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CRITICAL REVIEWS IN ORAL BIOLOGY & MEDICINE

A Critical Review of the Durability of Adhesion to Tooth Tissue: Methods and Results

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ABSTRACT

The immediate bonding effectiveness of contemporary adhesives is quite favorable, regardless of the approach used. In the long term, the bonding effectiveness of some adhesives drops dramatically, whereas the bond strengths of other adhesives are more stable. This review examines the fundamental processes that cause the adhesion of biomaterials to enamel and dentin to degrade with time. Non-carious class V clinical trials remain the ultimate test method for the assessment of bonding effectiveness, but in addition to being high-cost, they are time- and labor-consuming, and they provide little information on the true cause of clinical failure. Therefore, several laboratory protocols were developed to predict bond durability. This paper critically appraises methodologies that focus on chemical degradation patterns of hydrolysis and elution of interface components, as well as mechanically oriented test set-ups, such as fatigue and fracture toughness measurements. A correlation of *in vitro* and *in vivo* data revealed that, currently, the most validated method to assess adhesion durability involves aging of micro-specimens of biomaterials bonded to either enamel or dentin. After about 3 months, all classes of adhesives exhibited mechanical and morphological evidence of degradation that resembles *in vivo* aging effects. A comparison of contemporary adhesives revealed that the three-step etch-and-rinse adhesives remain the 'gold standard' in terms of durability. Any kind of simplification in the clinical application procedure results in loss of bonding effectiveness. Only the two-step self-etch adhesives approach the gold standard and do have some additional clinical benefits.

KEY WORDS: artificial aging, dental adhesives, enamel, dentin.

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(1) INTRODUCTION

The major shortcoming of contemporary adhesive restoratives is their limited durability *in vivo* (Van Meerbeek *et al.*, 1998). The most cited reasons for failure of adhesive restorations are loss of retention and marginal adaptation (Mjör *et al.*, 2002; Mjör and Gordan, 2002). Hence, a valuable approach to prolong the clinical lifetime of adhesives might be to focus on improving the stability of the bond of these biomaterials to tooth tissue. The immediate bonding effectiveness of most current adhesive systems is quite favorable (Inoue *et al.*, 2001b), regardless of the adhesive used. However, when these adhesives are tested in a clinical trial, the bonding effectiveness of some materials appears dramatically low, whereas the bonds of other materials are more stable (Van Dijken, 2000; Brackett WW *et al.*, 2002). The objective of this review is to discuss the potential *in vivo* degradation processes involved, to critically review study designs to assess these phenomena, and, eventually, to find out how well laboratory tests can predict *in vivo* bond durability.

(2) CLASSIFICATION OF CONTEMPORARY ADHESIVES

The basic mechanism of bonding to enamel and dentin is essentially an exchange process involving replacement of minerals removed from the hard dental tissue by resin monomers, which, upon setting, become micro-mechanically interlocked in the created porosities. This interlock was first described by Nakabayashi *et al.* in 1982 and is commonly referred to as 'hybridization', or the formation of a 'hybrid layer'. Based upon the underlying adhesion strategy, three mechanisms of adhesion are currently in use with modern adhesive systems (Fig. 1; Van Meerbeek *et al.*, 2001, 2003).

(2.1) Etch-and-Rinse Adhesives

'Etch-and-rinse' adhesives involve a separate etch-and-rinse phase. In their most common configuration, an acid (mostly 30-40% phosphoric acid) is applied and rinsed off. This conditioning step is followed by a priming step and application of the adhesive resin, resulting in a three-step application procedure. Simplified two-step etch-and-rinse adhesives combine the primer and adhesive resin into one application.

(2.2) Self-etch Adhesives

An alternative approach is based on the use of non-rinse acidic monomers that simultaneously condition and prime dentin, the so-called 'self-etch' adhesives. Regarding user-friendliness and technique-sensitivity, this approach seems clinically most promising. This approach eliminates the rinsing phase, which not only lessens the clinical application time, but also significantly reduces the technique-sensitivity or the risk of making errors during application. There are basically two types of 'self-etch' adhesives: 'mild' and 'strong' (Van Meerbeek *et al.*, 2001). 'Strong' self-etch adhesives have a very low pH (< 1) and exhibit a bonding mechanism and interfacial ultra-morphology in dentin resembling that produced by etch-and-rinse adhesives. 'Mild' self-etch adhesives (pH of around 2) dissolve the dentin surface only

partially, so that a substantial number of hydroxyapatite crystals remain within the hybrid layer. Specific carboxyl or phosphate groups of functional monomers can then chemically interact with this residual hydroxyapatite (Yoshida *et al.*, 2004). This two-fold bonding mechanism (*i.e.*, micro-mechanical and chemical bonding) is believed to be advantageous in terms of restoration durability. It has a micro-mechanical bonding component that may in particular provide resistance to abrupt de-bonding stress. The chemical interaction may result in bonds that better resist hydrolytic break-down and thus keep the restoration margins sealed for a longer period.

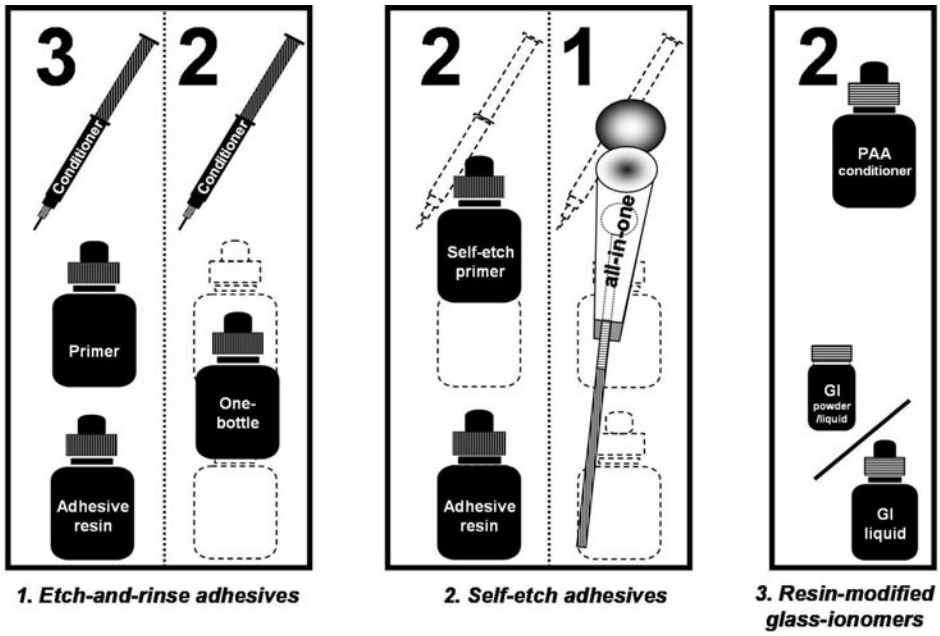

Figure 1. Classification of contemporary adhesives following adhesion strategy and number of clinical application steps. Gi = glass ionomer; PAA = polyalkenoic acid.

(2.3) Glass Ionomers and Glass-ionomer Adhesives

Glass-ionomers are still considered the only materials that self-adhere to tooth tissue (Yoshida *et al.*, 2000). A short polyalkenoic acid pre-treatment cleans the tooth surface; it removes the smear layer and exposes collagen fibrils up to about 0.5-1 μm deep (Inoue *et al.*, 2001a); therein, glass-ionomer components inter-diffuse and establish a micro-mechanical bond following the principle of hybridization (Lin *et al.*, 1992; Van Meerbeek *et al.*, 2001). In addition, chemical bonding is obtained by ionic interaction of the carboxyl groups of the polyalkenoic acid with calcium ions of hydroxyapatite that remained attached to the collagen fibrils (Yoshida *et al.*, 2000). This additional chemical adhesion may be beneficial in terms of resistance to hydrolytic degradation. Consequently, a two-fold bonding mechanism is established, similar to that mentioned above for mild self-etch adhesives. The basic difference with the resin-based self-etch approach is that glass ionomers are self-etching through the use of a relatively high-molecular-weight (from 8000 to 15,000) polycarboxyl-base polymer. This limits their infiltration capacity, so that only shallow hybrid layers are formed. In addition, because of this high molecular weight, they cannot infiltrate phosphoric-acid-decalcified dentin. Consequently, such aggressive conditioners should not be used in conjunction with glass ionomers (De Munck *et al.*, 2004).

(3) CLINICAL TRIALS

The ultimate test method for the assessment of bonding effectiveness remains a clinical trial. If the study objective is to investigate clinical effectiveness of adhesives, only studies involving non-carious class V adhesive restorations should be considered, for the following reasons (Van Meerbeek *et al.*, 1998): (1) Such lesions do not provide any macro-mechanical retention, so that ineffective bonding will result in early restoration loss; (2) retention, *i.e.*, evaluating if the restoration is present or not, is the only objective study parameter available; (3) any other type of cavity (I, II, III, and IV) will exhibit at least some macro-mechanical retention. Consequently, less-objective evaluation criteria, such as marginal integrity and discoloration, need to be quantified as a measure of bonding effectiveness; (4) class V restoration margins are located in enamel as well as in dentin; (5) lesions are commonly located on vestibular surfaces of anterior teeth and premolars, thus providing good access for the restorative procedure as well as for evaluation (visually, with the use of an explorer and magnifying glasses, and even by SEM, if epoxy replicas are made); (6) preparation and restoration of class V lesions are minimal and relatively easy, thereby somewhat reducing practitioner variability; (7) lesions are relatively widespread and occur on multiple teeth, facilitating patient selection and enabling balanced study designs to be developed; and (8) despite various cavity configuration factors of class V lesions (Feilzer *et al.*, 1987; Carvalho *et al.*, 1996), and thus resultant interfacial stress, the mechanical properties of the composite used are relatively unimportant (Browning *et al.*, 2000; Tyas and Burrow, 2001, 2002; Van Meerbeek *et al.*, 2005a,b). A drawback related to the use of non-carious class V lesions might be the substantial differences in the composition of the bonding surfaces. Non-carious class V lesions exhibit high degrees of sclerosis, and related high mineral content, as compared with intact or caries-affected dentin. Hybrid layer formation on this hypermineralized dentin is more difficult, and therefore less effective bonding is assumed (Van Meerbeek *et al.*, 1994; Prati *et al.*, 1999). Supporting this hypothesis is the observation of higher annual failure rates in the presence of sclerotic dentin (Van Dijken, 1994); however, this seems to be valid only for older adhesives (Van Meerbeek *et al.*, 1998; Van Dijken, 2000).

The outcome of a clinical study is dependent not only on the patient and the materials used. 'External' factors—such as the skills of the operator, type of light source, isolation method, finishing instruments used, etc.—significantly influence the outcome. Also, in many studies, patient-related factors—such as age, oral hygiene, occlusal loading, and dentin sclerosis—are more influential than any material property (Bayne *et al.*, 1991; Van Meerbeek *et al.*, 1998). Therefore, an appropriate study

design is paramount when clinical trials are conducted. The patient-related factors can be ruled out by the application of a balanced study design. In such a design, pairs of equal teeth (for instance, first and second premolars on the same side, left and corresponding right incisors, canines, or premolars, respectively) with similar lesions are chosen in each patient, and each tooth is assigned to one of the experimental treatments in a randomized way, so that the study hypothesis is tested at the patient level (Van Meerbeek *et al.*, 1998). However, when it comes to a comparison of different studies, especially from different research groups, all external and patient-related factors must still be considered and can be dealt with only by randomization and an adequate number of patients, rather than restorations. In that way, the results from the statistical sample can be extrapolated to the population. The number of patients required for this purpose can be determined with statistical power analysis. If the obtained results are to be compared with data in the literature, a control group using a well-established adhesive technique is also required. Hence, a study that uses only a simplified adhesive, will demonstrate only if that adhesive complies with, for instance, ADA standards. Only from a well-controlled experimental design can one conclude that this new material competes with the best available material. Besides adequate study design, longer observation times (up to 5 years and longer) are needed. Unfortunately, most currently published data are obtained from short-term studies and are often published only as meeting abstracts, without any study details.

Different causes that may interact synergistically can lead to clinical failure in class V studies. Eccentric occlusal stress is one of the main causes for the development of abfraction lesions, as revealed by finite element analysis (Rees, 2002) and clinical evidence (Braem *et al.*, 1992). The same stress that caused the lesions may also put tension on the restoration/tooth interface, resulting in increasing damage at the interface (Krejci *et al.*, 1994; Van Meerbeek *et al.*, 1998).

In addition to occlusal stresses, intra-oral temperature changes may also induce repetitive contraction/expansion stresses at the tooth-adhesive interface, due to the higher thermal contraction/expansion coefficient of the restorative material (as compared with that of tooth tissue) (Gale and Darvell, 1999).

The tooth-biomaterial bond may also degrade by exposure of the interface to water and/or human/bacterial enzymes present in saliva. Ingression of water into the hybrid layer (Sano *et al.*, 1995) and subsequent leaching out of resin components are believed to lead to inefficient *in situ* polymerization (Eick *et al.*, 1997) and degradation of resin components (Santerre *et al.*, 2001; Finer and Santerre, 2004; Jaffer *et al.*, 2002). Also, hydrolysis of hydroxyapatite-depleted or insufficiently resin-coated collagen fibrils compromises long-term bonding effectiveness (Hashimoto *et al.*, 2000, 2002, 2003b).

Thus, biomaterial-tooth interfaces are subjected to chemical as well as mechanical degradation. Chemically, the most important reactions are hydrolysis and plasticizing of the resin components, which are both related to the ingression of water. Since this ingression is a diffusion-like process, the related degradation mechanisms will also be diffusion-dependent. Hydrolysis can break up covalent bonds, linking the different units of collagen fibrils as well as resinous polymers (Hashimoto *et al.*, 2000). This process can be enhanced by enzymes released by bacteria (Santerre *et al.*, 2001) and by the dentin itself (Pashley *et al.*, 2004). Subsequently, the resultant breakdown products and residual monomers can leach out and so decrease the interfacial mechanics and allow more water to ingress. Water can also reduce the frictional forces between the polymer chains, which reduces the mechanical properties of the resin part and makes the polymer swell, a process known as the plasticization of resin. Also, repeated mechanical stress can affect interfacial integrity (De Munck *et al.*, 2005a,c). During each chewing cycle (or other mechanical stress), the interface is loaded. At some sites, stress concentrations may exceed interfacial fracture toughness, which results in the initiation of a crack. In some cases, this may also cause catastrophic failure of the restoration. In other cases, this initiated crack can act as even a bigger stress concentrator, so that the subsequent mechanical loads will enlarge the crack, a process known as crack propagation. Catastrophic failure will occur when crack propagation has extended to a level affecting the structural integrity of the material.

In the clinical situation, however, it is difficult to discriminate the specific factor(s) that caused the restoration to fail. In contrast to *in vivo* research, *in vitro* testing can elucidate the specific factors that are most detrimental to long-term bonding effectiveness. Future research can then focus on improving these specific factors and thereby enhance bond durability.

(4) LABORATORY STUDIES

(4.1) Bond Strength

(4.1.1) Test methodologies

Bond strength tests are the most frequently used tests to screen adhesives. The rationale behind this testing method is that the stronger the adhesion between tooth and biomaterial, the better it will resist stress imposed by resin polymerization and oral function. Different bond strength tests have been developed (Pashley *et al.*, 1995, 1999). Currently, the shear and micro-tensile bond strength (μTBS) test methods are the most used (Fig. 2). It is important to note that a bond strength value cannot be considered as a material property (Van Noort *et al.*, 1989). The data recorded depend largely upon experimental factors such as, for example, the type of composite, stress rate, sample size and geometry, and the actual test method (Phrukkanon *et al.*, 1998; Sudsangiam and Van Noort, 1999). Therefore, the absolute test values cannot be used to draw conclusions from, or be compared with, data gathered in other studies. Only relative study outcomes, in the sense of 'A is better than B', are a valid basis for further interpretation of the results. Nevertheless, bond-strength testing can reveal valuable clinical information, when gathered in a well-controlled design. For instance, by introducing an aging factor into the study design, one can assess the durability of adhesion. In this respect, the need for one or more controls to be included should be emphasized. In many studies (Tjan *et al.*, 1996; Dietschi and Herzfeld, 1998; Pilo and Ben-Amar, 1999; Frankenberger *et al.*, 2000; Meiers and Young, 2001; Cardoso *et al.*, 2002), all specimens are 'aged' (by, for example, thermo-cycling) so that more 'clinically' relevant data can be obtained. But if a proper control is absent, the study provides no information on durability. Different artificial aging techniques can be used, depending upon the specific types of bond degradation that are being investigated.

(4.1.2) In-house, short-term micro-tensile bond strength (μTBS) results

To assess long-term effectiveness, it is crucial that one first

determine the short-term bonding effectiveness of adhesives. These serve as baseline data. At Leuven, the μTBS of a large group of commercial and experimental adhesives to bur-cut enamel and dentin has been determined (Inoue *et al.*, 2001b, 2003; De Munck *et al.*, 2003a,b; Van Meerbeek *et al.*, 2003), always following the same experimental protocol (Fig. 2), with one particular restorative composite (Z100, 3M ESPE).

The pooled μTBS of all etch-and-rinse adhesives tested (Fig. 3a), when bonded to enamel, was 39 and 40 MPa for the three-step and two-step etch-and-rinse adhesives, respectively. As has been shown by Buonocore (1955), bonding to enamel requires only an acid-etch step followed by the application of a fluid resin, without the need for an intermediary primer step. Primers do not negatively influence bonding effectiveness and are mandatory when a 'wet-bonding' procedure is carried out. In general, self-etch procedures have resulted in significantly lower bonding effectiveness, although some two-step self-etch adhesives approached the bonding effectiveness of etch-and-rinse adhesives (De Munck *et al.*, 2005b). A pooled μTBS of about 30 MPa was obtained for two-step self-etch adhesives. No significant difference was recorded in favor of either a 'strong' or a 'mild' self-etch approach. Because of the superficial interaction of self-etch adhesives with enamel, and thus less potential for micro-mechanical interlocking than a phosphoric-acid treatment, it can be hypothesized that an additional chemical bonding capacity to hydroxyapatite contributed to the actual bonding effectiveness of 'mild' self-etch adhesives. Among all adhesives tested, one-step self-etch adhesives produced the lowest μTBS (Fig. 3a). The glass-ionomer adhesive Fuji Bond LC (GC) performed equally as well as the two-step self-etch adhesives. However, during bond-strength testing, the glass-ionomer adhesive tended to fail in the glass-ionomer material itself rather than at the interface. Thus, the actual bonding effectiveness to enamel was never assessed (Inoue *et al.*, 2001a).

In dentin, three-step etch-and-rinse adhesives still surpassed all other adhesives that use simplified application procedures (Fig. 3b). Statistical analysis of the pooled dentin μTBS data showed that three-step etch-and-rinse adhesives bonded significantly more strongly to dentin than did two-step etch-and-rinse and two-step self-etch adhesives. The latter two systems did not perform significantly differently from each other. Again, the significantly least favorable μTBS results

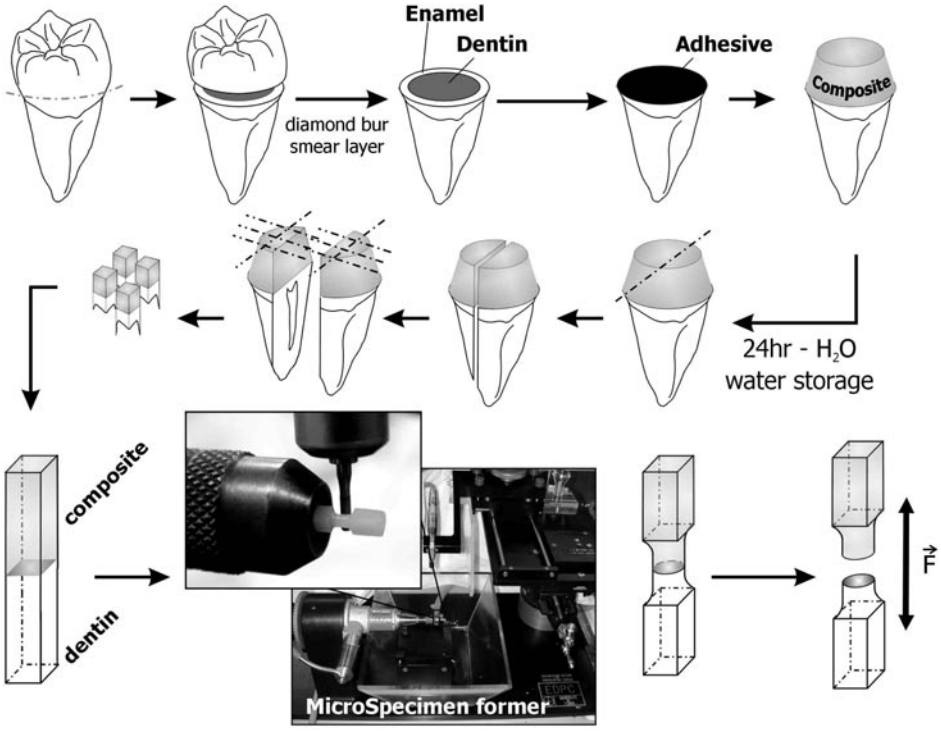

Figure 2. Schematic presenting the experimental design of micro-tensile bond strength testing.

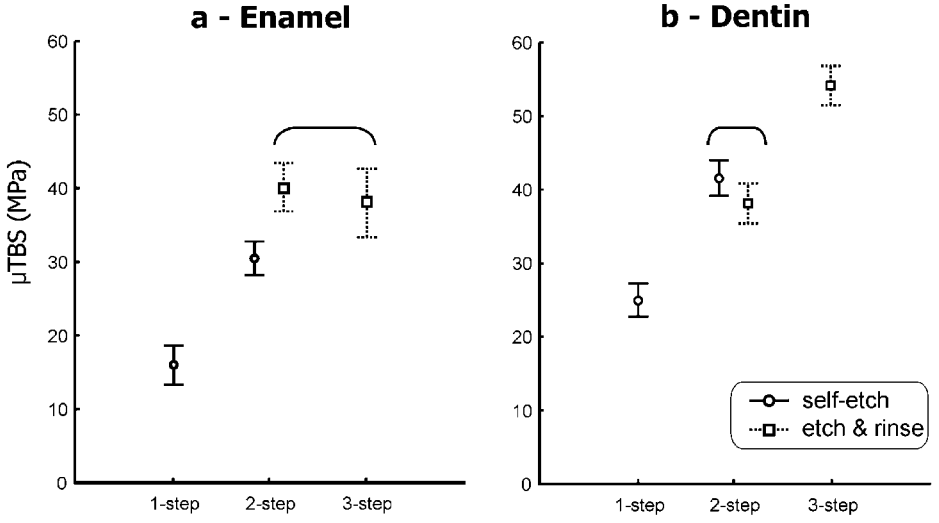

Figure 3. Pooled in-house μTBS data. **(a)** Statistical analysis of pooled enamel μTBS data *per* adhesive class, as gathered at the Leuven BIOMAT research cluster during the period 2001-2004, always using the same experimental protocol (Fig. 2). The central circle/rectangle represents the mean value, and vertical bars denote 95% confidence intervals. Adhesive classes in which the μTBS was not significantly different are connected by a horizontal line. **(b)** Statistical analysis of pooled dentin μTBS data *per* adhesive class, as gathered at the Leuven BIOMAT research cluster during the period 2001-2004, always using the same experimental protocol (Fig. 2). The central circle/rectangle represents the mean value, and vertical bars denote 95% confidence intervals. Adhesive classes in which the μTBS was not significantly different are connected by a horizontal line.

were recorded for one-step self-etch adhesives, and the μTBS of these adhesives was not significantly different from that of the resin-modified glass-ionomer adhesive.

(4.1.3) Aging by storage

The most commonly used artificial aging technique is long-term water storage. The bonded specimens are stored in fluid at 37°C for a specific period. This period may vary from a few months (Shono *et al.*, 1999) up to 4-5 years (Fukushima *et al.*, 2001; De Munck *et al.*, 2003b), or even longer. Most studies report significant decreases in bond strengths, even after relatively short storage periods (Burrow *et al.*, 1996; Kato and Nakabayashi, 1998; Shono *et al.*, 1999; Kitasako *et al.*, 2000; Armstrong *et al.*, 2001b, 2003; Meiers and Young, 2001; De Munck *et al.*, 2003b; Giannini *et al.*, 2003). Decrease in bonding effectiveness in this type of study is, first, supposed to be caused by degradation of interface components by hydrolysis (mainly resin and/or collagen). But, as previously mentioned, water can also infiltrate and decrease the mechanical properties of the polymer matrix, by swelling and reducing the frictional forces between the polymer chains, a process known as 'plasticization' (Ferracane *et al.*, 1998; Santerre *et al.*, 2001). Furthermore, some interface components, such as uncured monomers and break-down products of previous mechanisms, can elute and so weaken the bond (Hashimoto *et al.*, 2002). The storage solution is usually water. To prevent bacterial growth during the storage period, investigators have added sodium azide (Burrow *et al.*, 1996), chloramine (De Munck *et al.*, 2003b; Armstrong *et al.*, 2001a), or even antibiotics (Shono *et al.*, 1999). To mimic the clinical situation more closely, artificial saliva solutions can also be used, but bond strength reductions obtained were similar to those obtained with pure water degradation (Kitasako *et al.*, 2000). Even enzymes can be added to the storage medium. For example, esterases that can be produced by bacteria *in vivo* are able to catalyze the breakdown of resin components (Santerre *et al.*, 2001; Finer and Santerre, 2004). Most degradation processes are diffusion-rate-dependent. Consequently, the length of the diffusion path is as important as the diffusion time itself. A way to exclude diffusion-dependent effects is to age micro-specimens so as to render the diffusion path as short as possible. For example, when small μTBS sticks were stored, a significant decrease in bond strength to dentin was detected within as few as 90 days (Shono *et al.*, 1999; Armstrong *et al.*, 2001b). Storing tiny μTBS sticks may thus be considered as a form of accelerated aging. Enamel-resin bonds, when produced by etch-and-rinse adhesives, are more stable over time (Frankenberger *et al.*, 2000). They can seal off the path of water diffusion to the more vulnerable dentin-resin bond and so retard bond degradation (Hashimoto *et al.*, 2002; De Munck *et al.*, 2003b).

(4.1.4) Aging by thermo-cycling

Another widely used aging technique is thermo-cycling. The ISO TR 11450 standard (1994) indicates that a thermo-cycling regimen comprised of 500 cycles in water between 5 and 55°C is an appropriate artificial aging test. A literature review (Gale and Darvell, 1999) concluded that 10,000 cycles corresponds approximately to 1 year of *in vivo* functioning, rendering 500 cycles, as proposed by the ISO standard, as being very minimal in mimicking long-term bonding effectiveness. The artificial aging effect induced by thermo-cycling can occur in two ways: (1) Hot water may accelerate hydrolysis of interface components, and subsequent uptake of water and extraction of breakdown products or poorly polymerized resin oligomers (Miyazaki *et al.*, 1998; Hashimoto *et al.*, 2000); or (2) due to the higher thermal contraction/expansion coefficient of the restorative material (as compared with that of tooth tissue), repetitive contraction/expansion stresses are generated at the tooth-biomaterial interface. These stresses may lead to cracks that propagate along bonded interfaces, and, once a gap is created, changing gap dimensions can cause in- and outflow of oral fluids, a process known as 'percolation' (Gale and Darvell, 1999). In light of the first aging effect (diffusion-dependent hydrolysis and elusion), thermo-cycling should be applied to very small specimens, and any further preparation after aging is to be avoided. In that case, the most degraded interface is tested, corresponding to the vulnerable restoration margins. Aging of μTBS specimens might also be more appropriate than the larger shear-bond-strength specimens, because both resin composite and tooth tissue may protect the interfacial bond against thermal fluctuations. If the second aging effect (repetitive contraction/expansion stress) is considered, thermo-cycling should be applied to specimens in which stress similar to that in the clinical situation can be generated. *In vivo* stress will occur if the ratio of bonded to unbonded surfaces (the so-called 'C-factor') is high (Feilzer *et al.*, 1987). Therefore, thermo-cycling of the restored tooth will result in the highest clinically relevant stress.

A recent meta-analysis (Leloup *et al.*, 2001) of data published between 1992 and 1996 concluded that thermo-cycling has no significant effect on bond strength. Most studies included in the meta-analysis were carried out following the ISO standard of 500 cycles (mean number of cycles in the studies analyzed was 630). This number of cycles was probably too low for an aging effect to be obtained (Miyazaki *et al.*, 1998; Gale and Darvell, 1999; Nikaido *et al.*, 2002a). Also, specimen geometry has often not been taken into account. In most studies cited in that review, relatively large composite cylinders bonded to flat surfaces were thermo-cycled, prior to being pulled apart following a shear or tensile bond strength test protocol (Leloup *et al.*, 2001). As a result, the surrounding tooth and composite must have thermally protected a large part of the interface (Watts *et al.*, 1987). In addition, because of the low C-factor (about 1/6), little repetitive expansion/contraction stress must have been generated at the interface. Both reasons may explain why thermo-cycling did not affect bonding effectiveness in those studies. This hypothesis was confirmed by a study in which thermo-cycling of restored flat surfaces did not decrease the μTBS, whereas a similar aging protocol applied to restored cavities resulted in a significantly decreased μTBS (Nikaido *et al.*, 2002a). Thermo-cycling of tiny μTBS specimens (diffusion path < 1 mm) resulted in a significant decrease in bond strength (Xie *et al.*, 2002), thus supporting the assumption that thermo-cycling accelerates chemical degradation of the interface. Eventually, it can be concluded that thermo-cycling results in combined contraction/expansion stresses and accelerated chemical degradation. The relative contribution of each, however, is strongly dependent on the specific test set-up.

(4.1.5) Aging by occlusal loading

Mechanical loading may also affect resin adhesion to tooth structure. Again, to simulate this stress *in vitro*, it is important that one imposes stress similar to that occurring *in vivo* (Krejci *et al.*, 1994). One possibility is to 'age' restored cavities in a chewing simulator and afterward measure the bonding effectiveness (Nikaido *et al.*, 2002a; Frankenberger *et al.*,

2003a,b). A better alternative is to study dynamic mechanical phenomena, such as crack initiation and propagation, in well-controlled fracture toughness or fatigue test set-ups.

(4.1.6) *In vivo* degradation studies

The above-mentioned factors are expected to decrease bonding effectiveness, since they are *in vitro* equivalents of *in vivo* phenomena. Clinically, however, all these factors interact simultaneously and, consequently, may accelerate degradation. One way to overcome this mismatch between laboratory and clinical testing is to age specimens in diverse ways at the same time (Nikaido *et al.*, 2002a), or to age restorations in the oral cavity itself. Because of ethical reasons, the latter type of aging can be performed only on teeth already scheduled for extraction (Ferrari *et al.*, 1997; Iracki *et al.*, 2003), or on primary molars that require restorative treatment and that can be collected after exfoliation (Hashimoto *et al.*, 2000). Alternatively, animal studies can be conducted in which, after a certain period of oral functioning, the teeth are extracted and bond strengths measured (Sano *et al.*, 1999; Takahashi *et al.*, 2002).

The μTBS of *in vivo* resin-dentin bonds slowly decreases over time (Hashimoto *et al.*, 2000). Based on fractographic analysis, it has been concluded that bond degradation might be caused by deproteinization of collagen fibrils in demineralized non-protected dentin (Sano *et al.*, 1999; Hashimoto *et al.*, 2003a). It has been hypothesized that a rapid method of simulating this degradation is to expose the resin-dentin interface to a deproteinizing agent (Yamauti *et al.*, 2003). A solution of NaOCl in water is a non-specific deproteinizing agent. As an accelerated aging test, the bond strength of μTBS beams immersed in 10% NaOCl for one hour was determined (Yamauti *et al.*, 2003). After this short period, the μTBS significantly decreased, rendering this procedure a very rapid test method. Failure analysis also revealed that the drop in μTBS correlated with specific dissolution of the hybrid layer, similar to *in vivo* failure patterns. A drawback of this method is that, because of the non-specific properties, NaOCl also causes the mechanical properties of the dentin substrate itself to deteriorate (Sim *et al.*, 2001). Unfortunately, no data are as yet available to link this test directly to the clinical situation.

Of all the abovementioned tests, the fastest method to age tooth-biomaterial interfaces is to immerse μTBS specimens in NaOCl. A more commonly used and validated method is the storage of micro-specimens in water. After relatively short periods (from 90 days to 6 months) of storage in water, all classes of adhesives exhibited at least some decrease in bonding effectiveness (Shono *et al.*, 1999; Armstrong *et al.*, 2001b, 2003; Xie *et al.*, 2002) and a change in interfacial morphology similar to that of *in vivo*-aged specimens (Sano *et al.*, 1999; Hashimoto *et al.*, 2000; Takahashi *et al.*, 2002).

(4.2) Fracture Toughness

In fracture mechanics, the initiation and propagation of cracks in materials are studied. Fracture toughness can be defined as a measure of the material's resistance to crack propagation. In contrast to fracture strength—which is dependent on different factors, such as specimen geometry, surface roughness, and test configuration—fracture toughness is an intrinsic material property, independent of the type of test used. Conventional bond strength tests have a non-uniform stress distribution, as revealed by finite element analysis (Van Noort 1989, 1991; DeHoff *et al.*, 1995; Phrukkanon *et al.*, 1998). This accounts, in part, for the large variation in values obtained by different labs for micro-tensile as well as shear bond strengths (Van Noort *et al.*, 1989, 1991). Therefore, interfacial fracture toughness measurements should, in theory, provide more consistent results and are gaining popularity. Most research groups make use of an adapted short-rod test (Tam and Pilliar, 1994; Ruse *et al.*, 1996; Tam and Yim, 1997; Armstrong *et al.*, 1998, 2001a; Tantbirojn *et al.*, 2000; Tam *et al.*, 2001; Destoop, 2003), since it does not require fatigue pre-cracking for the formation of a sharp crack tip, and there is no need to perform any crack length measurement. Moreover, this test can be applied to small specimens, such as human teeth (Armstrong *et al.*, 1998). In all studies on fracture toughness, failure analyses revealed predominantly interfacial failures, in agreement with observed clinical failure modes (Tam and Pilliar, 1994). However, it has been hypothesized that the cured bonding resin of the adhesive may be a weak link at the interface, since its fracture toughness is in the same range as the interfacial fracture toughness (Khajotia *et al.*, 1997). This is corroborated by the observation that the interfacial fracture toughness is higher for filled than for unfilled adhesives (Tam *et al.*, 2001; Destoop, 2003).

Specimen preparation for fracture toughness measurements is difficult, and no standard procedure for dental adhesives is available. One point of concern is the presence of 'resin flashes' extending out of the chevron, if the required notch is prepared with Teflon tape. These 'flashes' may increase the values measured (Van Noort *et al.*, 1991; Tantbirojn *et al.*, 2000), but can be avoided if groove cuts are prepared afterward (Armstrong *et al.*, 2001a). However, the prepared grooves are more prone to micro-cracks, which may act as crack initiators and so lower the interfacial fracture toughness. Despite these differences in test set-ups, some consistent data have been reported by different research groups. For example, for Scotchbond MP (3M ESPE), a fracture toughness value of 0.45 MPa $\sqrt{m}$ has been recorded (Tam and Yim, 1997), which is in the same range as the value 0.38 MPa $\sqrt{m}$, obtained by Destoop (2003). Also, for All Bond 2 (Bisco), similar values of 0.88 and 0.80 MPa $\sqrt{m}$ were recorded (Tam and Yim, 1997; Armstrong *et al.*, 1998). The three-step etch-and-rinse adhesive OptiBond FL, in contrast, produced high values in one study (0.82 MPa $\sqrt{m}$; Armstrong *et al.*, 2001a), somewhat lower in another (0.63 MPa $\sqrt{m}$; Destoop, 2003), and could not be measured in a third study (Tam and Yim, 1997) because of very low bonding effectiveness.

Similar to bond strength tests, all kinds of 'aging' factors can be applied prior to fracture toughness measurements. However, in contrast to μTBS tests, it is not possible to prepare multiple specimens from the same tooth. Unfortunately, only a few studies have implemented such aging variables. Armstrong *et al.* (2001a) determined the μTBS and fracture toughness of a resin-dentin interface after 1 and 6 months of water storage. In contrast to μTBS, the fracture toughness did not decrease over that period.

(4.3) Fatigue Resistance

Typically, bonding effectiveness to tooth tissue is measured statically—for example, by shear bond or μTBS testing. In the clinical situation, however, tooth/composite bonds are seldom subjected to such acute tensile/shear stresses, but are subjected to cyclic sub-critical loads during function. Although each of these cycles alone will be insufficient to provoke failure, they will induce damage by generating cracks that grow with time and eventually result in marginal deterioration and loss of the

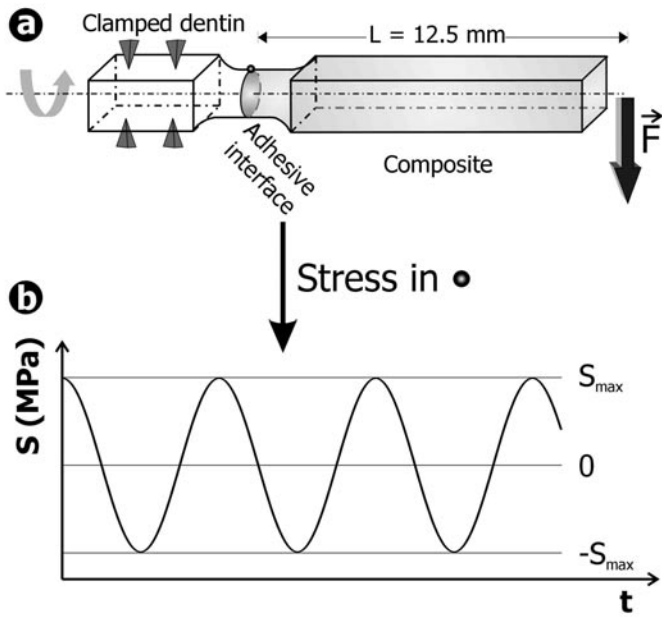

Figure 4. Working principle of the micro-rotary fatigue resistance (μRFR) test set-up. **(a)** A small rectangular beam with a rounded constriction at the tooth-biomaterial interface (diameter, 1.2 mm) is prepared by means of a diamond saw and a lathe. At a fixed distance of 12.5 mm from the interface (l = lever arm), a load (F) is applied, while the tooth part of the specimen is still clamped in the chuck of the lathe. Maximal stress (tension) is induced at the upper part of the interface (•). **(b)** When the specimen is rotated around its main axis, the outer layer of the interface (•) is subjected to sinusoidal tension-compression cycles (S = stress).

restoration. Fatigue can be defined as the failure of mechanical properties after repeated applications of stress, at a level well below the ultimate fracture strength of the material or interface. Consequently, fatigue tests provide information on the ability of a material or interface to resist the development of cracks as a result of a large number of cycles (Baran *et al.*, 2001).

Strength values are often looked at as indicators of structural performance. However, strength values are more determined by conditional factors such as stressing rate, stress concentrations, flaws, and test geometry rather than by material properties. Consequently, information regarding the material's microstructure, the test set-up, testing environment, and processing history is of critical value in the interpretation of strength data (Kelly, 1995). Especially, the importance of initiation of micro-cracks, flaws and other stress-raisers is often overlooked. Since a tooth-composite interface is complex and consists of materials with various properties, many potential initiation sites are present. A brittle (enamel) or semi-brittle material (dentin) is attached to an elastic-brittle resin composite (Jameson *et al.*, 1993; Baran *et al.*, 1999) with more elastic, ductile layers in between the adhesive resin and the hybrid layer (Van Meerbeek *et al.*, 1993). At all these interfaces, stress is easily built up and so can cause defects and flaws. Also, the heterogenic and anisotropic features of the involved materials are a source for initiation sites, with loosely cohering enamel prisms, porosities, and large composite glass fillers as obvious examples. Static bond strengths may not adequately demonstrate the effects these defects may have on bond durability, as can fatigue tests. Therefore, theoretically, *in vitro* fatigue testing of dental adhesives should serve as a good predictor of the *in vivo* mechanical performance of adhesives. Despite these inherent advantages, there are very little data on fatiguing of tooth-biomaterial interfaces (Dewji *et al.*, 1998). Even fewer studies address the fatigue resistance of contemporary adhesives bonded to enamel or dentin. In addition, to date, no standard fatigue test exists. Some research groups (Ruse *et al.*, 1995; Dewji *et al.*, 1998; Frankenberger *et al.*, 2003b) have applied cyclic stresses to standard shear bond strength specimens to determine the endurance limit of adhesives. Although such tests have drawbacks similar to those of static shear bond strength testing (Van Noort *et al.*, 1989; Sudsangiam and Van Noort, 1999), analysis of the data seems to provide a better insight into the *in vivo* behavior of adhesives (Ruse *et al.*, 1995). An alternative approach is a push-out set-up (Frankenberger *et al.*, 1999, 2003b): Standard conical cavities in dentin discs are restored with an adhesive and composite. Subsequently, these are pushed out in a (static or) cyclic way. This fatigue test yielded results similar to those obtained by static tests. One advantage of this push-out design is that it takes into account the effect polymerization stress might have in the clinical situation.

Another approach is based upon the classic rotating beam experiment (Wiskott *et al.*, 1994). With a miniaturized version of this test set-up, it is possible to apply tension-compression cycles to tooth-biomaterial interfaces (Fig. 4). An advantage of this method is that the specimens are very similar to standard μTBS specimens, thereby facilitating comparison with previous static results (De Munck *et al.*, 2005c). By this methodology, it was concluded that resin-tooth interfaces are vulnerable to progressive damage by subcritical loads, as was substantiated by SEM analysis that revealed typical fatigue fracture patterns. This set-up also allows for the preparation of multiple specimens *per* tooth, enabling balanced study designs to rule out the 'tooth' factor (De Munck *et al.*, 2005a).

(4.4) Leakage

One of the key functions of a dental restoration is to seal the exposed dentin from the oral environment, to prevent pulpal damage and further decay. Leakage of water and other products can occur along the interface through voids created during insertion or function. Based upon the size of these voids, two types of leakage can be distinguished: (1) If large voids are present, water, large molecules, and even bacteria can migrate along the restoration, in a process called 'microleakage'; or (2) if the voids are so small that only water and some small molecules can pass, the leakage is called 'nanoleakage'. The difference between both types is somewhat arbitrary, since both may occur simultaneously.

(4.4.1) Microleakage

Microleakage is defined as the clinically undetectable passage of bacteria, fluids, molecules, or ions between a cavity wall and the restorative material applied to it (Kidd, 1976). All resin-based restorative materials shrink and induce stress at the interface, which may lead to gap formation and interfacial stress. All current adhesives appear incapable of sealing the restoration margins and thus preventing microleakage (Pilo and Ben-Amar, 1999; Bouillaguet *et al.*, 2000; Grobler *et al.*, 2000; Hilton, 2002a). Many techniques have been used to assess microleakage, and the results vary considerably (Hilton, 2002b).

The use of organic dyes as tracers is one of the oldest and most common methods of detecting leakage *in vitro*. In general, this method for detecting microleakage involves the placement

of a restoration in an extracted tooth, followed by immersion of the tooth in a dye solution after the unfilled parts have been coated with a waterproof varnish. After a certain time interval, the specimens are removed, washed, and sectioned for visual examination to measure the extent of dye infiltration around the filling (Hilton, 2002b). Many dyes can be used with different particle sizes and affinity to substrates, but this does not seem to influence the test results significantly (Hilton, 2002b). In a well-controlled study design, it is theoretically possible to use the same aging factors as mentioned before. The main disadvantage of microleakage evaluation is that it is a qualitative method, which can be made semi-quantitative by the application of a non-parametric scale (Castelnuovo *et al.*, 1996). Generally, the results obtained in each study group differ only slightly, rendering interpretation of the results difficult and reducing the sensitivity of the test. Compared with bond-strength tests, the effect of artificial aging methods such as water storage and thermo-cycling on microleakage is minimal (Wendt *et al.*, 1992; Chan and Jones, 1994; Gwinnett and Yu, 1994; Gale and Darvell, 1999; Wahab *et al.*, 2003). However, microleakage seems more affected by mechanical load cycling (Abdalla and Davidson, 1990; Davidson and Abdalla, 1994; Jang *et al.*, 2001; Kubo *et al.*, 2001; Mitsui *et al.*, 2003), even more pronounced by additional thermo-cycling (Hilton, 2002b).

A quantitative method to assess microleakage is to measure the flow of fluid along the interface (Pagliarini *et al.*, 1996) or from the pulp to a sealed dentin surface (Derkson *et al.*, 1986; Bouillaguet *et al.*, 2000; Del-Nero *et al.*, 2000). The advantage of this method is that it is fully quantitative, and specimens can be followed longitudinally because of its non-destructive nature. The main disadvantage is that the nominal values are usually very low, so that the actual leakage path is sometimes unclear. Leakage may even occur through the dental substrate itself and so falsely increase the interfacial leakage values.

(4.4.2) Nanoleakage

Sano *et al.* (1994) revealed that leakage can occur between the hybrid layer and intact dentin, even when no gaps can be observed. This was morphologically assessed with extremely small Ag ions (Fig. 5). Because of the morphological and non-quantitative nature of this assessment, one must be very careful in interpreting the results of nanoleakage experiments, since appropriate controls are often absent (Agee *et al.*, 2003), and the results do not correlate with, for example, bond-strength tests. It is hypothesized that this tracer infiltration represents potential voids in the hybrid layer or within demineralized sub-micron spaces that have not effectively been filled by adhesive resin (Sano *et al.*, 1995). These voids are so small that bacteria may not be able to enter. Nevertheless, they make the bond more susceptible to hydrolytic degradation and bacterial by-products such as acids and enzymes (Paul *et al.*, 1999).

Recently, Tay *et al.* (2002a) reported that silver uptake may more likely represent areas of increased permeability within the resin matrix. In these zones, water is incompletely removed, resulting in regions of incomplete polymerization and/or hydrogel formation of the HEMA present in the adhesive systems. This water uptake along the cured adhesives was especially noted for one-step self-etch adhesives (Tay *et al.*, 2002b, 2003). One-step self-etch adhesives must consequently be regarded as semi-permeable membranes that attract water, as evidenced by a diffuse infiltration of the adhesive resin (Fig. 5).

One can also assess nanoleakage quantitively by measuring the dye penetration depth using confocal laser scanning microscopy (Dörfer *et al.*, 2000) or SEM (Li *et al.*, 2002a,b). The same artificial aging factors as used for other tests can also be applied to nanoleakage assessments. However, nanoleakage seems little affected by thermo-cycling (Li *et al.*, 2002a) or by mechanical load-cycling (Li *et al.*, 2002b). Water storage of the specimens, in contrast, resulted in increased nanoleakage, which even correlated well with a decrease in μTBS for some adhesives (Okuda *et al.*, 2001, 2002).

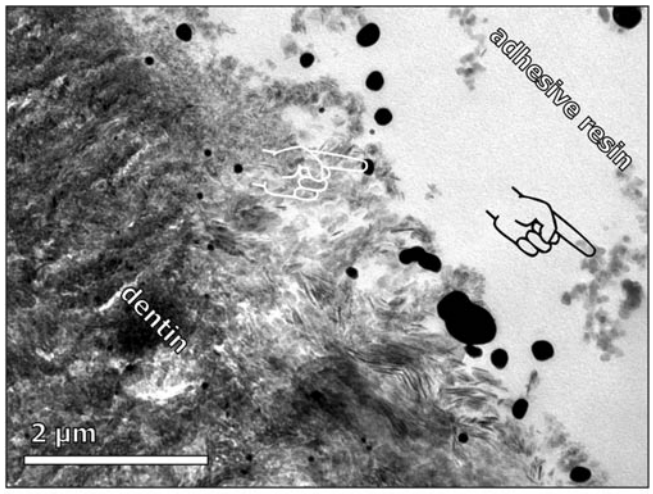

Figure 5. TEM photomicrograph showing the silver tracer penetration within an adhesive interface prepared with an experimental mild, one-step self-etch adhesive (acetone/water-based adhesive, containing HEMA and a carboxyl- and a phosphate-based functional monomer; GC, Japan). Tiny silver particles are scattered throughout the hybrid layer (white hand pointer) and the adhesive resin. Note also the nanofiller in the adhesive resin (black hand pointer).

(4.5) Marginal Analysis

Several *in vitro* studies have tested the performance of adhesives by evaluating the marginal gap formation around restorations placed in extracted teeth (Roulet *et al.*, 1989). This method assumes that if the forces generated by polymerization shrinkage or by thermo-mechanical strain exceed the bond strength, an observable gap will be formed at the margin of the restoration. Although there is no clear correlation between *in vitro* gap formation and interfacial failures observed *in vivo*, it is reasonable to assume that this marginal gap formation is clinically relevant (Roulet, 1994). The main advantage is that the original specimens can be used for longitudinal observation if epoxy replicas are used, rather than the original specimen. For that reason, measurements can be repeated after thermo-cycling, for example (Krejci *et al.*, 1993), or after long-term water storage (Blunck and Roulet, 2002). Even *in vivo* Class V restorations can be used for similar longitudinal marginal analysis studies (van Dijken and Hörstedt, 1997). A drawback is that it is a labor-intensive and time-consuming procedure.

(5) DURABILITY OF CURRENT ADHESIVES

The purpose of this section is to assess, based upon the *in vivo* and *in vitro* methodologies discussed above, the durability of resin-tooth interfaces. Because it is of no use to compare the results obtained with different adhesives in different studies, the durability was assessed *per* adhesive system. For some

contemporary adhesives, data on bond durability were gathered from published, controlled, *in vitro*, and *in vivo* studies, as listed in the Table. In an attempt at better interpretation of laboratory results in light of *in vivo* functioning of adhesives, *in vitro* data were linked to the results of Class V clinical trials, since they provide direct and objective information on bond durability (see above). Because of the different adhesion strategies, etch-and-rinse, self-etch, and glass-ionomer adhesives were analyzed separately.

In vivo, all possible aging factors interact simultaneously. Therefore, all possible artificial 'aging' methods were evaluated at the same time, to produce the best image possible of the *in vivo* behavior of adhesive restorations. Of all different tests, μTBS testing seems most appropriate for the application of artificial aging techniques, because: (1) this test is more sensitive to artificial aging than other tests, like fracture toughness, microleakage and nanoleakage tests (Gwinnett and Yu, 1994; Armstrong *et al.*, 2001a; Okuda *et al.*, 2001, 2002); (2) multiple μTBS specimens can be obtained *per* tooth, thus permitting balanced study designs to rule out 'tooth' variability; and (3) the μTBS test is widely used and accepted.

Table. List of *in vitro* and *in vivo* Studies Investigating Durability of Adhesion to Tooth Tissue

Reference	Test Method	Artificial Aging Method
Laboratory Testing		
Armstrong *et al.*, 2001a	μTBS, FT[a]	Water storage
Armstrong *et al.*, 2001b	μTBS	Water storage
Armstrong *et al.*, 2003	μTBS	Water storage
Blunck and Roulet, 2002	MA	Water storage
De Munck *et al.*, 2003b	μTBS	Water storage
De Munck *et al.*, 2005a	Fatigue	Cyclic loading
Drummond *et al.*, 1996	Fatigue	Cyclic loading
Frankenberger *et al.*, 1999	Fatigue	Cyclic loading
Frankenberger *et al.*, 2003b	Fatigue	Cyclic loading
Giannini *et al.*, 2003	SBS	Water storage
Gwinnett and Yu, 1994	SBS	Water storage
Hashimoto *et al.*, 2000	μTBS	*In vivo*
Hashimoto *et al.*, 2002	μTBS	Water storage
Hashimoto *et al.*, 2003a	μTBS	Water storage
Krejci *et al.*, 1994	MA	Mechanical loading, thermo-cycling
Meiers and Young, 2001	SBS	Water storage
Miyazaki *et al.*, 1998	SBS	Thermo-cycling
Miyazaki *et al.*, 2000	SBS	Thermo-cycling
Nikaido *et al.*, 2002a	μTBS	Mechanical loading, thermo-cycling
Nikaido *et al.*, 2002b	μTBS	Mechanical loading, thermo-cycling
Okuda *et al.*, 2001	μTBS, NL	Water storage
Okuda *et al.*, 2002	μTBS, NL	Water storage
Ruse *et al.*, 1995	Fatigue	Cyclic loading
Sano *et al.*, 1999	μTBS	*In vivo*
Shirai *et al.*, 2004	μTBS	Water storage
Shono *et al.*, 1999	μTBS	Water storage
Takahashi *et al.*, 2002	μTBS	*In vivo*
Xie *et al.*, 2002	μTBS	Thermo-cycling
Class V Clinical Trials	**Study Time (yrs)**	**Adhesives Tested**
Baratieri *et al.*, 2003	3	One-step
Boghosian, 1996	2	OptiBond FL
Brackett MG *et al.*, 2002	1	ScotchBond 1, Fuji II LC
Brackett WW *et al.*, 2002	1	Prompt L-Pop
Browning *et al.*, 2000	2	Scotchbond MP
Ianzano and Gwinnett, 1993	1	All Bond 2
Loguercio *et al.*, 2003	5	Vitremer, Dyract-PSA
Peumans *et al.*, 2003a	2	FujiBond LC
Peumans *et al.*, 2003b	2	Clearfil SE Bond
Swift *et al.*, 2001b	3	OptiBond Solo, Prime&Bond 2.1
Tyas and Burrow, 2001, 2002	3, 5	FujiBond LC
Türkün, 2003	2	Clearfil SE Bond, Prime&Bond NT
Van Dijken, 2000	3	EBS, One-step, Fuji II LC
Van Meerbeek *et al.*, 1996b	3	Bayer exp., Clearfil Liner Bond System, Scotchbond MP
Van Meerbeek *et al.*, 2004a	5	Permaquick, OptiBond FL

[a] μTBS = micro-tensile bond strength; SBS = shear bond strength; FT = fracture toughness; MA = marginal analysis by SEM; and NL = nanoleakage.

(5.2) Etch-and-Rinse Adhesives

From the 'traditional' three-step etch-and-rinse adhesives (Fig. 1), simplified two-step etch-and-rinse adhesives have been developed that combine the primer and adhesive resin into one application step. Because the three- and two-step etch-and-rinse adhesives produced by the same manufacturer mostly have similar compositions regarding solvent and adhesive monomers, they were considered together. Since the primer solvent within etch-and-rinse adhesives is a major factor affecting handling (Tay *et al.*, 1998) and performance (Carvalho *et al.*, 2003), the etch-and-rinse adhesives were categorized according to their respective solvent. In each category, the adhesive studied most frequently was chosen to represent its class of adhesives.

(5.2.1) Ethanol-based adhesives

The ethanol/water-based OptiBond adhesives (Kerr) are the most frequently studied commercial representatives of this category. The shear bond strength of the two-step version, OptiBond Solo (and later OptiBond Solo Plus), is significantly decreased by water storage (Meiers and Young, 2001; Giannini *et al.*, 2003), as well as by thermo-cycling (Miyazaki *et al.*, 1998). Also, the μTBS of OptiBond Solo decreased after 4 years of water storage, when the dentin interface was directly exposed to the storage medium (De Munck *et al.*, 2003b). Semi-quantitative marginal analysis (by SEM) after 1 year's water storage also revealed that the percentage of 'continuous' (gap-free) dentin margins decreased over time (Blunck and Roulet, 2002). The bonding effectiveness of the three-step etch-and-rinse version, in contrast, was not affected by water storage, thermo-cycling, and/or mechanical loading (Blunck and Roulet, 2002; De Munck *et al.*, 2003b, 2005c;

Frankenberger *et al.*, 2003b; Krejci *et al.*, 1994; Shirai *et al.*, 2005). Only when very small (cross-sectional areas of 0.4-0.6 mm^2) μTBS specimens were aged was a significant decrease in μTBS recorded for this three-step etch-and-rinse adhesive (Armstrong *et al.*, 2001a,b). The μTBS of other types of adhesives decreased at least to the same extent (Armstrong *et al.*, 2003). It seems reasonable to link this reduced *in vitro* durability of Optibond Solo to its reduced infiltration/hybridization capacity (Van Meerbeek *et al.*, 1999). Such a sub-optimal hybridization might explain, to a large extent, why the hybrid layer produced by the two-step version is more prone to hydrolytic degradation than that produced by the three-step etch-and-rinse version (De Munck *et al.*, 2003b). Despite these *in vitro* differences, both the two- and the three-step versions seem to function rather well *in vivo* (Boghosian, 1996; Swift *et al.*, 2001a,b; Van Meerbeek *et al.*, 2001, 2003, 2005a,b).

(5.2.2) Acetone-based adhesives

The representatives for this adhesive category were the three- and two-step adhesives, All-bond 2 and One-Step (BISCO), respectively. The bonding effectiveness of the two-step version decreased following thermo-cycling (Miyazaki *et al.*, 1998; Xie *et al.*, 2002) and water storage (Shono *et al.*, 1999; Okuda *et al.*, 2001). Just as with the other two-step etch-and-rinse adhesives, bond degradation could be prevented to a certain extent by a surrounding enamel seal (Hashimoto *et al.*, 2002). Only one study investigated the *in vitro* durability of the three-step etch-and-rinse adhesive, All-bond 2 (Gwinnett and Yu, 1994). In that study, the shear bond strength decreased significantly after 6 months of water storage, whereas no increase in microleakage could be detected over the same period. Although excellent *in vitro* bonding effectiveness can be obtained with acetone-based adhesives, the high technique-sensitivity of these types of adhesives may explain the less-than-optimal long-term results (Tay *et al.*, 1996a; Van Meerbeek *et al.*, 2001, 2003). These findings have been confirmed by clinical research. Almost 50% of the Class V restorations restored with One-step debonded during a three-year observation period (Burrow and Tyas, 1999; Van Dijken, 2000; Baratieri *et al.*, 2003). All-Bond 2 performed somewhat better, with retention rates of 98% after 1 year (Ianzano and Gwinnett, 1993) and 72% after 3 years (McCoy *et al.*, 1998).

(5.2.3) Water-based adhesives

Some supposedly lower-technique-sensitive adhesives use water-based primers. The most-studied commercial representatives are the three- and two-step etch-and-rinse adhesives, Scotchbond MP and ScotchBond 1, respectively (3M ESPE). No difference has been detected in short-term bonding effectiveness between the three- and two-step versions (Dunn and Söderholm, 2001; Armstrong *et al.*, 2003; De Munck *et al.*, 2003b). The bonds produced with the three-step version resisted dynamic loading in a fatigue test (Ruse *et al.*, 1995; Frankenberger *et al.*, 1999, 2003b). In the long run, the bonding effectiveness of Scotchbond MP is prone to some degradation by thermo-cycling as well as by water storage (Krejci *et al.*, 1994; Blunck and Roulet, 2002; Armstrong *et al.*, 2003; De Munck *et al.*, 2003b; Hashimoto *et al.*, 2003a). After *in vivo* functioning, the μTBS of ScotchBond MP decreased due to hydrolytic break-down of the interface (Hashimoto *et al.*, 2000). It has been hypothesized that this reduced durability is related to the incorporation of a high-molecular-weight polyalkenoic-acid co-polymer (De Munck *et al.*, 2003b). Phase separation was shown to occur, with the co-polymer being filtered out by the collagen network and deposited as a distinct gel on the surface of the collagen network (Van Meerbeek *et al.*, 1996a; Eliades *et al.*, 2001). In the extreme case, the gel may hinder adequate resin-interdiffusion, leading to hybrid layers consisting of collagen mainly infiltrated by the low-MW 2-hydroxyethylmethacrylate (HEMA) that was polymerized to linear poly-HEMA chains, and of residual water (solvent) that was insufficiently removed (and/or kept *in situ* due to HEMA). This rather poorly infiltrated and polymerized hybrid layer is more susceptible to degradation. In most studies, the two-step derivative, Scotchbond 1 (Single Bond outside Europe), seemed to lose much more of its bonding capacity, regardless of the artificial aging factor applied (Miyazaki *et al.*, 1998; Okuda *et al.*, 2001; Blunck and Roulet, 2002; Nikaido *et al.*, 2002b; Armstrong *et al.*, 2003; De Munck *et al.*, 2003b; Giannini *et al.*, 2003; Shirai *et al.*, 2005). However, the results from clinical studies with Scotchbond 1 do not always support the laboratory longevity studies. In one study, this two-step etch-and-rinse adhesive showed an excellent performance in a Class V clinical trial after 6 months of service (Perdigão *et al.*, 2001), while in a similar study the adhesive did not even fulfill the minimum ADA requirements (Brackett MG *et al.*, 2002; Brackett WW *et al.*, 2003). This considerable variability in bonding effectiveness is probably due to an operator-dependent technique-sensitivity. Over- or under-drying of acid-etched dentin, a very technique-sensitive step (Kanca, 1992; Tay *et al.*, 1996a,b), cannot explain this varying clinical effectiveness, since this particular adhesive is relatively insensitive to the amount of drying (Van Meerbeek *et al.*, 1998; Perdigão *et al.*, 2001). Conversely, *in vitro* research indicated that, with increasing thickness of the bonding layer (Zheng *et al.*, 2001), bond strengths decrease, probably because of incomplete solvent evaporation when thick layers of this water-based adhesive are applied. In the clinical study in which Scotchbond 1 performed rather poorly, each layer was only lightly air-dried (Brackett MG *et al.*, 2002). This may have resulted in poor solvent evaporation and thick adhesive layers. The application of a solvent-free bonding layer in a third step may overcome problems associated with residual solvent and fulfills the need (in light of the 'elastic bonding' concept) for a thick bonding layer at the same time (Kemp-Scholte and Davidson, 1990; Van Meerbeek *et al.*, 1993). This hypothesis is corroborated by the excellent clinical results (up to 3 years) for the three-step version, Scotchbond MP (Van Meerbeek *et al.*, 1996b; Browning *et al.*, 2000; Ozgunaltay and Onen, 2002).

(5.2.4) Conclusions regarding etch-and-rinse adhesives

Class V clinical trials have shown that most etch-and-rinse adhesives fulfill the ADA requirements, when the adhesive was applied correctly. Some adhesives are more difficult to apply and thus are less preferred in demanding clinical situations:

(1) Acetone-based adhesives require the use of the 'wet bonding' technique with a relatively small 'window of opportunity' to achieve optimal hybridization (Tay *et al.*, 1998). The resultant technique-sensitivity renders it difficult to apply these adhesives properly in the often-complex *in vivo* cavity configurations.

(2) It is more difficult for simplified two-step adhesives to infiltrate the demineralized collagen mesh fully and to remove all residual solvents, especially water, because of its low vapor pressure.

Consequently, three-step ethanol-water-based etch-and-rinse adhesives are still regarded as the 'gold standard' in terms of bond durability, especially in demanding cavity preparations that have exposed dentin margins.

(5.3) Self-etch Adhesives

Self-etch adhesives make use of acidic monomers that simultaneously etch and prime dentin. Without the need for rinsing, the application time of self-etch adhesives is shorter and the technique-sensitivity lower. In its most conventional form, the application of the self-etch primer is followed by the application of a hydrophobic bonding resin (Fig. 1). Just as was the case with etch-and-rinse adhesives, simplified adhesives that combine the (self-etch) primer with the adhesive resin were developed to create what is known as the one-step self-etch adhesives or so-called 'all-in-one' adhesives.

Because of the limited amount of *in vitro* and *in vivo* data available on these recently developed products, however, it is impossible to evaluate all one-step and two-step, mild and strong self-etch adhesives separately. Nevertheless, the bond produced by mild two-step self-etch adhesives to dentin seems quite stable *in vitro*: (1) No significant decrease in μTBS occurred after 1 year of function *in vivo* (Sano *et al.*, 1999; Takahashi *et al.*, 2002), although SEM fracture analysis revealed an increased porosity within the adhesive resin; (2) up to 30,000 thermal cycles did not significantly decrease the shear bond strength (Miyazaki *et al.*, 1998); (3) combined thermal and occlusal loading resulted in a small but statistically insignificant decrease of μTBS (Nikaido *et al.*, 2002a); and (4) long-term water storage decreased the μTBS of two-step self-etch adhesives (Armstrong *et al.*, 2003; Shirai *et al.*, 2005), but not more than other adhesive systems.

There is little information available regarding the durability of one-step self-etch adhesives. In general, their short-term bonding effectiveness is disappointing (Inoue *et al.*, 2001a; De Munck *et al.*, 2003a, 2005b), and must certainly compromise their long-term usefulness. An example of these one-step self-etch adhesives is the 'strong' self-etch adhesive Adper Prompt (3M ESPE), and its predecessor Prompt L-Pop, for which some information on bond durability is available. In two *in vitro* studies, the μTBS of water-stored specimens was so low that most specimens did not survive specimen processing (Armstrong *et al.*, 2003; Shirai *et al.*, 2005).

There is even less information available on the durability of self-etch adhesives bonded to enamel. In one study, the bond strength decreased after thermo-cycling (Miyazaki *et al.*, 2000). However, this reduced bonding capacity seemed to have little influence on the *in vivo* bonding to enamel (Peumans *et al.*, 2003b).

Despite the limited amount of *in vitro* data, it can be concluded that the bonds obtained by 'mild' two-step self-etch adhesives seem quite durable, in contrast to 'all-in-one' adhesives that produce less durable bonds *in vitro*. These findings are corroborated by clinical research: The 'strong' one-step self-etch adhesive, Prompt L-Pop, performed very poorly, with a retention rate of 65% after 1 year (Brackett WW *et al.*, 2002), in contrast to the 'mild' two-step self-etch adhesive, Clearfil SE Bond, that exhibited excellent results for up to 2 years (Peumans *et al.*, 2003b; Türkün, 2003).

(5.4) Glass Ionomers

Currently, glass ionomers are the only self-adhesive restorative materials, due to ionic-bond formation between the carboxyl groups of polyalkenoic acid with hydroxyapatite (HAp) at the tooth surface (Yoshida *et al.*, 2000). Currently, only one resin-modified glass-ionomer adhesive is commercially available (FujiBond LC, GC) to bond resin composites to enamel and dentin. Though the initial bond strength was quite favorable, the μTBS decreased over time as a result of water storage (De Munck *et al.*, 2004). This correlated well with the decrease in μTBS of almost 50% after 1 year of *in vivo* function (Takahashi *et al.*, 2002). This degradation process must probably be ascribed to decreased material properties rather than to decreased bonding potential. The clinical bonding effectiveness seems not to be affected, however, since the retention rates in clinical Class V trials (up to 5 years) are very high and approximate those achieved with the three-step etch-and-rinse 'gold standard' (Tyas and Burrow, 2001, 2002; Loguercio *et al.*, 2003; Peumans *et al.*, 2003a). Despite the esthetic disadvantages (Gladys *et al.*, 1999), resin-modified glass-ionomer restoratives provide a viable alternative for Class V restorations (Gladys *et al.*, 1999; Folwaczny *et al.*, 2000; Van Dijken, 2000; Brackett MG *et al.*, 2002).

(6) CONCLUSION

Non-carious Class V clinical trials remain the ultimate test method for the assessment of bonding effectiveness, but in addition to their high costs, they are time- and labor-consuming, and they cannot identify the true cause of clinical failure. Therefore, several techniques to predict bond durability *in vitro* have been developed. Most *in vitro* durability studies mimic one of the *in vivo* degradation factors involved, to disclose its effect on the general degradation process, in contrast to the clinical situation, where all these factors are operational simultaneously.

When *in vitro* and *in vivo* bonding effectiveness data were correlated, some clear associations were apparent. Adhesives that performed less well in several independent laboratory studies also appeared to be less clinically effective. Consequently, in contrast to common belief, clinical effectiveness of adhesives can be predicted. This analysis also revealed that, despite the fact that adhesives are sensitive to mechanical fatigue phenomena, the major factor affecting durability *in vivo* is hydrolysis of interface components, such as collagen and resin, and subsequent elution of the breakdown products. Currently, the most validated method for the assessment of this degradation process *in vitro* is the storage of micro-specimens in water. Within about 3 months, all classes of adhesives exhibited mechanical and morphological evidence of degradation that resembles *in vivo* aging. Consequently, the hydrolytic stability of cured adhesives is of crucial importance. The best way to achieve this goal is to apply a solvent-free, neutral-pH, hydrophobic adhesive resin layer in a separate step. This has been confirmed by the inferior *in vitro* and *in vivo* results obtained with two-step etch-and-rinse and one-step self-etch adhesives. These adhesives, because of their hydrophilic nature, act as semi-permeable membranes, attract water, and degrade faster than hydrophobic adhesives.

A comparison of contemporary adhesives reveals that the three-step, ethanol-water-based etch-and-rinse adhesives remain the 'gold standard' in terms of adhesion durability. Any kind of simplification in the clinical application procedure results in a loss of bonding effectiveness. Only two-step self-

etch adhesives most closely approach this standard, and have additional clinical benefits such as ease of manipulation and reduced technique-sensitivity.

(7) RECOMMENDATIONS FOR FUTURE RESEARCH

The purpose of this section is to point out some shortcomings in the currently available adhesive systems that, if improved, may enhance bond durability. A topic already mentioned is the hydrolytic instability of the various components at the tooth-biomaterial interface. Some adhesive monomers (*e.g.*, phenyl-P) are known to hydrolyze over time and so compromise long-term bonding effectiveness (Yoshida *et al.*, 2004). Also, hydrolysis of exposed collagen fibrils, even enhanced by host-derived metalloproteinases, is an issue (Pashley *et al.*, 2004). A solution to this problem might be achieved, for instance, by: (1) only partially exposing these fibrils, as do mild self-etch and glass-ionomer adhesives; or (2) incorporating the appropriate degradation inhibitors into the bonding procedure.

Micro-mechanical interlocking is believed to be a prerequisite to the achievement of a strong mechanical bond as shown by μTBS testing. Additional chemical adhesion may be beneficial in terms of durability, since it ensures an intimate adaptation of both the substrate and biomaterial components, thereby preventing nanoleakage (Sano *et al.*, 1999). Two components of the tooth substrate can be used to bond to collagen fibrils and hydroxyapatite crystals. Binding to collagen fibrils can be achieved only by hydrogen bonds; however, these are relatively weak and unstable, especially in an aqueous environment. However, the calcium available in hydroxyapatite can serve as as a receptor for stronger ionic bond formation (Yoshida *et al.*, 2004).

Most current durability studies focus on the adhesion to dentin and consider the enamel bond as strong and stable. Indeed, it has been well-established that strong and durable bonds to enamel can be produced by the well-established phosphoric-acid etch technique, followed by the application of a fluid hydrophobic adhesive resin. Contemporary two-step etch-and-rinse adhesives and self-etch adhesives, however, make use of resins that are more hydrophilic and conditioners that are less acidic (at least for the self-etch adhesives). Though the use of these new formulations raised the dentin bonding effectiveness of some new adhesives to a level comparable with that of the 'gold standard' three-step etch-and-rinse approach, their bonds to enamel may be compromised. Also, a tight protective enamel-resin seal may not necessarily be accomplished, since some of these adhesives act as semi-permeable membranes. Unfortunately, these are only speculations, since nearly no research has been performed to determine the durability of contemporary simplified adhesives bonded to enamel.

A trend in adhesive dentistry is to provide simpler and faster adhesives. Therefore, many manufacturers have launched an 'all-in-one' adhesive. None of the contemporary 'all-in-one' adhesives, however, can compete with the more traditional multi-step adhesives. Reasons for this inadequate performance are numerous, but the most important are that: (1) they are too hydrophilic and act, even after polymerization, as semi-permeable membranes; (2) because of the high solvent concentration, it is impossible to obtain an adhesive resin layer of adequate thickness and void from residual solvent; (3) during solvent evaporation, the monomer/water ratio may change and subsequently result in phase separations and blistering; and (4) the acidic components of these adhesives may also adversely interact with the initiator system of the composite and so weaken the bonding complex. If these problems are properly addressed, it must be possible to produce a universally applicable and reliable adhesive that is easier and faster to manipulate.

All current resin composites shrink by about 2-4%. The resultant polymerization shrinkage stress puts the immature bond under severe tension, which may lead to early failures of, especially, simplified adhesives. A non-shrinking composite may allow the bond to mature and so improve the short- as well as the long-term bonding effectiveness.

The ultimate goal is to develop self-adhesive restorative biomaterials that no longer need an adhesive for bonding to tooth tissue. Although glass ionomers and their derivatives can be considered as self-adhering restoratives, they lack other clinically relevant properties, such as sufficient mechanical strength, wear resistance, polishability, and, thus, esthetics. In brief, the concept of 'minimally invasive dentistry' may require a different set of restorative materials with physical and chemical properties adapted to the biomechanical needs of these new techniques.

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REFERENCES

Abdalla AI, Davidson CL (1990). Effect of mechanical load cycling on the marginal integrity of adhesive Class I resin composite restorations. *J Dent* 24:87-90.

Agee KL, Pashley EL, Itthagarun A, Sano H, Tay FR, Pashley DH (2003). Submicron hiati in acid-etched dentin are artifacts of desiccation. *Dent Mater* 19:60-68.

Armstrong SR, Boyer DB, Keller JC, Park JB (1998). Effect of hybrid layer on fracture toughness of adhesively bonded dentin-resin composite joint. *Dent Mater* 14:91-98.

Armstrong SR, Keller JC, Boyer DB (2001a). Mode of failure in the dentin-adhesive resin-resin composite bonded joint as determined by strength-based (μTBS) and fracture-based (CNSB) mechanical testing. *Dent Mater* 17:201-210.

Armstrong SR, Keller JC, Boyer DB (2001b). The influence of water storage and C-factor on the dentin-resin composite microtensile bond strength and debond pathway utilizing a filled and unfilled adhesive resin. *Dent Mater* 17:268-276.

Armstrong SR, Vargas MA, Fang Q, Laffoon JE (2003). Microtensile bond strength of a total-etch 3-step, total-etch 2-step, self-etch 2-step, and a self-etch 1-step dentin bonding system through 15-month water storage. *J Adhes Dent* 5:47-56.

Baran GR, McCool JI, Boberick KG, Zhang HQ (1999). Size effect in resin/glass composite flexure strengths. *J Oral Rehabil* 26:775-780.

Baran G, Boberick K, McCool J (2001). Fatigue of restorative materials. *Crit Rev Oral Biol Med* 12:350-360.

Baratieri LN, Canabarro S, Lopes GC, Ritter AV (2003). Effect of resin viscosity and enamel beveling on the clinical performance of class V composite restorations: three-year results. *Oper Dent* 28:482-487.

Bayne SC, Heymann HO, Sturdevant JR, Wilder AD, Sluder TB (1991). Contributing co-variables in clinical trials. *Am J Dent* 4:247-250.

Blunck U, Roulet JF (2002). Effect of one-year water storage on the effectiveness of dentin adhesives in class V composite resin restorations (abstract). *J Dent Res* 81(Spec Iss B):946 (www.dentalresearch.org).

Boghosian A (1996). Clinical evaluation of a filled adhesive system in Class 5 restorations. *Compend Contin Educ Dent* 17:750-754.

Bouillaguet S, Duroux B, Ciucchi B, Sano H (2000). Ability of adhesive systems to seal dentin surfaces: an in vitro study. *J Adhes Dent* 2:201-208.

Brackett MG, Dib A, Brackett WW, Estrada BE, Reyes AA (2002). One-year clinical performance of a resin-modified glass ionomer and a resin composite restorative material in unprepared class V restorations. *Oper Dent* 27:112-116.

Brackett WW, Covey DA, St-Germain HA Jr (2002). One-year clinical performance of a self-etching adhesive in class V resin composites cured by two methods. *Oper Dent* 27:218-222.

Brackett WW, Dib A, Brackett MG, Reyes AA, Estrada BE (2003). Two-year clinical performance of class V resin-modified glass-ionomer and resin composite restorations. *Oper Dent* 28:477-481.

Braem M, Lambrechts P, Vanherle G (1992). Stress-induced cervical lesions. *J Prosthet Dent* 67:718-722.

Browning WD, Brackett WW, Gilpatrick RO (2000). Two-year clinical comparison of a microfilled and a hybrid resin-based composite in non-carious class V lesions. *Oper Dent* 25:46-50.

Buonocore DH (1955). A simple method of increasing the adhesion of acryl filling materials to enamel surfaces. *J Dent Res* 34:849-853.

Burrow MF, Tyas MJ (1999). 1-year clinical evaluation of one-step in non-carious cervical lesions. *Am J Dent* 12:283-285.

Burrow MF, Satoh M, Tagami J (1996). Dentin bond durability after three years using a dentin bonding agent with and without priming. *Dent Mater* 12:302-307.

Cardoso PE, Placido E, Moura SK (2002). Micro-leakage of four simplified adhesive systems under thermal and mechanical stresses. *Am J Dent* 15:164-168.

Carvalho RM, Pereira JC, Yoshiyama M, Pashley DH (1996). A review of polymerization contraction: the influence of stress development versus stress relief. *Oper Dent* 21:17-24.

Carvalho RM, Mendonca JS, Santiago SL, Silveira RR, Garcia FC, Tay FR, *et al.* (2003). Effects of HEMA/solvent combinations on bond strength to dentin. *J Dent Res* 82:597-601.

Castelnuovo J, Tjan AHL, Liu P (1996). Micro-leakage of multi-step and simplified-step bonding systems. *Am J Dent* 9:245-248.

Chan MF, Jones JC (1994). Significance of thermal cycling in micro-leakage analysis of root restorations. *J Dent* 22:292-295.

Davidson CL, Abdalla AI (1994). Effect of occlusal load cycling on the marginal integrity of adhesive class V restorations. *Am J Dent* 7:111-114.

DeHoff PH, Anusavice KJ, Wang Z (1995). Three-dimensional finite element analysis of the shear bond test. *Dent Mater* 11:126-131.

De Munck J, Van Meerbeek B, Inoue S, Vargas M, Yoshida Y, Armstrong S, *et al.* (2003a). Micro-tensile bond strength of one- and two-step self-etch adhesives to bur-cut enamel and dentin *Am J Dent* 16:414-420.

De Munck J, Van Meerbeek B, Yoshida Y, Inoue S, Vargas M, Suzuki K, *et al.* (2003b). Four-year water degradation of total-etch adhesives bonded to dentin. *J Dent Res* 82:136-140.

De Munck J, Van Meerbeek B, Yoshida Y, Inoue S, Suzuki K, Lambrechts P (2004). Four-year water degradation of a glass-ionomer adhesive bonded to dentin. *Eur J Oral Sci* 112:73-83.

De Munck J, Van Meerbeek B, Van Landuyt K, Lambrechts P (2005a). Influence of a shock absorbing layer on the fatigue resistance of a dentin-biomaterial interface. *Eur J Oral Sci* 113:1-6.

De Munck J, Van Meerbeek B, Vargas M, Iracki J, Van Landuyt K, Poitevin A, *et al.* (2005b). One day bonding effectiveness of new self-etch adhesives to bur-cut enamel and dentin. *Oper Dent* 30:39-49.

De Munck J, Van Meerbeek B, Wevers M, Lambrechts P, Braem M (2005c). Micro-rotary fatigue of tooth-biomaterial interfaces. *Biomaterials* 26:1145-1153.

Del-Nero MO, Escribano N, de la Macorra JC (2000). Analysis of sealing vs. tensile bond strength of eight adhesive restorative material systems. *J Adhes Dent* 2:117-127.

Derkson GD, Pashley DH, Derkson ME (1986). Micro-leakage measurement of selected restorative materials: a new in vitro method. *J Prosthet Dent* 56:435-440.

Destoop V (2003). The cracking resistance and adhesion to dentine of dental restorative materials: a fracture mechanics approach (Doctoral thesis). Leuven: Université Catholique de Louvain, Belgium.

Dewji HR, Drummond JL, Fadavi S, Punwani I (1998). Bond strength of Bis-GMA and glass-ionomer pit and fissure sealants using cyclic fatigue. *Eur J Oral Sci* 106:594-599.

Dietschi D, Herzfeld D (1998). In vitro evaluation of marginal and internal adaptation of class II resin composite restorations after thermal and occlusal stressing. *Eur J Oral Sci* 106:1033-1042.

Dörfer CE, Staehle HJ, Wurst MW, Duschner H, Pioch T (2000). The nano-leakage phenomenon: influence of different dentin bonding agents, thermocycling and etching time. *Eur J Oral Sci* 108:346-351.

Drummond JL, Sakaguchi RL, Racean DC, Wozny J, Steinberg AD (1996). Testing mode and surface treatment effects on dentin bonding. *J Biomed Mater Res* 32:533-541.

Dunn WJ, Söderholm KJ (2001). Comparison of shear and flexural bond strength tests versus failure modes of dentin bonding systems. *Am J Dent* 14:297-303.

Eick JD, Gwinnett AJ, Pashley DH, Robinson SJ (1997). Current concepts on adhesion to dentin. *Crit Rev Oral Biol Med* 81:306-335.

Eliades G, Vougiouklakis G, Palaghias G (2001). Heterogeneous distribution of single-bottle adhesive monomers in the resin-dentin interdiffusion zone. *Dent Mater* 17:277-283.

Feilzer AJ, De Gee AJ, Davidson CL (1987). Setting stress in composite resin in relation to configuration of the restauration. *J Dent Res* 66:1636-1639.

Ferracane JL, Berge HX, Condon JR (1998). In vitro aging of dental composites in water—effect of degree of conversion, filler volume, and filler/matrix coupling. *J Biomed Mater Res* 42:465-472.

Ferrari M, Mannocci F, Cagidiaco MC, Kugel G (1997). Short-term assessment of leakage of class V composite restorations placed in vivo. *Clin Oral Invest* 1:61-64.

Finer Y, Santerre JP (2004). Salivary esterase activity and its association with the biodegradation of dental composites. *J Dent Res* 83:22-26.

Folwaczny M, Loher C, Mehl A, Kunzelmann KH, Hickel R (2000). Tooth-colored filling materials for the restoration of cervical lesions: a 24-month follow-up study. *Oper Dent* 25:251-258.

Frankenberger R, Krämer N, Petschelt A (1999). Fatigue behaviour of different dentin adhesives. *Clin Oral Invest* 3:11-17.

Frankenberger R, Krämer N, Petschelt A (2000). Long-term effect of dentin primers on enamel bond strength and marginal adaptation. *Oper Dent* 25:11-19.

Frankenberger R, Roth S, Kramer N, Pelka M, Petschelt A (2003a). Effect of preparation mode on Class II resin composite repair. *J Oral Rehabil* 30:559-564.

Frankenberger R, Strobel WO, Kramer N, Lohbauer U, Winterscheidt J, Winterscheidt B, *et al.* (2003b). Evaluation of the fatigue behavior of the resin-dentin bond with the use of different methods. *J Biomed Mater Res Part B: Appl Biomater* 67(B):712-721.

Fukushima T, Inoue Y, Miyazaki K, Itoh T (2001). Effect of primers containing N-methylolacrylamide or N-methylolmethacrylamide on dentin bond durability of a resin composite after 5 years. *J Dent* 29:227-234.

Gale MS, Darvell BW (1999). Thermal cycling procedures for laboratory testing of dental restorations. *J Dent* 27:89-99.

Giannini M, Seixas CAM, Reis AF, Pimenta LAF (2003). Six-month storage-time evaluation of one-bottle adhesive systems to dentin. *J Esthet Rest Dent* 15:43-49.

Gladys S, Van Meerbeek B, Lambrechts P, Vanherle G (1999). Evaluation of esthetic parameters of resin-modified glass-ionomer materials and a polyacid-modified resin composite in Class V cervical lesions. *Quintessence Int* 30:607-614.

Grobler SR, Oberholzer TG, Rossouw RJ, Grobler-Rabie A, Van Wyk Kotze TJ (2000). Shear bond strength, micro-leakage, and confocal microscopy of 4 amalgam alloy bonding agents. *Quintessence Int* 31:501-508.

Gwinnett AJ, Yu S (1994). Effect of long-term water storage on dentin bonding. *Am J Dent* 7:109-111.

Hashimoto M, Ohno H, Kaga M, Endo K, Sano H, Oguchi H (2000). In vivo degradation of resin-dentin bonds in humans over 1 to 3 years. *J Dent Res* 79:1385-1391.

Hashimoto M, Ohno H, Sano H, Tay FR, Kaga M, Kudou Y, *et al.* (2002). Micromorphological changes in resin-dentin bonds after 1 year of water storage. *J Biomed Mater Res* 63:306-311.

Hashimoto M, Ohno H, Sano H, Kaga M, Oguchi H (2003a). In vitro degradation of resin-dentin bonds analyzed by microtensile bond test, scanning and transmission electron microscopy. *Biomaterials* 24:3795-3803.

Hashimoto M, Tay FR, Ohno H, Sano H, Kaga M, Yiu C, *et al.* (2003b). SEM and TEM analysis of water degradation of human dentinal

collagen. *J Biomed Mater Res* 66(B):287-298.
Hilton TJ (2002a). Can modern restorative procedures and materials reliably seal cavities? In vitro investigations. Part 1. *Am J Dent* 15:198-210.
Hilton TJ (2002b). Can modern restorative procedures and materials reliably seal cavities? In vitro investigations. Part 2. *Am J Dent* 15:279-289.
Ianzano JA, Gwinnett AJ (1993). Clinical evaluation of Class V restorations using a total etch technique: 1-year results. *Am J Dent* 6:207-210.
Inoue S, Van Meerbeek B, Abe Y, Yoshida Y, Lambrechts P, Vanherle G, *et al.* (2001a). Effect of remaining dentin thickness and the use of conditioner on micro-tensile bond strength of a glass-ionomer adhesive. *Dent Mater* 17:445-455.
Inoue S, Vargas MA, Van Meerbeek B, Abe Y, Yoshida Y, Lambrechts P, *et al.* (2001b). Micro-tensile bond strength of eleven modern adhesives to dentin. *J Adhes Dent* 3:237-246.
Inoue S, Vargas MA, Abe Y, Yoshida Y, Lambrechts P, Vanherle G, *et al.* (2003). Micro-tensile bond strength of eleven contemporary adhesives to enamel. *Am J Dent* 16:329-334.
International Organization for Standardization (1994). ISO TR 11405, Dental materials—guidance on testing of adhesion to tooth structure.
Iracki J, De Munck J, Shirai K, Lambrechts P, Van Meerbeek B (2003). Micro-tensile bond strength of a contemporary total-etch and self-etch adhesive after in vivo degradation (abstract). *J Dent Res* 82(Spec Iss B):46 (www.dentalresearch.org).
Jaffer F, Finer Y, Santerre JP (2002). Interactions between resin monomers and commercial composite resins with human saliva derived esterases. *Biomaterials* 23:1707-1719.
Jameson MW, Hood JA, Tidmarsh BG (1993). The effects of dehydration and rehydration on some mechanical properties of human dentine. *J Biomech* 26:1055-1065.
Jang KT, Chung DH, Shin D, Garcia-Godoy F (2001). Effect of eccentric load cycling on micro-leakage of Class V flowable and packable composite resin restorations. *Oper Dent* 26:603-608.
Kanca J (1992). Effect of resin primer solvents and surface wetness on resin composite bond strength to dentin. *Am J Dent* 5:213-215.
Kato G, Nakabayashi N (1998). The durability of adhesion to phosphoric acid etched, wet dentin substrates. *Dent Mater* 14:347-352.
Kelly JR (1995). Perspectives on strength. *Dent Mater* 11:103-110.
Kemp-Scholte CM, Davidson CL (1990). Complete marginal seal of class V resin composite restorations effected by increased flexibility. *J Dent Res* 69:1240-1243.
Khajotia SS, Dhuru VB, Fournelle RA, McKinney MA (1997). Fracture toughness and load relaxation of dentin bonding resin systems. *Dent Mater* 13:151-156.
Kidd EAM (1976). Micro-leakage: a review. *J Dent* 4:199-206.
Kitasako Y, Burrow MF, Nikaido T, Tagami J (2000). The influence of storage solution on dentin bond durability of resin cement. *Dent Mater* 16:1-6.
Krejci I, Kuster M, Lutz F (1993). Influence of dentinal fluid and stress on marginal adaptation of resin composites. *J Dent Res* 71:490-494.
Krejci I, Häusler T, Sägesser D, Lutz F (1994). New adhesives in class V restorations under combined load and simulated dentinal fluid. *Dent Mater* 10:331-335.
Kubo S, Yokota H, Sata Y, Hayashi Y (2001). The effect of flexural load cycling on the micro-leakage of cervical resin composites. *Oper Dent* 26:451-459.
Leloup G, D'Hoore W, Bouter D, Degrange M, Vreven J (2001). Meta-analytical review of factors involved in dentin adherence. *J Dent Res* 80:1605-1614.
Li H, Burrow MF, Tyas MJ (2002a). The effect of load cycling on the nano-leakage of dentin bonding systems. *Dent Mater* 18:111-119.
Li H, Burrow MF, Tyas MJ (2002b). The effect of thermocycling regimens on the nano-leakage of dentin bonding systems. *Dent Mater* 18:189-196.
Lin A, McIntyre NS, Davidson RD (1992). Studies on the adhesion of glass ionomer cements to dentin. *J Dent Res* 71:1836-1841.
Loguercio AD, Reis A, Barbosa AN, Roulet J-F (2003). Five-year double-blind randomized clinical evaluation of a resin-modified glass ionomer and a polyacid-modified resin in noncarious cervical lesions. *J Adhes Dent* 5:323-332.
McCoy RB, Anderson MH, Lepe X, Johnson GH (1998). Clinical success of class V composite resin restorations without mechanical retention. *J Am Dent Assoc* 129:593-599.
Meiers JC, Young D (2001). Two-year composite/dentin bond stability. *Am J Dent* 14:141-144.
Mitsui FH, Bedran de Castro AK, Ritter AV, Cardoso PE, Pimenta LA (2003). Influence of load cycling on marginal micro-leakage with two self-etching and two one-bottle dentin adhesive systems in dentin. *J Adhes Dent* 5:209-216.
Miyazaki M, Sato M, Onose H, Moore BK (1998). Influence of thermal cycling on dentin bond strength of two-step bonding systems. *Am J Dent* 11:118-122.
Miyazaki M, Sato M, Onose H (2000). Durability of enamel bond strength of simplified bonding systems. *Oper Dent* 25:75-80.
Mjör IA, Gordan VV (2002). Failure, repair, refurbishing and longevity of restorations. *Oper Dent* 27:528-534.
Mjör IA, Shen C, Eliasson ST, Richter S (2002). Placement and replacement of restorations in general dental practice in Iceland. *Oper Dent* 27:117-123.
Nakabayashi N, Kojima K, Masuhara E (1982). The promotion of adhesion by the infiltration of monomers into tooth substrates. *J Biomed Mater Res* 16:1240-1243.
Nikaido T, Kunzelman KH, Chen H, Ogata M, Harada N, Yamaguchi S, *et al.* (2002a). Evaluation of thermal cycling and mechanical loading on bond strength of a self-etching primer system to dentin. *Dent Mater* 18:269-275.
Nikaido T, Kunzelmann KH, Ogata M, Harada N, Yamaguchi S, Cox CF, *et al.* (2002b). The in vitro dentin bond strengths of two adhesive systems in class I cavities of human molars. *J Adhes Dent* 4:31-39.
Okuda M, Pereira PN, Nakajima M, Tagami J (2001). Relationship between nano-leakage and long-term durability of dentin bonds. *Oper Dent* 26:482-490.
Okuda M, Pereira PNR, Nakajima M, Tagami J, Pashley DH (2002). Long-term durability of resin dentin interface: nano-leakage vs. microtensile bond strength. *Oper Dent* 27:289-296.
Ozgunaltay G, Onen A (2002). Three-year clinical evaluation of a resin modified glass-ionomer cement and a composite resin in non-carious class V lesions. *J Oral Rehabil* 29:1037-1041.
Pagliarini A, Rubini R, Rea M, Campese C, Grandini R (1996). Effectiveness of the current enamel-dentinal adhesives: a new methodology for its evaluation. *Quintessence Int* 27:265-270.
Pashley DH, Sano H, Ciucchi B, Yoshiyama M, Carvalho RM (1995). Adhesion testing of dentin bonding agents. *Dent Mater* 11:117-125.
Pashley DH, Carvalho RM, Sano H, Nakajima M, Shono Y, Fernandes CA, *et al.* (1999). The microtensile bond test: a review. *J Adhes Dent* 1:299-309.
Pashley DH, Tay FR, Yiu C, Hashimoto M, Breschi L, Carvalho RM, *et al.* (2004). Collagen degradation by host-derived enzymes during aging. *J Dent Res* 83:216-221.
Paul SJ, Welter DA, Ghazi M, Pashley D (1999). Nano-leakage at the dentin adhesive interface vs μ-tensile bond strength. *Oper Dent* 24:181-188.
Perdigão J, Carmo AR, Geraldeli S, Dutra HR, Masuda MS (2001). Six month clinical evaluation of two dentin adhesives applied on dry vs moist dentin. *J Adhes Dent* 3:343-352.
Peumans M, Van Meerbeek B, Lambrechts P, Vanherle G (2003a). Two-year clinical effectiveness of a resin-modified glass-ionomer adhesive. *Am J Dent* 16:363-368.
Peumans M, Van Meerbeek B, De Munck J, Lambrechts P (2003b). Two-year clinical effectiveness of a self-etch adhesive in cervical lesions (abstract). *J Dent Res* 82(Spec Iss B):911 (www.dentalresearch.org).
Phrukkanon S, Burrow MF, Tyas M (1998). The influence of cross-sectional shape and surface area on the microtensile bond test. *Dent Mater* 14:212-221.
Pilo R, Ben-Amar A (1999). Comparison of micro-leakage for three one-bottle and three multiple-step dentin bonding agents. *J Prosthet Dent* 82:209-213.
Prati C, Chersoni S, Mongiorgi G, Pashley DH (1999). Thickness and morphology of resin-infiltrated dentin layer in young, old, and sclerotic dentin. *Oper Dent* 24:66-72.
Rees JS (2002). The effect of variation in occlusal loading on the development of abfraction lesions: a finite element study. *J Oral Rehabil* 29:188-193.
Roulet JF (1994). Marginal integrity: clinical significance. *J Dent* 22:S9-S22.
Roulet J-F, Reich T, Blunk U, Noack M (1989). Quantitative marginal analysis in the scanning electron microscope. *Scanning Microsc* 3:147-158.

Ruse ND, Shew R, Feduik D (1995). In vitro fatigue testing of a dental bonding system on enamel. *J Biomed Mater Res* 29:411-415.

Ruse ND, Troczynski T, MacEntee MI, Feduik D (1996). Novel fracture toughness test using a notchless triangular prism (NTP) specimen. *J Biomed Mater Res* 31:457-463.

Sano H, Shono T, Takatsu T, Hosoda H (1994). Microporous dentin zone beneath resin-impregnated layer. *Oper Dent* 19:59-64.

Sano H, Takatsu T, Ciucchi B, Horner JA, Matthews WG, Pashley DH (1995). Nano-leakage: leakage within the hybrid layer. *Oper Dent* 20:18-25.

Sano H, Yoshikawa T, Pereira PN, Kanemura N, Morigami M, Tagami J, *et al.* (1999). Long-term durability of dentin bonds made with a self-etching primer, *in vivo. J Dent Res* 78:906-911.

Santerre JP, Shajii L, Leung BW (2001). Relation of dental composite formulations to their degradation and the release of hydrolyzed polymeric-resin-derived products. *Crit Rev Oral Biol Med* 12:136-151.

Shirai K, De Munck J, Yoshida Y, Inoue S, Lambrechts P, Shintani H, *et al.* (2005). Effect of cavity configuration and ageing on the bonding effectiveness of six adhesives to dentin. *Dent Mater* (in press).

Shono Y, Terashita M, Shimada J, Kozono Y, Carvalho RM, Russell CM, *et al.* (1999). Durability of resin-dentin bonds. *J Adhes Dent* 1:211-218.

Sim TP, Knowles JC, Ng Y-L, Shelton J, Gulabivala K (2001). Effect of sodium hypochlorite on mechanical properties of dentine and tooth surface strain. *Int Endod J* 34:120-132.

Sudsangiam S, Van Noort R (1999). Do dentin bond strength tests serve a useful purpose? *J Adhes Dent* 1:57-67.

Swift EJ Jr, Perdigão J, Heymann HO, Wilder A-D Jr, Bayne SC, May KN Jr, *et al.* (2001a). Eighteen-month clinical evaluation of a filled and unfilled dentin adhesive. *J Dent* 29:1-6.

Swift EJ Jr, Perdigão J, Wilder AD Jr, Heymann HO, Sturdevant JR, Bayne SC (2001b). Clinical evaluation of two one-bottle dentin adhesives at three years. *J Am Dent Assoc* 132:1117-1123.

Takahashi A, Inoue S, Kawamoto C, Ominato R, Tanaka T, Sato Y, *et al.* (2002). In vivo long-term durability of the bond to dentin using two adhesive systems. *J Adhes Dent* 4:151-159.

Tam LE, Pilliar RM (1994). Fracture surface characterization of dentin-bonded interfacial fracture toughness specimens. *J Dent Res* 73:607-619.

Tam LE, Yim D (1997). Effect of dentine depth on the fracture toughness of dentine-composite adhesive interfaces. *J Dent* 25:339-346.

Tam LE, Khoshand S, Pilliar RM (2001). Fracture resistance of dentin-composite interfaces using different adhesive resin layers. *J Dent* 29:217-225.

Tantbirojn D, Cheng YS, Versluis A, Hodges JS, Douglas WH (2000). Nominal shear or fracture mechanics in the assessment of composite-dentin adhesion? *J Dent Res* 79:41-48.

Tay FR, Gwinnett JA, Wei SH (1996a). Micromorphological spectrum from overdrying to overwetting acid-conditioned dentin in water-free acetone-based, single-bottle primer/adhesives. *Dent Mater* 12:236-244.

Tay FR, Gwinnett AJ, Pang KM, Wei SH (1996b). Resin permeation into acid-conditioned, moist, and dry dentin: a paradigm using water-free adhesive primers. *J Dent Res* 75:1034-1044.

Tay FR, Gwinnett JA, Wei SH (1998). Relation between water content in acetone/alcohol-based primer and interfacial ultrastructure. *J Dent* 26:147-156.

Tay FR, Pashley DH, Suh BI, Carvalho RM, Itthagaruna A (2002a). Single-step adhesives are permeable membranes. *J Dent* 30:371-382.

Tay FR, King NM, Chan KM, Pashley DH (2002b). How can nano-leakage occur in self-etching adhesive systems that demineralize and infiltrate simultaneously? *J Adhes Dent* 4:255-269.

Tay FR, Pashley DH, Peters MC (2003). Adhesive permeability affects composite coupling to dentin treated with a self-etch adhesive. *Oper Dent* 28:610-621.

Tjan AHL, Castelnuovo J, Liu P (1996). Bond strength of multi-step and simplified-step systems. *Am J Dent* 9:269-272.

Türkün SL (2003). Clinical evaluation of a self-etching and a one-bottle adhesive system at two years. *J Dent* 31:527-534.

Tyas MJ, Burrow MF (2001). Clinical evaluation of a resin-modified glass ionomer adhesive system—results at three years. *Oper Dent* 26:17-20.

Tyas MJ, Burrow MF (2002). Clinical evaluation of a resin-modified glass ionomer adhesive system—results at five years. *Oper Dent* 27:438-441.

Van Dijken JW (1994). Clinical evaluation of four dentin bonding agents in class V abrasion lesions. A four year follow up. *Dent Mater* 10:319-324.

Van Dijken JW (2000). Clinical evaluation of three adhesive systems in class V non-carious lesions. *Dent Mater* 16:285-291.

Van Dijken JW, Hörstedt P (1997). Marginal adaptation to enamel of a polyacid-modified resin composite (compomer) and a resin-modified glass ionomer cement in vivo. *Clin Oral Invest* 1:185-190.

Van Meerbeek B, Willems G, Celis JP, Roos JR, Braem M, Lambrechts P, *et al.* (1993). Assessment by nano-indentation of the hardness and elasticity of the resin-dentin bonding area. *J Dent Res* 72:1434-1442.

Van Meerbeek B, Braem M, Lambrechts P, Vanherle G (1994). Morphological characterization of the interface between resin and sclerotic dentine. *J Dent* 22:141-146.

Van Meerbeek B, Conn LJ Jr, Duke ES, Eick JD, Robinson SJ, Guerrero D (1996a). Correlative transmission electron microscopy examination of nondemineralized and demineralized resin-dentin interfaces formed by two dentin adhesive systems. *J Dent Res* 75:879-888.

Van Meerbeek B, Peumans M, Gladys S, Braem M, Lambrechts P, Vanherle G (1996b). Three-year clinical effectiveness of four total-etch dentinal adhesive systems in cervical lesions. *Quintessence Int* 27:775-784.

Van Meerbeek B, Perdigão J, Lambrechts P, Vanherle G (1998). The clinical performance of adhesives. *J Dent* 26:1-20.

Van Meerbeek B, Vargas M, Inoue S, Yoshida Y, Peumans M, Lambrechts P, *et al.* (1999). Hybridization effectiveness of a two-step versus a three-step smear layer removing adhesive system examined correlatively by TEM and AFM. *J Adhes Dent* 1:7-23.

Van Meerbeek B, Vargas S, Inoue S, Yoshida Y, Peumans M, Lambrechts P, *et al.* (2001). Adhesives and cements to promote preservation dentistry. *Oper Dent* 26:S119-S144.

Van Meerbeek B, De Munck J, Yoshida Y, Inoue S, Vargas M, Vijay P, *et al.* (2003). Buonocore memorial lecture: adhesion to enamel and dentin: current status and future challenges. *Oper Dent* 28:215-235.

Van Meerbeek B, De Munck J, Van Landuyt K, Kanumilli P, Lambrechts P, Peumans M (2005a). Restoring cervical lesions with flexible adhesives and composites. *J Dent Res* (submitted).

Van Meerbeek B, Kanumilli P, De Munck J, Van Landuyt K, Lambrechts P, Peumans M (2005b). A randomized controlled trial evaluating the three-year clinical effectiveness of two etch-and-rinse adhesives in cervical lesions. *Oper Dent* (in press).

Van Noort R, Noroozi S, Howard IC, Cardew G (1989). A critique of bond strength measurements. *J Dent* 17:61-67.

Van Noort R, Cardew GE, Howard IC, Noroozi S (1991). The effect of local interfacial geometry on the measurement of the tensile bond strength to dentin. *J Dent Res* 70:889-893.

Wahab FK, Shaini FJ, Morgano SM (2003). The effect of thermocycling on micro-leakage of several commercially available composite Class V restorations in vitro. *J Prosthet Dent* 90:168-174.

Watts DC, McAndrew R, Lloyd CH (1987). Thermal diffusivity of composite restorative materials. *J Dent Res* 66:1576-1578.

Wendt SL, McInnes PM, Dickinson GL (1992). The effect of thermocycling in micro-leakage analysis. *Dent Mater* 8:181-184.

Wiskott AHW, Nicholls JI, Belser UC (1994). Fatigue resistance of soldered joints: a methodological study. *Dent Mater* 10:215-220.

Xie B, Dickens SH, Giuseppetti AA (2002). Microtensile bond strength of thermally stressed composite-dentin bonds mediated by one-bottle adhesives. *Am J Dent* 12:177-184.

Yamauti M, Hashimoto M, Sano H, Ohno H, Carvalho RM, Kaga M, *et al.* (2003). Degradation of resin-dentin bonds using NaOCl storage. *Dent Mater* 19:399-405.

Yoshida Y, Van Meerbeek B, Nakayama Y, Snauwaert J, Hellemans L, Lambrechts P, *et al.* (2000). Evidence of chemical bonding at biomaterial-hard tissue interfaces. *J Dent Res* 79:709-714.

Yoshida Y, Nagakane K, Fukuda R, Nakayama Y, Okazaki M, Shintani H, *et al.* (2004). Comparative study on adhesive performance of functional monomers. *J Dent Res* 83:454-458.

Zheng L, Pereira PN, Nakajima M, Sano H, Tagami J (2001). Relationship between adhesive thickness and microtensile bond strength. *Oper Dent* 26:97-104.