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Review article

BIOMIMETIC STRATEGIES AND ADHESIVE PROTOCOLS IN THE RESTORATION OF SEVERELY COMPROMISED POSTERIOR TEETH - A CONTEMPORARY REVIEW

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ABSTRACT

Severely compromised distal teeth present significant challenges in restorative dentistry, necessitating innovative approaches that align with natural biological structures. Biomimetic principles offer a promising framework for reconstruction, emphasizing materials and techniques that mimic the mechanical and aesthetic properties of natural teeth. This review explores key biomimetic strategies, including advanced adhesive systems, dentin-enamel interface replication, and regenerative protocols that enhance long-term functionality. Additionally, biomimetic frameworks guide the selection of materials and methods that optimize tooth restoration while minimizing biological disruption. Stress-reducing techniques/protocols, such as improved occlusal design and reinforcement strategies, further contribute to the longevity and resilience of restorations. The role of matrix metalloproteinases (MMPs) in dentin degradation and adhesive failure is also examined, highlighting strategies for their inhibition to enhance restoration durability and longevity. By integrating these principles, clinicians can achieve restorations that closely resemble natural dentition, promoting durability and patient comfort.

Key words: adhesion, biomimetic, cavity preparation, indirect restorations, posterior teeth,

INTRODUCTION

The concept of minimally invasive intervention in the management of hard dental tissues remains a fundamental principle in contemporary dental practice. The conservative approach in tooth preparation, biocompatible materials, and effective adhesion, combined with the desire for highly esthetic restorations, lays the foundation of biomimetic dentistry.

The advantages of this approach in restorative dental care in the posterior regions include increased strength of the adhesive bond, maximum preservation of tooth structures (even in teeth considered non-restorable), minimization of extensive crown preparation, reduction of postoperative sensitivity [1], and the elimination of many postoperative injuries to the dental pulp and the associated endodontic treatments. Biomimetic materials replicate the function of natural enamel, dentin, and the enamel-dentin junction (EDJ), resulting in a restored tooth that is biomechanically and aesthetically similar to natural dental tissues [2]. Biomimetic restorations in posterior regions include direct composite fillings, indirect partial coverage restorations (inlays and onlays made of ceramic or composite), and, where necessary, overlays (ceramic/composite full coverage restorations).

Biomimetic strategies and adhesive protocols

The restoration of extensively damaged teeth presents a significant clinical challenge, requiring not only the replacement of lost structure but also the recreation of functional, aesthetic, and biomechanical integrity. In this context, biomimetic dentistry has emerged as a progressive philosophy, aiming to replicate the natural properties and hierarchical architecture of dental tissues through minimally invasive and adhesive techniques. Central to this approach are the principles of stress reduction and adhesive optimization, which collectively seek to preserve the vitality of the tooth and ensure the longevity of the restoration.

A critical examination of modern adhesive protocols reveals a shift towards biologically driven methodologies that prioritize the preservation of dentin integrity, the improvement of the adhesive interface, and the use of materials and techniques that mimic the natural mechanical behavior of teeth. Simultaneously, contemporary stress-reduction protocols are designed to mitigate the functional loads transferred to the bonded interface, thereby minimizing the risk of adhesive failure, crack initiation and propagation, and postoperative sensitivity. The integration of these strategies within restorative procedures forms the foundation of biomimetic adhesive protocols, which aim not only to restore, but to preserve and protect, aligning restorative outcomes with the natural biomechanics of dentition.

This article aims to explore the current evidence-based protocols and innovations in biomimetic adhesive dentistry, with particular emphasis on the interplay between stress modulation and adhesive performance in the restoration of structurally compromised teeth.

Contemporary principles of tooth preparation are based on specific structural and geometrical criteria that must be thoroughly analyzed before planning an indirect adhesive restoration. These criteria can be effectively applied to all restorations that are adhesively cemented. They include the tooth surface with the greatest circumference (buccally and palatally/lingually), the sigmoidal nature of the enamel-dentin junction (*EDJ*), and the orientation of enamel prisms in relation to the axial and proximal surfaces/walls [3]. Over recent decades, restorative approaches have been undergoing continuous development, gradually shifting from mechanical retention strategies towards those emphasizing optimal adhesive performance [4]. Composite materials and adhesive dentistry have evolved into an integrated and balanced system, enabling the functional, anatomical, and aesthetic restoration of hard dental tissues. The principles of biomimetic dentistry are directed towards increasing bond strength, ensuring effective marginal sealing, reducing residual stress, and preserving the vitality of the dentition [5].

The biomimetic restorative protocol was first published by Dr Deliperi in 2002 in the Journal of the American Dental Association (*JADA*). The implementation of this protocol allows for the maximization of adhesive bond strength and the minimization of stress during restoration, with the objective of replicating the functional and optical characteristics of the intact natural tooth [6]. Both the maturation of the adhesive interface and the incremental placement and polymerization of the restorative material are essential components of the protocol aimed at reducing stress over the remaining tooth structure. Initially described as a six-step process, the protocol has evolved into a ten-step approach as biomimetic techniques have been improved.

Aspects of contemporary stress-reduction protocol:

1. Indirect techniques
2. Decoupling with time
3. Incorporation of reinforcing fibers
4. Use of soft-start or pulse-activated polymerization techniques
5. Incremental horizontal dentin replacement - ≤1 mm
6. Biomimetic materials
7. Restoration of non-vital teeth
8. Crack detection and management
9. Cusp reduction
10. Verticalization of occlusal forces

Indirect techniques for posterior restorations are designed to minimize polymerization shrinkage and the resulting residual stresses within the restorative material [1]. In indirect restorations, polymerization occurs extra-orally, thereby minimizing the stresses transferred to the tooth structure. This significantly reduces the potential for marginal microleakage and the complications arising therefrom. Decoupling with time – it is recommended that the thickness of the initial composite increment does not exceed 1.5 mm. This approach prevents the immediate bonding of deep dentin to enamel or superficial dentin before the hybrid layer has fully matured and achieved optimal mechanical strength, a process which typically requires approximately five minutes. This technique prevents degradation of the adhesive interface and the formation of a micro-gap between the composite restoration and the pulpal floor, which, over time, can result in postoperative sensitivity and discomfort. The "decoupling with time" strategy neutralizes the so-called "connectivity hierarchy," which posits that composite shrinkage stress tends to migrate or "flow" towards the most mineralized and dry walls of the cavity preparation, and away from the moist dentinal surfaces [7].

Extensive structural loss and endodontic treatment of posterior teeth often result in a significant reduction of hard dental tissues, compromising the mechanical integrity of the tooth. The integration of reinforcing fibers into dental restorations expands the application potential of both direct and indirect restorative techniques. These fibers not only enhance the strength of the restoration [8, 9] but may also function as a stress-absorbing layer. The effectiveness of this reinforcement is influenced by the type, size, and orientation of the fibers used [10,11].

Several studies have demonstrated that the use of polyethylene fibers - with a high elastic modulus and favorable tensile strength - in conjunction with flowable composites beneath the main restorative layer increases fracture resistance by modifying the tooth–restoration interface [9,10]. There is also evidence suggesting that fiber-reinforced composites reduce microleakage, regardless of the fiber type employed [9,12]. According to Lassila et al., restorations incorporating a bulk core made of glass-fiber-reinforced composite and a thin (0.5–1 mm) superficial layer of a highly polishable composite exhibit promising outcomes in terms of fracture resistance and compressive strength.

Polymerizing composite resins using a gradual increase in light intensity has proven to significantly reduce polymerization stress across various composite systems [13]. Studies involving a 5-second initial low-intensity exposure show a beneficial effect on stress development during the polymerization process. Specifically, slow-curing protocols have been employed to mitigate complications such as enamel fractures, marginal leakage, microcracks in hard dental tissues, postoperative sensitivity, marginal discoloration, and secondary caries [14]. These techniques reduce polymerization stress during the curing reaction, resulting in improved clinical outcomes.

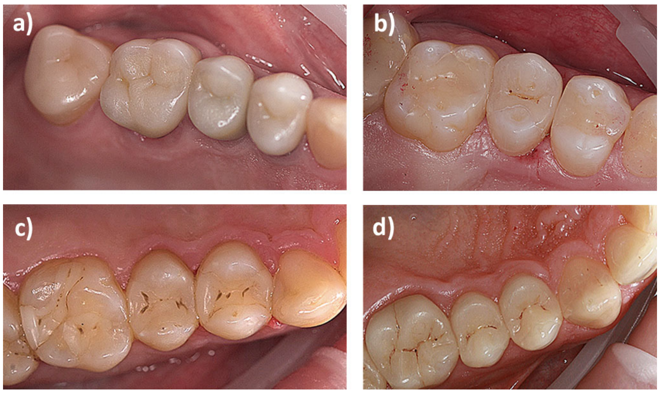
Layered incremental placement of composite material, not exceeding 1 mm, is recommended in dentin replacement. Although the technique has been debated - particularly regarding the resulting configuration factor (*C-factor*). Yantcheva demonstrated that nanocomposites and silorane-based composites, which require incremental application, provide improved marginal adaptation and reduced microleakage [15]. The reduction in stress is attributed to the smaller composite volumes, which generate significantly less contraction stress on the cavity walls during polymerization [16]. Incremental build-up also facilitates uniform and efficient polymerization due to a lower ratio of bonded to unbonded surfaces [17]. The dual-layered technique is considered a novel biomimetic restorative approach, designed to emulate the structural integrity of the dentine–enamel complex. It consists of a fiber-reinforced composite base and a superficial layer of a highly polishable, wear-resistant composite [8]. The glass fibers serve as a crack-stopping barrier, preventing the propagation of internal fractures within the restoration.

The application of biomimetic materials in restorative dentistry remains a challenge, largely due to the complex and dynamic nature of the oral environment. Restorative materials are exposed to wide variations in temperature, pH, microbial activity, and dietary factors. Additionally, individual differences such as age, ethnicity, and lifestyle can influence oral conditions. Materials used to restore dental structure and function should ideally mimic the properties of natural tissue, particularly in terms of elastic modulus, tensile strength, and compressive resistance [18]. Dentin replacement composites are recommended to have polymerization shrinkage below 3% and an elastic modulus in the range of 12–20 GPa [19].

Recent studies have explored novel bioactive nanocomposites designed to reduce secondary caries, extend the longevity of restorations, and promote overall oral health [20, 21]. Such materials are Cention N and Cention Forte (*Ivoclar, Liechtenstein*) [22]. Promising results have also been reported for a novel monomer - (*3,9-diethyl-1,5,7,11-tetraoxaspiro[5,5] undecane-3,9-diyl)bis (methylene) bis((2-(3-(prop-1-en-2-yl)phenyl)propan-2-yl)carbamate*), known as DDTU-IDI - which exhibits post-curing volumetric and hardness enhancement. The development of low-shrinkage composites and the introduction of DDTU-IDI-based polymers present a positive strategy for reducing polymerization shrinkage and potentially enhancing the long-term durability of composite restorations [23]. According to Zihuan et al., a polymer containing 20% DDTU-IDI demonstrated a polymerization shrinkage of just 1.83 ± 0.53% [23]. Wang et al. reported on a novel siloxane-modified polyurethane monomer featuring both acrylate and siloxane functionalities. This monomer forms chemical bonds with both dentinal collagen and hydroxyapatite, and has been formulated as a potential alternative to bisphenol A-glycidyl methacrylate. The siloxane–polyurethane-based adhesive is designed to enhance dentin bonding quality and the long-term performance of adhesive restorations.

The restoration of non-vital teeth presents a significant challenge in restorative dentistry due to the substantial loss of hard tooth tissues. De Kuijper et al. suggested that in the short term (2.5 to 3 years), available low-quality evidence indicates no significant differences in tooth survival or restoration quality among various restoration types. To better understand the impact of restoration type on the survival and restorative outcomes of endodontically treated posterior teeth, robust clinical trials are warranted. These trials should carefully account for factors such as the amount of remaining coronal tooth tissue and other relevant baseline characteristics [24]. On the other hand, Shu et al. investigated those indirect restorations, particularly crowns, that are suggested as a preferable option for restoring endodontically treated teeth with extensive coronal damage. Indirect restorations, primarily crowns, demonstrate superior survival rates in the short term (*5 years*) and medium term (*10 years*) when compared to direct restorations, such as composite or amalgam (Fig. 1) [25,26].

Fig. 1. A 10-year follow-up of: **a/** ceramic restoration on tooth #16; **b/** ceramic restoration on tooth # 15; **c/** indirect composite restorations on teeth #14 and 15; **d/** ceramic restorations on teeth #14 and 15.



In endodontically treated teeth, biomimetic strategies advocate for the elimination or reduction of post-and-core preparations, and instead recommend adhesive protocols aimed at reinforcing the remaining tooth structure and minimizing stress within the restoration and tooth preparation [27]. The use of a dual-cure composite with a chemically initiated polymerization phase during the first five minutes is advised. The volume of the composite is less critical in this scenario due to the slow initiation of chemical polymerization, which typically occurs over a period of 4 to 5 minutes. This delayed polymerization allows sufficient time for the formation of a stable hybrid layer at the adhesive–dentine interface [28]. Accurate detection and localization of dentinal cracks is virtually impossible without the use of magnification. However, the precise extent of crack propagation often remains uncertain at the time of clinical examination. Consequently, no universally accepted method currently exists for early, non-invasive quantitative crack diagnosis [29].

Posterior teeth, particularly mandibular molars, are most frequently affected. A modern diagnostic approach combining Diagnodent *(KaVo Dental Technologies, Biberach, Germany*) (a method used for early caries detection) with the application of dyes can help determine the extent of carious tissue or cracks and assist in delineating the peripheral margin of the sealed zone. It is recommended that all cracks within the dentin be carefully removed within 5 mm from the occlusal surface and within 3 mm proximally from the axial wall in areas of marginal sealing [30]. Residual cracks beneath the restoration may propagate due to micro-stress during function. Larger cracks tend to propagate under lower stress compared to smaller ones [30]; therefore, it is advisable to remove as many cracks as possible without exposing the pulp. Conventional rotary burs used to remove dentinal cracks often induce additional microcracks and may exacerbate existing ones. The extent of dentine loss is influenced by the shape and size of the bur. Contemporary minimally invasive protocols recommend air abrasion with aluminum oxide (*Al, Of*) as a technique that generates the fewest new microcracks, while preserving more tooth structure compared to traditional methods [31].

The presence of cuspal structures thinner than 2 mm at the cavity base - after removal of carious and cracked dentine - should be avoided when possible. [32]. A smoother preparation design, free of complex geometric forms, is encouraged. This transition alters the stress distribution across the hybrid layer from tensile to compressive forces, thereby reducing fatigue at the adhesive interface [33].

Special attention should be given to occlusal mapping and the verticalization of occlusal loads in order to minimize tensile stress on the restoration and cervical portion of the tooth.

Aspects of adhesive protocols for effective bonding

1. Adhesive systems
2. Inhibition of Matrix Metalloproteinases (*MMPs*)
3. Creating a peripheral sealing zone free
4. Surface preparation - air abrasion
5. Optimizing the enamel margins
6. Freshly prepared dentin
7. Flowable composite application
8. Coronal margin relocation

Restorative dentistry has made remarkable advancements in recent years, particularly in the development and application of adhesive protocols that aim to preserve tooth form and color. The adhesion of dental materials to tooth structures relies on three fundamental mechanisms: *1) surface wetting*, which facilitates intimate contact between the material and the substrate; *2) microretention*, also known as micromechanical interlocking, which enhances mechanical stability; and *3) chemical interaction*, which promotes molecular bonding. To achieve durable adhesion, it is essential to optimize the application of these primary bonding principles in clinical practice [34]. With advancements in dental technology, adhesive systems have evolved through seven generations - from no-etch techniques to total-etch and, ultimately, self-etch adhesives. This progression has enhanced bond strength, simplified procedures, and improved clinical outcomes, reflecting the continuous innovation in restorative dentistry (Table 1).

Table 1. Classification of Contemporary Bonding Agents

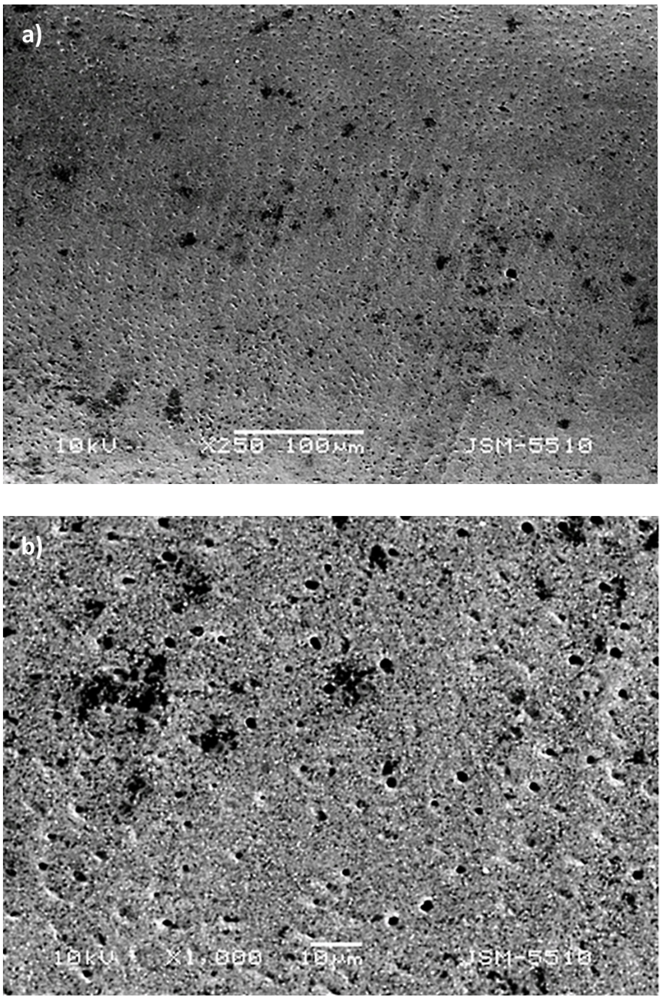
Evolvment of dental adhesives	**Main features and number of steps**	**Number of components**	**Advantages**	**Limitations/ Disadvantages**	**Critical analysis**
4th	Three-step total-etch (etch, prime, bond); complete smear layer removal; hybrid layer formation	3	High bond strength (17–25 MPa); predictable results; long-term stability; reduced post-op sensitivity	Technique sensitive; risk of over-etching; time-consuming.	Gold standard for durability and bond strength, but complex and sensitive to operator error [35]
5th	Two-step total-etch (etch, then combined prime/bond); single-bottle system	2	Simplified application; reduced chair time; good bond strength (20–24 MPa)	Still technique sensitive (moisture control); possible post-op sensitivity; multiple coats may be needed. Two-step systems prone to hydrolytic degradation [36]	Balances performance and ease, but still prone to errors if moisture is not well controlled [35]
6th	Two-step self-etch (etch/prime combined, then bond); no separate etching	2	Less technique sensitive; reduced post-op sensitivity; no rinsing step, bond strength to dentin (18-23 MPa)	Lower bond strength to enamel; variable substrate effectiveness; mixing required	Improved user-friendliness, but enamel bonding is weaker, and mixing can introduce errors [35]

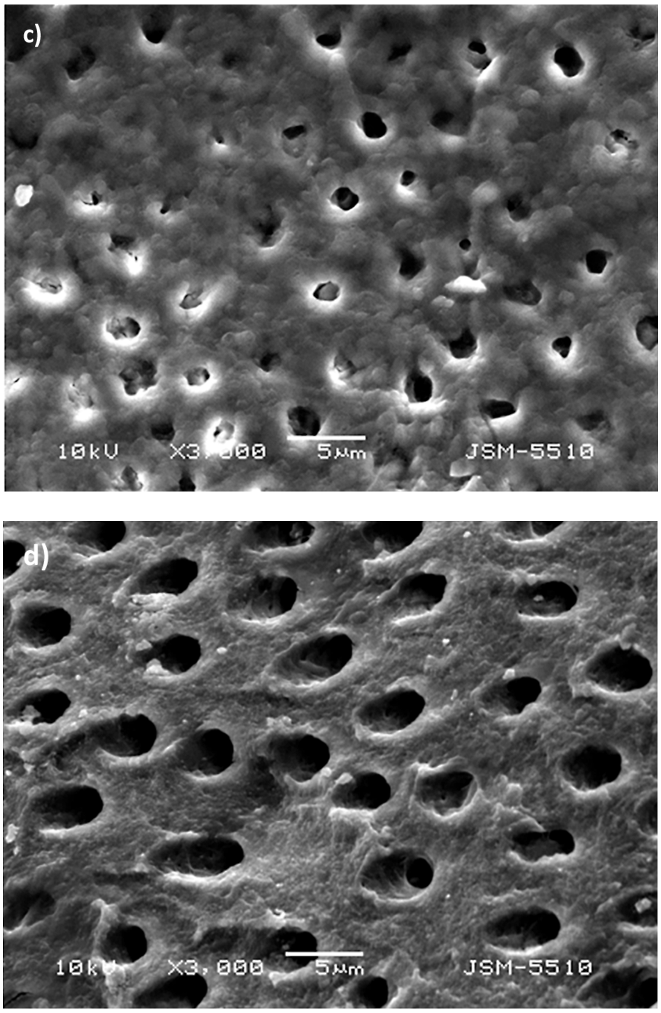
7th	One-step self-etch (all in one bottle); no separate mixing	1	Simplest application; minimal technique sensitivity; fast (18-35 MPa)	Lower bond strength than earlier generations; possible long-term durability issues	Highly convenient, but may compromise bond strength and longevity, especially on enamel One-step systems prone to hydrolytic Degradation
8th	Universal adhesives: can be used as self-etch, total-etch, or selective-etch; improved monomer chemistry	1	Highest bond strength (to both enamel and dentin); versatile; improved hybrid layer; reduced sensitivity(25-35 MPa) [37]	Newer, less long-term data; cost; technique still matters Combination of hydrophilic/ hydrophobic monomers make them susceptible to hydrolytic degradation [38]	Superior bond strength and versatility, outperforming previous generations in studies, but long-term clinical evidence is still emerging [39]

Biomimetic replication of lost dental tissue has become increasingly achievable through sophisticated adhesive techniques and the use of advanced nanocomposites and ceramic materials. A durable adhesive interface is achievable when appropriate materials are used in Combination with well-defined, clinically applicable protocols. Eight such protocols have been systematized; when implemented in conjunction with stress-reduction strategies, they contribute to predictable and long-lasting biomimetic restorations [5].

The quality of adhesion is influenced by numerous factors, particularly the type of adhesive system used. In biomimetic protocols, both total-etch and self-etch systems are employed. These systems represent the gold standard in dental bonding and can achieve bond strengths of 25–35 MPa to enamel and 40–60 MPa to dentin [5]. Literature indicates that three-step total-etch and two-step self-etch systems yield the most favorable clinical outcomes [40,41]. However, the long-term durability of dentin bonding remains suboptimal due to the inherent difficulty of bonding to dentin compared to enamel. The micromechanical interaction between enamel and adhesive is a result of monomer diffusion and interlocking within the micro-porosities created by acid demineralization [42]. This interaction facilitates the formation of resin tags within the micro-porosities, resulting in a highly reliable and durable adhesive interface. Such predictable adhesion is a fundamental factor in the long-term success of adhesive restorations. Given its high degree of mineralization - approximately 92% by weight, predominantly in the form of hydroxyapatite - enamel offers an ideal substrate for stable and robust bonding. Among available surface conditioning methods, phosphoric acid etching continues to be considered the gold standard for achieving effective adhesion to dental hard tissues, owing to its ability to create a consistent etching pattern that optimizes surface energy and micro-retention [43]. Dentin, on the other hand, contains a high proportion of organic components, water, and tubules connected to the pulp, along with fluid within those tubules. Additionally, a smear layer is formed inevitably during the mechanical preparation [44] (Fig. 2).

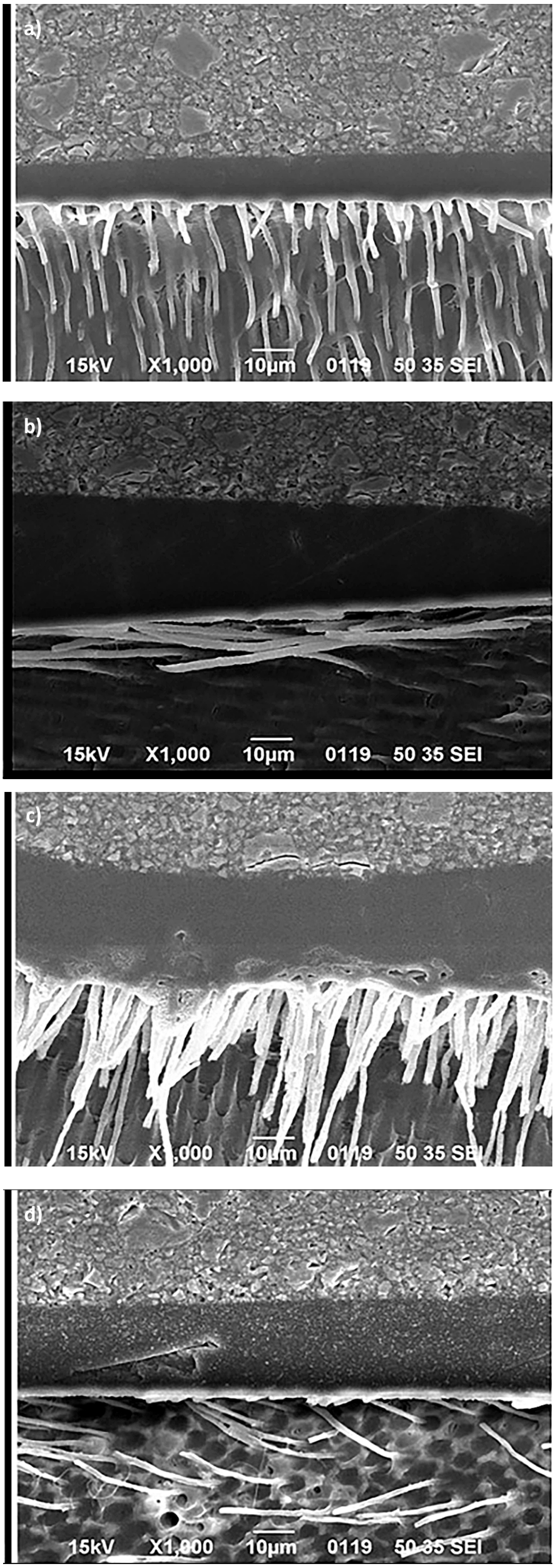
Fig. 2. SEM of smear layer - medication of dentin after the preparation with chlorhexidine – ***a)*** *magnification x 250*; ***b)*** *magnification x 1000*; ***c)*** *magnification x 3000*; ***d)*** SEM of opened dentin tubules after the application of 37% phosphoric acid – *magnification x 3000.*





Gateva and Kabakchieva demonstrated that application of 37.5% phosphoric acid for 15 seconds to sound dentin teeth effectively removes the smear layer, both from the dentinal tubule orifices and from the intertubular areas [45]. This procedure effectively removes the smear layer and demineralizes approximately 5/ ìm of the underlying dentin, thereby exposing a three-dimensional network of Type I collagen fibrils that constitutes the organic framework of the dentinal matrix [46]. The interfibrillar space - approximately 30 ± 11 nm - acts as a diffusion channel, allowing low-viscosity adhesive monomers to infiltrate the demineralized collagen network to a depth of ~5 µm [47]. Upon polymerization, the adhesive forms a micromechanical bond with the collagen fibrils, resulting in the formation of the hybrid layer, a structurally acid-resistant zone that is central to the durability of adhesive bonds [48]. The hybrid layer was first identified by Nakabayashi in 1982 and described as an interdiffusion zone formed at the molecular level between demineralized dentin and the polymerized adhesive system [48]. The stability of this hybrid layer is essential to the efficacy of bonding. Its failure is most commonly attributed to the presence of water and acidic components, which contribute to enzymatic and hydrolytic degradation over time [49]. In daily clinical practice, adhesive monomers often fail to completely encapsulate the collagen matrix, leaving collagen fibrils at the base of the hybrid layer partially or entirely unprotected (Fig. 3).

Fig. 3. Hybrid layer: *Magnification x 1000* **a/** and **c/** - c/-parallel dentin tubules orientation; and **b/** and **d/** - d/-perpendicular tubules orientation to the bonded surface [50].



This poorly infiltrated region is susceptible to nanoleakage, and is observed in both self-etch and total-etch systems - even in the absence of visibly demineralized zones [51, 52]. The infiltration of monomers into the water-filled collagen matrix is incomplete, allowing water to persist in or later penetrate the hybrid layer [51, 52]. Transmission electron microscopy with water-soluble markers has confirmed that parts of the hybrid layer are filled with water instead of adhesive [52]. Although initially minimal, these water-rich zones enlarge over time [52], indicating progressive water replacement of hybrid layer components. The absence of protective polymerized adhesive and the presence of water leave demineralized collagen fibrils vulnerable to hydrolytic degradation [53]. This degradation, combined with the breakdown of hydrophilic components within the adhesive system, results in loss of hybrid layer integrity and decreased bond strength over time [51]. The enzymatic mechanisms contributing to this process - particularly the roles of matrix metalloproteinases (*MMPs*) and cysteine cathepsins - have been extensively studied in recent years, with significant advancements in understanding their involvement in adhesive interface breakdown [53]. MMPs are a group of enzymes embedded within the mineralized dentinal matrix. Most MMPs are synthesized and secreted by odontoblasts in the form of proenzymes, requiring activation to degrade components of the extracellular matrix. Acidic conditioning of dentine surfaces activates dormant MMPs present in the dentinal matrix, which then become responsible for the degradation of collagen within the hybrid layer. These enzymes hydrolyze the organic matrix of demineralized dentine, leading to the deterioration of exposed collagen fibrils beneath the hybrid layer, thereby significantly compromising the bond strength at the adhesive–dentine interface [54,55]. Clinically, this may result in increased dentinal hypersensitivity, recurrent caries, marginal discoloration (Fig.4), reduced bond durability, and both reversible and irreversible pulpitis [56]. Several studies have aimed to develop inhibitory strategies targeting MMPs in order to enhance the functional stability of the adhesive–dentin interface [57,58]. Such MMP inhibitors can be incorporated into dental materials or applied topically within the cavity. The application of cross-linking agents prior to adhesive placement has been shown to improve hybrid layer stability [59]. Examples of MMP-inhibiting compounds include: tissue inhibitors of metalloproteinases (TIMPs), quaternary ammonium methacrylate's, collagen cross-linkers such as ethylenediaminetetraacetic acid (EDTA), galardin, chitosan, and riboflavin [60], protease inhibitors, chlorhexidine, benzalkonium chloride, tetracycline and chemically modified tetracyclines and adhesive systems containing MDP (10-Methacryloyloxydecyl dihydrogen phosphate) [61].

Adhesive systems such as Clearfil Protect Bond™ (*Clearfil SE Bond Kuraray Noritake Dental, Tokyo, Japan*) incorporate MDPB, which exhibits bactericidal activity through disruption of bacterial cell membranes. This mechanism inhibits biofilm formation and bacterial colonization at the tooth–restoration interface, thereby potentially enhancing restoration longevity. *In vitro* studies have demonstrated significant reductions in bacterial counts [62,63]. Even after polymerization, the antibacterial monomer MDPB does not leach out, stays immobilized through co-polymerization and continues to exert its antibacterial properties [64]. Nevertheless, despite these encouraging findings, further longitudinal clinical investigations are required to assess long-term efficacy and the potential role of such systems in preventing recurrent caries under clinical conditions. The incorporation of antimicrobial agents into adhesive systems not only improves their functional properties but also aligns with the growing emphasis on preventive strategies in contemporary dentistry.

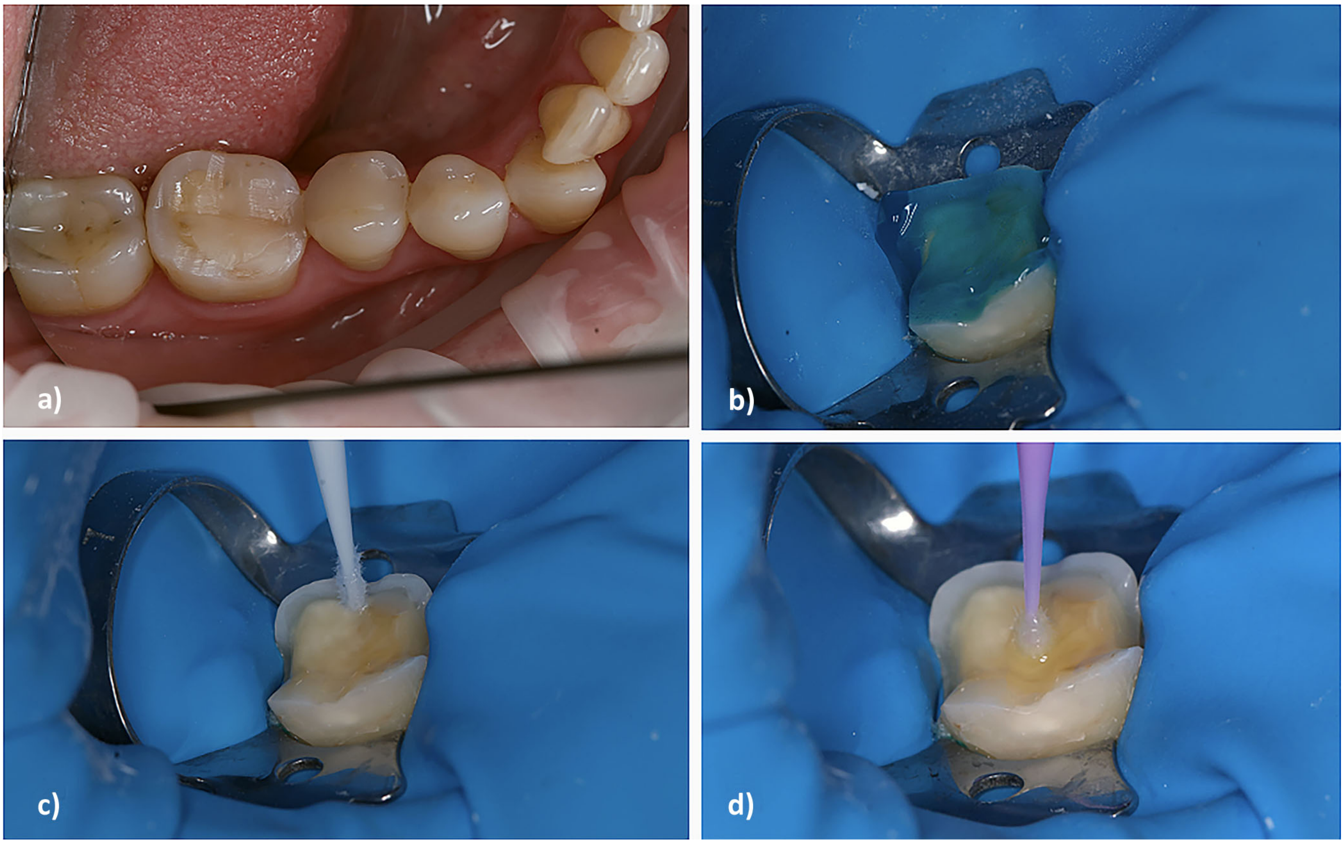
Fig. 4. a) Isthmus fracture and marginal discoloration around composite indirect restoration (#46); **b**) Marginal discoloration around ceramic restoration (#16).

Recent evidence supports that the application of 2% chlorhexidine for 30 seconds effectively deactivates MMP activity [53, 58]. Benzalkonium chloride binds strongly to demineralized dentine, and at concentrations of 0.5 - 1.0% or higher, it has been shown to inhibit MMP-2, MMP-8, and MMP-9 by 100% [65]. Hence, benzalkonium chloride is considered a promising addition to the growing class of quaternary ammonium compounds with dual inhibitory and antibacterial properties. Deactivation of MMPs can prevent the degradation of approximately 25 - 30% of the bonding interface [5].

The conventional approach to dentin bonding is often regarded as insufficiently stable, largely due to the structural heterogeneity of dentine, which impairs the formation of a consistent and durable adhesive seal. This instability is further compounded by the susceptibility of hydrophilic adhesive monomers to hydrolytic degradation, as well as the enzymatic activity of MMPs, which can break down exposed collagen fibrils. In recent decades, adhesive technologies have evolved substantially, with the development of novel dental adhesives and composite systems aimed at simplifying clinical protocols by reducing the number of application steps and components. The efficacy of an adhesive system is typically not dependent on a single compound but rather on the synergistic action of a well-optimized formulation incorporating multiple ingredients, each fulfilling distinct roles [53]. A key requirement for contemporary adhesives is the ability to establish a reliable and long-lasting bond to various dental substrates. To this end, continuous efforts are being made to refine the chemical composition and application techniques of adhesive materials. Innovations in this domain include the use of advanced monomers with enhanced hydrolytic stability, bioactive compounds, and alternative application strategies. Incorporating functional monomers that promote both micromechanical retention and chemical interaction with dental substrates has shown to significantly improve adhesive performance. Moreover, the integration of bioactive molecules into adhesive formulations is increasingly seen as a promising strategy to enhance mechanical resilience while suppressing enzymatic degradation of the tooth structure, thereby contributing to the longevity of the adhesive–dentine interface [66,67].

A fundamental aspect of the biomimetic approach to cavity preparation is the preservation and strategic utilization of structurally sound dentin, particularly in the periphery of the lesion. Establishing a peripheral sealing zone consisting of 2–3 mm of caries-free, mechanically sound dentine - without pulpal exposure - is essential for optimizing the substrate conditions for adhesive procedures. This circumferential zone serves as a biologically favorable interface that enhances the effectiveness of dentin hybridization and reinforces the mechanical stability of the adhesive restoration. The presence of sound dentin in this region facilitates reliable micromechanical retention and promotes durable chemical interactions between the adhesive system and the dental tissues. It also contributes to the reduction of marginal microleakage and improves resistance to bacterial penetration, thereby minimizing the risk of recurrent caries and pulpal irritation. From a biomimetic standpoint, this protocol aligns with the principle of restoring the tooth in a manner that emulates natural structure and function, supporting a sealed, stress-distributing interface that integrates predictably with the remaining tooth substrate. Furthermore, preservation of peripheral dentin integrity is critical in cases where additional restorative strategies such as Immediate Dentin Sealing (*IDS*) (Fig.5), Deep Margin Elevation (*DME*), or adhesive onlays placement are employed, as the quality of this marginal zone directly influences the long-term success of the restoration. As such, the deliberate creation and preservation of a caries-free peripheral sealing zone should be regarded as a core component of the biomimetic cavity design protocol.

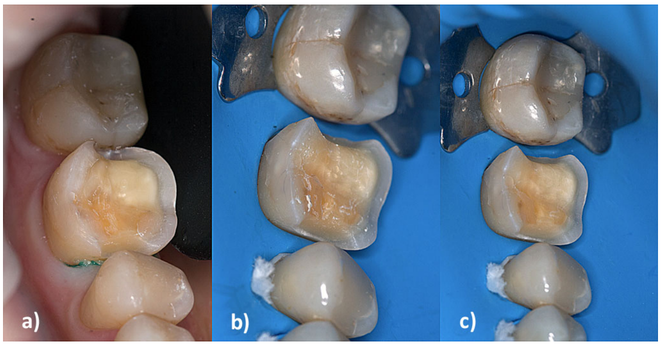
Fig. 5. a) Initial clinical situation; **b)** The application of etching gel for *IDS* after the biomimetic preparation of the tooth #46; **c, d)** Application of IV generation adhesive system Optibond FL (Kerr, Orange, USA) to realize IDS over the freshly cut dentin.



Surface preparation through air abrasion results in internal contours that are more rounded than those created with cylindrical burs, potentially improving restoration longevity by reducing stress concentrations that predispose to fracture. The use of aluminum oxide (*Al, Of*) particles during air abrasion has been found to significantly enhance the bond strength between dentin and composite materials (Fig. 6).

Findings from the scientific literature confirm that microabrasion using both 27 µm and 50 µm aluminum oxide particles led to a notable increase in the force required to de-bond the composite from the dentin surface, regardless of particle size. These results differ from other reports suggesting air abrasion has no significant effect on bond strength [11,68].

Fig. 6. **a)** Intraoral view of tooth #46 after the old filling removal and preparation for IDS; **b)** Isolation of tooth with Rubber dam, and **c)** The use of an air abrasion with Al, O*f* particles for better conditioning the dentin for hybrid layer formation.



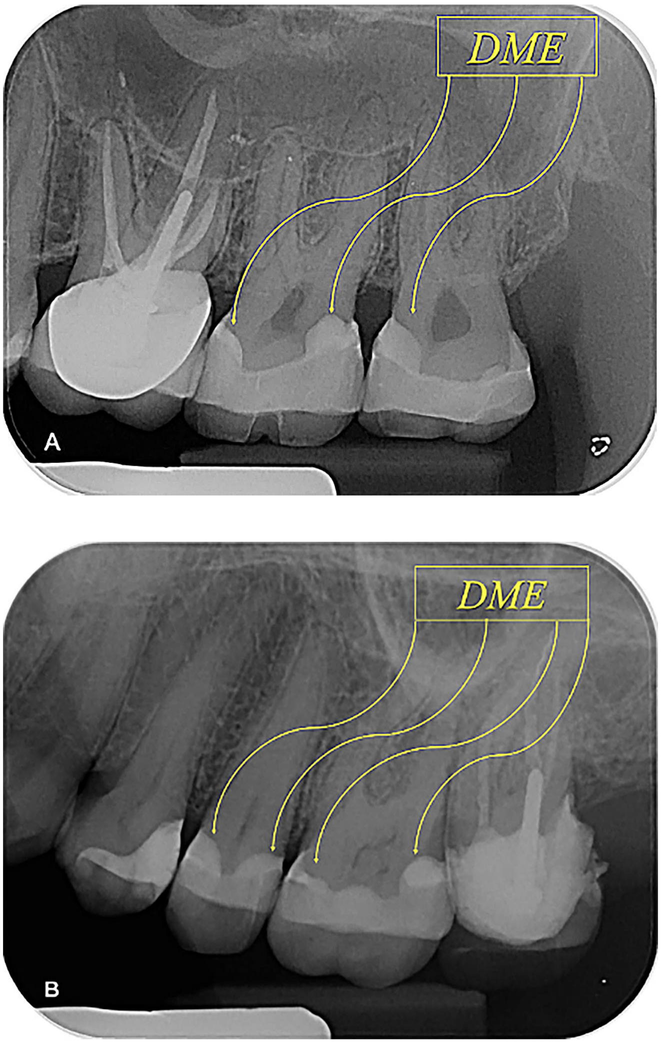
Beveling and optimizing the enamel margins to create an appropriate design of the interface phase contribute to improved marginal adaptation and bonding efficacy of both self-etch and total-etch systems in primary and permanent dentitions [69,70]. Freshly prepared dentine represents the streamlined substrate for bonding procedures [33]. However, conventional protocols for indirect aesthetic restorations can significantly compromise bond strength due to contamination from temporary materials. The immediate application of an adhesive system to freshly cut dentin, prior to impression taking, is referred to as Immediate Dentin Sealing (*IDS*) (Fig. 5). This approach is proposed as an alternative to Delayed Dentin Sealing (*DDS*), in which hybridization occurs immediately before the cementation of the indirect restoration. Applying multiple layers of adhesive contributes to the formation of a thicker adhesive film, which facilitates better stress distribution and results in superior bond strength and stability [48]. A critical aspect of the bonding process is the formation of the hybrid layer between the adhesive resin and demineralized dentine, which plays a vital role in the long-term retention of the restoration [4, 71].

Moreover, the hybrid layer formed during IDS has demonstrated enhanced stability, particularly when filled adhesives are used [1]. Filled adhesive systems applied in IDS have been reported to provide bond strengths comparable to or greater than those achieved with conventional IDS protocols. IDS also reduces the formation of microgaps between the dentin surface and the restoration, thereby limiting bacterial infiltration and reducing pulpal sensitivity following tooth preparation [72,73]. The application of a flowable composite as a reinforcing intermediate layer after IDS has been shown to enhance microtensile bond strength across various adhesive systems, with reported improvements ranging from 23.3% (*Scotch Bond MP, 3M ESPE, St. Paul, MN, USA*) to 56.0% (*Clearfil SE Bond Kuraray Noritake Dental, Tokyo, Japan*) [74,75]. The elastic modulus of these materials (*approximately 12 GPa*) is comparable to that of coronal dentin. A thin layer of flowable composite ensures complete polymerization of the adhesive system, even under conditions of dentinal fluid transudation, which may otherwise result in an overly thin, incompletely cured adhesive layer. Once the adhesive interface is covered with composite and light-cured, the effects of oxygen inhibition and transudation are halted [5]. This step also establishes a ‘secure bond’, meaning that even in the event of restoration de-bonding, the flowable composite layer remains bonded to the sealed dentin [40]. This is particularly important for simplified adhesive systems, helping to protect the hybrid layer against oxygen inhibition and preserving the integrity of the IDS coating [76]. The final adhesive layer may range from 60 to 80 ìm on smooth convex surfaces to 200–300 ìm on concavities, depending on surface geometry, helping to eliminate undercuts and producing a smooth preparation surface. Bond strength to dentin continues to develop over time, possibly due to the completion of co-polymerization reactions involving various monomers [33]. Notably, IDS allows for stress-free dentin bonding, as cementation is delayed, and occlusal loading is postponed-conditions typical of indirect restorations - thereby improving marginal adaptation. This technique also enhances adhesion in situations involving short clinical crowns or highly divergent cavity walls. Following final polymerization of the adhesive during IDS, an oxygen-inhibited layer remains on the surface, typically 4–40 ìm thick. This layer can interfere with the polymerization of vinyl polysiloxane impression materials [77]. Its thickness may be reduced by applying glycerine gel to the sealed surface (“*air blocking*”) followed by an additional 10-second light-curing cycle, a step often recommended in IDS protocols [33,78].

A thinner oxygen-inhibited layer will result in a correspondingly thinner layer of unpolymerized impression material, which is unlikely to affect the fit of restorations, as conventional or digital workflows anticipate cement space. Various methods have been proposed to manage this challenge. For example, Magne and Nilsen suggest pumicing the sealed surface, although this may risk compromising impression accuracy [78], while others recommend wiping with 70% ethanol. As these strategies may only reduce, but not eliminate, the oxygen-inhibited layer, thorough cleaning of the sealed surface with a fine-grit diamond bur at low speed or air abrasion immediately before cementation is generally advised [33,78]. Further research and clinical trials are warranted to better understand the clinical implications and effectiveness of IDS in the long-term success of indirect restorations and dentine bonding.

Deep Margin Elevation (*DME*), also referred to as coronal margin relocation, is a clinical strategy used to reposition subgingival margins to a supragingival level by applying restorative material (Fig.7).

Fig. 7. Control radiographs after the cementation of ceramic restorations. The DME with composite material of the mesial and distal proximal part of the teeth has been created before an impression (*yellow arrows*): **A/** The DME on teeth #26 and 27; **B/** The DME on teeth #25 and 26.



This facilitates improved marginal integrity and enhances bond strength [79]. When executed properly, DME may help reduce bacterial colonization and the incidence of secondary caries, while also supporting periodontal health [75]. The natural gingival attachment to the base of deep lesions is compromised in such cases, and DME does not re-establish it, but instead creates a new interface composed of an extended junctional epithelium alongside the restorative material and a shortened connective tissue attachment along the underlying dentine. Elevating the margin to a supragingival level is necessary to achieve biomimetic tensile strength exceeding 30 MPa. This repositioning of the apically located margin, when performed in conjunction with IDS and the application of adhesive and composite to serve as a "*dentine substitute*", is termed the "*bio-base*" [79]. The "*bio-base*", as defined by the Academy of Biomimetic Dentistry, refers to a stress-reducing foundation upon which the indirect restoration is adhesively cemented.

Recent findings suggest that the composite material used to elevate the subgingival margin does not adversely affect the long-term performance of the bonded restoration [13, 15, 80]. Similar to natural tooth structure, adhesively restored occlusal surfaces are capable of withstanding, and in some cases exceeding, normal functional loads [17]. As a result, biomimetically restored teeth demonstrate reduced gap formation beneath the restoration and decreased dentinal crack propagation due to stress concentration, contributing to diminished postoperative sensitivity and preservation of pulpal vitality [5].

CONCLUSION

A significant limitation in adhesive dentistry remains the long-term deterioration of resin–dentin interfaces, primarily resulting from the ageing of adhesive systems. In response, various experimental strategies have been proposed to enhance the durability of dentin bonding, though with differing degrees of effectiveness. These approaches often focus on increasing the resistance of the dentinal collagen matrix to enzymatic degradation, either through direct inhibition of collagenolytic enzymes or by reinforcing the matrix against their activity. Emerging technologies, particularly in the field of nanotechnology, have enabled the development of novel materials and the refinement of existing adhesive systems. Potential advancements encompass the inhibition of matrix metalloproteinases, enhancement of collagen stability, incorporation of antimicrobial features, and the stimulation of regenerative processes within the dental hard tissues. Equally important are the strategies for strengthening the dentin tissue, which is a hierarchically organized biological composite. We could speculate that, in the near future, technological innovations aimed at mitigating collagenolytic hydrolysis and establishing more stable resin–dentin bonds are expected to become increasingly accessible and clinically relevant in all types of preparation designs.

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