

A critical review of dental biomaterials with an emphasis on biocompatibility

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Abstract

This paper presents the major achievements in the field of biomaterials in restorative dentistry and tissue regeneration reported over the past 3 years. The review aims to summarize the knowledge on important biomaterials and the emerging modification strategies to improve their biointegration, biological activity, mechanical properties, and resistance to the harsh oral environment. We also discuss the main opportunities and challenges associated with the use of biomaterials in dentistry.

Much contemporary research focuses on the interactions between biomaterials and the surrounding tissues in the oral environment regarding adhesion, associated stresses and strains, and the durability of dental restoration materials. Dental biomaterials should support cell adhesion and activity, leading to dental tissue regeneration, and are also expected to effectively prevent bacterial infections and inhibit material corrosion in saliva. The degradation, dissolution or corrosion of restorative materials due to exposure to body fluids can alter the structure and mechanical properties of the material, causing various adverse effects.

Another aspect addressed in recent literature is the improvement of the mechanical properties and esthetics of restorative materials. The surfaces of biomaterials are usually modified with polymers or nanomaterials to reduce friction while maintaining biocompatibility.

Although all modern biomaterials are promising, there is an urgent need for more in vivo and clinical studies to investigate their biological advantages and disadvantages in detail. The computational techniques used to assess the properties of modern dental materials, particularly the mechanical ones, could assist in the development of the materials. Such an approach can help bring new biomaterials to the market by reducing complicated, tedious and expensive experimentation.

Keywords: biomaterials, orthodontics, restorative dentistry, prosthodontics, periodontology

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Introduction

Only a few commercially available dental biomaterials have passed all biocompatibility screening assays, thus confirming their low toxicity and patient health protection.^{1,2} Most dental materials have been approved based on the grandfathering process, which allows for sale without prior toxicity tests if a biomaterial is characterized by a similar chemical composition, sterilization procedure, production procedure, and the same dose of active substances as compared to the marketed products.³ Since May 2021, the European Union (EU) have been implementing a new regulation for marketing and using medical devices,⁴ Regulation (EU) 2017/745 or the Medical Device Regulation (MDR), which replaces the former Medical Device Directive (MDD) 93/42/EEC.⁵ The new regulation will substantially impact those involved in manufacturing, distributing and using medical devices, as it requires the entire lifecycle of a medical device to be represented by a comprehensive set of dental product data, including clinical outcomes.^{4–6}

Biocompatibility is vital for all treatment strategies and refers to the ability of the material to function in the oral environment without causing local or systemic harm, essentially meaning the interaction between the material and the host must be harmonious. Generally, adverse reactions in patients can be classified as local or systemic. The first category concerns a direct interaction with the oral mucosa and pulp, which may cause mucosal irritation or oral lichenoid reactions, while systemic adverse reactions (mainly hypersensitivity and anaphylactic shock) relate to the overreaction of the immune system.⁷ Interestingly, after many years of exposure to dental materials, patients and dental staff experience various adverse reactions, from cracking or flaking skin, swelling and irritation to peripheral neuropathy.⁸ Hence, an objective assessment of dental material biocompatibility is crucial for ensuring patient safety and successful treatment. Additionally, it is equally important to emphasize that proactive diagnostics and material selection can substantially decrease the likelihood of complications and the need for follow-up treatment.

The most commonly used dental biomaterials are restorative materials applied to fill tooth cavities or treat dental caries, and materials for hard and soft tissue repair. The former group includes resin composites, titanium (Ti) and zirconium (Zr) alloys, polymers, ceramics, casting investments, and impression materials. The latter category comprises biomaterials that may serve as scaffolds for cell adhesion and proliferation, as well as carriers in drug delivery systems to treat fractures, and for temporomandibular joint reconstruction, dentin/enamel reconstruction, periodontal ligament (PDL) replacement, and the pre-osseointegration of dental implants.^{9,10} Examples of the applications of dental materials are presented in Fig. 1.

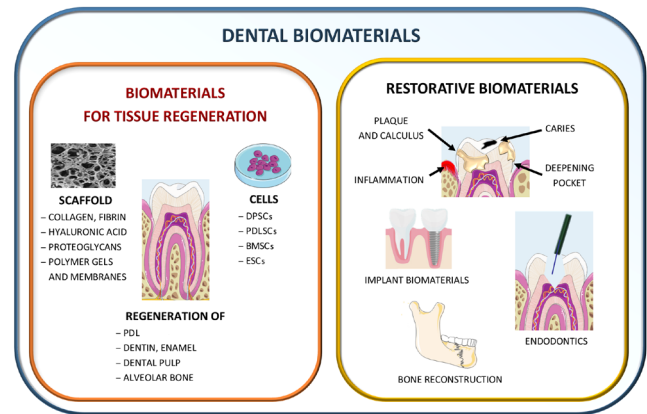


Fig. 1. Various applications of biomaterials in dentistry

PDL – periodontal ligament; DPSCs – dental pulp stem cells; PDLSCs – periodontal ligament stem cells; BMSCs – bone marrow stem cells; ESCs – embryonic stem cells.

Despite the wide availability of dental biomaterials, no material has ideal properties. The selection of biocompatible materials depends on several factors, such as their mechanical and biological characteristics, stability in the oral environment (including corrosion in saliva), functionality, the final cost, and esthetics. Furthermore, biomaterials are expected to be multifunctional, biologically active, and offer combined features, as in the case of composite dental fillings that exhibit antibacterial and remineralization effects.^{11,12} Dental biomaterials have evolved extensively over the last 10 years, with their functionality being progressively improved. However, there is a vast space for further investigations on the longevity of biomaterials, their wear behavior in the changing environment of the oral cavity, their bioactive potential, and the enhancement of their biological, optical and mechanical properties.

The repair and regeneration of injured hard and soft tissues remains challenging. There have been many attempts to favor the regrowth process of different soft tissues with advanced dental materials. However, these approaches could not re-establish the complex structure–function interactions with other tissues, and additional studies are required.^{13–15} In the case of hard tissues, the primary problem is polymerization shrinkage at the composite–tooth interface, which usually leads to micro-leakage and secondary caries.^{16–20} Thus, improving the prolonged release of active components from various dental restorative materials, taking into account their wear in the oral environment, remains a significant challenge in dentistry.^{21–23}

This review presents the major achievements in the field of biomaterials reported over the past 3 years (Fig. 2), and aims to summarize the emerging modification strategies to improve the biointegration, biological activity and mechanical properties of the materials, as well as their resistance to the oral environment. We also discuss the main opportunities and challenges associated with the use of biomaterials in dentistry.

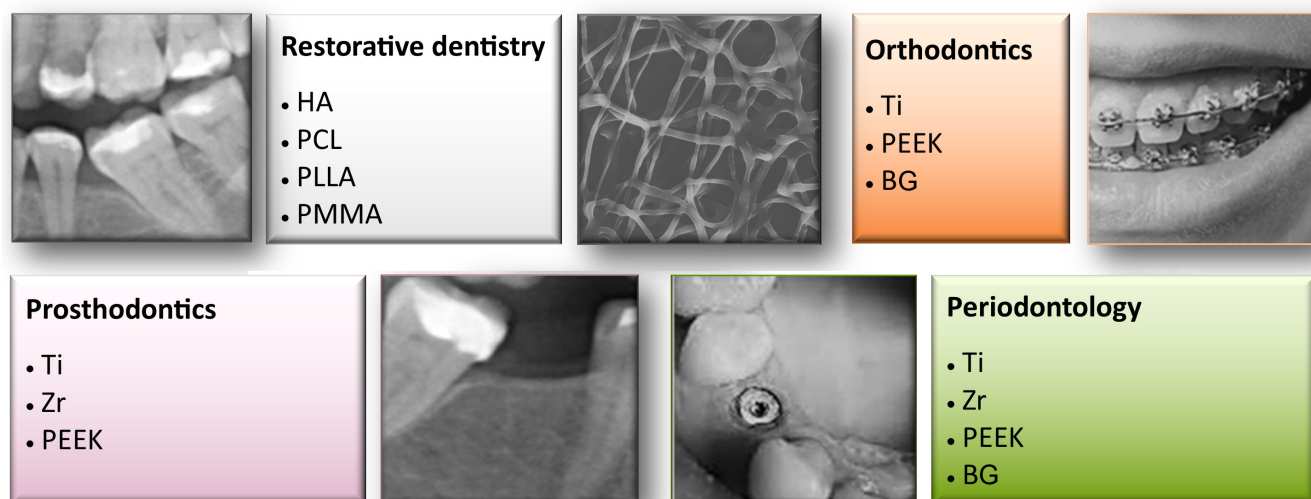


Fig. 2. Various materials used in dentistry

HA – hydroxyapatite; PCL – poly(ϵ -caprolactone); PLLA – polylactic(L-lactic) acid; PMMA – polymethyl methacrylate; Ti – titanium; PEEK – polyetheretherketone; BG – bioactive glass; Zr – zirconium.

Examples of the most important reports on biomaterials published over the past 3 years are presented in Table 1 and discussed in the relevant sections.

Methods

The PubMed, Scopus and Google Scholar search engines were used in the bibliometric analysis, using a combination of the following keywords: ‘dental material’ with ‘biocompatibility’, ‘tissue regeneration’, ‘restorative dentistry’, ‘orthodontics’, ‘prosthodontics’, ‘Ti’, ‘polyetheretherketone’ (PEEK), ‘bioactive glass’ (BG), ‘resin’, ‘ceramic’, ‘implant’, ‘polymethyl methacrylate’ (PMMA), ‘in vivo’, ‘in vitro’, ‘clinical studies’, ‘simulation’, and ‘deep learning’.

The exclusion criteria were manuscripts written in a language other than English, those not available, and articles published before 2020 (with a few exceptions of articles essential to the development of the techniques described). At the same time, to ensure originality and accuracy, the search focused on research papers and excluded review articles. As a result, articles with titles containing words such as ‘review’, ‘meta-analysis’ or ‘overview’ were not included, with few exceptions. Additionally, we added a description of the method used for conducting the systematic literature review in the supplementary materials (available on request from the corresponding author).

Biomaterials for soft and hard tissue regeneration

Over the past 3 years, there has been a significant increase in research related to dental biomaterials for tissue regeneration and reconstruction as compared to other restorative materials.²⁴ Dental tissue engineering allows

the replacement of missing teeth with bioengineered products and the regeneration of damaged dental tissues with the use of dental stem cells.²⁵ Appropriate stem cells are seeded on the surfaces of biomaterials (bioscaffold surfaces), which stimulate them to create a biocomplex. Various mesenchymal stem cells are found in the tooth, such as dental pulp stem cells (DPSCs), periodontal ligament stem cells (PDLSCs), dental follicle stem cells (DFSCs), and stem cells from the dental apical papilla or the exfoliated deciduous teeth. However, the first 2 cell lines are recognized as the most powerful in dental tissue engineering.^{25–27} Biomaterials for scaffolds are designed to facilitate cell proliferation, differentiation, adhesion, and migration. Additionally, scaffolds loaded with appropriate growth factors or biomolecules can mimic tissue-specific micro-environments, and regulate the cell–matrix interactions, angiogenesis and the formation of the extracellular matrix (ECM).²⁸

Various polymers (natural and synthetic) are suitable bioscaffolds for the proliferation and differentiation of dental stem cells.²⁹ Natural scaffolds are usually made of polysaccharides, such as alginate, hyaluronic acid and its derivatives, or chitosan, and are endowed with various proteins, including collagen, fibrin and silk. Natural scaffolds exhibit excellent biocompatibility and degrade faster than synthetic polymers, without releasing toxic components. However, their mechanical properties are much worse as compared to synthetic bioscaffolds.³⁰ On the other hand, synthetic bioscaffolds, such as poly(ϵ -caprolactone) (PCL), polylactic acid (PLA) and polyethylene glycol (PEG), display better physicochemical properties, but degrade much slower and have lower biocompatibility. Synthetic polymers are often enriched with various bioactive compounds, such as nano-hydroxyapatite (nHA), nanofluoroapatite or BG, to reduce their cytotoxicity or add new features.^{31–36}

Table 1. Biomaterials in dentistry reported during the last 3 years

Area	Biomaterials	Functionality/results	Research advancement	Reference number
Biomaterials for soft and hard tissue regeneration				
Resin composites	Bis-GMA/TEGDMA resin composites modified with Zn/Sr-doped HA	– restorative materials for hard tissue treatment; – improvement of antibacterial activity and mineralization capacity without the loss of biocompatibility	in vitro studies: cytotoxicity (L929 fibroblasts); antibacterial test (<i>S. aureus</i>)	53
	silica aerogel/Bis-GMA/TEGDMA resin composites (size of silica aerogel particles: 15 nm and 50 nm)	– restorative materials for hard tissue treatment; – improved mechanical and antimicrobial properties, higher hardness and lower water absorption than in the case of pure composites	in vitro antibacterial studies (<i>S. aureus</i>)	54
	CP/Bis-GMA/TEGDMA resin composites	– restorative materials for hard tissue treatment; – remineralization of caries-affected dentin and the prevention of caries lesions under orthodontic brackets, controlled release of ions after 2–3 months	in vitro/ex vivo remineralization studies with human teeth and artificial saliva (review article)	55
	SiO ₂ - and Al ₂ O ₃ -based UDMA resin composites	– restorative materials for hard tissue treatment; – increased surface roughness and porosity; – only Al ₂ O ₃ -enriched resins showed sufficient physicomaterial properties to be used as resin fillings	lack of biological studies	57
GIC	encapsulated commercial GIC: Fuji II LC, Fuji IX, Ketac™ Fil Plus, and EQUIA Forte™ HT Fil	– restorative materials for hard tissue treatment; – encapsulation eliminated the manual mixing problem and improved the surface hardness of GIC in the post-aging studies	in vitro aging studies investigating mineral deposition	171
	RMGIC modified with ZnO NPs (20–40 nm, 2 wt%)	– restorative materials for hard tissue treatment; – improvement of antibacterial activity without sacrificing fluoride release properties and flexural strength	in vitro antibacterial studies (<i>S. mutans</i>)	60
	commercial GIC (Fuji II LC) modified with a propolis extract	– restorative materials for hard tissue treatment; – lack of antibacterial properties after the addition of the propolis extract, the deterioration of flexural and shear strength	in vitro antibacterial studies (<i>S. mutans</i>)	61
	GIC (Fuji II) modified with 3 active components: nHA (4 wt%), Zn L-carnosine (6 wt%) and ciprofloxacin (1.5 wt%)	– restorative materials for hard tissue treatment; – improved thermal, mechanical and biological properties of biomaterials; – combination of GIC and bioactive components can help treat caries in non-compliant patients, including children	in vitro studies: cytotoxicity (human gingival fibroblasts BSCL138, human keratinocytes BSCL143L); antibacterial test (<i>S. mutans</i>)	62
Bioscaffolds	chitosan/gelatin/HA scaffolds	– restorative materials for tissue engineering; – excellent biomimetic microenvironment for cells, supporting their odontogenic differentiation and biomineralization in vitro	in vitro studies (DPSCs)	38
	ECM from DPSCs	– restorative materials for tissue engineering; – improved osteogenic differentiation/mineralization of gingival fibroblasts	in vitro/ex vivo tests (DPSCs were isolated from the teeth or gingival tissues of healthy adult patients)	39
	laminin-DPEM	– restorative materials for tissue engineering; – the introduction of laminins to DPEM enhances the adhesion of DPSCs and promotes their odontogenic differentiation	in vitro/ex vivo tests (the dentin matrix was extracted from the premolars of beagles)	40
	decellularized bioscaffolds isolated from rat DP tissue	– restorative materials for tissue engineering; – ability to support dental stem cell repopulation	in vitro/ex vivo studies (DP was isolated from rat jaws, and the decellularized scaffolds were recellularized with human DPSCs in vitro)	42
	L-arginine-containing mesoporous SiO ₂ NPs	– restorative materials for tissue engineering; – controlled release of L-arginine inhibits bacterial growth and neutralizes the acidic environment responsible for the development of secondary caries	in vitro antibacterial studies (<i>S. mutans</i> , <i>L. casei</i>)	64
nHA	commercial toothpaste containing F and HA (F1400, F500, Biorepair®)	– restorative materials for tissue engineering; – the toothpaste reaches the enamel matrix and the apatitic mineral phase by penetrating the enamel layer, thereby improving remineralization	in vitro/ex vivo studies (8 primary teeth extracted for orthodontic reasons)	66
	HA-modified commercial dental flosses (Oral-B®)	– restorative materials for tissue engineering; – efficient drug delivery system for the prevention and treatment of early caries; – ability to remove the bacterial biofilm from interproximal areas	in vitro studies (<i>S. salivarius</i> K12)	67

Area	Biomaterials	Functionality/results	Research advancement	Reference number
Biomaterials in restorative dentistry				
Ti and Ti alloys	Ni-Ti orthodontic wires	<ul style="list-style-type: none"> – biomaterials in orthodontics; – Ni-Ti orthodontic wires are susceptible to corrosion in the oral cavity, especially at friction points 	in vitro studies on the corrosion of orthodontic wires in the oral cavity	78
	Ti implants	<ul style="list-style-type: none"> – biomaterials in orthodontics; – mechanical treatment of Ti implants may increase the dissolution of Ti in peri-implant tissues, potentially contributing to the development of peri-implantitis 	ex vivo studies (a model of organic polymicrobial peri-implant biofilms)	68
	Ti implants	<ul style="list-style-type: none"> – biomaterials in orthodontics; – Ti was detectable in PICF and GCF, even in healthy subjects 	clinical study evaluating the fissure fluid from both implants and the adjacent teeth for the possibility of Ti contamination (77 patients with 117 implants)	69
	CM and a synthetic BS combined with TM	<ul style="list-style-type: none"> – biomaterials in orthodontics; – application of CM and a synthetic BS combined with TM did not facilitate lateral bone augmentation; – in vivo results were inconclusive 	in vivo studies investigating the lateral bone augmentation of chronic peri-implant defects (6 canine mandibles)	70
	Ti and Zr implants coated with β -TCP	<ul style="list-style-type: none"> – Ti and Zr implants coated with β-TCP can generate periodontal tissue and form biohybrid implants 	in vivo studies (the implants were implanted in rabbits after the extraction of lower right central incisors, and examined at 45 and 90 days)	128
	Ti and Zr disks	<ul style="list-style-type: none"> – biomaterials in orthodontics; – air-polishing, the ultrasonic scaler and the Er:YAG laser significantly reduced the amount of biofilm on Ti and Zr surfaces 	in vitro studies examining the decontamination methods to remove the bacterial biofilm from biomaterial surfaces	130
	Ag/HA NPs and ZnO NP coatings on orthodontic Ti mini-screws	<ul style="list-style-type: none"> – biomaterials in orthodontics; – orthodontic Ti mini-screws coated with ZnO NPs revealed the highest antimicrobial activity against bacteria and fungi, and showed better cytocompatibility with oral epithelium cells, bone cells and fibroblasts as compared to the Ag/HA NP coating 	in vitro antibacterial tests (<i>E. aeruginosa</i> , <i>S. aureus</i> , <i>S. mutans</i> , <i>E. faecalis</i> , <i>E. coli</i> , <i>C. albicans</i>) and cytotoxicity tests (fibroblasts, osteocytes, osteoblasts, and oral epithelial cells)	81
complete-arch implant-supported fixed maxillary prostheses made of Ti or monolithic Zr	<ul style="list-style-type: none"> – biomaterials in prosthodontics; – Zr prostheses showed less plaque accumulation and less inflammation of the adjacent soft tissues as compared to Ti prostheses 	clinical study comparing plaque accumulation and soft tissue inflammation	77	
PEEK	PEEK FDP	<ul style="list-style-type: none"> – biomaterials in prosthodontics; – 95% of patients maintained their PEEK FDP without fracture, while 5% reported decementation; – 10% of PEEK FDP showed marginal discoloration 	clinical study examining the efficacy of PEEK FDP over 1 year; 20 patients received three-unit posterior PEEK FDP	98
	PEEK and sandblasted PEEK disks	<ul style="list-style-type: none"> – biomaterials in orthodontics; – sandblasted PEEK was more susceptible to bacterial adhesion; – bacterial adhesion to PEEK is lowest on materials with a rough surface 	in vitro tests (<i>S. sanguinis</i> , <i>S. oralis</i> , <i>E. faecalis</i> , and <i>S. gordonii</i>)	85
	PEEK and Ti healing abutments	<ul style="list-style-type: none"> – biomaterials in orthodontics; – PEEK healing abutments induced a stronger inflammatory response in the tissues as compared to Ti healing abutments 	clinical study examining and comparing the response of soft tissues to biomaterials (22 implants with PEEK or Ti healing abutments were placed in 11 patients for 3 months)	87
	PEEK and Ti scaffolds	<ul style="list-style-type: none"> – biomaterials in orthodontics; – PEEK scaffolds showed lower biomechanical strength than Ti scaffolds; – both scaffolds provide excellent osteogenic space retention as compared to traditional GBR surgery 	in vivo studies investigating alveolar bone augmentation (3 beagles, 18 bone defects were created in the mandibles of 3 dogs (6 per dog))	88
	orthognathic surgery combined with simultaneous PEEK bone augmentation	<ul style="list-style-type: none"> – biomaterials in orthodontics; – orthognathic surgery with PEEK bone augmentation significantly improved facial symmetry, even in patients with combined soft and hard tissue hypoplasia 	clinical study comparing the facial symmetry results after digitally planned surgery and bone augmentation with PEEK (30 patients, including those with and without laterognathia, patients with and without syndesmosis, and patients with and without PEEK bone augmentation)	103

Area	Biomaterials	Functionality/results	Research advancement	Reference number
Biomaterials in restorative dentistry				
BG	GIC, GIC with CP, Ag NP-modified GIC, and 45S5 Bioglass® paste	– biomaterials in orthodontics; – GIC with CP exhibited the strongest bond	ex vivo study examining the effects of bonding agents on the luting strength of orthodontic brackets (48 healthy human premolars)	108
	BioMin® F and NovaMin®	– biomaterials in orthodontics; – orthodontically induced WSLs can be diminished through BioMin F remineralization therapy	clinical study comparing the treatment of orthodontically induced WSLs with 2 types of BG (60 patients aged 14–26 years, with a total of 60 WSLs, the formulations were tested for 5 weeks)	111
Resins	epoxy resin-coated Ni-Ti orthodontic wires	– biomaterials in orthodontics; – epoxy resin coating ensures increased corrosion resistance and reduced leakage of Ni into saliva	corrosion studies using artificial saliva	84
	ZnO NP-PMMA nanocomposite (a denture base material)	– biomaterials in prosthodontics; – nanocomposite was prone to color changes after exposure to various solutions; – modification of PMMA with ZnO NPs is esthetically acceptable at a concentration of 2.5% or 5%	lack of biological studies; the degradation test was performed for 6 months to examine stability and color changes after exposure to water, coffee, red wine, black tea, and a denture cleaning solution	113
	PMMA modified with TiO ₂	– biomaterials in prosthodontics – adding TiO ₂ NPs ensured a significant reduction in bacterial adhesion to the biomaterial surfaces	in vitro antibacterial studies (<i>S. mutans</i>)	115
	graphene-PMMA composites	– biomaterials in prosthodontics; – significant improvement of the mechanical properties of composites with a low content of graphene (0.1027%)	lack of biological studies	117
	CAD/CAM PMMA resins	– biomaterials in prosthodontics; – improved mechanical and biological features, i.e., a higher modulus of elasticity, lower cytotoxicity and slight changes in cell morphology	in vitro studies (keratinocytes): cytotoxicity test, morphological changes of the cells after exposure to the tested material	118
	PEKK-based double-crown dental prostheses (modified with Au and Co-Cr)	– biomaterials in prosthodontics; – PEKK/PEKK and Au/PEKK primary/secondary crown combinations exhibited superior surface wear than the control group	lack of biological studies; stabilization studies for the double-crown system in a wet environment simulating 13 years of use to investigate the retentive forces of several material combinations between primary and secondary crowns	96
Ceramics	multi-layered Zr ceramics (cantilever IRFDP)	– biomaterials in prosthodontics; – acceptable fracture resistance	in vitro studies (natural teeth were used as abutments to simulate clinical conditions and create the ideal matching of the adhesive interface)	121
	metal-ceramic and ceramic FDP	– biomaterials in prosthodontics; – the highest incidence of chipping occurred in Zr FDP with a complete veneer, followed by metal-ceramic FDP with a high noble metal framework	cohort study evaluating the chipping and failure rates of FDP supported by metal-ceramic and ceramic implants and combined tooth-implant-supported FDP (434 FDP placed in 324 patients, an observation period of 0.5–12.6 years)	124
	ceramic brackets (Forestadent, G&H Orthodontics, GC Orthodontics, DynaFlex, and American Orthodontics)	– biomaterials in orthodontics; – all ceramic brackets were prone to discoloration – coffee had the greatest effect on color stability	in vitro studies examining the color stability of ceramic brackets in various fluids (100 ceramic brackets dipped in coffee, Coca-Cola®, Cedevida®, and artificial saliva)	82

GIC – glass ionomer cement; nHA – nano-hydroxyapatite; Ti – titanium; PEEK – polyetheretherketone; BG – bioactive glass; Bis-GMA – bisphenol A-glycidyl methacrylate; TEGDMA – triethylene glycol dimethacrylate; Zn – zinc; Sr – strontium; HA – hydroxyapatite; *S. aureus* – *Staphylococcus aureus*; CP – calcium phosphate; SiO₂ – silicone dioxide; Al₂O₃ – aluminum oxide; UDMA – urethane dimethacrylate; RMGIC – resin-modified glass ionomer cement; ZnO – zinc oxide; NP – nanoparticle; *S. mutans* – *Streptococcus mutans*; Zn – zinc; DPSCs – dental pulp stem cells; ECM – extracellular matrix; laminin-DPEM – laminin-modified native dental pulp extracellular matrix; DP – dental pulp; *L. casei* – *Lactobacillus casei*; F – fluorine; *S. salivarius* – *Streptococcus salivarius*; Ni – nickel; PICF – peri-implant cavity fluid; GCF – gingival crevicular fluid; CM – collagen membrane; BS – bone substitute; TM – Ti mesh; Zr – zirconium; β-TCP – beta-tricalcium phosphate; Er:YAG – erbium-doped yttrium-aluminum garnet; Ag – silver; *E. aeruginosa* – *Enterobacter aeruginosa*; *E. faecalis* – *Enterococcus faecalis*; *E. coli* – *Escherichia coli*; *C. albicans* – *Candida albicans*; FDP – fixed dental prosthesis; *S. sanguinis* – *Streptococcus sanguinis*; *S. oralis* – *Streptococcus oralis*; *S. gordonii* – *Streptococcus gordonii*; GBR – guided bone regeneration; WSL – white spot lesion; PMMA – polymethyl methacrylate; TiO₂ – titanium dioxide; CAD/CAM – computer-aided design/computer-aided manufacturing; PEKK – polyetheretherketone; Au – gold; Co – cobalt; Cr – chromium; IRFDP – inlay-retained fixed partial prosthesis.

Another promising group of biomaterials that have shown advantages as dental scaffolds are hydrogels (HGs). They are soft, three-dimensional (3D) networks made of hydrophilic polymers, which can be natural, synthetic, or a combination of both. Hydrogels provide a tissue-like micro-environment and, due to their elasticity and flexibility, can mimic the native ECM. Moreover, various nanomaterials and bioactive compounds are incorporated into the polymer matrix of HGs to increase the efficiency of the scaffold.³⁷ The potential of chitosan/gelatin/hydroxyapatite (HA) scaffolds to enhance the viability and proliferation of DPSCs was examined by Vagropoulou et al., who found that these hybrid scaffolds provided a biomimetic micro-environment for cells, supporting their odontogenic differentiation and biomineralization *in vitro*.³⁸

Bioscaffolds for tooth engineering can be prepared from the native ECM, which is unique for each cell type, provides tissue architecture and delivers specific growth factors. For instance, Nowwarote et al. reported that ECM from DPSCs exhibited improved osteogenic differentiation/mineralization of gingival fibroblasts.³⁹ In turn, Fu et al. proposed an excellent dental pulp (DP) tissue regeneration strategy via the laminin-modified native DP ECM (laminin-DPEM).⁴⁰ Based on *in vitro* tests, the authors showed that introducing laminins to DPEM enhanced the adhesion of DPSCs and promoted their odontogenic differentiation.⁴⁰

Wang et al. fabricated a novel, biologically active scaffold for tooth engineering based on dentin, which was freeze-dried to maintain its mechanical and biological properties.⁴¹ Dental pulp stem cells cultured on the freeze-dried dentin showed improved attachment, growth, viability, and collagen secretion.⁴¹ The ability to support dental stem cell repopulation on the decellularized bioscaffold was evaluated by Matoug-Elwerfelli et al.⁴² The bioscaffold isolated from rat DP tissue demonstrated positive expression of odontoblastic markers and growth factors.⁴²

Metallic biomaterials are of great interest in dentistry due to their excellent mechanical features and biocompatibility.⁴³ They are applied as dentures, plates, joints, screws, and implants to restore the functions of missing tissues. Cobalt-chromium (Co-Cr), stainless steel, gold (Au), Zr, and Ti alloys are predominant among all metallic biomaterials. However, Ti- and Zr-based alloys exhibit better osseointegration than other metals and alloys. Moreover, Ti alloys possess superb mechanical properties. Thus, Ti and its alloys are still the primary materials used for dental implants.⁴³ However, Ti-based dental implants need to be improved, as they cause allergic reactions and the discoloration of the mucosa. Another significant drawback of Ti dental implants is corrosion, which results in the release of Ti particles into the tissues close to the implants and local lymph nodes. Conditions in the oral environment, including the application of fluoride-enriched toothpastes or mouthwashes, or high glucose

levels, may enhance this unfavorable process. Zirconium-based dental materials are suitable for biomedical applications due to their low porosity, high density, high flexural strength, and resistance to fracture and corrosion. Zirconium restorative materials have other advantages, such as degradation and aging in water or water vapor.⁴⁴ Generally, both Zr and Ti implants reveal similar osseointegration. The modification of the surfaces of metal-ceramic implants improves their mechanical properties, fracture toughness and wear resistance, and inhibits bacterial adhesion. The most common modification methods are sandblasting, laser ablation, polishing, acid etching, ultraviolet (UV) treatment, or the addition of nanocomposites (e.g., nHA). Preclinical studies indicate that the surface modification of metallic biomaterials brings an enormous benefit in terms of improved osseointegration.⁴⁵

Biomaterials can be used as carriers in drug delivery systems to facilitate implantation or treat various infections and oral diseases, and may come in multiple forms, such as nanosystems/nanoparticles (NPs), nanofibers, thin films, HGs, or scaffolds. They can be made of natural or synthetic polymers, organic or inorganic NPs, ceramic materials, or metal compounds. Such carriers protect the active components of the drugs against degradation or deactivation in the oral environment, and allow their controlled release and targeting pathogenic bacteria.^{46,47} For instance, a chitosan-agarose HG was applied for the biomimetic remineralization of a native enamel surface, and a significant increase in the microhardness of the enamel-like layer was observed after a 7-day remineralization process in artificial saliva.⁴⁵ In turn, a chitosan-based HG enriched with an amelogenin-derived peptide (QP5) was suitable to inhibit the growth of cariogenic bacteria and promote the remineralization of initial caries lesions.⁴⁵

In the last few years, regenerative therapies based on guided bone regeneration (GBR) and guided tissue regeneration (GTR) have attracted a great deal of attention.⁴⁸ Guided bone regeneration focuses on the regeneration of the alveolar bone in edentulous regions, while GTR repairs periodontal tissues.^{49,50} Both GBR and GTR use a porous membrane to physically prevent unwanted cells from entering the lesion area. Such membranes should have excellent biocompatibility, and ensure the spatial and biomechanical stability of the lesion site. Based on their composition and bioactivity, polymeric membranes for GBR and GTR can be classified into absorbable, non-resorbable and inorganic-based materials.⁴⁸ The first group primarily comprises natural polymers, including collagen-, gelatin- and chitosan-based materials. The non-resorbable membranes are typically made of synthetic polymers, such as expanded or dense polytetrafluoroethylene (PTFE), while the inorganic-based membranes include calcium sulfate (CaSO₄) and HA compounds.⁴⁹ Guided tissue regeneration also requires the presence of osteogenic cells, as well as osteoconductive and osteoinductive materials, since biomaterials act as cell carriers

that activate the cellular processes required for tissue regeneration. The delivery of stem cells through biomaterials appears to help regenerate and restructure the oral cavity. However, more research is needed to assess their long-term efficacy.⁴⁹

Biomaterials in restorative dentistry

Restorative biomaterials constitute the largest group among all materials in dentistry. They include those used to treat caries (resin composites, glass ionomer cement (GIC) and polymers), materials for tissue regeneration and reconstruction (bioscaffolds, drug delivery systems and implants), and multifunctional toothpastes, mousses or flosses for tooth remineralization (Fig. 3). These biomaterials have been the focus of research in recent years with the aim to improve their functionality and biocompatibility.

Dental resin composites are the dominant materials for filling tooth cavities and restoring the biting surface of damaged teeth. They have been used for direct restoration since 1998 to replace amalgam fillings, which are toxic due to the mercury (Hg) content, and are usually made of a dental resin reinforced with a powdered glass filler. The color of the resin can be adapted to the surrounding teeth, with the fillings often blue light-cured to build the final restoration.^{51,52}

The primary issues associated with the application of resin composites are polymerization shrinkage, discoloration and cytotoxicity, though composite materials with antibacterial properties and mineralization capacity may help overcome polymerization shrinkage problems. Inhibiting bacterial growth prevents secondary caries, while the deposition of minerals can facilitate bonding

to the tooth structure. For instance, Li et al. designed advanced resin composites consisting of the monomer bisphenol A-glycidyl methacrylate (Bis-GMA) and the diluent triethylene glycol dimethacrylate (TEGDMA), with improved antibacterial and mineralization properties by incorporating zinc (Zn)/strontium (Sr)-doped-HA.⁵³ Furthermore, the Zn/HA and Sr/HA modification did not affect resin biocompatibility *in vitro* when using fibroblasts, which is crucial for preventing micro-leakage and secondary caries.⁵³ Cheng et al. achieved the mechanical and antimicrobial improvement of Bis-GMA and TEGDMA-based resins by adding silica aerogel (15 mm and 50 mm).⁵⁴ The silica aerogel/resin composite showed significantly lower water absorption and higher hardness than a pure resin matrix.⁵⁴ Bis-GMA and TEGDMA resins can also be modified with multifunctional fillers, such as calcium (Ca) orthophosphates.⁵⁵ Calcium phosphates (CPs) are the main constituents of bones and teeth, and significantly improve the remineralization of enamel and dentin. In composite materials, Ca phosphates contribute to the remineralization of caries-affected dentin and preclude caries lesions under orthodontic brackets. Additionally, Bis-GMA and TEGDMA resins are excellent for short-term treatment due to the release of ions, which subsides after 2–3 months.⁵⁵

Composite materials based on the monomer urethane dimethacrylate (UDMA) have also been investigated as dental fillings. UDMA resins exhibit lower polymerization shrinkage than Bis-GMA/TEGDMA resins, and due to the lack of hydroxyl groups, they are less prone to water sorption. Thus, UDMA-based composites are used alternatively to prepare dental restorative materials.⁵⁶ Khan et al. designed silicone dioxide (SiO₂) and aluminum oxide (Al₂O₃)-based UDMA resin composites enriched with a spherical micro-filler (30 nm).⁵⁷ These composites were characterized by increased surface roughness and porosity. However, only the resins enriched with Al₂O₃ showed sufficient biomechanical properties to be used as a resin filling.⁵⁷

Another versatile material with a broad spectrum of uses in restorative dentistry is GIC, a powder-liquid formulation that usually contains a fluoroaluminosilicate glass filler, which releases fluoride over time, and a polyacrylic acid solution. The most important modification of GIC involves the incorporation of components that exhibit regenerative or self-curing potential, such as nano-sized fillers, natural resins (e.g., propolis or chlorhexidine (CHX)), nano-sized bioceramics, HA, nanofluoroapatite, various metal NPs (e.g., Zn, silver (Ag) or Ti), and natural antibiotics.^{58,59}

Malekhoseini et al. examined the effects of incorporating zinc oxide (ZnO) NPs, sized 20–40 nm, on the antibacterial and mechanical properties of resin-modified glass ionomer cement (RMGIC).⁶⁰ Based on *in vitro* studies, the authors concluded that the modification of the RMGIC via ZnO NPs (2 wt%) improved the release of fluoride ions

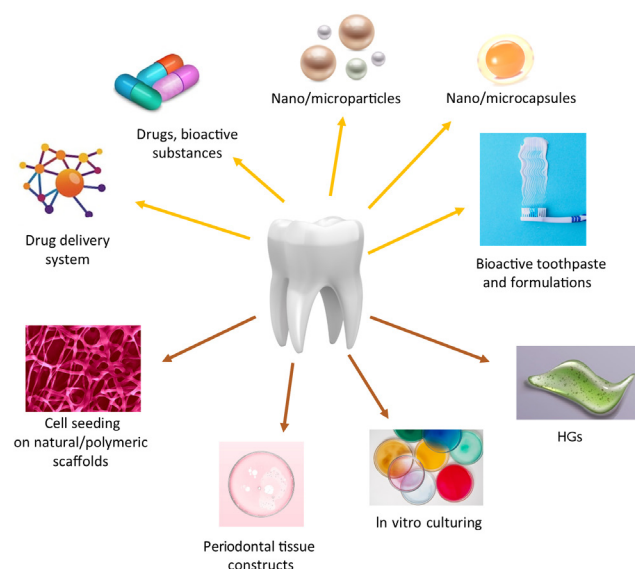


Fig. 3. Various biomaterials in periodontology
HG – hydrogel.

and its antibacterial activity against *Streptococcus mutans* (*S. mutans*), while it did not affect its flexural strength or modulus of elasticity.⁶⁰ Similar in vitro tests were performed by Panahandeh et al.⁶¹ The commercial Fuji II LC RMGIC powder was modified with a propolis extract. Adding propolis did not enhance the antibacterial properties of the RMGIC; instead, it deteriorated its flexural and shear strength. The lack of the antibacterial activity of the propolis-modified RMGIC can be attributed to the high viscosity of the Fuji IX cement, which may disturb the release of the antibacterial agent.⁶¹ Pagano et al. also carefully studied the improvement of mechanical and biological properties of GIC as a result of incorporating various additives.⁶² They designed advanced GIC (based on Fuji II LC), modified with 3 active components: HA (4 wt%) to enhance biocompatibility and mechanical properties; a mucosal defense agent – Zn L-carnosine (6 wt.%) to protect and repair mucous membranes; and an antibacterial agent – ciprofloxacin (1.5 wt%) to achieve bactericidal features. The combination of RMGIC and bioactive components helped treat caries in non-compliant patients.⁶²

The most common polymeric materials used in dentistry are based on polycarbonate (PC), PCL, PMMA, poly(lactic(L-lactic) acid (PLLA), and hexamethyldisilazane (HMDC). These materials can be used as polymer coatings to improve biocompatibility, prevent the formation of the bacterial biofilm, inhibit the corrosion of restorative materials in saliva, and reduce the friction force on orthodontic elements, such as metal wires. For instance, nanofibres made of PCL or poly(p-dioxanone) (PDO), loaded with various antibiotics, such as ciprofloxacin, doxycycline or metronidazole, can be applied as efficient drug delivery systems to treat bacterial infections of oral mucosa.⁶³ López-Ruiz et al. designed a dental drug delivery system based on L-arginine-containing mesoporous SiO₂ NPs to prevent secondary caries.⁶⁴ The controlled release of L-arginine effectively inhibited the growth of *S. mutans* and *Lactobacillus casei* (*L. casei*), and neutralized the acidic environment responsible for the development of secondary caries.⁶⁴

Nano- and microparticles can act as a delivery system for fluoride ions, which prevent the growth of caries-related bacteria and further acidification of saliva. In addition, fluoride ions in saliva reduce the demineralization of enamel. For example, in vitro studies showed that sodium fluoride (NaF)-loaded ethylcellulose and gelatin microparticles provided the sustained release of fluoride ions over 8 h.⁶⁵ These microparticles released fluoride ions in acidic conditions, accelerating the remineralization of hard tissues.⁶⁵

Biomaterials have been introduced to daily-use oral care products, such as toothpastes, mousses, mouthwashes, and dental flosses, to restore enamel and dentine tissue. Fluoride- and HA-containing toothpastes or mousses are among the most popular methods of restoring the tooth structure by promoting tooth remin-

eralization. The ability to remineralize dental surfaces has been widely examined and reported for deciduous and permanent teeth. Bossù et al. tested the effects of 3 commercial toothpastes containing fluorine (F) and HA on tooth remineralization.⁶⁶ Based on ex vivo studies (8 primary teeth extracted for orthodontic reasons), the authors concluded that all types of toothpaste reached the enamel matrix and the apatitic mineral phase by penetrating the enamel layer. The remineralization ability was associated with the chemical composition of the toothpastes and the tailored synthetic graininess of active components in the biofluid media.⁶⁶

Various active compounds, such as fluoride, HA, CHX, and povidone-iodine, can be incorporated into dental flosses to serve as an efficient drug delivery system for the prevention and treatment of early caries.⁶⁷ Improving dental floss is essential as it helps remove the bacterial biofilm from interproximal areas particularly prone to early caries.

Developing novel advanced restorative materials provides new methods for effectively treating oral diseases and for dental tissue regeneration. Materials are modified with bioactive substances, drugs or functional additives to improve their final properties. However, different shortcomings of dental restorative biomaterials are still raising doubts, leaving room for continuous enhancement.

Titanium and titanium alloys

Titanium is widely used in dental implants because of its biocompatibility, chemically inert character, resistance to corrosion, superior stability, and various physical and mechanical characteristics. Since its introduction to dentistry, it has been the gold standard for dental implant connectors and abutments. No cases of Ti-based allergic reactions have been reported in the dental literature. Indeed, one of the main factors that make Ti suitable for use in dental and medical implants is its ability to form a strong bond with the living bone and soft tissue, a process known as osseointegration, which is essential for the long-term success of the implant; Ti is particularly well-suited for this purpose. When Ti is implanted into the body, it stimulates the growth of new bone tissue, which helps anchor the implant in place and promotes healing. However, the growing demand for esthetics has led to the advancement of alternative materials that resemble the teeth, such as ceramic and Zr-based implants. Although Ti-based materials are widely used, much research still focuses on determining their long-term use and modification.

The effects of cleaning the surfaces of Ti implants were studied by Kotsakis et al., who found that the mechanical treatment of Ti implants may increase the dissolution of Ti in peri-implant tissues, potentially contributing to the development of peri-implantitis.⁶⁸ Their results were supported by an ex vivo model of organic polymicrobial

peri-implant biofilms, which was more representative of clinical conditions than other single- or three-species biofilm models.⁶⁸ The findings were also biologically relevant, as the tests regarded the crucial cell types involved in the homeostasis of peri-implant tissues.⁶⁹ Furthermore, the study showed that Ti was detectable in peri-implant crevicular fluid (PICF) and gingival crevicular fluid (GCF), even in healthy subjects. Also, the concentrations of inflammatory mediators were increased in peri-implant disease and significantly associated with Ti concentrations, even when adjusted for the peri-implant health. The authors suggest that the effects of Ti on peri-implant and periodontal tissues require further research.⁶⁹

An *in vivo* study investigated the effects of a collagen membrane (CM) and a synthetic bone substitute (BS) combined with a Ti mesh (TM) on lateral bone augmentation in a chronic peri-implant defect model in 6 canine mandibles.⁷⁰ The study found that using CM and/or BS did not appear to brought an additional benefit to lateral bone augmentation in peri-implant defects with TM. However, the study had a small sample size and the results were inconclusive.⁷⁰

Using Ti-platelet-rich fibrin (T-PRF) as a donor site membrane during free gingival graft (FGG) surgery was recommended by Koca-Ünsal et al.⁷¹ The research confirmed that T-PRF increased vascularity at the donor site, which might improve soft tissue healing. The study also found a positive correlation between the tissue thickness at the right and left donor sites, but no significant differences between the two. Furthermore, the study indicated that using ultrasound (US) to assess the tissue thickness and vascular density at the donor site during FGG surgery could contribute to the clinical success and reduce the risk of complications; it was the first study to evaluate the effectiveness of T-PRF using US imaging.⁷¹

A retrospective case series study on the use of TM in the jaw for the development of the implant site was presented by Levine et al.⁷² A total of 58 mesh procedures were performed in 48 patients, using various bone grafts and biologics. The average initial ridge width was 2.0 ± 1.0 mm, and the horizontal increase after TM procedures was 4.7 ± 1.6 mm. Titanium mesh exposure occurred in 22% of cases, with middle-aged and older patients more likely to have mesh exposure than younger patients. All implants were placed successfully, but 56% required additional contour augmentation after placement in the appropriate prosthetic position. The study indicates that TM procedures result in significant bone regeneration in narrow alveolar ridges, but the rate of TM exposure associated with age, as well as the frequency of additional contour grafting, should be discussed with patients.⁷²

Majewski assessed the application of a customized TM for GBR in atrophied alveolar ridges to achieve the optimal crest volume for implant placement.⁷³ Six patients who had been evaluated for at least 3 years were included in the study. A custom-made TM was used to protect the

contour of the augmentation site and the stability of the xenograft particles. After 6 months, the mesh was removed and the implants were placed in the planned positions. The average volume increase of the augmented sites amounted to 5.2 mm horizontally and 2.75 mm vertically. Minor soft tissue perforation occurred in 50% of cases, but it did not affect the implant placement procedure. No implant failure was observed during the follow-up period. The study concluded that a customized TM was a predictable technique for bone regeneration in advanced 3D defects.⁷³

The properties of Ti implants favor their use in prosthodontics. Recent studies have mainly focused on evaluating the mechanical properties and possible cytotoxicity of Ti, though it is essential to consider the properties of dental alloys and carefully choose materials to ensure their effectiveness and safety in clinical use. Romero-Resendiz et al. investigated the feasibility of using Ti-indium (In) alloys for dental prostheses through powder metallurgy methods.⁷⁴ They found that In acted as a grain refiner, reducing the grain size of the alloys and improving their mechanical behavior. The total porosity of the alloys decreased with an increasing In content, but the grain size and the In content had a more significant impact on the mechanical properties of the alloys than porosity. The alloys also showed non-classic mechanical performance due to the heterogeneous distribution of In, which was predominantly found on the grain boundaries and in porous regions. The release of Ti^{3+} and In^{3+} ions was below toxic concentrations, and the corrosion behavior was affected by the formation of a protective oxide layer, leading to low corrosion rates. Among the 3 prepared alloys, the Ti-10In alloy showed the most promising properties for use as a dental implant due to its smaller grain size, higher open porosity percentage, lower ion release, and lower corrosion rate.⁷⁴

Atanasova et al. investigated the relationship between the strength of the bond of dental porcelain to selective laser-melted (SLM) Ti and the temperature of Ti pre-oxidation.⁷⁵ They found that the oxide scale covering Ti surfaces thickened significantly at temperatures of 750°C and above, but the bond strength was negatively correlated with the pre-oxidation temperature. The results suggest that the pre-oxidation of SLM Ti frameworks prior to the application of porcelain is not necessary, and room-temperature passivation in the air after the surface airborne-particle abrasion of SLM Ti results in a Ti-ceramic bond that is above the minimum recommended values for metal-ceramic systems. These findings indicate that SLM Ti can be clinically applied in porcelain-fused-to-metal (PFM) prostheses.⁷⁵

Recent studies have shown that Ti cannot always compete with other available biomaterials. Abou-Ayash et al. investigated the trueness and marginal fit of computer-aided design/computer-aided manufacturing (CAD-CAM) complete-arch implant-supported screw-retained

fixed prostheses made of PEEK, polyetherketoneketone (PEKK) and Ti.⁷⁶ They found that the material type significantly affected the trueness of the frameworks, with PEEK having the lowest deviations, followed by PEKK and Ti. For marginal gaps, only the location of the abutments had a significant effect, with gaps in abutment 4 being significantly larger within the PEKK group than in abutments 2 and 3. Overall, the trueness of the frameworks differed according to the material type, but the marginal fit of the frameworks was similar and was smaller than 90 µm on average.⁷⁶

In a clinical study, Curiel-Aguilera et al. compared complete-arch implant-supported fixed maxillary prostheses made of Ti or monolithic Zr in terms of plaque accumulation and soft tissue inflammation.⁷⁷ They found that Zr prostheses had slightly lower plaque levels than Ti prostheses, and the levels significantly decreased over time in the Zr group while remaining constant in the Ti group. The study also found that Ti prostheses had significantly higher plaque levels than Zr prostheses across all time points, and that patients with Zr prostheses responded well to plaque control measures, while those with Ti prostheses had more difficulty with controlling plaque. Overall, the results suggest that Zr prostheses may present with less plaque accumulation and less inflammation of the adjacent soft tissues than Ti prostheses.⁷⁷

Titanium alloys have become firmly established in orthodontics due to their durability. Nevertheless, their durability is still under investigation, especially in the case of alloys containing other metals. A study by Chahine et al. aimed to evaluate the corrosion behavior of nickel (Ni)-Ti orthodontic wires in the oral cavity, using scanning electron microscopy (SEM), electrochemical analysis, and transmission electron microscopy (TEM) mapping.⁷⁸ The SEM and electrochemical analysis results showed that Ni-Ti orthodontic arches were able to initiate the corrosion process in the oral cavity, especially at the site of friction in contact with the braces. The TEM mapping revealed the presence of double or multiple layers of Ti, Ni and Al oxides on the surface of the wires. The study suggests that Ni-Ti orthodontic wires may be susceptible to corrosion in the oral cavity, especially at friction points.⁷⁸

Nur'aini et al. aimed to compare the permanent deformation properties of 3 different Ni-Ti orthodontic wire products – IMD Orthoshape™, American Orthodontics Ni-Ti heat-activated wire and Ormco Ni-Ti thermal wire.⁷⁹ A total of 27 samples were used, divided into 3 groups, each containing 9 samples of a different wire product. The wires were placed into the brace slots on the test prototype and subjected to force loading for 28 days. Then, the permanent deformation of the wires was measured using a digital caliper, and compared to the deflection of the new or control wires. The results showed a significant difference in the permanent strain values between the 3 thermal Ni-Ti wire products, with the smallest being reported for Ormco, followed by American Orthodontics and IMD

Orthoshape. The study concluded that using 0.014-inch-diameter thermal Ni-Ti wire with the least permanent strain was suitable in the early stages of orthodontic treatment to allow maximum and effective tooth movement.⁷⁹

The issue of Ti alloy biocompatibility is not without significance, as only suitably modified surfaces can meet the specific requirements of, among other things, the environment of the application. The goal of the work by Im et al. was to improve the biocompatibility and retention of orthodontic mini-screws by imparting bioactive properties to their surfaces.⁸⁰ The proposed method consisted of performing anodization, periodic pre-calcification and heat treatment on the Ti-6Al-4V ELI alloy mini-screws. The anodization process consisted of applying 20 V to a glycerol solution containing 20 wt% water and 1.4 wt% hydrofluoric acid for 60 min, resulting in the formation of a layer of titanium dioxide (TiO₂) nanotubes on the surfaces of the mini-screws. Cyclic decalcification and heat treatment generated fine-grained Ca phosphate deposits on the surfaces of the mini-screws. The samples were then immersed in simulated body fluid (SBF) to confirm the presence of densely structured protrusions and elevated concentrations of Ca and phosphorus (P), which bind and concentrate endogenous bone morphogenetic protein (BMP). They also measured the time of the removal of the mini-screws after they were fixed in the tibias of rabbits for 4 weeks. The results showed that the mini-screws had a significantly longer removal time than the untreated ones, and could be used as orthodontic mini-screws.⁸⁰

The aim of an in vitro study conducted by Fathy Abo-Elmahasen et al. was to evaluate the microbial activity of Ag/HA NPs and ZnO NPs on orthodontic Ti mini-screws in terms of inhibiting microbial growth.⁸¹ The study also tested the in vitro cytotoxicity and cytocompatibility of the synthesized nano-coatings, as well as the animal models of 4 cell types (fibroblasts, osteocytes, osteoblasts, and oral epithelial cells). The results showed that the mini-screws coated with ZnO NPs had the highest antimicrobial activity against a range of bacteria and fungi, and ZnO NPs also showed better cytocompatibility with oral epithelium cells, bone cells and fibroblasts as compared to Ag/HA NPs. The authors concluded that the proposed nano-coating was a promising strategy to overcome the development of the inflammatory zone around fixed mini-screws.⁸¹

As mentioned earlier, in research on the alloys used in orthodontics, the esthetic aspect is taken into account. Šimunović et al. conducted an in vitro study to assess the color stability of esthetic ceramic brackets and adhesive samples after immersion in commonly consumed beverages.⁸² There were a total of 100 ceramic brackets sourced from 5 different producers (Forestadent, G&H Orthodontics, GC Orthodontics, DynaFlex, and American Orthodontics) and a total of 120 adhesive samples (3M Transbond™ XT, and American Orthodontics

BracePaste® color change adhesive and BracePaste® adhesive) dipped in 4 different solutions – coffee, Coca-Cola®, Cedevida®, or artificial saliva (control group). The color readings were assessed at various intervals. The results showed that all brackets showed significant discoloration, with coffee having the greatest effect on color stability. The BracePaste color change adhesive showed the greatest discoloration, while Transbond XT the least.⁸²

To improve the corrosion and esthetic properties of Ni-Ti orthodontic wires, biocompatible Al-SiO₂ coatings are proposed. Such materials are characterized by better physicochemical properties and far greater esthetics, and do not cause cytotoxicity.⁸³ As an alternative to uncoated Ni-Ti wires, esthetically pleasing epoxy-coated or thermally rhodium (Rh)-plated wires are also available to improve the esthetics. Furthermore, in vitro and corrosion studies using artificial saliva have shown that epoxy resin coatings increase corrosion resistance and release less Ni into saliva.⁸⁴

Polyetheretherketone

Polyetheretherketone is a type of thermoplastic polymer of various applications, including medical and dental implants. The material is known for its high strength and stiffness, and its resistance to heat, chemicals and wear, which helps prolong the life of medical devices that are made of this polymer. Due to its durability, it can handle high stresses and deformations, and that is why it is suitable for manufacturing medical implants. Moreover, PEEK is often used as an alternative to metals in medical implants because of its biocompatibility. It does not damage or irritate the living tissues, which makes it a safe and effective material for medical and dental applications. Polyetheretherketone is commonly used in orthopedic and dental rehabilitative treatment because of its beneficial biomechanical characteristics. Nevertheless, the material is still susceptible to bacterial attachment and biofilm development.

Several surface properties are associated with biofilm development on the PEEK surfaces, one of which is roughness, with *Streptococcus sanguinis* (*S. sanguinis*) shown to build up a biofilm on rough PEEK surfaces over 72 h, and comparable findings reported for *Streptococcus oralis* (*S. oralis*), *Enterococcus faecalis* (*E. faecalis*) and *Streptococcus gordonii* (*S. gordonii*). The research by Barkarmo et al. also implies that bacteria are more likely to adhere to the PEEK surfaces if they are sandblasted.⁸⁵ The plasma spraying of the PEEK surfaces with Ag NPs effectively blocked the growth of Gram-negative *Escherichia coli* (*E. coli*) and Gram-positive *Streptococcus aureus* (*S. aureus*). However, PEEK materials that have been modified with antibiotic coatings and peptide-functionalized NPs exhibit minimal adherence and growth of *Pseudomonas aeruginosa* (*P. aeruginosa*) and *Staphylococcus epidermidis* (*S. epidermidis*) as

compared to traditional PEEK products. These findings suggest that bacterial adhesion to PEEK is lowest on materials with a rough surface.

Two strategies for modifying the surface of PEEK to make it resistant to bacterial adhesion and biofilm formation were discussed in the work by Gao et al.⁸⁶ The 1st strategy consisted in coating the PEEK surface with antibiotics or other antimicrobial agents, such as natural extracts, antimicrobial peptides or metal oxides. The 2nd strategy involved modifying the surface morphology of PEEK to create microstructures that can kill bacteria or prevent them from adhering to the surface. The review discussed several specific methods for modifying PEEK with these strategies and presented research results indicating their effectiveness in inhibiting bacterial growth. Furthermore, the study referred to several antimicrobial agents that can be used to coat the surface of PEEK to make it resistant to bacterial adhesion and biofilm formation. These include antibiotics, such as gentamicin sulfate, minocycline, vancomycin, and tobramycin, as well as natural extracts, antimicrobial peptides, and metal oxides, such as ZnO and silicon nitride (Si₃N₄). The review also discussed the use of selenium (Se) and fluoride as antimicrobial agents for coating PEEK.⁸⁶

Milinkovic et al. compared the response of peri-implant soft tissues to polyethylene and Ti healing abutments, using histological and immunohistochemical analyses.⁸⁷ They found that PEEK healing abutments induced a more intense inflammatory response in the tissues than Ti healing abutments, as demonstrated by the activation of histocytes and plasma cells. On the other hand, Ti healing abutments induced an inflammatory response of lower intensity, which was mainly mediated by B cells. These results suggest that PEEK healing abutments may be associated with a more intense inflammatory response in the soft tissues around the implant than Ti healing abutments.⁸⁷

In a study by Li et al., patient-specific PEEK scaffolds proved to be a promising option for individualized alveolar bone augmentation, demonstrating similar space-holding and osteogenic properties to their Ti counterparts.⁸⁸ Such scaffolds can achieve excellent osteogenic space retention, making them a potential alternative to traditional GBR surgery. Although PEEK scaffolds showed lower biomechanical strength than Ti scaffolds, they can be used for customized alveolar bone augmentation and may be a better option than traditional collagen periosteal membranes.⁸⁸

Improving the seal between soft tissues and PEEK implants by mimicking the chemistry of the tooth surface poses a significant problem described in the literature, is very important in dental practice and presents a challenge in material engineering. An interesting example in this respect comes from Saad et al., who modified the PEEK surface with collagen I and compared it with a Ti alloy (Ti-6Al-4V), the most widely used biomaterial

for percutaneous procedures.⁸⁹ The results showed that collagen-modified PEEK and Ti surfaces were characterized by an increased adsorption of the key proteins of the basement membrane and improved epithelial cell viability as compared to unmodified PEEK and Ti. These findings suggest that the proposed modification technique can potentially improve the PEEK–epithelial tissue sealing and expand the use of PEEK as a biomaterial for percutaneous implants. Moreover, the use of collagen-modified PEEK in percutaneous implants offers several potential advantages over unmodified PEEK and Ti. The surface of collagen-modified PEEK more effectively promotes the adsorption of essential basement membrane proteins, which are necessary for establishing a strong seal between the implant and the surrounding soft tissues, and can reduce the risk of infection and improve long-term implant stability. Furthermore, the collagen-modified PEEK surface promotes better cell viability and growth as compared to unmodified PEEK and Ti, suggesting better integration with the surrounding tissues. These benefits make collagen-modified PEEK a promising biomaterial for percutaneous implants.⁸⁹

Another possibility for modifying scaffolds to enhance their therapeutic effect is worth mentioning at this point. Due to its high affinity, collagen can be combined with several bioactive agents to improve its effect, with the collagen scaffolds incorporating recombinant human-cartilage oligomeric matrix protein–angiopoietin 1 (rhCOMP-Ang1) and coumaric acid shown to facilitate bone formation.⁹⁰ Indeed, *in vitro* and *in vivo* models of critically sized mandible defects have shown that this material enhances the proliferation, mineralization and migration of cultured human periodontal ligament fibroblasts (hPLFs) through the activation of the angiopoietin 1 (Ang1)/TEK (Tie2) signaling axis.⁹⁰ As discussed earlier, Ti and Zr with collagen scaffolds have already been proposed, and their further modification with bioactive agents should contribute to their development into even more functional materials.

Another important aspect to consider is material durability. The influence of 3 denture cleaners upon immersion in a chemical solution that was applied to PEEK and other denture base materials was studied and compared with respect to long-term water sorption and solubility.⁹¹ The study concluded that denture cleaners can affect the water sorption and solubility of PEEK and other denture materials over time. Specifically, the PEEK group showed a significant difference in the average water sorption values among all cleaning agent groups and a substantial difference in average solubility with regard to the distilled water and sodium hypochlorite (NaClO) groups. These results suggest that the type of denture cleaner used may affect the long-term performance of PEEK and other denture base materials.⁹¹

Evaluating the effects of loading and grafting on osseointegration and soft tissue healing in the implant area with

immediately placed, self-loaded, progressive implants at the tissue level in a minipig model was the subject of a study by Parvini et al.⁹² The researchers put 56 TLX implants (commercial Straumann® TLX RT, Roxolid®, SLActiv®, with durable PEEK matrices) immediately after the bilateral extraction of mandibular first and second premolars in 14 minipigs. The implant sites were assigned to 4 groups, including unloaded with simultaneous grafting with the use of bovine bone mineral, unloaded without grafting, loaded with simultaneous grafting, and loaded without grafting. The researchers found at weeks 4 and 12 that implant loading and grafting had no significant effect on osseointegration and soft tissue healing in the TLX implant area. However, they noted that the values tended to vary between the buccal and lingual aspects of the implants. These results suggest that TLX implants may be a promising option for dental implants, especially when immediate loading and grafting are not possible or necessary.⁹²

Polyetheretherketone is being increasingly used to manufacture removable and fixed prostheses, such as dental crowns, bridges and denture clasps in removable dental prostheses, which is due to its low potential for causing allergies, low water solubility, superior biocompatibility, high thermal and chemical resistance, moderate biofilm formation, and excellent mechanical properties.⁹³ The material, with its good physical and mechanical properties, including high melting temperature and compressive strength as compared to other polymers, as well as good biocompatibility, is a potential alternative to Ti for long-term dental applications.⁹⁴ Research related to the use of PEEK in dental prostheses focuses on the problem of its chemical stability, which can hinder adhesive bonding due to the inert surface of the material, and on comparison with other materials.

Gentz et al. compared the retentive forces of removable partial denture clasps made of Co-Cr and 2 thermoplastic polymers (PEEK and PEKK), using the CAD/CAM processes.⁹⁵ The clasps were tested with a chewing simulator for 15,000 cycles to simulate 10 years of use, and the results showed that Co-Cr clasps had significantly higher retentive forces than thermoplastic polymer clasps. The researchers also examined the specimens under an SEM and observed that Co-Cr clasps showed wear on the glaze layer of the ceramic crowns, whereas the thermoplastic polymer group did not. Such wear may explain the reduction in retentive forces observed with Co-Cr over insertion and removal cycles as compared to the consistency noted with thermoplastic polymers. Nonetheless, PEEK and PEKK clasps had similar retentive forces, yet lower than those of Co-Cr clasps. All 3 groups of clasps demonstrated an initial increase in retentive forces, followed by a gradual decrease, still all maintained similar or higher retentive forces as compared to the baseline measurement. The study suggests that thermoplastic polymer clasps are appropriate for

clinical use due to their resistance to fatigue and the possibility to fabricate them through CAD/CAM.⁹⁵

Igarashi et al. described the results of an *in vitro* study conducted to assess the use of PEKK as an alternative material for double-crown dental prostheses.⁹⁶ The study involved testing the retentive forces of primary crowns made of various materials, including PEKK, and secondary crowns made of PEKK, and comparing them with the gold standard (primary crowns made of Au and secondary crowns made of galvano-gold (GA)) after 20,000 connections and disconnection cycles. The study used a linear torsion all-electric dynamic test instrument to place the secondary crown on the primary crown with a force of 50 N-cm for 1 s, and then remove it with a frequency of 1 Hz. The results showed significant differences between the various test materials regarding their retentive forces, demonstrating that PEKK was a suitable alternative material for double-crown prostheses. Furthermore, the authors concluded that the PEKK/PEKK and Au/PEKK primary/secondary crown combinations were better in terms of retention forces than the Au/GA combination, and the combination of Co-Cr/PEKK showed stable retention throughout the testing period and superior retention strength after a total of 20,000 insertion/removal cycles. Since PEKK/PEKK and Au/PEKK showed superior surface wear than the control group, it can be concluded that PEKK offers good clinical prospects.⁹⁶

Wang et al. discussed the use of PEEK in fixed dental prostheses (FDP), such as crowns, partial dentures and post-and-core.⁹⁷ They noted that PEEK showed excellent mechanical properties, including good stress distribution, and was biocompatible, non-mutagenic, non-cytotoxic, and non-allergenic. However, the chemical stability of PEEK can be considered an advantage or a disadvantage, as it minimizes intraoral corrosion, but makes adhesive bonding difficult due to the inert surface of the material. The authors described various strategies that had been explored to improve the adhesive properties of PEEK, including acid etching, plasma treatment, airborne-particle abrasion, laser treatment, and adhesive systems. They concluded that while PEEK was a promising alternative to conventional materials for FDP, it had some disadvantages, such as the lack of esthetics, and its inert and hydrophobic surface could make bonding with composite resins and abutment teeth difficult. They suggested that further research was needed to overcome these challenges and facilitate the wider adoption of PEEK in fixed prosthodontics.⁹⁷

Raj et al. conducted a clinical study to evaluate the efficacy of PEEK FDP over 1 year.⁹⁸ The study included 20 patients who received three-unit posterior PEEK FDP. Clinical examinations and patient recalls were conducted at intervals of 0, 3, 6, 9, and 12 months to evaluate the longevity of restorations, using the modified Ryge criteria and the System for California Oral Health Reporting (SCOHR). Radiographic assessments were also per-

formed after 12 months. The study results showed that 95% of patients maintained their PEEK FDP without fracture during the study period, while 5% reported the decementation of their FDP. Furthermore, 10% of the PEEK FDP showed marginal discoloration, but no significant changes in marginal adaptation, oral hygiene or periodontal health were observed over the study period. The authors concluded that PEEK FDP had satisfactory clinical efficacy and acceptable clinical outcomes during the 12-month observation period, but further research with a larger sample size was needed to build evidence on the use of PEEK for FDP in the long term.⁹⁸

Soldatovic et al. determined the fracture load of implant-supported four-unit cantilever FDP with frameworks made of 2 differently filled PEEK compounds and veneered using 3 different techniques.⁹⁹ The study included 120 duplicate four-unit FDP frameworks, which were milled from PEEK with 20% TiO₂ filler or pressed with 30% TiO₂ filler, and veneered using digital veneers, conventional composite resin veneers or pre-fabricated veneers. Fixed dental prostheses were adhesively bonded to Ti abutments, and the fracture load was measured before and after artificial aging in a mastication simulator. The results showed that the filler content and the veneering technique significantly affected the fracture load, with the 30% filler content and pre-fabricated veneers providing the highest resistance to fracture. Aging did not affect the fracture load. The authors concluded that the filler content of PEEK compounds and the veneering technique influenced the fracture load of implant-supported four-unit PEEK FDP, and selecting the appropriate veneering method could improve the long-term success of bilayered structures. They also noted that all of the FDP in the study had a higher fracture load than the maximum occlusal forces in the posterior region, and that mastication simulation did not impact the fracture resistance of the examined PEEK FDP.⁹⁹

A very interesting summary of works on the use of PEEK for dental prostheses was presented by Khurshid et al., who assessed if PEEK had superior mechanical and esthetic properties as compared to other materials used in the construction of dental prostheses.¹⁰⁰ The review included 12 articles, with 2 case studies, 3 observational studies, and 1 randomized controlled trial (RCT). The quality of the research was evaluated using various tools, and the overall quality of most studies was classified as low or medium. The review found that the evidence on the long-term viability of PEEK-based dental prostheses was insufficient, and most of it came from case reports and non-randomized observational studies. The authors concluded that future studies should focus on large-scale multicenter trials comparing the survival rate of PEEK-based prostheses with other materials, and that implant-supported PEEK prostheses should be further studied as a potential replacement for conventional materials and designs.¹⁰⁰

The effects of amine group modification on the osseointegration behavior of carbon fiber-reinforced polyethylene (CPEEK) in rabbits was the purpose of a study by Wang et al.¹⁰¹ Two groups of implants were used – 30%-CPEEK and A-30%-CPEEK (amine modification), with pure Ti as a control. Bone-forming capacity and osseointegration were assessed in vivo by microcomputed tomography analysis, SEM observations and histological evaluation. The results showed that all parameters differed significantly between the 2 groups, with those in the A-30%-CPEEK group being equal to or better than pure Ti. The study also found that modifying the amine group could positively affect bone regeneration and suggested that A-30%-CPEEK could be a promising non-metallic implant material. In conclusion, this study showed that the amine group modification of PEEK improved osseointegration in rabbits. Moreover, A-30%-CPEEK implants showed higher levels of new bone formation and better bone integration than unmodified implants with 30%-CPEEK.¹⁰¹

Boonpok et al. studied the effect of hydrothermal treatment on the bioactivity of the HA-titanium nitride (TiN) coating on PEEK by immersion in SBF.¹⁰² The coating was produced by pulsed direct current magnetron sputtering. Its dissolution in SBF was studied at different time points for up to 56 days. The results showed that the dissolution of the coating and the precipitation of the Ca phosphate complex from SBF occurred continuously throughout the immersion period, causing physical and chemical changes in the coating. However, after 56 days, the coating remained on the PEEK surfaces and had a 1.16 Ca/P ratio. These results suggest that the hydrothermal treatment of the HA-TiN coating improves its bioactivity, and may have potential applications in orthopedics and dentistry.¹⁰²

Kerkfeld et al. compared the facial symmetry results after simultaneously performed, digitally planned orthognathic surgery based on patient-specific implants (PSI) and bone augmentation with PEEK in patients with craniofacial defects.¹⁰³ The research involved 5 groups of patients, including those with and without laterognathia, patients with and without syndesmosis, and patients with and without PEEK bone augmentation. The digital process workflow involved cone-beam computed tomography (CBCT) and virtual surgery planning for all patients to produce patient-specific cutting guides and osteosynthesis plates. In addition, the deformed skulls were superimposed on a non-deformed skull and/or the healthy side was mapped to produce PEEK PSI for augmentation. The results of both surgical approaches were evaluated using conventional posterior-anterior radiographs, and en-face images taken before and 9 months after surgery. The findings showed that simultaneous orthognathic surgery with PEEK bone augmentation significantly improved facial symmetry when compared to conventional orthognathic surgery (6.5%P (3.2–9.8%P)). Indeed, PSI-based orthog-

nathic surgery improved horizontal bone alignment in all patients, while simultaneous PEEK bone augmentation improved facial symmetry, even in patients with combined soft and hard tissue hypoplasia. A digital workflow, including virtual surgical planning, led to improved balance in all patients.¹⁰³

Bioactive glass

Bioactive glass is a type of biocompatible glass of various applications, made from a combination of silicon (Si), Ca, sodium (Na), and P, and designed to fuse with the living tissues in the body. When implanted, BG stimulates the growth of new bone tissue, which can help repair or regenerate damaged or lost bone, making it valuable in dentistry, orthopedics and other medical fields. In addition to its ability to stimulate bone growth, BG has several other properties that make it a useful biomaterial. Indeed, it is biocompatible, resistant to infections, and can help prevent bacteria from growing on its surface. Moreover, BG is strong, durable, and can withstand the stresses and strains of daily use. Among the main advantages of BG is its ability to fuse with the living tissues; once implanted, it forms a chemical bond with the surrounding bone and soft tissues, which favors implant anchorage and promotes healing. This bonding process, known as osseointegration, is essential for the long-term success of medical implants, and is one of the key factors that make BG such a valuable biomaterial.

Ongphichetmetha et al. compared the effectiveness of a paste containing 5% calcium sodium phosphosilicate (CSPS) and 8% arginine in alleviating dentin hypersensitivity (DH) in patients receiving non-surgical periodontal therapy.¹⁰⁴ This double-blind RCT involved 45 volunteers who were treated with one of 3 dental formulations immediately after non-surgical treatment and continued brushing twice daily for 8 weeks. The results showed that the CSPS preparation immediately reduced DH, which declined by week 8. The study concluded that the CSPS paste and arginine were beneficial in terms of reducing discomfort in patients with periodontitis immediately and during the first 2 weeks after non-surgical periodontal treatment.¹⁰⁴

Williams discussed the evidence on bioactivity mechanisms in some biomaterials, including BG, especially in case the material was modified to promote such activity.¹⁰⁵ The article covered a basic understanding of bioactivity phenomena and their relations with biocompatibility mechanisms in biomaterials. The author analyzed the performance of bioactive materials in various areas, including bone induction, cell adhesion, immunomodulation, thrombogenicity, and antimicrobial behavior. The effectiveness of bioactive materials was shown to be based on solid scientific evidence in a variety of applications, but their successful clinical translation remains problematic. Indeed, it is suggested

that a focus on the 'bioactivity zone' at the interface between the material and the host tissue may provide a better understanding of the mechanisms of bioactivity, and help improve the design and performance of biomaterials. Finally, the article discussed the challenges and barriers to the successful clinical translation of bioactive materials.¹⁰⁵

Some reviews in the field indicate that the subject of applying BG in periodontology is well-researched. Cannio et al. reviewed the literature on the potential bioactivity and biocompatibility of some BG types, such as 45S5 Bioglass®, BonAlive® and 19-93B3, in the biomedical field.¹⁰⁶ The paper discussed various forms in which these materials can be obtained and their potential applications, including dentistry and reconstructive surgery. The article also highlighted the need for further research and clinical trials to fully understand the performance of these materials and optimize their design for future applications. In their systematic review, Behzadi et al. evaluated the potential effectiveness of BG and HA in dentinal tubule occlusion, which may be useful in treating DH.¹⁰⁷ The review included 35 *in vitro* studies, which revealed a low risk of bias and demonstrated the effectiveness of BG and HA in dentinal tubule occlusion. The review suggests that desensitizers containing BG and HA can be used to treat DH, but more long-term clinical studies are needed to make definitive recommendations.¹⁰⁷

In orthodontics, BG is used as a bonding and cleaning agent. For example, Chopra et al. evaluated the effects of different bonding agents on the luting strength of orthodontic brackets.¹⁰⁸ The study involved 48 healthy human premolar teeth that were randomly divided into 4 groups, including a control group that used GIC, a group that used GIC with CPs, a group that used GIC with Ag NPs, and a group that used the 45S5 Bioglass paste. The teeth were bonded with metal locks, and a universal testing machine (UTM) was used to remove the locks and measure the strength of the luting cement. The thickness of the remaining cement was also measured using computed tomography (CT) and SEM. The results showed that the CP GIC group had the highest bond strength, followed by the luting GIC, Ag NP GIC and 45S5 Bioglass groups. The luting GIC group had the greatest thickness of the remaining cement, followed by the Ag NP GIC, CP GIC and 45S5 Bioglass groups. The study found that CPs in GIC provided the strongest bond and left the least cement on the tooth surface as compared to the other luting agents tested.¹⁰⁸

Moslemi et al. proposed using the AutoCAD® and SPSS software for advanced statistical analysis of the data collected during orthodontic tests.¹⁰⁹ The research evaluated the effects of toothpastes with BG on the remineralization of orthodontically induced white spot lesions (WSLs). Orthodontic brackets were bonded to extracted premolar teeth, which were then immersed in a demineralization

solution to create artificial carious lesions on enamel. The samples were divided into 2 groups, with one treated with a toothpaste containing NaF, and the other treated with a toothpaste containing BG. The samples were analyzed using a polarizing microscope, and the results showed that both toothpastes were effective in remineralizing WSLs, but the BG toothpaste was more effective than the toothpaste with NaF.¹⁰⁹

Al Shehab et al. investigated the influence of 2 types of sealants, namely fluoride bioactive glass (FBAG) paste and the Alpha-Glaze™ resin, on the shear bond strength of orthodontic brackets to enamel, as well as their protective effects against a simulated cariogenic acid attack.¹¹⁰ The study included 135 extracted premolar teeth, which were divided into 3 groups: FBAG; Alpha-Glaze; and control. The shear bond strength of the brackets was measured using an Instron UTM, and the protective effects of the sealants was evaluated using a toothbrushing simulator and light microscopy. The results showed that the shear bond strength values did not differ significantly between the FBAG (28.1 ±5.5 MPa), Alpha-Glaze (32.5 ±7.4 MPa) and control (30.7 ±6.5 MPa) groups. The Alpha-Glaze sealer provided a mechanical barrier on the enamel surface within seconds of polymerization, but did not considerably protect enamel from a simulated cariogenic acid attack. On the other hand, FBAG was able to protect the enamel surface around orthodontic brackets, but its relatively long application time posed some clinical difficulties. The study suggests that FBAG can be used as an orthodontic sealant that does not affect the bond strength of orthodontic brackets and causes minimal damage to enamel during the removal of brackets.¹¹⁰

Salah et al. evaluated the effectiveness of 2 types of BG (45S5) – BioMin® F and NovaMin® – in comparison with casein-phosphopeptide-amorphous calcium phosphate (CPP-ACP) in the treatment of orthodontically induced WSLs.¹¹¹ Sixty post-orthodontic WSLs were randomly assigned in a double-blind RCT with 3 parallel arms (*n* = 20): group I (Bio-BAG) received the BioMin F slurry and toothpaste; group II (N-BAG) received the NovaMin slurry and toothpaste; and the positive control group (CPP-ACP) received the Recaldent toothpaste. The products were applied daily in a dental office for 1 week, and then reinforced by self-application at home for 4 weeks. The results showed that at a 6-month follow-up, all 3 groups revealed a statistically significant regression of WSL as compared to baseline, and there was a highly significant percentage reduction in the lesion size in the Bio-BAG group as compared to the control group. The average lesion area decreased by 64.8%, 32.2% and 31.6% in respective groups. The study concluded that using the BioMin F toothpaste in a dental office and at home for 4 weeks resulted in a more significant esthetic improvement of post-orthodontic WSLs as compared to NovaMin and CPP-ACP.¹¹¹

Acrylic resins

For acrylic resins, new research focuses mostly on esthetics, including color fastness, and on mechanical resistance and biocompatibility. For example, Almuraikhi studied the effects of different disinfecting solutions on the color stability of 2 types of denture substructure materials – Meliodent® and ProBase® Hot.¹¹² The materials were immersed in chemical disinfectants (2% alkaline glutaraldehyde, 0.5% chlorhexidine gluconate or 0.5% NaClO solutions) or distilled water (as control), and color stability was measured at different time points. The results indicated that all disinfectant solutions had some impact on the color stability of base materials, with the smallest effect observed with 0.5% chlorhexidine gluconate and the greatest effect observed with 0.5% NaClO. Color stability was the lowest when the materials were immersed in distilled water. These results suggest that professionals should consider the effects of different disinfectant solutions on the color stability of denture base materials when selecting a disinfectant for use on dentures, which is particularly important, as color stability is an important factor affecting the final denture appearance.¹¹²

Szerszeń et al. evaluated the color stability of a ZnO NP-PMMA nanocomposite as a denture base material.¹¹³ The nanocomposite was exposed to various solutions (distilled water, coffee, red wine, black tea, and denture cleaning tablet) for 6 months and color changes were measured using a digital colorimeter. The results showed that all materials experienced significant color changes after exposure to various solutions, with the greatest changes observed for red wine and the least for distilled water. The researchers found that the modification of PMMA with ZnO NPs is esthetically acceptable at a concentration of 2.5% or 5% by weight, but color changes become more noticeable when the NP content is higher, and the use of the nanocomposite should be discussed with patients.¹¹³

In terms of biological, mechanical and structural properties, modified PMMA may represent a promising approach to improving denture performance and longevity.¹¹⁴ Zore et al. studied the effect of adding TiO₂ NPs to PMMA on the adhesion of *S. mutans* to the material through comprehensive tests of mechanical strength, color fastness and biocompatibility.¹¹⁵ The surface properties of modified PMMA, including roughness, the contact angle, zeta potential, and color parameters, were measured. Tensile strength was also measured. The results showed that adding TiO₂ NPs decreased the roughness and contact angle of the material, increased its zeta potential, and changed its color. Adding TiO₂ NPs also decreased the uniaxial tensile strength of the material and had a significant effect on the formation of the *S. mutans* biofilm on its surface, with concentrations of 10% and 20% reducing the bacterial adhesion by 58% and 60%, respectively. The authors concluded that PMMA modified with TiO₂

NPs could be a promising material for fabricating acrylic resin-based dental materials, but further studies are needed to test its antimicrobial properties and color matching with gingival tissues.¹¹⁵

Malisic et al. studied the effect of gamma radiation on the microbiological purity and material properties of a PMMA composite containing Al₂O₃ NPs.¹¹⁶ The material was irradiated with doses of 0, 10, 20, and 25 kGy, and the microbiological purity, mechanical properties, thermal stability, microstructure, and the color changes were tested. The results showed that a dose of 25 kGy was sufficient for the complete sterilization of the material, and improved its mechanical properties and thermal stability. However, the dose also caused microstructural changes in the material, including the formation of cracks and pores and color changes. The authors concluded that gamma radiation could sterilize PMMA/Al₂O₃ NPs composites, but the optimal dose would depend on the intended application of the material.¹¹⁶

Punset et al. found that adding graphene to PMMA improved its mechanical properties, including compressive strength and the modulus of elasticity, and reduced its specific wear rate, determined by the mechanical compression test and the pin-on-disk wear test.¹¹⁷ The presence of graphene in PMMA was studied using Raman spectroscopy and field emission scanning electron microscopy (FESEM). Shore hardness and Vickers microhardness were also determined. Despite promising results, further studies are needed to determine the optimal percentage range of reinforcement, the influence of graphene morphology, and the biocompatibility and fatigue of the composite.¹¹⁷

Pagano et al. compared the mechanical and biological characteristics of a PMMA disk for CAD/CAM prostheses (test samples) with traditional resin (control samples).¹¹⁸ The test samples had a higher modulus of elasticity than the control samples and a different Brillouin frequency. Furthermore, SEM showed that keratinocytes in the test samples appeared flattened, with lamellipodia, while those in the control samples had cytoplasmic filaments. The test samples were also significantly less cytotoxic than the control samples. However, no significant differences in apoptosis were found between the 2 types of samples. Real-time polymerase chain reaction (PCR) showed increased *p53* expression in keratinocytes in both types of samples, but no significant variations in *p21* or *bcl2* expression. The authors concluded that the PMMA disc for CAD/CAM prostheses had improved mechanical and biological features as compared to traditional resin, including a higher modulus of elasticity, better keratinocyte morphology and lower cytotoxicity.¹¹⁸

Since it is important for the application of materials in dentistry that the material allows for simple processing to create accurate models, research is being carried out to determine the best possible fabrication technique variants. Sidhom et al. evaluated the precision of PMMA

working models and the marginal fit of PMMA provisional prostheses produced using 2 digital fabrication techniques – CAD/CAM milling and 3D printing.¹¹⁹ The samples were evaluated using a coordinate-measuring machine (CMM), an SEM and a stereomicroscope. The results showed that the CAD/CAM-milled models had lower mean distances between the reference points as compared to the 3D-printed models, and the marginal fit of the CAD/CAM-milled provisional prostheses was better than that of the 3D-printed prostheses. The authors concluded that CAD/CAM milling is a more accurate technique for the fabrication of PMMA working models and provisional prostheses than 3D printing.¹¹⁹

The analysis of recent literature indicates that it is possible to use PMMA in dental applications, with particular emphasis on its mechanical and biological properties. Furthermore, modifying PMMA with several additives has been shown to alter its mechanical properties, including compressive and tensile strength and the modulus of elasticity, and to significantly affect biofilm formation on its surface.

Ceramic materials

Ceramic materials are now firmly established in prosthodontics, and research continues regarding their mechanical resistance and biocompatibility. The question of esthetics is also of great importance, with studies focusing on commercially available and new materials, mainly based on modifications. The aim of a study by Juntavee et al. was to evaluate the ability of different types of ceramics of varied thickness to mask the color of various substructures.¹²⁰ Ceramics used in the study were BruxZir[®] Anterior, Celtra[™] Duo and VITA SUPRINITY[®], and the substructures included natural dentine, tetracycline-stained dentine, Zr, a resin composite, and a cast metal. The researchers used a spectrophotometer to measure the color of the specimens, and determined the masking ability by comparing the color difference before and after combining the ceramics with the substructures. The results showed that the type and thickness of the ceramic and substructure significantly affected the masking ability, with tetracycline-stained dentine having the greatest impact on the appearance of the ceramic restoration. The study concluded that BruxZir Anterior, Celtra Duo and VITA SUPRINITY all had the ability to mask tetracycline-stained dentine, with BruxZir Anterior requiring a minimum thickness of 0.6 mm, VITA SUPRINITY requiring a minimum thickness of 1.2 mm and Celtra Duo requiring a minimum thickness of 1.6 mm to achieve an ideal masking capability. Monolithic Zr had a higher masking ability than a lithium silicate/phosphate glass ceramic.¹²⁰

Al-Dwairi et al. conducted an *in vitro* study to examine the effect of the design of the framework on the fracture resistance and failure modes of cantilever inlay-retained fixed partial dentures (IRFPDs) made of 2 types of multi-

layered monolithic Zr materials.¹²¹ The researchers prepared 72 natural premolar teeth as abutments for IRFPDs, using 3 different designs, and then fabricated full-contoured IRFPDs from the 2 Zr materials. The samples were subjected to thermocycling and mechanical loading, and the surviving samples were then loaded until failure on UTM. The results showed that the mean failure load was not significantly different between the different designs or materials. However, during the dynamic fatigue test, the IPS e.max[®] ZirCAD Prime material had a significantly higher failure rate than the Zolid Gen-X material. The researchers also found that the type of attachment structure significantly affected durability. Dentures with a cantilever design, which maximizes adhesion to enamel, showed promising results, while IPS e.max ZirCAD Prime was more prone to fracture with the long palatal wing design.¹²¹

Daou conducted an *in vitro* study to compare the fit of Co-Cr alloy FDP fabricated using different techniques before and after ceramic layering.¹²² The researcher prepared a Co-Cr alloy master model and manufactured 60 frameworks, using selective laser melting (SLM), soft milling and conventional casting. The replica technique was used to measure the marginal and internal discrepancies of the frameworks before and after they were layered with ceramics, and compared the results within each group. The data showed significant differences within the groups before and after ceramic layering for SLM and soft milling, but not for conventional casting. The study also found that soft milling resulted in increased gap values in the marginal and occlusal regions. However, there was no statistical difference in the marginal region between the conventional casting group and the soft milling and SLM groups. The author concluded that ceramic layering increased the discrepancy between the laser-sintered and milled frameworks, particularly in the marginal region.¹²²

Another *in vitro* study was conducted by Spitznagel et al., who investigated the failure load and fatigue behavior of monolithic and bilayer Zr FDP supported by one-piece ceramic implants.¹²³ The researchers prepared 80 three-unit FDP supported by 160 Zr implants, which were divided into 4 groups: the monolithic 3Y-TZP Zr (Vita YZ[®] HT) group (Z-HT); the monolithic 4Y-TZP Zr (Vita YZ ST) group (Z-ST); the 3Y-TZP Zr (Vita YZ HT) group with a facial veneer (Vita VM[®]9) (FL); and the polymer-infiltrated ceramic network (PICN) 'tabletop' group with a 3Y-TZP framework (Vita YZ HT) (RL). Half of the samples in each group were subjected to fatigue in a mouth-motion chewing simulator with simultaneous thermocycling, and all specimens were then exposed to single-load-to-failure testing. The results showed that all samples withstood the fatigue application and that the choice of material significantly affected the failure load, with the FL group recording the highest failure load, followed by the Z-ST, Z-HT and RL groups. All FDP mate-

rial combinations survived chewing forces that exceeded physiological levels, with the bilayer FL and monolithic Z-ST groups showing the highest resilience, meaning they could serve as reliable prosthetic reconstruction concepts for three-unit FDP in ceramic implants.¹²³

Due to the widespread use of implants, it is possible to carry out long-term studies that can clearly indicate the advantages and disadvantages of the materials used. Ramelsberg et al. conducted an observational cohort study to evaluate the chipping and failure rates of FDP supported by metal-ceramic and ceramic implants and combined tooth–implant-supported FDP.¹²⁴ The study included 434 FDP placed in 324 patients, with 213 implant-supported FDP, 66 implant-supported cantilever FDP, and 155 tooth–implant-supported FDP. Metal-ceramic FDP were made with a high noble metal alloy or a Co-Cr base metal alloy framework, while ceramic FDP were all Zr-based with a monolithic, completely veneered or partially veneered framework. The researchers found that during the observation period of 0.5–12.6 years, 17 FDP failed due to implant failure, tooth loss, major chipping, or the loosening of the abutment screw. The survival probability was 96% after 5 years and 91% after 10 years, and the Cox regression analysis showed that age, sex, the location of FDP, the type of FDP support, and the FDP material had no significant effect on the failure of the prostheses. However, chipping was significantly affected by the material of the framework and the type of veneer, with the highest incidence of chipping occurring in Zr FDP with a complete veneer, followed by metal-ceramic FDP with a high noble metal framework. The authors concluded that implant–implant-supported and combined tooth–implant-supported FDP have promising long-term survival rates, and that chipping seems to occur less frequently in monolithic or partially veneered FDP than in FDP with complete veneers.¹²⁴

Balmer et al. wrote a position paper on the current level of evidence regarding Zr implants in clinical trials.¹²⁵ The authors note that Ti oral implants are considered the standard in implant dentistry, but their grey color and a high prevalence of peri-implant infections have led to controversy over whether tooth-colored, metal-free Zr ceramic implants provide sufficient potential to be considered equal in terms of treatment outcomes. The authors stated that the most available and scientifically documented Zr implant systems were one-piece implants requiring experienced surgeons and prosthodontists due to their limited flexibility in compromised angulation or vertical positioning cases. They also noted that there was evidence of a comparable outcome for one-piece Zr implants as in the case of Ti implants for the fixed replacement of 1–3 missing teeth. However, the available clinical data evaluating two-piece Zr implants with an adhesively bonded implant–abutment interface suggest an inferior outcome. The authors also mentioned that data evaluating the clinical applicability of screw-retained solutions, although

revealing sufficient fracture resistance in laboratory investigations, are still missing. They concluded that more RCTs assessing patient-reported outcome measures and two-piece Zr implant systems, as well as further clinical research on the selection of materials for monolithic reconstructions are needed to allow for a comparison with Ti at the implant level.¹²⁵

Zirconium-based ceramic implants have proven biocompatible through the tests conducted on various forms of Zr, including an yttria-stabilized ceramic, and magnesium oxide (MgO)-, Al and Ca-added ceramics. These tests demonstrated that ceramics were biocompatible materials, although Zr wear products showed some toxicity.¹²⁶ Dental implants based on Zr are also biocompatible with immune cells, including monocytes, lymphocytes and macrophages, since tests showed the absence of toxicity.¹²⁷ Also osteoblasts exhibited no toxicity during investigations. Meanwhile, in vivo tests of hard and soft tissues showed their biocompatibility with Zr-based implant materials.¹²⁷

Several variables can affect the biocompatibility of the implant surface, such as the energy, topography and chemical composition of the surface. These factors may play an important role in the development of biofilms in implanted dental materials. Both Ti and Zr are hydrophobic materials, meaning they do not interact with water, and therefore, do not promote the growth of microorganisms. In addition, Gram-positive bacteria have a thick peptidoglycan layer and hydrophobic characteristics that allow them to be attracted to implants made of Ti or Zr. Despite this attraction, microbiological studies have not reported considerable bacterial adhesion to either material. Nonetheless, Ti and Zr differ in their electrical properties. Unlike Zr, Ti is a semiconductor due to a bioactive dioxide layer, and its electrical conductivity ultimately leads to greater plaque accumulation on Ti surfaces. Additionally, albumin present in saliva is adsorbed on Ti surfaces because of divalent Ca ions, which are attracted to the negatively charged Ti surface, and bond to Ti and bacterial surfaces.

Using stem cells for PDL tissue reconstruction in osseointegrated implants was studied by Safi et al., with Ti and Zr implants coated with beta-tricalcium phosphate (β -TCP) assessed using a long-pulse neodymium-doped yttrium-aluminum garnet (Nd:YAG) laser.¹²⁸ Isolated bone marrow mesenchymal cells and PDLSCs were tested for periosteal markers. After extraction, the coated implants were transferred to the rabbit lower right central incisors and examined after 45 and 90 days. The results showed that placing coated Ti and Zr implants without a cell sheet resulted in a well-seated implant at both healing intervals. The use of PDLSCs alone or co-cultured with bone marrow mesenchymal stem cells (BMMSCs) formed natural periodontal tissue, with no significant difference between Ti and Zr implants, resulting in a biohybrid dental implant. The study concluded that Ti and Zr

implants coated with β -TCP could generate periodontal tissue and form biohybrid implants when mesenchymal cell sheets are isolated from PDLSCs alone or co-cultured with BMMSCs.¹²⁸

Assery et al. studied the effect of erbium-doped yttrium-aluminum garnet (Er:YAG) laser treatment on Zr and Ti disks, and differences in biofilm formation due to surface changes.¹²⁹ The disks were exposed to a laser, and the surface changes, roughness and elemental mass of the material were evaluated using SEM and atomic force microscopy (AFM). At the 2nd stage, 4 participants wore the disks in custom-made intraoral stents overnight, and the biofilm-covered disks were stained and visualized using multi-photon confocal laser scanning microscopy. The results showed that the Ti and Zr disks treated with the Er:YAG laser had visible surface changes, but showed no significant alterations in the mean surface roughness or elemental mass. Furthermore, there were no significant differences in biofilm biomass, thickness or the ratio of live to dead bacteria in the laser-treated Ti and Zr disks as compared to the non-laser-treated groups. The study concluded that the Er:YAG laser treatment of Ti and Zr implant surfaces did not significantly affect surface roughness, elemental mass or early oral biofilm formation.¹²⁹

Investigating the efficacy of different implant decontamination methods in terms of reducing biofilm modification, as well as their potential cytotoxicity was the goal of a study by Stein et al.¹³⁰ Titanium and Zr disks were contaminated with a highly adherent biofilm consisting of 6 bacterial species. Decontamination was performed using various methods, including a Ti curette, an ultrasonic scaler, air-polishing with glycine and erythritol powder, an Er:YAG laser, 1% chlorhexidine (CHX), 10% povidone-iodine, 14% doxycycline, and a 0.95% NaOCl solution. The results showed that only air-polishing, the ultrasonic scaler and the Er:YAG laser significantly reduced the amount of biofilm on Ti and Zr surfaces. These methods also resulted in favorable cytocompatibility on both materials. In contrast, the chemicals caused potential cytotoxic effects.¹³⁰ The application of Er:YAG laser irradiation as a support for Zr materials used in dentistry, including *in vitro* confirmation, is also described in other works.^{131–133}

The analysis of the most recent literature shows that at present, Zr implants, despite their advantages, are not a substitute for commonly used Ti implants. Comparative studies show that Ti is still superior in terms of long-term stability and satisfactory osseointegration. On the other hand, Zr implants are the preferable option when esthetics is required. According to recent reports, they are also the material of choice for protection against implants, as clinical studies indicate a better response of soft tissues as compared to Ti implants. Long-term studies are still needed in this area, particularly regarding the antibacterial effects.

Three-dimensional printing technology

From a practical point of view, researchers are increasingly focusing on questions related to the possibility of using 3D printing technology in prosthodontics, including the selection of the appropriate biomaterials. Son et al. conducted a study to evaluate the intaglio surface trueness of interim dental crowns fabricated using 3 different 3D printing and milling technologies.¹³⁴ The study used a CAD reference model as a baseline for comparison, and interim dental crowns were fabricated using the stereolithography apparatus (SLA), digital light processing (DLP) and milling machine technologies. The intaglio surface trueness of the fabricated crowns was assessed using a 3D inspection software program, and statistical analysis was conducted to compare the results. The study showed significant differences in intaglio surface trueness between the 3 different technologies, with the milling group demonstrating the highest trueness values. In addition, the milling group showed significant differences in trueness according to the location of the intaglio surface. In general, the findings suggest that 3D printing technologies may be more accurate and uniform in manufacturing interim dental crowns as compared to the milling technology.¹³⁴

Shin et al. conducted a study to analyze the effect of the internal structure and the presence of a cross-arch plate on the accuracy of 3D-printed dental models.¹³⁵ The models were designed with a U-shaped arch or a cross-arch plate attached to the palate area, and the internal structure was divided into 5 types. The accuracy of the models was measured in terms of trueness and precision. The study showed that the presence of a cross-arch plate significantly improved the accuracy of the 3D-printed models, with lower trueness and precision values in the cross-arch plate group as compared to the U-shaped group. In addition, the internal structure of the models affected accuracy, with higher trueness values in the 1.5 mm shell group, and lower values in the roughly and fully filled models. The findings suggest that a cross-arch plate is necessary for the accurate 3D printing of dental models, and that the internal structure of the models also plays a role in determining accuracy. Overall, the results of this study highlight the importance of considering the internal structure and the presence of a cross-arch plate in the design of 3D-printed dental models.¹³⁵

Mai et al. conducted a study to evaluate the effect of a newly developed CHX-loaded polydimethylsiloxane (PDMS)-based coating material on the surface properties and antibacterial activity of 3D-printed dental polymers.¹³⁶ The coating material was synthesized by encapsulating CHX in mesoporous silica NPs and adding them to PDMS. The coating was applied to the 3D-printed polymer specimens, using oxygen plasma and thermal treatment to form a thin film. The results of the study showed that the coating significantly reduced surface irregularity

and increased the hydrophobicity of the specimens. In addition, the coated specimens had a significantly lower count of bacterial colony-forming units (CFUs) in culture media as compared to the non-coated specimens, indicating the effective antibacterial activity of the coating. The findings suggest that coating substances may improve the surface properties and antibacterial activity of 3D-printed dental materials.¹³⁶

Schönhoff et al. investigated the mechanical properties of polyphenylene sulfone (PPSU) and PEEK processed using fused filament fabrication (FFF) to evaluate the suitability of PPSU as an alternative material for the 3D printing of dental restorations.¹³⁷ After aging, the study tested three-point flexural strength, two-body wear, Martens hardness, and the indentation modulus. The results showed that PPSU printed with FFF had lower flexural strength than PPSU cut from pre-fabricated molded material, indicating the need to optimize the 3D printing parameters for PPSU. Polyphenylene sulfone also had lower hardness and indentation modulus values than PEEK, but comparable results for flexural strength and two-body wear. In general, the findings suggest that PPSU may be a suitable alternative to PEEK for the manufacturing of removable and fixed dental prostheses, but that the quality of the filament used in the 3D printing process is important in determining the mechanical properties of the printed material.¹³⁷

Park et al. compared 3D-printed provisional three-unit FDP with conventionally fabricated and milled restorations in terms of flexural strength.¹³⁸ The study used 3 additive manufacturing (AM) technologies – SLA, DLP and fused deposition modeling (FDM) – as well as subtractive manufacturing (SM) and conventional methods as controls. The 3D-printed prostheses were made of a PMMA-based resin (SLA and DLP) or a PLA-based resin (FDM). The flexural strength of the prostheses was measured using UTM and analyzed statistically. The study showed that the SLA and DLP groups had significantly higher flexural strength than the conventional group, but there were no significant differences between the SLA and DLP groups or between the DLP and SM groups. The FDM group showed only dents, but no fractures. The findings suggest that 3D-printed provisional restorations made with the SLA and DLP technologies have adequate flexural strength for dental use.¹³⁸

The discussed studies evaluated various aspects of the use of 3D printing in dentistry, including the development and application of coating materials, the accuracy and trueness of interim dental crowns, the mechanical properties of different materials, the effect of the internal structures and cross-arch plates on the accuracy of dental models, and the flexural strength of 3D-printed dental prostheses. Overall, the studies suggest that 3D printing can be useful in dentistry, but further research is needed to optimize its use in fabricating prostheses, models and restorations.^{134–138}

In summary, removable and fixed removable dental prostheses are commonly used to replace missing teeth, or support and stabilize other dental restorations. Such devices are usually made of various materials, including metals, ceramics or composite resins, and can be manufactured using various techniques, such as casting, milling or AM. Research has shown that the design and material of dental prostheses can affect their performance, with particular materials and designs being more resistant to damage or chipping than others. Research is underway to evaluate the performance and clinical applicability of different dental prostheses and materials, with a focus on improving patient outcomes.

Simulations as support for material design

Structural analysis

One of the most common computational techniques used in dentistry, and especially in orthodontics, is the finite element method (FEM), a numerical technique used to solve complicated structural engineering problems. The fundamental idea of FEM is to decompose a complex geometry problem into smaller and simpler parts called ‘elements’, which can be easily analyzed. These elements are then combined to create a complete solution to the original problem. The FEM computations are often used in engineering fields, such as mechanical, civil and aerospace engineering, to analyze and design structures like buildings, bridges and aircraft.

The initial step in FEM calculations creates a mathematical model of the problem that includes details about the material composition, geometry and the loading conditions of the structure. The model is then divided into smaller elements that can be analyzed using mathematical equations. Next, the internal forces and stresses of each element are calculated with a combination of mathematical equations and computer algorithms. Finally, the forces and stresses of each element are combined to determine the overall behavior of the structure. Numerous software programs utilize FEM calculations for various uses. Popular examples are ANSYS, Abaqus, COMSOL Multiphysics®, SOLIDWORKS® Simulation, and Solid Edge, which are mainly used by engineers and scientists to evaluate and design complicated structures and systems. These software programs are also used in other industries, such as biotechnology, chemical engineering and energy production.

The work of Schmidt and Schrader was divided into 2 parts.^{139,140} In the 1st part, the authors investigated the fracture behavior of a three-piece dental bridge restoration under different chewing speeds (1.0 mm/min and 130 mm/s), using digital image correlation (DIC). The results

showed that the material exhibited significantly different responses at different test speeds, and the forces at fracture were substantially lower at the average chewing speed (130 mm/s) than in the quasi-static test. The work underscores the importance of considering different speeds when evaluating the mechanical properties of dental materials, as well as the usefulness of the DIC method for studying the fracture performance of materials. Furthermore, these results may be important for future research on the application of FEM to predict the behavior of dental restorations under clinical conditions.¹³⁹ In the 2nd part of the study, the use of FEM for predicting the mechanical performance of a PMMA temporary dental bridge under clinically relevant loads was proposed, with the nonlinear FEM predictions validated through experiments. The analysis indicated that when a material model for PMMA in dental applications is determined, the influence of the stress-state-dependent plastic flow is negligible, and the von Mises yield criterion is sufficiently accurate. Finally, the results showed good agreement when applying the von Mises yield criterion, and the Schmachtenberg hardening law was used to account for plastic deformations. However, the study also emphasized that simplifying the assumptions of the linear elastic properties of the material should be avoided in FEM studies, as they do not consider rate dependencies or plastic flow. Therefore, accurate preliminary investigations for material characterization are necessary for precise FEM predictions.¹⁴⁰

Wahju Ardani et al. conducted a study to test the feasibility of using modified PEEK with nHA as a biomaterial for orthodontic mini-implants.¹⁴¹ Using numerical molecular docking simulation, the binding affinity of nHA, PEEK and a PEEK-nHA complex with 12 osseointegration-related target proteins was analyzed. The results showed that the PEEK-nHA complex had a more negative binding affinity than either PEEK or nHA alone, indicating that it has greater potential than either of these materials as a biomaterial for osseointegration and the fabrication of orthodontic mini-implants.¹⁴¹

A similar approach was represented in other works in this area. For example, Mieszala et al. determined the possibility of using PEEK in the manufacturing of braces for orthodontic treatment.¹⁴² A variety of transpalatal arch (TPA) geometries were designed by the researchers with the use of CAD, with 4 of the designs selected and fabricated by milling PEEK. Then, the researchers conducted FEM and in vitro mechanical tests to analyze the forces acting on first upper molars. The results showed that the PEEK TPAs were capable of generating forces ranging from 1.3 to 3.1 N, and moments in the oro-vestibular direction ranging from 2.1 to 6.6 N·mm. However, some areas of the TPAs experienced von Mises stress in excess of 154–165 MPa, which could lead to the permanent deformation of the devices. Despite this, none of the TPAs showed visible deformation or cracking during in vitro tests. The researchers concluded that

PEEK might be a suitable material for manufacturing orthodontic TPAs.¹⁴²

The simulation of the tooth movement induced by orthodontic treatment can be performed with the use of FEM, which is designed to study multi-body system interactions. Orthodontic tooth movement refers to the process of moving teeth to their desired positions by using orthodontic appliances, such as braces or aligners. The process is a vital part of orthodontic treatment, and aims to correct misaligned teeth and improve the function and appearance of the patient's bite. Anh et al. simulated the mechanical behavior of a newly designed closing loop connected to the gable bends to investigate the optimal loop activation conditions to achieve the desired tooth movement during orthodontic treatment.¹⁴³ The closure loop is a commonly used system in orthodontics to close the space left after extractions, and peak bending is a type of bend in the arch that provides torque control for the anterior teeth and anchorage control for the posterior teeth. The researchers constructed a 3D model of the maxillary dentition, and used FEM to simulate the movement of both anterior and posterior teeth while varying the degree of peak bending. The results showed that using a 5° gable bend in the loop caused the lingual deviation of the crown of a central incisor and the corporeal movement of a first molar. Meanwhile, using 10° and 15° gable bends caused the corporeal movement and root movement of a central incisor and the distal deviation of a first molar. The researchers concluded that the new closing loop design, which involves reducing the thickness of the teardrop-shaped loop by 50% and using different degrees of peak bending, is effective in achieving torque control for the anterior teeth and anchorage control for the posterior teeth, and can be easily performed in a dental office.¹⁴³

In another study on orthodontic tooth movement, researchers compared the simulated orthodontic treatment results, obtained using the Incognito™ Lite Appliance System,¹⁴⁴ and the actual results to assess the accuracy of the system.¹⁴⁵ The Incognito Lite Appliance is a lingual orthodontic system that uses CAD and CAD/CAM to create digital treatment settings. The study included 17 Angle's Class I or II malocclusion participants who received the Incognito Lite standard arch sequence. The simulation and actual results were compared using Final Surface® software and the best-fit point-to-triangle method with 1,000 reference points. The results showed that the Incognito Lite Appliance System accurately achieved the simulated tooth movement in terms of tip, torque and rotation parameters, with most discrepancies within $\pm 3^\circ$. However, there were significant discrepancies between the simulated and actual tooth positions in the translational parameter, with a difference in position of 0.6–1.0 mm. The researchers concluded that while the Incognito Lite Appliance System was accurate in terms of tip, torque and rotational parameters, significant discrepancies in

the translational parameter might impair the treatment outcome and could be clinically significant.¹⁴⁵

Assessment of mechanical properties

The field of dental implants has seen significant advancements in recent years, with the development of new materials and designs that aim to improve the osseointegration process and increase success rates. In the works summarized below, innovative approaches to dental implants, which have shown promising results in clinical trials, are presented. Work by Milone et al. compared stress distribution around the cortical bone for dental implants made of Ti and Zr, using FEM.¹⁴⁶ The authors found that the stress evaluated for the Zr implant was more distributed around the cortical bone, suggesting that using Zr could improve the osseointegration process and increase the lifespan of the implant.¹⁴⁶

In a study by Patil et al., the use of finite element analysis (FEA) was explored to evaluate the mechanical behavior of Ti dental implants coated with graphene or graphene oxide.¹⁴⁷ Bones and soft tissues were modeled as homogeneous, isotropic and linearly elastic materials, and the assumption was made that the Ti implant was 100% osseointegrated. The FEA was performed using the CATIA and ANSYS Workbench software tools to analyze von Mises stress, strain and deformation at the implant and the implant–cortical bone interface. An ideal implant preload was applied to the occlusal surface of the crown, with preload values of 0.2 N·m in an anticlockwise direction and an axial load of 100 N, 150 N, 200 N, and 250 N. The results showed that the Ti implant coated with graphene oxide had better mechanical behavior than graphene, with the mean von Mises stress values of 39.64 MPa, 23.65 MPa and 37.23 MPa in pitches 1, 2 and 3, respectively (1.0 mm, 1.4 mm and 2.2 mm). The study also found that functionalizing the Ti implant helped reduce stress in the implant system. Overall, the use of FEA for solving biomechanical issues related to medical and dental devices was emphasized, and the potential for in vivo studies and practical applications was noted.¹⁴⁷

Miljanovic et al. designed a mandibular implant using the Mimics[®] and 3-Matic software to address mandibular defects in patients suffering from trauma or disease.¹⁴⁸ The implant was improved by planning the positions for dental implants prior to mandibular reconstruction surgery, using the Blue Sky Plan[®], v. 4, software. A surgical guide was designed in this software and 3D-printed using the SLA technology, while FEA was performed on the surgical guide with the ANSYS FEM software to evaluate its mechanical behavior during the surgery. The results showed that the surgical guide was able to withstand the forces encountered during the procedure. The proposed method significantly reduced the surgical and recovery time, increased accuracy, and provided a predictable and visualized restorative solution.¹⁴⁸

Hussein evaluated the mechanical properties of a graphene-based polymer (GBP) and PEEK as materials for esthetic clasps in removable partial dentures.¹⁴⁹ The study included 32 latches made with the use of the CAD/CAM technology, which were subjected to retention force tests after 10,000 insertion and removal cycles and thermocycling. The deformation of the clasp arms was also measured, and the areas of stress and strain concentration were analyzed using the FEM software (ANSYS, v. 21). The results showed that PEEK had a significantly higher retention force (2.248 ± 0.315 N) than GBP (2.018 ± 0.298 N), with a p -value < 0.001 . The buckle arm strain was also significantly higher in GBP as compared to PEEK. The concentration of stress and strain were observed at the connection of the retentive arm to the minor connector and at the retentive arm clamp in both materials. Owing to the FEA of the clasp materials, it was possible to estimate maximum principal stress. The results of this study suggest that PEEK has superior mechanical properties as an esthetic bracket material as compared to GBP, and that the optimization of GBP may be necessary to improve its suitability for this application. The possibility of using calculation methods to unambiguously indicate stress distribution in a material was confirmed, which greatly facilitates the design of new materials and the assessment of their durability. Stress and strain concentration was observed in both materials, but further optimization of GBP may be necessary to improve its suitability for use as an esthetic latch material. These results may be helpful to dentists when selecting materials for esthetic clasps in removable partial dentures. Furthermore, this work highlights the potential of new materials and designs in dental implants to improve success rates and patient satisfaction.¹⁴⁹

Deep learning

Deep learning is a machine learning (ML) subfield that involves the training of artificial neural networks (ANN) on large data sets to allow the network to learn and make intelligent decisions on its own. Deep learning has been successful in many applications, including image and speech recognition, natural language processing, and even games. As such, it has enabled major advances in fields such as computer vision, robotics and healthcare. Also, in the widely understood issues of dental materials, ANN have proven to be useful.^{150,151}

The research of Kose et al. centered around dental biomaterials and aimed to assess the precision of ML regression models in predicting the final color of leucite-reinforced glass ceramic CAD/CAM veneer restorations.¹⁵⁰ The study leveraged the color space parameters within the CIELab system (the International Commission on Illumination – Commission internationale de l'éclairage), specifically L (lightness), a (green to red) and b (blue to yellow), which are fundamental for quantifying and characterizing color in this context. Leucite-reinforced glass

ceramics designed for dental use were used in different shades and thicknesses, ranging from 0.3 to 1.2 mm. Full-color measurements were taken for each sample against different background colors, such as black, white, A1, and A3. The dataset included the color difference values (CIEDE2000) and all CIELab coordinates relevant to the experimental groups. The researchers used experimental translucent resin cement and a precisely calibrated spectrophotometer for measurements. Afterward, 28 distinct regression models were applied and fine-tuned for optimal performance by considering the weights associated with the CIELab color space parameters. The findings of this study underscore the influence of various factors on the L, a and b coordinates in the CIELab color space, which collectively determine the color characteristics of dental biomaterials. It is noteworthy that the shade of the ceramic restoration was primarily affected by the type of tooth substrate, followed by the thickness of the restoration, and specific values for L, a and b. The decision tree regression model proved to be the most effective, exhibiting the lowest mean absolute error and the highest accuracy in predicting the shade of the restoration based on these CIELab coordinates. From a clinical perspective, the ML regression model presented in that study has substantial potential for dental professionals. It streamlines the forecast of the final color outcome of ceramic veneers produced using leucite-reinforced glass CAD/CAM ceramic, a material exclusively designed for dental purposes. Whether the veneers are low-translucency (LT) or high-translucency (HT), and whether they are cemented with translucent cement, this predictive tool depends on the initial color of the tooth substrate and the thickness of the ceramic material. Employing this technique enhances the predictability and precision of esthetic outcomes in dental restorations, ultimately providing advantages to both clinicians and patients in the field of dental biomaterials.¹⁵⁰

With regard to Zr biomaterials, a study by Lerner et al. investigated the role of artificial intelligence (AI) in fabricating implant-supported monolithic Zr crowns (MZCs) on custom-made hybrid abutments.¹⁵¹ The methodological process involved the intraoral scanning, CAD-based design, precise milling, and clinical application of hybrid abutments and provisional crowns. Artificial intelligence aided in designing the final crown with the automated margin line design. Outcome parameters covered various aspects, from the assessment of the precision of fabrication to clinical evaluations, including the marginal adaptation, interproximal contacts, occlusal harmony, chromatic integration, and survival of the MZCs. The study cohort consisted of 90 patients, predominantly female (55), with a mean age of 53.3 ± 13.7 years. Over a follow-up period ranging from 6 months to 3 years, the careful evaluation of individual hybrid abutments revealed a mean deviation of $44 \pm 6.3 \mu\text{m}$ from the original CAD design. Notably, the MZCs achieved commendable results in terms of clinical performance, characterized by superior marginal adapta-

tion, favorable interproximal and occlusal contacts, and harmonious chromatic integration. Crucially, the 3-year cumulative statistics indicated a 99.0% survival rate and a 91.3% success rate for the MZCs.¹⁵¹

The work by Suryawanshi and Behera focused on the evaluation of ML models used for predicting the wear of dental composite materials.¹⁵² Dental materials degrade over time and need replacement, and resin composites are commonly used for dental restorations. In their study, the authors utilized the *in vitro* test results obtained from the pin-on-disk tribometer following the American Society for Testing and Materials (ASTM) standards (ASTM G99-04) to assess the performance of 3 different ML models in analyzing the wear of dental composite materials when exposed to a chewing tobacco solution. The research involved 4 distinct dental composite material samples that were immersed in a chewing tobacco solution for a specific duration, and then subjected to a wear test. Among the models under consideration there was a multi-layer perceptron (MLP), a type of ANN. The structural similarity of MLP to biological neural networks makes it versatile and applicable to a variety of tasks within the scope of ML, including regression and classification. The underlying mechanism is based on the emulation of interconnected neurons, enabling them to identify intricate patterns in data. Another important AI approach in this study is the *k*-nearest neighbors (KNN) algorithm. This algorithm, known for its simplicity and intuitive methodology, is useful for classifying and regressing tasks. The KNN approach is based on making predictions by using the majority class outcomes or calculating the averages from the *k*-nearest data points in the training dataset. The 3rd model is XGBoost – an acronym that stands for “eXtreme Gradient Boosting”, an algorithm that is renowned for its effectiveness in predictive modeling situations. The XGBoost ML model stood out, as it achieved an impressive R^2 value of 0.9996, indicating a very strong predictive capability. The results suggest that XGBoost significantly outperformed the other ML approaches in predicting the wear of dental composite materials, making it a promising tool for predictive applications in the field of dentistry.¹⁵²

Drug discovery

In the field of drug design, molecular docking is a widely used numerical approach to find the optimized protein–ligand system. The purpose of molecular docking is to find the optimal orientation and conformation of a ligand when it binds to a protein, and to predict the strength of the binding interaction. Such information can be used to assess the potential of the ligand as a drug candidate and to optimize its structure to improve its binding affinity. Molecular docking algorithms typically use a set of geometric, physical and chemical principles to predict the binding of the ligand to the protein¹⁵³ through a combination of quantum computing and molecular mechan-

ics. Quantum computing is used to predict the electronic properties of the ligand and the protein, such as electron distribution and chemical bond strength. Meanwhile, molecular mechanics calculations predict the shapes and behavior of the ligand and the protein based on their physical properties, such as size, mass and charge. These 2 types of calculations are often used together in molecular docking algorithms to provide a more accurate prediction of the ligand–protein binding. For example, PyRx is a program designed for small-molecule ligand-to-protein docking and analysis, and is commonly used in drug discovery and development to study interactions between ligands and proteins, and predict the affinity of a ligand to a target protein. In addition, PyRx can be used to optimize the positions of ligands and evaluate how ligands bind to proteins, to study the structural properties of proteins, as well as to enable the virtual screening of large libraries of compounds.

Prahasanti et al. presented an *in silico* study showing that HA-PMMA composites have the potential to function as dental implant biomaterials due to their advantageous mechanical, chemical and biological properties.¹⁵⁴ These composites not only induce osseointegration, with biocompatibility and minimal allergic reactions, but also they do not release metal ions and can be obtained from natural Indonesian resources. The 3D structure, molecular weight and identification number of the HA-PMMA complex were obtained from the PubChem database and minimized using the Open Babel software. The 3D structures of bone morphogenetic protein (BMP) 2, BMP4, BMP7, alkaline phosphatase (ALP), osteonectin, osteopontin, and osteocalcin were obtained from the Research Collaboratory for Structural Bioinformatics Protein Data Bank (RCSB PDB) and sterilized with the use of the PyMol software to remove water molecules. Molecular docking simulations were performed using PyRx and analyzed using the Discovery Studio software to visualize the types of chemical bonds formed. The results showed that the HA-PMMA complex could increase the activity of osseointegration-related proteins such as BMP2, BMP4, BMP7, ALP, osteonectin, osteopontin, osteocalcin. The complex had the strongest binding to osteonectin and was predicted to increase the activity of ALP. Finally, the study suggested that HA-PMMA composites might be potential candidates as biomaterials for dental implants.¹⁵⁴

Riaz et al. evaluated the binding affinity of 3 newly designed hydroxyquinoline compounds based on the amino acid residues at the active site of each protein and drug-like properties, including sulfanilamide, 4-amino benzoic acid and sulfanilic acid, against 5 bacterial protein targets.¹⁵⁵ Hydroxyquinolines have previously been shown to have various biological properties, including antibacterial activity. The researchers used molecular docking software to assess the affinity of the compounds with proteins and found that they had binding energy values ranging from -2.17 to -8.45 kcal/mol. Compounds 1 and 3 had

the best binding results toward bacterial protein targets 1ZIO/3VOB and 1JII/4CJN, respectively, and, as the authors suggest, may serve as novel antibiotic scaffolds. The researchers conducted molecular dynamics simulations to further evaluate the potential of the compounds as bacterial inhibitors, particularly against methicillin-resistant *S. aureus*. The simulation showed that the compounds had good stability and did not form aggregates. The study identified 2 hydroxyquinoline derivatives showing a strong affinity for binding to specific proteins in certain bacterial strains. These compounds can effectively treat infections caused by these bacteria, particularly *S. aureus* and *E. coli*. The synthesis of these compounds is relatively straightforward, facilitating further research investigating their effectiveness in treating bacterial infections. It can be concluded that hydroxyquinoline compounds have the potential to develop as bacterial inhibitors and warrant further experimental studies through preclinical and clinical trials.¹⁵⁵

Opportunities and challenges

A few main limitations regard all types of biomaterials in dentistry. They are associated with the biocompatibility of biomaterials, their degradation in the complex oral environment, and features that affect their cost and esthetics.

Biomaterials in dentistry are exposed to the aggressive oral environment, changes in saliva pH and flow, and various forms of gingival inflammation due to an erosive diet, rich in sugars and acids, or stress-related diseases, such as anorexia or bulimia nervosa. A highly acidic oral environment is also related to gastroesophageal reflux disease (GERD), which is becoming increasingly common in the young population due to an improper diet, severe vitamin D deficiency, obesity, and food allergies.¹⁵⁶ These factors contribute to the loss of the mineralized tooth structure, early caries, bacterial infections, and the loss of dental tissues.

Restorative biomaterials still suffer from signs of aging, such as marginal or surface discoloration, chipping, and changes in shape and transparency. Palacios et al. examined changes in the mechanical properties of 3 commercial resin composites immersed in artificial saliva.¹⁵⁷ After 30 days of incubation, the flexural strength, fracture toughness, hardness, and modulus of elasticity of the tested composites were significantly reduced.¹⁵⁷ Similar results were reported by Kielbassa et al., with the authors showing that high-viscosity GIC and a glass hybrid restorative system do not provide long-term protection against abrasive wear.¹⁵⁸

Over the last decade, scientists have made a considerable effort to enhance the mechanical properties of biomaterials and their stability in complex media without compromising their biocompatibility. Their research

regards mainly the chemical composition of restorative materials and advanced modification techniques.^{159,160} Nowadays, nanotechnology plays an essential role in developing advanced restorative biomaterials and their further improvement.¹⁶¹ The application of nanomaterials in dentistry includes dental diagnostics, preventive dentistry, prosthodontics, endodontics, periodontics, implantology, and regenerative dentistry. They are used as NPs, nanocomposites, nanofibers, or implant nanocoatings. Nano-enhanced biomaterials display excellent antimicrobial activity and improved mechanical properties, especially resin composites enriched with Ag NPs, ZnO NPs or copper (Cu) NPs.¹⁶² However, the number of *in vitro* and *in vivo* studies confirming these positive effects is limited. Additionally, only a few long-term clinical studies indicate resin composites can be used for the restoration of the posterior teeth with long-lasting durability.^{163–165}

Another critical limitation of advanced dental materials is preventing the formation of salivary protein coating on the surfaces of biomaterials. Salivary proteins attach to the material surface and serve as adhesion substrates for the colonizing bacteria, reducing the bacteriostatic activity of biomaterials.¹⁶¹ Improving biomaterials to achieve protein-repellent surfaces is a great challenge for material engineering, with *in vitro* studies indicating that the adsorption of saliva proteins on the surfaces of biomaterials is mainly determined by the surface characteristics. The lowest protein adsorption is observed for hydrophobic and negatively charged coatings. However, some studies show that the adsorption of proteins cannot be linked to the physicochemical properties of the surface. The negatively charged glycoproteins mucin-7 (MUC7) and zinc alpha 2-glycoprotein (ZAG) adsorb not only to positively charged surfaces, but also to the silica- and PEG-modified biomaterials, which are hydrophilic and exhibit negative electrokinetic potential. Scientists suggest that this effect can be explained by the unique and complex interactions between the proteins involved in salivary micelles, which are formed due to the accumulation of MUC7, lactoferrin and immunoglobulin A, and positively charged lysozyme, which mainly occurs as a single component. The proteins attach to the surface of the biomaterial through a multitude of physicochemical interactions to maintain homeostasis in the complex oral environment.^{166,167}

In recent years, scientists have faced the emerging problem of monomer cytotoxicity due to incomplete composite resin polymerization reactions. The unreacted monomers remain in the polymer matrix and may be released into saliva, accumulating in the surrounding tissues. It should be pointed out that the unreacted monomers deteriorate the stability of polymer fillings, which results in their shorter clinical lifetime. Developing new resin monomer technology based on silorane and UDMA resins is an important area of dentistry research.^{168,169} These new materials ensure low shrinkage stress at the tooth–biomaterial interface, and minimize contraction gaps, micro-leakage

and the recurrence of caries. Although modern biomaterials are promising, more *in vivo* and clinical studies are urgently needed to investigate their biological advantages and drawbacks in detail (Fig. 4).

Developing modern dental materials should be supported by computational techniques to evaluate their properties, predominantly mechanical features. Such an approach can facilitate the introduction of new biomaterials to the market by reducing the number of complicated, tedious and expensive experiments. In this regard, more cooperation between dentists and engineers is needed to ensure the development of the optimal solutions (Fig. 4). Furthermore, advanced treatment methods in dentistry should include personalized strategies to design biomaterial–drug combinations specific to each individual's health state. Personalized dental biomaterials could be enhanced based on data acquisition at the individual level, including saliva composition and saliva biomarker levels.^{170,171}

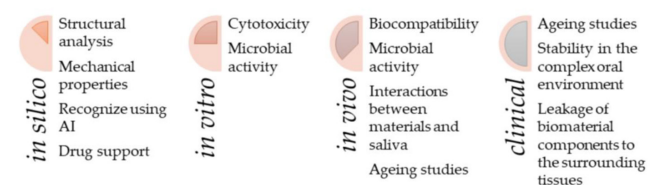


Fig. 4. Development of dental materials – necessary research steps

Conclusions

This paper summarizes the most important biomaterials and emerging modification strategies that improve their biointegration, biological activity, mechanical properties, and resistance to the harsh oral environment.

Although biomaterials are widely used, a great deal of research is still being conducted to improve their long-term use and introduce modifications to support dental tissue regeneration. Dental biomaterials are also expected to prevent bacterial infections and effectively inhibit material corrosion in saliva. However, restorative biomaterials are still susceptible to bacterial attachment and biofilm formation.

Another aspect addressed in recent literature reports is the improvement of the mechanical properties and esthetics of restorative materials. The surfaces of biomaterials are usually modified with polymers or nanomaterials to reduce friction while maintaining biocompatibility.

All modern biomaterials are promising; however, there is an urgent need for more *in vivo* and clinical studies to investigate their biological advantages and disadvantages in detail. The computational techniques used to assess the properties of modern dental materials, particularly the mechanical ones, could assist in the development of the materials. Such an approach can help bring new biomaterials to the market by reducing complicated, tedious and expensive experimentation.

Ethics approval and consent to participate

Not applicable.

Data availability


All data generated and/or analyzed during this study is included in this published article.


Consent for publication

Not applicable.

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