

***In Vitro* Performance of Class I and II Composite Restorations: A Literature review on Nondestructive Laboratory Trials—Part II**

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Clinical Relevance

In vitro research remains of primary importance to selecting and validating the techniques and products to be used *in vivo*. However, the clinical predictive value of such tests needs to be appraised and ranked to provide meaningful help toward the clinical decision-making process.

ABSTRACT

A literature review was conducted on adhesive Class I and II restorations and nondestructive *in vitro* tests using the PubMed/Medline database for the 1995-2010 period. The first part of

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this review has presented and critically appraised selected literature dealing with the quality and *in vitro* behavior of adhesive Class II restorations using photoelasticity, finite element analysis, and microleakage study protocols. This second part reviews additional parameters, which are deformation and fracture resistance to cyclic loading, shrinkage stress and tooth deformation following restoration placement, bond strength (microtensile, tensile, and shear tests), and marginal and internal adaptation. In addition, a “relevance score” has been proposed that aims to classify the different study protocols according, firstly, to the resulting quality, quantity, and consistency of the evidence and then, secondly, to their potential clinical relevance, as estimated by their ability to simulate oral and biomechanical strains. The highest clinical relevance was attributed to marginal and internal adaptation studies, following cyclic

loading in a moist environment. However, a combination of *in vitro* protocols will have an even greater predictive potential and has to be considered as a crucial preclinical research approach with which to investigate the numerous restorative configurations that cannot be efficiently and rapidly tested *in vivo*.

INTRODUCTION

Posterior adhesive restorations, as a substitute for metal-based restorations, have become the “standard of care” in an increasing number of dental offices and clinics.¹⁻³ However, the abundant number of available restorative options implies a limited standardization of these techniques, and this may lead to the possible application of improper clinical protocols. The time and effort demanded by *in vivo* trials does not permit all adhesive systems, base liners, and restorative products/techniques to be evaluated in prospective clinical studies and over a sufficient period of time. Therefore, the need for and the advantages of preclinical *in vitro* trials is undeniable. Unfortunately, the many laboratory evaluation protocols and their variability and complexity, coupled with an already-intricate study field, means that there is a clear need to organize *in vitro* research on Class II adhesive restorations. Furthermore, this organization should be based on the ability of the research protocol to reproduce the most important oral strains, to evaluate and tentatively appraise the potential clinical relevance, and to follow a thinking process successfully applied in clinical biomedical science.⁴⁻¹²

Part one of this review selected literature dealing with the quality and *in vitro* behavior of adhesive Class II restorations using photoelasticity, finite element analysis (FEM), and microleakage study protocols. Photoelasticity demonstrated that higher stresses could be observed in large cavities and those restored using a light-curing material compared to a chemically curing one.¹³⁻¹⁵ However, photoelasticity did show atypical results when comparing layering and bulk-filling techniques.^{16,17} Unfortunately, this method carries several conceptual and methodological limitations and therefore is characterized by improper quality and consistency of the evidence. It has been advantageously replaced by FEM.

The crucial role of the FEM protocol was validated by comparing stress levels in similar restorative configurations using natural teeth and strain gauges.^{18,19} This method then confirmed the influence of cavity design and dimensions,²⁰⁻²³ layering techniques,^{24,25} and the physical characteristics of the

materials, such as stiffness,²⁶⁻³³ with a good consistency of the evidence. Despite the fact that FEM neither emulates the effect of moisture nor that of cyclic masticatory function (fatigue), the recent three-dimensional modeling approach shows a good quality of the evidence for stress distribution within the tooth-restoration as a whole.

The use of the microleakage protocol only allowed a few hypotheses to be confirmed with a good consistency of results. Only cavity and margin design,^{34,35} light-curing type,^{36,37} and composite structure and technology³⁸⁻⁴¹ had an influence on microleakage. However, there are a lot of studies utilizing this protocol, possibly because of its simplicity. When more of these studies were reviewed, the conclusions proved highly inconsistent. This strongly indicates that further use of the microleakage protocol should be limited as a result of the overall poor quality and consistency of the evidence associated with this protocol.

The second part of this review will cover the remaining nondestructive *in vitro* protocols, which are 1) deformation resistance and fracture resistance to cyclic loading, 2) shrinkage stress and related tooth deformation, 3) bond strength (microtensile, tensile, and shear tests), and 4) marginal and internal adaptation. In addition, a “relevance score” will be proposed based on the aforementioned criteria (quality, quantity, and consistency of the evidence), taking into consideration the ability of the protocol to simulate oral biomechanical strains.

MATERIALS AND METHODS

The search strategy, detailed in Part I of this review, included an appraisal of the PubMed/Medline database using the following primary key words: *in vitro*, Class II, posterior composites, inlays and onlays, tooth colored, and composite. For this second part, additional key words related to study hypothesis, such as cavity configuration, polymerization, or light-curing, or to study methodology, such as resistance to fracture and deformation, shrinkage stress, tooth deformation, bond strength and microtensile bond strength, and marginal and internal adaptation, were used to identify all existing references. The search was conducted with the limit “Dental Journal” and from 1995 to 2010. Perusal of the references of relevant articles allowed completion of the review (references of the references). A few older “major” references were cited, when appropriate. Articles were first classified according to the experimental protocol, each one corresponding to a specific review table, and were then subclassi-

fied according to the parameters/hypothesis investigated. For microleakage, bond strength, and marginal adaptation protocol, the type of restoration (direct and indirect) was also considered, and then the references were analyzed according to the subparameters previously described in part one of this review). The overall strength of evidence was appraised according to the three factors of quality, quantity, and consistency. Whenever possible and appropriate, the approach applied was the same as introduced in 1994 by Gyorkos and Abrahamowicz.⁷ This process is now well established and largely used to develop practice guidelines and other health-related policy advice.⁸⁻¹²

References related exclusively to indirect ceramic and CAD-CAM/Cerec® restorations (Sirona, Bensheim, Germany) or restoration fit, as well as those dealing with restoration of deciduous teeth, were excluded from this review. In addition, wear tests and studies measuring restoration fracture resistance to monotonic stress/loading (in general, all kinds of destructive tests) were not taken into consideration for this literature review.

I. Deformation and Resistance to Cyclic Loading

The studies that were reviewed are presented in Table 1. When comparing the deformation of intact and restored teeth using composite or ceramic in MOD cavities, the mean tooth compliance (relative deformation) after preparation was about 2.0, and mean tooth compliance was back to 1.1 in composite and 1.0 in the ceramic group. This demonstrated the ability of both restorative materials to reinstall tooth resistance under a load of 11.17 Kg.⁴² However, after cyclic loading, more samples fractured in the composite group than in the ceramic group, although this was not significant in terms of mean cycles to failure.

The resistance to fracture following cyclic loading and increasing force (200 to 1000 N) for composite MOD onlays (buccal cusp replacement) with or without additional palatal partial coverage demonstrated an increasing resistance to fracture with full occlusal coverage. However, at the same time, more dramatic failure patterns were observed.⁴³ Therefore, clinical recommendations could not be drawn, as lowering the remaining cusp could eventually lead to untreatable failures. The aforementioned results were submitted to additional FEM analysis, and this substantiated the superior resistance to fracture of the overlay configuration and also provided a more detailed picture of the various

Table 1: *Selected references for deformation and resistance to cyclic loading*

Shor and others, 2003 ⁴²
Fennis and others, 2004 ⁴³
Fennis and others, 2005 ²¹
Kuijs and others, 2006 ⁴⁴
Magne and Oganessian 2009a ⁴⁵
Magne and Knezevic, 2009a ⁴⁶
Magne and Oganessian 2009b ⁴⁷
Magne and Knezevic, 2009b ⁴⁸
Magne and Knezevic 2009c ⁴⁹

stresses (tensile, shear, and compressive) that account for adhesive interface or restoration failure.²¹ It was also concluded that adhesive failures are more likely to occur with a high E-modulus composite and that lowering the E-modulus might trigger cohesive restoration fractures. Another study⁴⁴ from the same authors included ceramic overlays, which were compared to direct and indirect composite restorations. In this study, no significant difference was observed with regard to overall fatigue resistance among the three restorative options, while a combination of adhesive and cohesive failures was predominantly observed in the indirect groups.⁴⁴ These latter results might be attributed to a lower mechanical resistance of the adhesive interface and cement layer underneath indirect restorations and, in particular, to the lower stiffness of the cement, compared to a highly filled composite (82 vol% and 92 wt%) or ceramic restoration. The aforementioned studies thus concluded that in a vital tooth configuration, with cyclic loading ranging from normal function (200 N) to parafunctional forces (1000 N), the choice of material might not be a crucial factor for overall mechanical resistance and clinical success. However, it must be pointed out that the tested composites (direct and indirect) were conventional, highly filled hybrids, with high E-modulus (19.6 GPa and 23.0 GPa), and these are markedly higher than the current nano-hybrid materials with moduli around 10 GPa or lower.

Magne and coworkers⁴⁵⁻⁴⁸ interestingly applied a similar protocol to a nonvital tooth configuration with forces ranging from 200 N to 1000 or 1400 N. In their first article, the influence of restoration thickness (1.5 to 3.5 mm) using a composite system developed for CAD-CAM technology (Paradigm MZ100®, 3M, St Paul, MN, USA) was tested. They observed that increasing the thickness of the restoration improved the resistance to fatigue and

also reduced the occurrence of subgingival fractures. This demonstrated the protective effect of thick composite overlays made of high mechanical strength and E-modulus composite.⁴⁶ When comparing 3-mm-thick ceramic (Vita MKII CEREC, VITA Zahnfabrik, Bad Säckingen, Germany) and composite (Paradigm MZ100) overlays, the fatigue resistance of the composite material was significantly superior, and the efficiency of immediate dentin sealing (to establish adhesion prior to impression) was also effective, as demonstrated by an absence of adhesive failures.⁴⁹ The same protocol was repeated with a restorative nano-hybrid composite, and these composite overlays showed a better resistance to fatigue than did the ceramic restorations.⁴⁸ When comparing both composites, Paradigm MZ100 exhibited a higher survival rate (73%) compared to the nano-hybrid brand (50%), even though this was not statistically significant. In the same test, none of the ceramic restorations survived the last test phase at 1400 N. Moreover, ceramic restorations showed a much higher proportion of subgingival, nonrepairable fractures.^{46,48,49} These two series of studies dealing with either a vital or nonvital tooth configuration evaluated the behavior of restorations under physiological and nonphysiological parafunctional forces. The protocol included a FEM to tentatively explain the findings with a natural substrate. In the vital tooth configuration, the choice of material appeared less influential than the restoration configuration with regard to fracture resistance and failure pattern. Conversely, in a nonvital tooth situation, the choice of material and the restoration thickness markedly influenced the stress distribution, fracture resistance, and fracture pattern.

Conclusion: Deformation and Resistance to Fatigue Loading—The aforementioned findings might have a crucial impact on our understanding of restoration reaction and resistance to cyclic forces. Specifically, the potential impact of the material's physical characteristics (ie, E-modulus and flexural strength) on medium- and long-term restoration behavior might largely depend on the extent of the preparation and the intrinsic capacity of the remaining tooth structure to resist functional stresses. In a vital tooth, it can be logically assumed that the restoration plays a less important protective role than it does in a nonvital configuration. In addition, a less rigid (significantly less than dentin; ie, nano-hybrid composite) or stiff and brittle material (ie, feldspathic porcelain) would likely increase the risk of restoration/tooth failure when treating fragile teeth (nonvital) in high stress-bearing areas. The quality and consistency of the evidence here are satisfactory.

However, the quantity of the evidence is rather limited, although such criteria seem less crucial as a result of the protocol applied (same tooth/teeth used for testing different cavity configurations or FEM stress simulation).

Only nondestructive tests or those involving cyclic loading were taken into consideration for this review because of the fact that mere resistance to fracture ("classical" fracture-resistance protocol) mimics the reaction of the system to extreme monotonic, linearly increasing stresses, and these are considered as poorly relevant as simulations for *in vivo* failures. Such tests neither reproduce accidental fracture (totally different stress kinetics) nor simulate other restoration failure patterns such as marginal leakage, tissue demineralization, pulpal complication, or fractures triggered by repeated stresses (fatigue). Likewise, the fracture patterns observed in such tests (which include axial or severe cusp and restoration fractures of vital tooth configurations) are practically nonexistent *in vivo*, with the exception of rather rare traumatic tooth fractures.⁵⁰ One can therefore assume that the quality of evidence would be insufficient, and this justifies the exclusion of such research in the present review.

II. Deformation of Teeth and Shrinkage Stress During and After Restoration Placement

The studies that were reviewed are presented in Table 2.

Layering Techniques—When comparing different composite filling techniques (bulk, bulk + re-restoration and incremental) to amalgam restoration in Class II MOD cavities of different widths (1, 2.5, and 5 mm), more deformation resulted from adhesive techniques, with the highest deformation being measured in 5-mm bulk composite restorations.⁵¹ The concept of re-restoring a tooth involves the placement of a bulk-fill composite restoration that is fully polymerized, and then a new slot is subsequently cut into the composite after polymerization. This slot is subsequently restored with more composite, and this technique has been proposed as a means to dissipate stress in the final restored tooth. In this study, it was observed that re-restoration did reduce stress compared to initial values.

In Class I cavities, tooth deformation proved to be minimal in comparison to Class II MO (medium or large) or MOD cavities. The size and cavity design or configuration factor proved to be influential factors for tooth deformation⁵² and also for stress development. This occurred in an inverse relationship at the

Table 2: Selected references for deformation of teeth and stress during and after restoration placement
Layering techniques
Versluis and others, 2004 ¹⁹
Shor and others 2003 ⁴²
Kamel and others 1995 ⁵¹
Tantbijorin and others 2004 ⁵²
Gonzalez Lopez and others 2007 ⁵³
Park and others 2008 ⁵⁴
Curing protocols
Versluis and others, 2004 ¹⁹
Fleming and others 2007 ³⁷
Comparaison of materials and brands:
Fleming and others 2007 ³⁷
Palin and others 2005 ⁴¹
Fleming and others 2007 ⁵⁵
Bouillaguet and others 2006 ⁵⁶
Fleming and others 2007 ⁵⁷

restorative interface, as measured directly on teeth and by FEM study.¹⁹ More recent studies have confirmed the increased deformation observed in Class II MOD restorations when compared to two-surface MO design⁵³ as well as the reduction of tooth deformation that is observed with layering techniques.⁵⁴ However, in this later study, no significant difference was observed between the horizontal and oblique layering techniques.

The deformation of intact and restored teeth using composite or ceramic in MOD cavities was also reviewed. The studies showed a mean tooth “compliance” of 2.0 (relative deformation) following preparation, and then the “compliance” reverted to 1.1 in the composite group and 1.0 in the ceramic group. This demonstrated the ability of both restorative materials to return the tooth’s resistance to flexure under a load of 11.17 Kg.⁴²

Curing Protocols—Versluis and coworkers¹⁹ studied the effect of the curing protocol by using various combinations of light intensity and exposure time (but corresponding to similar curing energy) and observed large variations in shrinkage strain, as measured by both FEM and experimental methods. Their results actually revealed the positive impact of extending curing time with a reduced light intensity.¹⁹ Various curing light units and polymerization protocols were compared with regard to cuspal deflection of MOD restorations made of various materials (resin composites and an ormocer). The curing light type proved influential (LED induced less deformation), as did the restorative materials. The curing protocol of using a

halogen curing unit (standard vs soft-start) had no influence on cuspal deformation³⁷; however, microleakage was observed to be inversely proportional to cuspal deformation, even though the authors could not explain the possible link between lower deformation and higher leakage.

Comparison of Materials and Brands—The influence of the composition of the matrix resin was also evaluated to assess cuspal flexure following the placement of each composite layer as well as after treatment completion. It was shown that the classical bisphenol A diglycidyl ether dimethacrylate and triethylene glycol dimethacrylate (TEGMA) resin blend augmented cuspal flexure compared to ethoxylated bisphenol A glycol dimethacrylate (Bis-EMA) and urethane dimethacrylate (UDMA) compositions.⁵⁵ However, the authors did not comment on the material E-modulus, which largely differed among the tested materials and which is also likely to have influenced tooth deformation.

Electronic speckle pattern interferometry (ESPI) proved to be a viable method with which to monitor tooth dimensional changes during composite placement as the device doesn’t contact the tooth.⁵⁶ The same authors also measured the influence of various composite systems on cuspal deflection following a single increment placement in 2 × 2.5 × 11-mm MOD cavities. The least amount of deformation was recorded with the experimental silorane system, while the flowable composite did not induce more deformation than a conventional hybrid. Among the nano-hybrid materials, variable, cumulative cusp displacement was also recorded, though it was significantly less than that associated with the conventional hybrid. The stiffness of the material proved once again to influence the reaction to composite polymerization shrinkage.

Fleming and coworkers^{55,57} compared previous data obtained with a halogen light-curing unit (LCU) to new data generated with LED technology. Despite large numerical differences in favor of the ormocer material compared to the Z100 system, no statistical significance was revealed between both of these light-curing technologies.³⁷ The same authors investigated the cuspal deformation of experimental oxirane and silorane materials and compared it to that of monomodal composite systems (Z100 and Z250, 3M).⁴¹ They observed a significant reduction in cuspal deflection with the oxirane and then the silorane but with, respectively, an increase or no difference in microleakage values. The authors then put the relative “impact” of cuspal deformation on cavity seal into perspective.

Conclusion: Tooth Deformation and Shrinkage Stress—The cavity size and design (configuration factor) as well as material physico-chemical composition (filler and matrix and consequently the material's stiffness) proved to influence tooth deformation and stress development within the tooth structure or the restorative interface. When considering the design of the studies under review, the quality of the evidence has to be considered to be high, with good consistency. The light curing type (LED vs halogen) only proved to influence cuspal deformation (less deformation for LED curing) in some studies but had no influence on microleakage. The curing mode (soft-start vs conventional curing mode with halogen LCU) had no influence on either of these parameters. Therefore, the ability of a hypothetically "improved" curing approach, such as soft-start curing, appeared to be ineffective in reducing tooth deformation, while an extended curing time with continuous, lower irradiance did demonstrate reduced tooth deformation, even though it was tested in a different experimental setup. With regard to these hypotheses about curing modality, the quantity and consistency of the evidence were rather limited.

Conclusion: Tooth Deformation and Shrinkage Stress Methodology—The tooth deformation observed following the placement and polymerization of various composite materials and curing protocols validates the results obtained by FEM studies. Therefore, when measurements produced on natural teeth are compared to FEM, it confers on these tests a high quality of evidence. The ESPI approach without direct interference with the restored tooth appears to be a promising alternative to conventional strain gauges.

III. Microtensile and Shear Tests

The adhesion studies that were reviewed are presented in Table 3.

Comparison of Restorative and Layering Techniques—Several studies compared the influence of layering vs bulk-fill approaches on dentin bond-strength (BS). They all concluded that a bulk-fill technique did lead to lower bond strength compared to restorations placed incrementally.⁵⁸⁻⁶¹ The results regarding the influence of different layering approaches proved rather controversial, with some studies⁵⁹ showing higher bond strength values for the horizontal technique, while two other studies^{58,60} concluded that there was no difference between horizontal and oblique or vertical layering techniques. When combining three to four horizontal and

oblique layers in different geometries, the highest microtensile bond strength (MTBS) values were observed with the four increments. All other combinations of three horizontal and oblique layers exhibited similar MTBS values, and all were lower than that observed for four increments.⁶²

Other Restorative Variables (Cervical Margin Position, Cavity Dimensions, and C-Factor)—Cavity depth proved influential for bond strength, with lower values in deep dentin and the highest values observed on a flat preparation with low C-factor (CF=1). When a higher C-factor (CF=3) was used, all values fell, which demonstrated the impact of restricted free-surface and composite flow.⁶³ Consequently, the C-factor, and therefore bond strength, also proved to influence failure modes at the adhesive interface.⁶³ The cavity size was also shown to be an influential factor for dentin adhesion, and with an appropriate layering technique the negative impact of larger cavity dimensions could be counteracted.⁶¹ When attempts were made to evaluate the impact of preparation wall location (gingival, pulpal, and axial) on MTBS, no trend was found. The results actually demonstrated that adhesion was influenced by the adhesive system rather than by the preparation surface or location.⁶⁴

Sandwich Techniques—In one study,⁵⁸ the presence of a flowable resin composite (FRC) liner did not improve MTBS in Class II cavities restored incrementally using either a horizontal or oblique layering technique. In another study,⁶⁵ the differences in MTBS were specific to the product rather than influenced by the presence of a flowable composite liner underneath bulk or incrementally filled restorations. It was observed that a lining of FRC improved adhesion when vertical or oblique layering techniques were applied but had no apparent effect underneath horizontal increments. Once again, these findings were product specific.⁵⁹ Other authors concluded again that the use of a FRC liner alone did not improve MTBS underneath bulk-filled restorations with a high C-factor, while the presence of fibers or a combination of FRC together with fibers did increase MTBS.⁶⁶ Incorporation of glass fibers also showed stable BS values regardless of the C-factor.⁶⁶

Polymerization Protocol—Incremental techniques provided better MTBS than did bulk filling for the two different irradiation modes tested (continuous and stepped). MTBS values on flat dentin specimens were also higher than in a Class I cavity configuration, with the exception of the combination of incremental technique and stepped curing mode.⁶⁰

Table 3: <i>Selected References for Microtensile and Shear Bond Strength</i>
Comparison of restorative and layering techniques
Figueiredo Reis and others, 2003 ⁵⁸
Nikolaenko and others, 2004 ⁵⁹
dos Santos and others, 2004 ⁶⁰
He and others, 2007 ⁶¹
Niu and others, 2009 ⁶²
Other restorative variables (Cervical margin position, cavity dimensions, and C-factor)
Hez and others, 2007 ⁶¹
Yoshikawa and others, 1999 ⁶³
Cavalcanti and others, 2010 ⁶⁴
Sandwich techniques
Figueiredo Reis and others, 2003 ⁵⁸
Nikolaenko and others, 2004 ⁵⁹
Cavalcanti and others, 2008 ⁶⁵
Belli and others, 2006 ⁶⁶
Polymerization protocol
dos Santos and others, 2004 ⁶⁰
D'Alpino and others, 2006 ⁶⁷
Ilie and others, 2006 ⁷¹
Comparison of materials
Cavalcanti and others, 2008 ⁶⁵
Nikaido and others, 2002 ⁶⁸
Purk and others, 2004 ⁶⁹
Purk and others, 2006 ⁷⁰
Ilie and others, 2006 ⁷¹
Indirect restorations
Coelho Santos and others, 2005 ⁷²
Paul and Schaerer 1997 ⁷³
Magne and others, 2005 ⁷⁴
Frankenberger and others, 2007 ⁷⁵
Comparison of direct and indirect techniques
Aggarwal and others, 2008 ⁷⁶
Frankenberger and others, 1999 ⁷⁷
de Andrade and others, 2007 ⁷⁸
Purk and others, 2004 ⁷⁹

Different combinations of light sources (plasma, halogen and LED) were used to cure the dentin bonding agent (DBA) and composite in Class I cavities, and this revealed the significant influence of irradiation conditions. Overall, bond strength was more dependent on the light source used for curing the DBA rather than that used for curing the composite. In this study, the LED curing of the DBA together with halogen curing of the restorative composite produced the lowest MTBS values.⁶⁷

Comparison of Materials—Two adhesive systems (self-etch one and two step) were tested after

mechanical and thermal fatigue. The one-step system presented lower MTBS values and more than 50% of sample debonding during the testing, which was presumably due to an overwet phenomenon. In this study,⁶⁸ the short period of mechanical loading (50,000 cycles) did not influence the results. In an attempt to evaluate the impact of contact time of the primer on the tooth substrate, additional priming times of 30, 60, and 120 seconds were added after normal application duration, but these did not influence MTBS, as measured on the gingival wall of Class II cavities.⁶⁹ In another study⁷⁰ from the same authors, it was concluded that MTBS values were not influenced by location (pulpal or gingival wall) for the various adhesives tested. However, the three-step total-etch, water-based adhesive and the two-step acetone-based prime and bond systems produced lower values than the two-step water-based self-etch and two-step total-etch ethanol-based systems.⁷⁰

Several composite types and brands were tested for polymerization shrinkage and their interface quality, microhardness profile, flexural strength, and elasticity-modulus following a bulk application in a Class I configuration. It was found that MTBS was correlated to elasticity modulus and the velocity of contraction stress development within restrictive cavity configuration.⁷¹ Therefore, one cannot predict that a high MTBS will be based only on a low E-modulus since the polymerization kinetics play an important role in the development of interfacial stresses and adhesion.⁷¹

Indirect Restorations—Various adhesives (one-step, two-step, and three-step systems) were compared following two modes (pre-cured or non-pre-cured) before the placement of indirect composite inlays. The effect of pre-curing appeared to be material and location specific, and the thickness of the adhesive layer appeared to be increased in the case of pre-curing.⁷² However, the relevance of the aforementioned results in relation to pre-curing the adhesive system for the cementation of indirect restorations would seem to be dubious since the concept of “dual bonding”⁷³ was not fully implemented in this study (adhesive layer thinned and light-cured just prior to adhesive cementation). This latter concept is also supported by more recent results^{65,74} obtained on flat dentin or overlay-like preparations demonstrating that light-activation of the adhesive layer before indirect cementation, renamed “immediate dentin sealing,” is crucial to obtaining high MTBS.

The presence of temporary cement used for the interim restoration reduced MTBS values in Class I

inlays, and to overcome this effect, cleaning of the cavity or immediate dentin sealing was needed.⁷⁵ The removal of cement excesses with a scaler or air polishing with a soft glass were effective treatments, while another air-polishing paste with round particles was unable to restore good MTBS values.⁷⁵

Comparison of Direct and Indirect Techniques—The effect of cyclic loading was evaluated on direct and indirect Class II composite restorations. It was shown⁷⁶ that next to marginal adaptation, MTBS values were superior in the indirect group. When evaluating the influence of different generations of adhesives (third self-etch, fourth total etch, and fifth one bottle) in combination with direct composite and indirect ceramic restorations, the former multistep adhesive generations produced higher bond strengths, while the pre-curing of the adhesive before cementation of indirect restorations also increased the bond strength.⁷⁷ In a similar study configuration,⁷⁸ with simplified cavity design, the dual bonding concept once again noticeably increased the bond strength at buccal walls while reducing MTBS at pulpal walls. When interposing a layer of low-viscosity resin composite, the bond strength measurements were significantly lowered as a result of cohesive fractures in the low-filled liner. Interestingly, a comparison⁷⁹ between *in vivo* and *in vitro* MTBS bond strength on axial and gingival walls demonstrated lower values *in vivo*, which were particularly pronounced at the gingival walls, most likely as a result of higher substrate wetness.

Conclusion: Microtensile and Shear Tests—Within the limitations of this study protocol, the most relevant conclusions, based on a satisfactory quantity and consistency of the evidence, are that

- higher bond strengths were obtained with layering techniques (vs bulk);
- for indirect restorations, “dual bonding” or “immediate dentin sealing,” as opposed to an application and curing of the DBA just before placing the restoration, increased bond strength; and
- the cavity C-factor is an influential factor for bond strength (high CF reduces MTBS).

All other study variables, including curing protocols, cavity depth, the presence of flowable composite liner, light source, and various adhesive systems, did not have a clear impact on MTBS, and, therefore, no recommendations can be drawn as a result of the limited evidence related to quantity and consistency.

Conclusion: Microtensile and Shear Test Methodology—Bond strength and, in particular, microtensile

bond strength tests measure the capacity of an adhesive interface to resist stresses induced by polymerization and occlusal function. They actually represent the first attempt to evaluate the potential of a specific restorative system or technique to establish the biomechanical balance needed to maintain sealed margins and reinforce the remaining tooth structure. Such features are crucial in Class I and II adhesive restorations in order to obtain satisfactory medium- and long-term clinical behavior. When combined with mechanical and thermal stressing (oral environment simulation), MTBS tests most likely increase their potential clinical relevance and adequately complement marginal adaptation studies. MTBS also have the potential to measure regional variations of bond strength, something that was not possible with conventional tensile or shear bond strength tests. However, this latter potential ability requires more investigation. The MTBS methodology does potentially suffer from tissue inhomogeneity, but on the other hand, it provides a precise, quantitative evaluation method, which confers an acceptable quality of evidence.

IV. Marginal Adaptation

The marginal adaptation studies that were reviewed are presented in Table 4.

Comparison of Restorative and Layering Techniques—In the absence of mechanical loading, two studies^{80,81} did not find any significant difference in marginal adaptation between bulk-fill and layering techniques, while a third report⁸² presented opposing findings of significantly more cervical defects in the bulk-fill technique group. In proximal microcavities, more sophisticated filling techniques, such as the three-site layering concept and ceramic inserts, did not show any advantage over a simple two-layer technique using either a restorative or flowable composite.⁸³ Accordingly, “overengineering” the restorative technique appeared useless for small volumes.

In an attempt to evaluate the benefit of additional retentions in small box preparations simulating restoration repair, the smallest box-only composite additions (without undercuts or occlusal retentions) provided the best resistance to cyclic loading.⁸⁴

Other Restorative Variables (Cervical Margin Position, Cavity Dimensions, Matrix Systems, etc)—The beveling of margins proved beneficial to marginal adaptation,^{83,85,86} but mainly when enough tissue remained above the cemento-enamel junction.^{87,88} When less than 1 mm of enamel height remained,

the bevel no longer had a positive influence, and in such situations, an indirect technique provided better adaptation.⁸⁷ The instruments used for finishing and beveling margins proved to be influential with regard to marginal adaptation. Specifically, ultrasonic-driven instruments induced more marginal defects compared to sonic instruments^{83,85} or a fine diamond round bur.⁸³ The vibration induced by ultrasonic energy during composite placement also proved to be beneficial for Class II adaptation of nonbeveled cavities.⁸⁵

Sandwich Techniques—Sandwich techniques with conventional glass ionomer cement as a lining downgraded the adaptation to dentin when compared to full composite restorations^{87,88} or sandwich restorations using resin modified glass ionomer cement (rmGIC) liner or full composite restoration.⁸⁹ A rmGIC liner or base did show⁹⁰ the potential to improve marginal adaptation *in vitro*. The same potential was also demonstrated by a compomer; however, the adaption was only improved in a closed sandwich configuration.^{86,91,92} But the rationale for using a fluoride-releasing material in an open sandwich configuration was finally questioned, as literature reviews^{93,94} have not confirmed the protective role of GICs against recurrent caries. Other materials, such as chemically curing or flowable composites, were considered to facilitate restoration placement and/or reduce the negative impact of polymerization shrinkage. This literature review found that the presence of either a flowable liner or chemically curing composite base actually improved marginal adaption, but without totally suppressing marginal defects.^{77,84,95,96} The aforementioned findings were confirmed recently another study,⁹⁷ which showed a significant reduction of imperfect margins after loading when applying rmGIC or flowable composite liners with lower E-modulus. In another study,⁹⁸ a positive effect was only observed when a thin, pre-cured flowable composite lining was applied. The cervical gap size in lined composite restorations was linearly correlated to the strain absorption capacity (negative correlation) and shrinkage (positive correlation).

Influence of Polymerization Protocol—It was first suggested by Goracci and de Martinis⁹⁹ that a slow polymerization mode could reduce marginal defects in Class II restorations. Since then, only a few reports have evaluated and confirmed the impact of curing protocol on the quality of adaptation in the Class II restoration. The adaptation to enamel of Class II MOD restorations was not influenced by the curing light energy (medium intensity conventional

halogen or high-intensity plasma), while the step-curing protocol produced better occlusal and cervical adaption than did pulse-delay or ramp-curing protocols.¹⁰⁰ This partially supports other *in vitro* studies in which the authors studied the effect of various polymerization protocols on contraction force¹⁰¹ or distribution.¹⁹ In an attempt to confirm the advantage of the three-sided light-curing protocol over a conventional occlusal curing, it was shown that a reduced light intensity is likely to be the influential factor that improves restoration adaptation.¹⁰² In a recent study,¹⁰³ the impact of curing time and energy density on contraction stress and marginal adaptation was evaluated. It was shown that a minimal radiant exposure was needed to reach a satisfactory adaption and that a further increase in light density did not significantly affect contraction stress or adaptation. Nevertheless, relevant and conclusive studies clarifying the role and potential impact of curing protocols and light intensity on marginal adaptation are still needed.

Comparison Between Adhesive and Composite Types or Systems—Marginal adaptation to enamel was not affected by gingival fluid contamination when this happened just after acid etching. However, gingival fluid did adversely affect adaption when the contamination happened after adhesive placement.¹⁰⁴ These results should not necessarily be considered valid for blood or saliva contamination.

The use of a filled adhesive system improved the marginal and internal adaptation of mixed Class II cavities when compared to a nonfilled, thinner “prime and bond” adhesive system. The thicker and consequently elastic bonding resin was considered to act as a stress-breaking layer.⁹¹ The performance of simplified adhesive systems used with their respective composite also proved inferior to the multicomponent system that served as the control.¹⁰⁵

The comparison between ormocers and a traditional hybrid composite used in Class II cavities was clearly in favor of the hybrid composite, which presented very high percentages of perfect adaptation both in occlusal and cervical enamel. The adhesive used for the ormocer tested in this study was believed to be responsible for the unsatisfactory adaptation observed with the ormocer.¹⁰⁶ The influence of ceramic inserts on proximal adaptation of Class II restorations was dependant on the level of the cervical margin and the type of insert used.¹⁰⁷ Anatomically shaped inserts improved adaptation to enamel only, while round-shaped, beta-quartz inserts had no influence at all on adaptation when compared to full composite restorations. In dentin,

Table 4: *Selected References for Marginal and Internal Adaptation*

Comparison of restorative and layering techniques
Tjan and others, 1992 ⁸⁰
Idriss and others, 2003 ⁸¹
Stoll and others, 2007 ⁸²
Hugo and others, 2001 ⁸³
Frankenberger and others, 2003 ⁸⁴
Other restorative variables (Cervical margin position, cavity dimensions, matrix system, etc)
Hugo and others, 2001 ⁸³
Schmidlin and others, 2007 ⁸⁵
Dietschi and others, 2002 ⁸⁶
Dietschi and others, 1995a ⁸⁷
Dietschi and others, 1995b ⁸⁸
Sandwich techniques
Belli and others, 2001 ³¹
Frankenberger and others, 1999 ⁷⁷
Frankenberger and others, 2003 ⁸⁴
Dietschi and others, 1995a ⁸⁷
Dietschi and others, 1995b ⁸⁸
Dietrich and others, 1999 ⁸⁹
Dietrich and others, 2000 ⁹⁰
Dietschi and others, 2002a ⁸⁶
Dietschi and others, 2002b ⁹¹
Dietschi and others, 2003 ⁹²
Randall and Wilson, 1999 ⁹³
Wiegand and others, 2007 ⁹⁴
Garberoglio and others, 1995 ⁹⁵
Belli and others, 2001 ⁹⁶
Kwon and others, 2010 ⁹⁷
Chuang and others, 2004 ⁹⁸
Influence of polymerization protocol
Versluis and others, 2004 ¹⁹
Goracci and Martinis, 1996 ⁹⁹
Hofmann and Hunecke, 2006 ¹⁰⁰
Sakaguchi and others, 2004 ¹⁰¹
Losche, 1999 ¹⁰²
Prado and others, 2010 ¹⁰³
Comparison between adhesive and composite types or systems
Dietschi and others, 2002 ⁹¹
Spahr and others, 2000 ¹⁰⁴
Göhring and others, 2003 ¹⁰⁵
Kournetas and others, 2004 ¹⁰⁶
Strobel and others, 2005 ¹⁰⁷
Indirect composite restorations
Dietschi and others, 2003 ⁹²
Comparison between direct and indirect class II restorations
Manhart and others, 2001 ¹
Manhart, 2004 ³
Paul and Sharer, 1997 ⁷³

Table 4: Continued.

Aggarwal and others, 2008 ⁷⁶
Frankenberger and others, 1999 ⁷⁷
Dietrich and others, 1999 ⁸⁹
Dietschi and others 2002 ⁹¹
Bertschinger and others, 1996 ¹⁰⁸
Dietschi and Herzfeld, 1998 ¹⁰⁹
Papathanasiou and Bardwell, 2001 ¹¹⁰
Iida and others, 2003 ¹¹¹
Evaluation of marginal and internal adaptation of class II restorations following short-term clinical function
van Dijken and others, 1998 ¹¹²
Lindberg and others, 2000 ¹¹³
Andersson-Wenckert and others, 2002 ¹¹⁴
Andersson-Wenckert and others, 2004 ¹¹⁵
Opdam and others, 2007 ¹¹⁶
Lindberg and Van Dijken, 2005 ¹¹⁷

the inserts had no positive impact on restoration quality.

Indirect Composite Restorations—The influence of resinous bases with increasing E-modulus underneath Class II MOD composite inlays was evaluated after mechanical loading. The best results were obtained with a “highly filled” flowable material, while the restorations having no base, a compomer, or a “low-filled” flowable or a restorative material lining showed more marginal defects.⁹² These results indicated that material mechanical properties such as rigidity/elasticity and viscosity have the potential to influence restoration adaptation after loading. It is interesting to mention that these differences appeared only after loading, which supports the use of cyclic loading to evaluate the impact of different materials or treatment protocols on Class II restoration adaptation and quality.

Comparison Between Direct and Indirect Class II Restorations—In the presence of thin cervical enamel (0.5-mm thickness and 1-mm height) the indirect composite restorations had a better adaptation compared to a direct, multilayered composite filling.⁸⁸ The presence of a bevel also improved the cervical adaptation in both direct and indirect restorations, but only when there was “thick” (>1 mm) enamel remaining. With a butt margin design, thick enamel was beneficial to indirect restorations only.⁸⁸ In a study⁸⁸ evaluating the influence of restorative technique (direct vs indirect composites) and liners (GIC or rmGIC), the inlay technique proved overall to be superior to the direct composite option. In this study, the presence of GIC or rmGIC liners lowered the excellent adaption percentages in

both direct and indirect restorations. Once again, the benefit of glass ionomers used as liners was not substantiated by *in vitro* studies when evaluated in a protocol that was more clinically relevant.

The combination of the dual bonding technique (applying the adhesive system before impression or further restorative procedures)^{73,108} together with an inlay or insert technique yielded better adaptation than did direct or indirect techniques using a conventional adhesive cementation technique (applying the adhesive at the time of cementation).¹⁰⁹ In addition, when comparing a direct technique to ceramic inlays using the dual bonding technique, better results were obtained with this latter approach.⁷⁷ Moreover, in this same study, third- and fourth-generation adhesives showed better performance than did those of the fifth generation. In another test,⁷⁶ in which the test samples underwent cyclic loading, the performance of composite inlays was observed to be superior to the direct technique. When comparing a direct technique to direct chair-side inlays or laboratory indirect inlays, the lowest amount of gaps was observed in the indirect group. A reduction in gaps was also observed in the direct inlay group compared to the group in which the direct technique was utilized, but this finding was not significant.¹¹⁰

Comparing different inlay materials in mixed Class II cavities (composite, low-fusing ceramic, Spinell and aluminous porcelains) did not show any significant difference in either marginal or cervical adaptation between these three ceramic materials, which had differing structure and stiffness.¹⁰⁹ The composite inlay, however, showed a better marginal adaptation in cervical dentin. In a similar study, the cement type appeared to be the influential factor for cervical adaptation to dentin. Better cervical adaptation to dentin was also observed with ceramic inlays compared to a direct technique, although once again, this was dependant on the luting material.^{1,110}

Finally, it was observed that the proportion of gap-free resin-dentin interface was not influenced by the restorative technique (direct or CEREC inlay) but instead by the presence of a low-elasticity flowable composite liner, which significantly decreased the amount of defects at the same interface.¹¹¹

Evaluation of Marginal and Internal Adaptation of Class II Restorations Following Short-term Clinical Function—An interesting approach to testing the marginal and internal adaptation of Class II adhesive restorations was developed by van Dijken and coworkers.¹¹² They sought to integrate the clinical

environment and strains, and their concept was to restore premolars scheduled to be extracted (one month after restoration placement) for orthodontic reasons and then to apply the same evaluation protocol as was used for *in vitro* investigations.¹¹² This approach confirmed the advantage of using a multicomponent adhesive system over a simplified one, and it also verified that the directed shrinkage technique (placing a base of self-curing composite underneath a light-curing restorative material) produced a dentin adaptation that was comparable to that obtained using a horizontal multilayering technique.¹¹² The adaptation for sandwich restorations using a compomer or rmGIC base was superior to full composite restorations after this short period of clinical service^{113,114} and confirmed the findings of many *in vitro* investigations.⁸⁹⁻⁹¹ However, it has to be considered that these findings were not confirmed after longer *in vivo* observation periods.^{115,116} Using the same protocol, the one-month adaption of Class II restorations with a FRC was observed to be equivalent to a full composite filling. Using this same test model and time frame, no influence on restoration adaptation was reported¹¹⁷ between a soft-start curing and continuous irradiation curing technique.

Conclusion: Marginal Adaptation—Within the limitations of this study protocol, the most relevant conclusions based on a satisfactory quantity and consistency of the evidence are that

- the position of restorative margins influenced the marginal adaptation (less defects observed at enamel margins);
- a bevel improved cervical adaptation in both direct and indirect restorations when enough enamel was present (>1 mm);
- the dual bonding technique (application of the adhesive system before impression and cementation) improved restoration adaptation;
- multicomponent adhesive systems showed better margins than did simplified ones;
- the use of a FRC with low E-modulus or a chemically curing composite base showed a potential for better marginal adaption underneath both direct and indirect restorations; and
- a better overall adaptation was obtained with indirect techniques.

The influence on marginal adaptation of other variables, such as the filling technique, the curing protocol and light intensity, the presence of a GIC or rmGIC liner, or the composite type used for direct restorations or material type (composites or ceram-

ics) for indirect restorations, could not be ascertained as a result of the insufficient quantity or consistency of the available evidence.

Conclusion: Marginal Adaptation Methodology—Phenomena such as nano-leakage, leakage, pulpal complications, and secondary caries, which are induced by interface breakdown, represent the majority of clinical failures observed in all types of direct restorations.^{3,118} Therefore, evaluating the behavior of adhesive restorations and interfaces with natural tissues under simulated function, pulpal pressure, and a moist environment helps to identify weak points and allows a better understanding of how to reduce the incidence of defects around or underneath a restoration.^{92,119-121} This undoubtedly confers upon such a research approach the highest quality among all protocols used to test Class II restorations.

In fact, observing the restoration marginal adaptation without mechanical loading will only reflect the behavior of the system used to fabricate the restoration or placement/insertion stresses and will not provide information about the reaction of the overall system to function. Studies^{86,92,109,122} using multiple loading cycle steps have actually shown the impact of mechanical load magnitude and stress duration on the quality of marginal and internal adaptation of the restoration. For instance, a restorative system that exhibited a good immediate adaptation due to the increased flexibility of the liner later showed an unsuccessful behavior due to increased deformation under load and adverse behavior to fatigue once it was mechanically stressed. In other words, satisfactory initial adaptation of a restorative system can neither predict an optimal clinical behavior nor inform us about the reaction to long-term functional stresses or the oral cavity environment. The effect of long-term exposure to moisture is also an important test condition in order to reveal phenomena such as hydrolytic degradation and expansion of the restorative system due to water sorption.^{115,116,123} The limited duration of *in vitro* investigations therefore still represents a weak aspect of such testing protocols and further justifies the need for *in vivo* trials, despite their numerous aforementioned practical limitations.

The sensitivity threshold and overall “quality” of evidence for marginal adaptation protocols should also be addressed, as procedural confounders exist for the laboratory stages (ie, control of sample moisture, polishing technique, experience of the operator, real load applied, etc), all of which can affect the significance of some studies and explain

the conclusions of a recent and controversial review¹²⁴ questioning the relevance of marginal-internal adaptation tests of Class V restorations. As a result, the “apparent” absence of a correlation between clinical and *in vitro* studies regarding the performance of Class V restorations was erroneously interpreted as a possible irrelevance of marginal leakage tests instead of as an indication that confounders and sensitivity issues exist, which affect both the *in vitro* and clinical studies under review. This underlines once again the importance of extremely well-standardized study protocols and proper simulation of the oral environment (ie, functional loading) for *in vitro* trials.

V. Comparison of Methods and Evidence Hierarchy for In Vitro Trials

Clinically, restorations can potentially fail because of restoration/tooth fracture, loss of anatomy and function (chemical and mechanical wear), or interface degradation, leading to marginal leakage, pulpal pathology, and recurrent decay. Such failures are therefore of three types: structural breakdown, surface degradation, or loss of cohesiveness between the restoration and tooth structure. Oral cavity strains responsible for those failures are of a mechanical, chemical, thermal, and bacteriological nature. In addition, the repetitive occurrence of those stresses, known as “fatigue,” is of particular importance for both *in vivo* and *in vitro* research.¹²⁵ Therefore, the best approach to evaluate the ability of a restorative system to resist such strains and degradation patterns is a clinical trial, and scientists and clinicians thus continue to call for medium- to long-term studies to discriminately appraise the various operative protocols and material choices. Unfortunately, clinical evaluation times shorter than three to five years^{126,127} seem insufficient, and this strengthens the need for preclinical, *in vitro* evaluation protocols.¹²⁶⁻¹²⁸

In a similar fashion to the accepted hierarchy of evidence in clinical research, there is also an obvious and increasing need to assess the relevance of laboratory protocols. Therefore, a first important consideration is to evaluate the capacity of *in vitro* tests for adhesive posterior restorations to replicate major oral strains, such as functional forces, thermal changes, and moist environment. This represents the initial rationale and assessment model for developing a hierarchy of the predictive value or evidence level of *in vitro* trials, such as we have proposed in Table 5.

Table 5: Proposed Hierarchy of Evidence for Class II In Vitro Trials, Based on the Capacity of the Laboratory Protocol to Simulate Oral Cavity Strains. Relevance or Hierarchy Degree Is Ranked on a 1-5 Scale, 5 Being the Highest Score

In Vitro Protocol	Stress Conditions ^a		Relevance Score
	Monotonic Mechanical Loading	Cyclic	
Resistance to fracture	+	–	1
Photoelasticity	+	–	2
Marginal leakage	–	–	1
		+T&ML	2
Bond strength	+	–	2
		+T&ML	3
Resistance to deformation	+	–	2
		+ML ^b	3
Finite element analysis			
Two dimensional	+	–	2
Three dimensional			3
Resistance to fracture	–	+ML ^b	3
Polymerization-induced tooth deformation	+	–T&ML	3
Wear resistance	–	+T&ML	4
Marginal adaptation	–	–	3
		+ T&ML	4
Marginal and internal adaptation	–	–	4
		+T&ML	5

Abbreviations: ML, cyclic mechanical loading; T, thermal cycling; –, without; +, with.
^a Most frequent study design.
^b Cyclic strains may be applied prior to testing.

For instance, resistance to fracture tests without cyclic stressing induce fracture patterns that are irrelevant to the failures observed clinically and were therefore attributed the minimal score (1). As well, microleakage tests, which show poorly consistent results and use a semiquantitative evaluation scale, were also considered poorly relevant to clinical conditions and were thus given scores of 1 or 2 when thermal cyclic or mechanical loading was used. Photoelasticity also suffers from main technological limitations, as previously described, and it was thus also attributed a low relevance score (2). Despite the fact that the evaluation of wear in contact areas following cyclic loading was not reported in this review (as the related references were not in the selected review period), this methodology was attributed a high score of relevance (4), even though wear resistance tests appear nowadays to be less crucial as a result of the considerable improvements in the physical properties of composites.

The reaction of posterior adhesive restorations to intraoral strains is the result of complex interactions among the filling material, the tooth substrate, and their environment. To date, there is no single *in vitro* test able to simulate all of the aforementioned strains and degradation patterns and then able to

reliably predict the clinical performance of a restorative system. Therefore, considering a combination of protocols would appear to be the safest approach at the present time. For instance, information collected from computer simulation (FEM) or tooth deformation (score of 2 to 3 for each) can contribute to a better understanding of stress development and management in adhesive restorations. Bond strength tests (score of 2 to 3) would complete this first level of evaluation by enabling an understanding of how well the adhesive interface reacts to the placement of the restoration and the subsequent functional load.

The second evaluation level would be provided by adaptation studies (score of 3) and, in particular, those studies that submit samples to cyclic loading (scores of 4 to 5). Such protocols appear more discriminative in terms of predicting clinical behavior since they mimic a global interaction of the restorative system with the tooth in a simulated oral environment. They also provide meaningful information about the quality of interfaces following fatigue.^{88,91,92,120,129-131} However, it may be necessary to perform these studies with an increase of load and number of cycles in order to simulate parafunctional forces and long-term behavior. A

force feedback through stress sensors could also improve loading control and should be considered as part of a desired implementation for most of the existing “mastication simulators,” which presently lack such a feedback system.

In clinical studies potential confounders exist. Some of these are sample size, patient selection (ie, age and gender, social background, hygiene, existence of parafunctions, etc), observation period, patient drop-out, clinician skill, and clinical evaluation thresholds, to cite only the most important ones. This logically explains why only multicenter and multioperator, randomized controlled studies with medium- to long-term observation periods are truly conclusive.⁴⁻⁶ The unfortunate reality is that such studies are either totally missing or cannot investigate detailed parameters, such that preclinical, *in vitro* studies remain a valid and decisive evaluation approach.

In order to improve the quality of the evidence in *in vitro* trials, hidden or confounding variables thus have to be identified and tentatively eliminated or controlled. Depending on the protocol, those procedural confounds that have to be considered are

- origin and condition of teeth (human or animal origin, type of teeth, age, presence of decay, storage conditions, etc),
- control of sample moisture,
- finishing of the restorations (thermal and mechanical stresses), and
- control of forces (ie, magnitude, stress profile, frequency).

Therefore, it seems advisable to avoid drawing clinical conclusions from *in vitro* protocols showing relevance scores that are below 3, unless these are combined with other evaluation methods. Following such a thinking process in dentistry would seem advantageous for editors, reviewers, and readers and would limit the risk of misinterpretation of *in vitro* research and the subsequent dissemination of insufficiently founded clinical guidelines.

GENERAL CONCLUSIONS

An abundant number of study hypotheses corresponding to almost unlimited combinations of preparation techniques, adhesive procedures, restorative options, and materials were submitted to various *in vitro* protocols. Some of these hypotheses were repeatedly tested and some consensus arose in regard to the quantity and consistency of the evidence. However, many other combinations re-

main yet to be validated by either additional *in vitro* research or clinical trials as a result of the insufficient quantity, quality, or consistency of the available evidence.

The following conclusions can therefore be made based on the systematic conclusiveness of various *in vitro* studies, and some recommendations can conceptually be made to guide clinicians toward their operative choices, even though some caution might still apply in the absence of absolute confirmation through clinical research.

- 1) Stress management remains an issue with modern composite technology because of the substantial volumetric polymerization shrinkage that occurs as a byproduct of this chemistry. As yet, there is no new composite formulation in existence that can significantly limit or totally eliminate shrinkage and still maintain all of the proven performance of hybrid composites, even in *in vitro* testing situations.
- 2) The stresses occurring during restoration placement (direct techniques) or function can be controlled by a number of methods.
- 3) The control of curing light energy (low irradiance with extended polymerization time) helps reduce stresses transmitted to the restoration, adhesive interface, and tooth structure. However, the advantages of modified light-curing protocols such as ramp curing, soft-start curing, and step curing were not fully verified.
- 4) Multilayering is mandatory for direct restorations. No protocol seems especially superior; however, cavity size and configuration are influential factors.
- 5) Dual bonding (IDS) improves the adhesion and adaptation to dentin for indirect techniques.
- 6) The “elastic” base lining concept (placement of a stress-breaking layer) proved efficient and superior to “traditional” full composite restoration techniques; however, the thickness and E-modulus of such liners are influential factors.
- 7) Indirect restorations proved better than direct ones in most *in vitro* conditions, when used in large cavities.
- 8) The material’s stiffness, restoration thickness, and configuration (no coverage, partial coverage, or full occlusal coverage) play a crucial role in treating large cavities or nonvital teeth as a result of the imperative need for tooth stabilization and reinforcement. It seems advisable to use “stiffer” composites or ceramics for restoring weakened posterior teeth, such as those that have been endodontically treated.

Conflict of Interest

The authors of this manuscript certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

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