primary: keeping the average grain size below a critical threshold (often < 1 μm) substantially lowers the driving force for the t→m transformation, achieved through tight control of powder characteristics and sintering cycles²⁶. Compositionally, adding a small fraction of alumina to form alumina-toughened zirconia (ATZ) inhibits grain growth and markedly improves hydrothermal aging resistance; notably, some ATZ systems even show increased flexural or fatigue strength after aging, contrasting with behaviors observed in certain 3Y-TZP grades^{33,34}. Alternative stabilizers such as ceria (CeO₂) impart excellent LTD resistance; modern Ce-TZP-based composites (e.g., Ce-TZP/Al₂O₃/aluminate) show strong anti-aging performance, although conventional monolithic Ce-TZP typically exhibits lower initial flexural strength than 3Y-TZP due in part to larger grain sizes³⁵. Finally, post-sintering surface finishing (precision polishing) can remove surface flaws and introduce compressive stresses that help stabilize the tetragonal phase and suppress LTD initiation³³.

(3) *Engineering the surface for optimal osseointegration*

The biological response to an implant is dictated by its surface characteristics. While bulk properties determine mechanical integrity, the surface topography, chemistry, and energy govern the initial interactions with proteins

and cells that orchestrate the process of osseointegration. As-sintered zirconia has a relatively smooth surface, which is considered bio-inert and does not actively promote bone apposition. Therefore, various modification techniques are employed to create a micro-rough and more bioactive surface to enhance and accelerate osseointegration. A summary of these techniques is presented in **Table 2**.

(a) *Physical and chemical surface modifications*

The most common methods for modifying zirconia surfaces involve physical or chemical means to increase micro-roughness. Sandblasting (airborne-particle abrasion with ceramic particles, e.g., Al₂O₃) is widely used and effectively creates a rough surface; preclinical evidence shows increases in bone-to-implant contact (BIC) and removal torque versus machined surfaces. For example, *in vitro* data have shown up to ~175% higher initial osteoblast adhesion on sandblasted zirconia compared with polished controls^{36,37}. However, this method is not without drawbacks: the aggressive mechanical process can induce surface/subsurface damage, introduce residual compressive residual stresses, and trigger the t→m phase transformation, any of which may accelerate low-temperature degradation (LTD). There is also a risk of abrasive contamination (e.g., embedded alumina)^{18,38,39}.

Table 2: Influence of processing and surface modification on zirconia implant properties.

Treatment Method	Primary Mechanism	Effect on Microstructure/Surface	Effect on Osseointegration (Pros)	Potential Drawbacks (Cons)	Risk Control/Best Practice
Sintering Control	Thermal densification	Controls grain size, density, phase composition	Indirectly affects LTD resistance	Trade-off between toughness and LTD	Do: Adhere strictly to powder-specific time/temp protocols. Don't: Deviate without validation.
Sandblasting	Abrasive particle impact	Increases micro-roughness	Enhances BIC and removal torque	Alumina contamination, induces t→m, may accelerate LTD	Do: Use low pressure (≤0.2 MPa) & small particles (~50 μm). Don't: Use aggressive high-pressure abrasion.
Acid Etching	Chemical dissolution	Creates micro/nano-pits	Increases surface area, enhances BIC (superior to Ti)	Less aggressive than sandblasting	Do: Strictly control time and concentration. Don't: Exceed validated etching windows (e.g., time/conc.).
Laser Texturing	Ablation/melting	Creates defined grooves/patterns	Controlled topography for cell guidance	Thermal effects, potential for micro-cracks	Do: Use ultrashort pulse lasers (fs/ps) for "cold ablation". Don't: Use parameters that cause significant thermal diffusion.

Treatment Method	Primary Mechanism	Effect on Microstructure/Surface	Effect on Osseointegration (Pros)	Potential Drawbacks (Cons)	Risk Control/Best Practice
UV Irradiation	Photochemical reaction	Reduces surface hydrocarbons	Increases hydrophilicity and surface energy	Effect may diminish over time	Do: Apply UV treatment immediately before implantation. Don't: Store treated samples long-term without reactivation.
NTP Treatment	Plasma-surface interaction	Cleans and functionalizes surface	Increases wettability and cell adhesion	Effect may not be permanent, potential for increased bacterial adhesion	Do: Optimize plasma gas type and duration for desired chemistry. Don't: Rely solely on plasma activation without proper storage control.
Bioactive Coating	Material deposition	Adds a layer of HA, etc.	Promotes osteoconduction	Risk of delamination, long-term stability unknown	Do: Ensure strong interfacial bonding via pre-treatment or gradient coating. Don't: Use thick or poorly adhered coatings without mechanical validation.

Acid etching is a chemical alternative that uses strong acids (e.g., hydrofluoric acid) to selectively dissolve the surface, creating micro-/nano-scale pits and increasing the area for protein/cell attachment. When optimized, etching tends to be less mechanically damaging than aggressive grit-blasting; nevertheless, excessive acid concentration or long exposure can reduce strength, so parameter windows matter^{40,41}. Notably, several studies and reviews report that acid-etched zirconia achieves BIC values comparable to – and in some models even exceeding – SLA titanium, underscoring the strong osseointegration potential of properly etched zirconia¹⁴. Laser texturing offers a more controlled approach: laser ablation/melting can generate precise micro-grooves that guide cell alignment and improve early biological response; as with any thermal technique, improper parameters may induce micro-cracking, so process control is critical⁴⁰.

(b) *Advanced surface coatings and treatments*

Beyond altering topography, surface chemistry can be tailored to enhance bioactivity. Thin hydroxyapatite (HA) or calcium-phosphate coatings are osteoconductive and can accelerate bone formation at the interface; recent sol-gel HA methods on zirconia have shown > 40 MPa adhesion and markedly improved *in vivo* osteoconductivity, though long-term coating stability/adhesion remains a clinical consideration and depends on processing (e.g., avoiding high-temperature reactions)⁴². More recently, physicochemical activation approaches that alter surface energy without changing the microtopography have gained traction. Ultraviolet (UV) photo-functionalization and non-thermal atmospheric plasma (NTP/CAP) can remove hydrocarbon contaminants and enrich surface hydroxylation, shifting zirconia from hydrophobic to super-hydrophilic; preclinical work

(including large-animal and cell models) links these treatments to improved protein adsorption, osteoblast attachment/spreading, and earlier osseointegration. Importantly, these methods can be applied chairside immediately prior to placement^{43,44}.

(4) *In-vivo performance and long-term clinical evidence*

Ultimately, the viability of zirconia implants is determined by their long-term clinical performance. While preclinical data are largely positive, the translation to clinical practice has yielded a complex and sometimes contradictory body of evidence, highlighting the influence of implant design, patient selection, and the continuous evolution of the materials themselves.

(a) *Survival and success rates: a heterogeneous landscape*

Systematic reviews of short-term clinical studies often report promising survival for zirconia implants – typically ~95–98.4% at 1–5 years – comparable to titanium in selected indications. It must be noted that these data are aggregated across variable follow-up horizons (e.g., 1, 5, and 10 years), which reflects the heterogeneity of the available literature as long-term data for modern zirconia systems is still emerging. A recent comprehensive meta-analysis (n = 4017 implants) reported a 10-year cumulative survival rate (CSR) of 95.1% and also showed that two-piece designs had significantly lower survival than one-piece (p = 0.017)¹⁵. However, other long-term studies report markedly lower CSRs (Table 3). For example, a 5-year study on custom-made two-piece zirconia implants reported a CSR of 75.8% and deemed the system “clinically unacceptable”¹⁵. Likewise, a 5-year prospective study of one-piece zirconia implants supporting three-unit fixed dental prostheses found a

Table 3: Long-term (≥5 years) clinical outcomes of zirconia dental implants.

Implant Design	No. of Implants/Patients	Follow-up Period	Cumulative Survival Rate (%)	Success Rate (%)	Mean Marginal Bone Loss (MBL) (mm)	Key Findings/Complications	Key References
One-piece (3 surface types)	831/378	Up to 5 years	95.0 % (overall); 97.6 % (acid-etched)	-	-	Acid-etched surface showed significantly better success.	51
Two-piece	91/39	5 to 12 years	100 %	-	MBL < 1.65 mm	High survival rates, low prevalence of biologic complications.	52
Commercially available	277/221	5 years	97.2 %	-	1.1 mm	Reliable clinical performance based on meta-analysis.	3
Custom two-piece	30 patients	5 years	75.8 %	71.0 %	-	Deemed “clinically unacceptable” due to low survival.	53
One-piece (supporting FDPs)	54/27	5 years	66.7 %	-	1.89 mm	Low survival attributed to peri-implantitis.	54
Mixed	4 017/2 083	Up to 10 years	95.1 % (10-year CSR)	-	0.63–2.06 mm	High overall 10-year survival; two-piece had lower survival than one-piece.	15

CSR of 66.7 %, with failures primarily due to progressive bone loss and peri-implantitis ⁴⁵. Together, these findings emphasize that “zirconia” is not monolithic; outcomes depend on material generation, manufacturing process, implant design, and specific clinical application.

This picture is further complicated by a validation lag. Manufacturing and materials have evolved substantially over the past two decades; meta-analytic data indicate that clinically available (current-generation) systems show far fewer fractures than earlier/non-commercial prototypes (e.g., fracture prevalence decreasing from ~3.4 % in early literature to ~0.2 % in commercially available systems aggregated up to ~2017) ⁴⁶. Consequently, 10-year cohorts initiated a decade ago may be evaluating materials and connections that are obsolete relative to today’s products ¹⁵. This underlines the need for advanced, predictive characterization (e.g., accelerated aging, in-silico/ML-assisted risk modeling) to complement decade-long clinical trials.

(b) The one-piece vs. two-piece debate

Much of the clinical controversy surrounds the two primary implant designs. The majority of early and currently available zirconia implants are of a one-piece (or monobloc) design, where the implant and abutment are fabricated as a single unit. The primary advantage of

this design is the elimination of the implant-abutment microgap, which is a known site for bacterial colonization and micromovement in two-piece systems, potentially leading to reduced marginal bone loss (MBL) ⁴⁷. However, the clinical disadvantages are significant. Surgical placement is far more challenging, as the implant must be positioned perfectly to meet both osseous and prosthetic requirements simultaneously, with no possibility for post-surgical angulation correction. Any attempt to grind or prepare the integrated abutment to correct its alignment drastically reduces the implant’s fracture strength – in one study, from 2 084 N to 804 N.

Two-piece zirconia implants were developed to address these limitations, offering the same prosthetic flexibility as conventional titanium systems. However, their introduction has brought new challenges ⁴⁸. The connection between the ceramic implant and the ceramic or hybrid abutment is a point of mechanical weakness, and early designs were plagued by low fracture strength ⁴⁹. While newer designs have improved, some systematic reviews have found that two-piece systems have a statistically significant lower survival rate than one-piece systems. This ongoing debate highlights the difficulty in engineering a reliable ceramic-to-ceramic connection that can withstand long-term masticatory forces.

(c) Failure modes and complications

The main technical complication is fracture. Risk is highest in early-generation devices and in reduced-diameter fixtures (e.g., $3.5\text{--}3.75\text{ mm}$), which have shown unacceptably low survival in several cohorts⁴⁸. Fractography of retrieved implants suggests bending-overload as the dominant mechanism, with initiation at the thread constriction for one-piece and at the abutment/connection region for two-piece designs⁵⁰. Although zirconia exhibits relatively low plaque/biofilm affinity in several experimental and clinical observations, it is not immune to peri-implant disease; peri-implantitis was a leading cause of failure in the 5-year FDP cohort noted above⁴⁹. Another reported mode is “aseptic loosening,” i.e., loss of osseointegration with implant mobility in the absence of overt infection, documented in prospective two-piece series and long-term cohorts.

III. Characterizing the Bone-Implant Interface: From 2D Histology to 4D Multimodal Imaging

The assessment of osseointegration – the direct connection between bone and implant – is fundamental to preclinical implant research. The methods used to characterize this interface have evolved significantly, moving from two-dimensional microscopic snapshots to comprehensive four-dimensional analyses that capture the structural, chemical, and mechanical properties of the newly formed tissue over time.

(1) The gold standard: 2D histomorphometry

For decades, 2D histomorphometry has been the undisputed gold standard for the quantitative evaluation of osseointegration⁵⁵. The technique involves embedding the explanted implant-bone block in a hard resin (e.g., polymethylmethacrylate), followed by precise cutting and grinding to produce thin, undecalcified sections⁵⁶. These sections are then stained and analyzed under a light microscope (Fig. 4). Key quantitative metrics, such as the Bone-to-Implant Contact (BIC) ratio – the percentage of the implant surface in direct contact with bone – and Bone Area Fraction Occupancy (BAFO) or Bone Volume/Total

Volume (BV/TV) in the surrounding region of interest, are meticulously measured⁵⁷. This method provides unparalleled microscopic resolution, allowing for the visualization of cellular activity at the interface and offering what has long been considered the definitive “ground truth” for bone apposition⁵⁶. However, the limitations of this technique are substantial. It is inherently destructive, precluding any further analysis of the sample. The process is also exceptionally labor-intensive and time-consuming. Most critically, it provides only a few 2D slices to represent a complex, heterogeneous 3D structure, raising significant questions about how representative a single slice truly is⁵⁸.

(2) The rise of Micro-CT for 3D quantitative analysis

(a) Principles and advantages

Micro-computed tomography (micro-CT) has emerged as a powerful, non-destructive alternative for assessing osseointegration⁵⁹. This technique uses X-rays to generate a series of 2D projection images of a sample from multiple angles, which are then computationally reconstructed into a 3D volumetric dataset. Achieving high-quality, reproducible data is critically dependent on the standardization and reporting of acquisition parameters. While isotropic voxel resolutions are typically in the range of $5\text{--}10\ \mu\text{m}$ for this application⁶⁰, other parameters such as tube voltage (e.g., $70\text{--}90\ \text{kVp}$), tube current, the use of physical filters to reduce beam hardening, and the rotation step fundamentally determine image contrast, noise levels, and artifact presence. In preclinical studies, acquisition protocols commonly employ a tube voltage in the $50\text{--}90\ \text{kV}$ range and a current adjusted for optimal signal, often using a thin aluminum or copper filter to shape the X-ray spectrum. High-quality reconstructions are achieved using a small rotation step (e.g., $<0.5^\circ$) over a 180° or 360° rotation. A critical methodological consideration, particularly for high-density materials like zirconia, is the mitigation of metal artifacts which can obscure the peri-implant bone. This is often addressed through

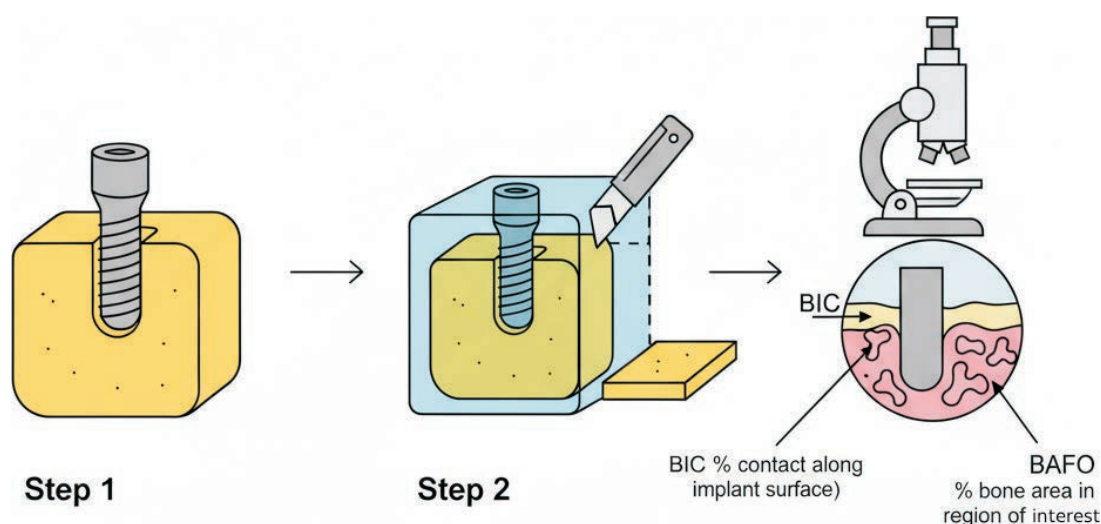


Fig. 4: Schematic illustration of the 2D histomorphometry workflow for osseointegration assessment.

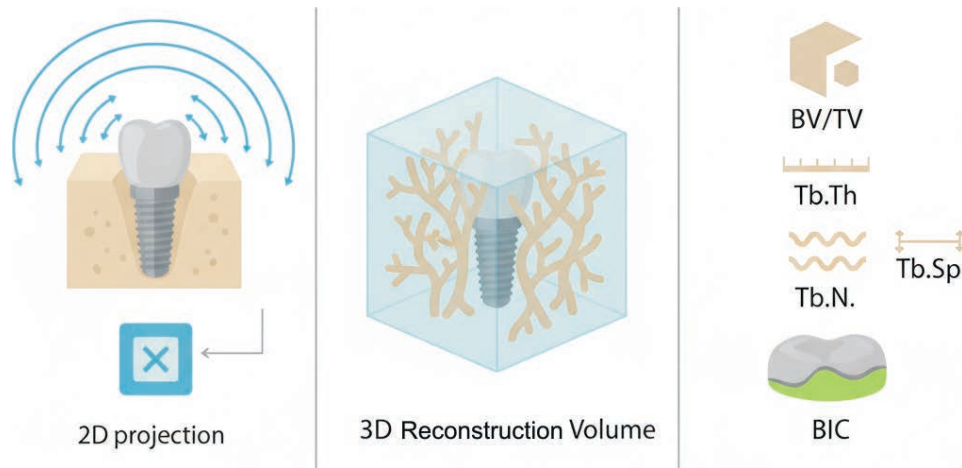


Fig. 5: Schematic illustration of micro-CT workflow for assessing osseointegration.

a combination of optimized scanning parameters and the use of specialized metal artifact reduction (MAR) algorithms during reconstruction. For the quantitative analysis, segmentation of bone from the background is most commonly achieved using a global thresholding strategy based on the grayscale histogram, though more advanced local or algorithm-based thresholding methods also exist. To ensure objectivity, robust studies must report high inter- and intra-rater reliability, with intraclass correlation coefficients for key metrics like BIC and BV/TV often exceeding 0.95. The primary advantage of micro-CT is its ability to provide a complete, 3D visualization of the entire bone-implant interface without physically sectioning the sample (Fig. 5). From this 3D data, a host of crucial morphometric parameters describing the bone microarchitecture can be calculated, including BV/TV, trabecular number (Tb.N), trabecular thickness (Tb.Th), trabecular separation (Tb.Sp), and, importantly, a true 3D BIC value for the entire implant surface⁶¹. Its non-destructive nature also means that the same sample can be used for subsequent analyses, such as histology or mechanical testing⁵⁶.

(b) **The critical controversy: correlation between micro-CT and histology**

Given the established role of histology, a central question has been the degree to which micro-CT data correlates with the gold standard. The evidence on this point is notably contentious and has revealed fundamental questions about the nature of “ground truth” itself. Several studies have found strong and statistically significant correlations when comparing 2D histomorphometric BIC with the BIC measured from a single, carefully registered 2D micro-CT slice from the same location⁶². For instance, one study reported a Pearson correlation coefficient of 0.762 between the two 2D methods. These findings suggest that, on a slice-by-slice basis, micro-CT can accurately reflect the bone contact seen in histology.

However, a critical discrepancy arises when the 2D histological measurement is compared to the comprehensive 3D BIC calculated from the entire micro-CT volume. While 2D micro-CT slices can correlate well with their 2D histological counterparts, multiple studies have reported a

poor or non-existent correlation when a single 2D histological metric is compared against the true 3D volumetric value. This is the “numerical synthesis” that the reviewer rightly pointed out was missing.

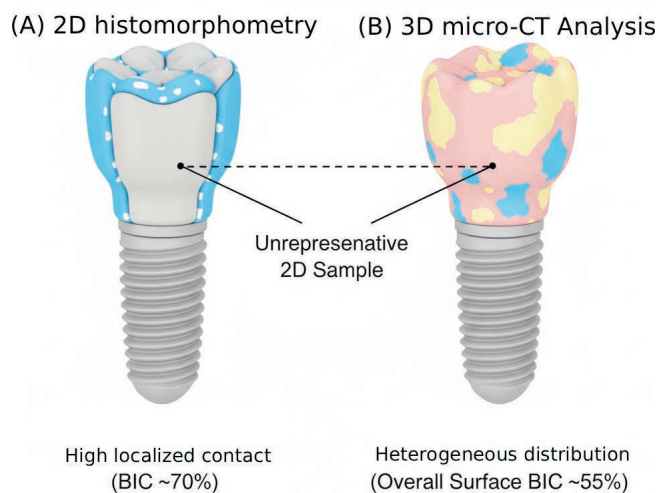


Fig. 6: Schematic illustrating the concept of sampling bias in osseointegration assessment. (A) Traditional 2D histomorphometry provides a high-resolution analysis of a single, arbitrary plane, which may show a high BIC. (B) A comprehensive 3D micro-CT reconstruction of the entire implant reveals the true, heterogeneous nature of the BIC.

For example, a foundational study⁶³ directly quantifying this relationship in a rabbit tibia model found no significant correlation (Pearson’s $r = -0.165$, $p = 0.499$) between 2D histomorphometric BIC and 3D micro-CT BIC. Similarly, a study by Park *et al.*⁸⁰ concluded that a single 2D mid-implant section was a poor predictor of the overall 3D BIC, further challenging the validity of the 2D ‘gold standard’ as a representative measure. This lack of correlation does not indicate a failure of the micro-CT technique. Instead, it exposes the inherent sampling bias of the 2D gold standard itself. As illustrated in Fig. 6, the bone-implant interface is highly heterogeneous; BIC can vary dramatically along the length and around the circumference of an implant⁵⁸. A single 2D histological section is merely one arbitrary

plane through this complex structure and is therefore a fundamentally unrepresentative sample of the whole. The poor correlation between 2D histology and 3D micro-CT is a mathematical inevitability stemming from this sampling bias. This challenges the very notion of 2D histology as a sufficient ground truth for validating 3D assessment tools and suggests that micro-CT, by providing a complete volumetric assessment, may in fact be the more accurate and representative method for quantifying overall osseointegration. A comparison of these assessment techniques is detailed in **Table 4**.

(c) *Beyond morphology: multimodal and multiscale characterization*

A complete understanding of the bone-implant interface requires moving beyond morphology to assess the quality and mechanical competence of the newly formed bone. This has led to the development of multimodal imaging approaches, where micro-CT is combined with other analytical techniques to provide a more holistic characterization⁶⁵. For example, a powerful combination involves correlating micro-CT data with site-matched analysis using Raman spectroscopy and nanoindentation⁶⁴. After micro-CT scanning, the sample can be sectioned, and the same region of newly formed bone at the interface can be analyzed further. Raman spectroscopy provides nanoscale information about the chemical composition, such as the mineral-to-matrix ratio and collagen cross-link quality. Nanoindentation measures microscale mechanical properties like Young's

modulus and hardness. A study using this multimodal approach on a rabbit model demonstrated that the newly formed bone at the implant interface was significantly different from the mature, pre-existing bone; it had a lower mineral-to-matrix ratio, lower crystallinity, and a lower Young's modulus (12.8 GPa vs 15.7 GPa). This reveals that successful osseointegration is not just about the quantity of bone contact, but also the quality and maturation of that bone, adding a crucial property dimension to the 3D spatial data.

(4) *In-vivo and longitudinal imaging*

The non-destructive nature of micro-CT opens the door for longitudinal studies in preclinical animal models, adding time as a fourth dimension to the analysis⁶¹. *In-vivo* micro-CT scanners allow for the same animal to be scanned at multiple time points throughout the healing process (e.g., 2, 6, and 12 weeks post-implantation)⁶¹. This provides invaluable dynamic data on the rate of bone formation, changes in bone microarchitecture over time, and the process of bone remodeling in response to the implant⁶⁰. This 4D approach allows researchers to move from a static picture of the final outcome to a dynamic understanding of the entire biological process of osseointegration, something that is impossible to achieve with destructive, single-timepoint methods like histology. This capability is essential for evaluating the efficacy of new implant surfaces or biomaterials designed to accelerate or enhance healing.

Table 4: Applications of ML/DL across imaging modalities for osseointegration assessment. Abbreviations: BIC, bone-to-implant contact; BAFO, bone area fraction occupancy; BV/TV, bone volume fraction; CBCT, cone-beam computed tomography; ISQ, implant stability quotient; XAI, explainable artificial intelligence.

Technique	Principle	Information Provided	Pros	Cons	Key References
2D Histomorphometry	Light microscopy of stained tissue sections	2D BIC, BAFO, cellular activity	Gold standard, high resolution, cellular detail	Destructive, 2D only, labor-intensive, high variability	58
Micro-CT	X-ray attenuation	3D BV/TV, Tb.N, Tb.Th, 3D BIC, connectivity	Non-destructive, 3D quantification, high throughput	Lower resolution than histology, artifacts, no cellular info	61
Raman Spectroscopy	Inelastic light scattering	Nanoscale chemical composition (mineral: matrix, crystallinity)	Non-destructive, molecular information	Surface technique, complex data analysis	64
Nanoindentation	Mechanical probing	Microscale mechanical properties (Young's modulus, hardness)	Direct mechanical data, high spatial resolution	Destructive, sensitive to surface preparation	64

IV. ML-Assisted Analysis: A New Paradigm in Osseointegration Assessment

The advent of high-resolution, 3D imaging modalities like micro-CT has revolutionized the characterization of the bone-implant interface, but it has also created a new challenge: data overload. A single micro-CT scan can generate thousands of high-resolution images, making manual segmentation and analysis a significant bottleneck that is both time-consuming and prone to operator-dependent variability⁶⁶. This deluge of complex data has created a clear and pressing need for automated, objective, and scalable analysis tools. ML, and particularly its subfield DL, has emerged as a transformative solution, offering a new paradigm for extracting meaningful and predictive information from medical imaging data⁶⁷.

(1) DL architectures for medical image analysis

DL models, particularly Convolutional Neural Networks (CNNs), are exceptionally well-suited for image analysis tasks. Inspired by the human visual cortex, CNNs use a series of learnable filters (or kernels) to automatically extract a hierarchical set of features from raw pixel data, ranging from simple edges and textures in the initial layers to complex, abstract patterns in deeper layers⁶⁸. This ability to learn relevant features directly from data, without the need for manual feature engineering, is their primary advantage over traditional image processing methods.

For tasks requiring pixel-level classification, such as delineating the precise boundaries of bone tissue, encoder-decoder architectures have become the standard. The U-Net architecture, originally developed for biomedical image segmentation, is particularly prominent⁶⁹. It consists of a contracting path (the encoder) that captures

context and a symmetric expanding path (the decoder) that enables precise localization, with “skip connections” linking the two paths to preserve high-resolution feature information⁶⁷. These architectures have demonstrated state-of-the-art performance in segmenting a wide range of anatomical structures from various medical imaging modalities⁶¹.

(2) Applications of ML in zirconia implant assessment

The application of ML in dental implantology is rapidly expanding, moving from simple automation of existing tasks to sophisticated predictive modeling that can inform clinical decision-making. A summary of key applications and reported performance is provided in **Table 5**.

(a) Automated segmentation and morphometry

One of the most immediate applications of DL is the automated segmentation of bone from micro-CT and Cone-Beam Computed Tomography (CBCT) scans⁷⁰. Studies have successfully trained U-Net-based models to accurately delineate bone compartments, such as the epiphyseal and metaphyseal regions in preclinical models, with high fidelity (e.g., mean F1-scores or Dice coefficients often reported between 0.85–0.95)⁷⁰. However, a significant limitation of the current literature, as highlighted in recent systematic reviews, is the wide heterogeneity in methodological reporting. Dataset sizes vary dramatically, from small preclinical cohorts to larger clinical sets, and are not always clearly specified. While common data augmentation techniques like rotation and flipping are often mentioned to improve model robustness, the specific parameters are rarely detailed. This automation enables the high-throughput

Table 5: Applications of ML models in dental implant imaging

Application Task	Imaging Modality	ML/DL Model(s) Used	Key Performance Metrics Reported	Main Finding/Contribution	Key References
Osseointegration prediction	Plain radiography	ResNet, DenseNet, MobileNet	Accuracy: 79.9–83.6 %, AUROC: 0.89–0.92	Feasibility of predicting osseointegration from 2D images	71
Implant stability (ISQ) prediction	CBCT	Cascade network (MobilenetV2- DeeplabV3+ & ResNet-50)	Accuracy: 92.9–96.1%	High-efficiency, automated ISQ classification from 3D data	72
ADDIN ZOTERO_ITEM CSL_CITATION	micro-CT + FEA	Statistical correlation	Strong correlation between micro-CT parameters and FEA-derived stiffness	Links morphology to mechanical competence	74
Osseointegration monitoring	Electro-mechanical impedance	1D CNN	Prediction accuracy: > 94 %	Non-imaging based method for autonomous monitoring	74

and reproducible calculation of the key morphometric (e.g., BV/TV, Tb.N, BIC), effectively eliminating the tedious and subjective nature of manual analysis. In a clinical context, AI-powered segmentation of alveolar bone from CBCT scans has been shown to be up to 116 times faster than manual methods, drastically improving workflow efficiency.

(b) *Predictive modeling of osseointegration and stability*

Beyond descriptive analysis, the true power of ML lies in its predictive capabilities. Several pioneering studies have demonstrated the potential of DL models to predict clinical outcomes directly from standard radiographic images. In one notable study, a suite of CNNs, including ResNet and DenseNet architectures, were trained on a large dataset of post-operative plain radiographs⁷¹. The models were able to predict the ultimate success or failure of osseointegration with high performance, achieving mean accuracies between 79.9% and 83.6% and Area Under the Receiver Operating Characteristic Curve (AUROC) values as high as 0.922. This suggests that subtle radiographic patterns, potentially imperceptible to the human eye, contain predictive information about the biological state of the bone-implant interface.

This predictive capacity extends to 3D imaging as well. A multi-task cascade network has been developed to analyze CBCT images, first using a segmentation model (MobilenetV2-DeeplabV3+) to identify the peri-implant bone region of interest, and then feeding this volume into a classification model (ResNet-50) to predict the Implant Stability Quotient (ISQ), a clinical measure of stability. This system achieved prediction accuracies of over 96% for binary classification of stability⁷². Furthermore, ML can be used to bridge the gap between imaging and biomechanics by correlating micro-CT-derived structural parameters with outputs from finite element analysis (FEA) to create models that can predict the mechanical stiffness of the peri-implant bone from imaging data alone⁷³.

(3) *The “black box” problem and the imperative of explainable AI (XAI)*

(a) *Defining the challenge*

Despite their impressive performance, a major barrier to the clinical adoption of deep learning models is their inherent opacity, often referred to as the “black box” problem⁷⁵. A deep neural network can make a highly accurate prediction, but the complex, non-linear pathway through millions of interconnected parameters makes it nearly impossible for a human to understand the specific reasoning behind its decision⁷⁶. This lack of transparency is a critical issue in high-stakes fields like medicine, where it erodes trust and complicates accountability. If a model predicts a high risk of implant failure, a clinician needs to understand why to make an informed treatment decision. Without this understanding, the AI remains a “black box” that renders verdicts without justification, hindering its integration into clinical workflows.

(b) *Solutions through explainability*

The emerging field of eXplainable AI (XAI) aims to address this challenge by developing methods to peer inside the black box and make model decisions more transparent and interpretable⁷⁴. Rather than just providing a prediction, XAI techniques generate an “explanation” that accompanies it. For image-based tasks, these explanations often take the form of saliency or heat maps, which highlight the specific pixels or regions in the input image that were most influential in the model’s decision-making process⁷⁶. Methods like LIME (Local Interpretable Model-agnostic Explanations) and SHAP (SHapley Additive exPlanations) can be applied to trained models to quantify the contribution of different input features to a given prediction. For example, a SHAP analysis of a model predicting peri-implantitis risk was able to identify that patient race and history of osteoporosis were unexpectedly strong predictors in the dataset, providing insights that could guide further clinical investigation. By providing this explanatory layer, XAI transforms the AI from an opaque oracle into an interactive and auditable decision-support tool, fostering the trust and confidence necessary for clinical adoption.

(4) *The future horizon: personalized implants and digital twins*

The true transformative potential of AI in implantology lies in its ability to synthesize vast amounts of patient-specific data to enable truly personalized medicine. The convergence of the technologies and concepts discussed throughout this review points toward a future centered on the “digital twin”⁷⁷. A digital twin is a high-fidelity, virtual replica of a patient’s specific anatomy – in this case, the jawbone and surrounding structures – created from high-resolution imaging data like CBCT scans⁷⁸.

This digital twin serves as a virtual testbed for treatment planning and simulation. AI algorithms can analyze this patient-specific model to automatically identify critical anatomical structures, assess bone quality, and recommend an optimal implant size, position, and angulation. This information can then be used to design a fully personalized, patient-specific implant that is perfectly adapted to the individual’s anatomy, which can then be fabricated using 3D printing⁷⁹.

Furthermore, the digital twin represents the ultimate synthesis of the core themes of this review. It is a multi-scale model that must incorporate information about the implant’s material properties, which are derived from its processing and microstructure. It must then simulate the complex biological interactions at the bone-implant interface, using rules and parameters informed by data from micro-CT and multimodal imaging. Finally, the long-term performance – the prediction of osseointegration success and biomechanical stability under physiological loads – can be simulated using a predictive engine powered by machine learning models trained on vast clinical datasets. This integrated approach promises to move implant dentistry from a reactive to a predictive discipline, allowing clinicians to test and optimize treatment strategies in a virtual environment to maximize

the probability of long-term success before ever making an incision.

Moreover, the application of AI extends beyond mere automation of known processes; it functions as a powerful engine for scientific discovery. By training deep learning models to predict outcomes from raw imaging data, and then using XAI to interpret what those models have learned, researchers can identify novel, previously unrecognized imaging biomarkers of osseointegration. These subtle textural or micro-architectural features, once validated, can be incorporated into future clinical assessments, creating a virtuous cycle where AI not only improves clinical efficiency but also deepens our fundamental understanding of the underlying biology.

V. Conclusions

The pursuit of an ideal dental implant has driven significant innovation, leading from the established success of titanium to the promising advent of zirconia ceramics. This review has critically examined the complex, interconnected factors that govern the performance of zirconia implants, establishing a clear linkage from initial material processing and surface modification to the resulting microstructure and, ultimately, to *in-vivo* osseointegration and long-term clinical outcomes. The evidence demonstrates that the success of zirconia is not an intrinsic material property but a carefully engineered balance of competing demands for mechanical toughness, resistance to degradation, and surface bioactivity. The heterogeneity observed in clinical studies is a direct reflection of the varying degrees of success with which different material generations and designs have navigated this fundamental “zirconia trilemma”.

To navigate this complexity and unlock the full potential of ceramic implants, a paradigm shift in assessment methodology is required. Traditional 2D histomorphometry, while valuable for its cellular-level detail, is an insufficient and unrepresentative gold standard for characterizing the complex 3D reality of the bone-implant interface. High-resolution, non-destructive micro-CT, especially when combined with multimodal techniques that probe the chemical and mechanical properties of the peri-implant bone, offers a far more comprehensive and accurate picture of osseointegration.

The vast and complex datasets generated by these advanced imaging modalities necessitate the integration of machine learning. AI and deep learning are proving to be indispensable tools, not merely for automating analysis and improving efficiency, but for their transformative potential to predict clinical outcomes from standard imaging and to discover novel, data-driven biomarkers of healing. By leveraging explainable AI (XAI), we can translate the “black box” decisions of these powerful algorithms into clinically interpretable insights, fostering trust and facilitating their adoption.

Looking forward, the convergence of these fields – advanced materials science, multimodal imaging, and artificial intelligence – points toward a future of truly personalized implant dentistry. The development of patient-specific digital twins, which integrate anatomical data with predictive simulations of biological and

mechanical performance, represents the ultimate synthesis of this approach. This will enable clinicians to design and validate customized treatment strategies in a virtual environment, moving the field from a reactive to a predictive and preventative model of care. While significant challenges related to data standardization, algorithmic transparency, and regulatory approval remain, the pathway is clear. The continued, synergistic development of advanced materials and intelligent analytical tools holds the key to realizing the full promise of zirconia implants and defining the next generation of dental restorative care.

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