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SOURCE (OR PART OF THE FOLLOWING SOURCE):

Type	Dissertation
Title	Clinical performance of resin composite restorations: the value of accelerated in-vitro testing
Author	F. Garcia-Godoy
Faculty	Faculty of Dentistry
Year	2012
Pages	118

FULL BIBLIOGRAPHIC DETAILS:
http://dare.uva.nl/record/419552

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CHAPTER 6

General discussion:

Is the clinical performance of bonded restoratives predictable in the laboratory?

Introduction

Dental biomaterials are subjected to considerable degradation processes during clinical service over time.[1-5] After amalgam, having been the standard restorative for posterior restorations for more almost two centuries, today tooth-colored materials such as resin-based composites are the treatment option of choice for the majority of patients.[6-13] Adhesive dentistry's long-term success is proven for pit and fissure sealing, direct and indirect resin composites, and ceramic inlays.[11,13-25] Nevertheless, even in the era of nano-optimized resin-based composites, polymerization shrinkage still relies on durable adhesion to enamel and dentin as a fundamental prerequisite, and vice versa, without successful adhesion, gap formation potentially jeopardizes clinical long-term success.[4,26-36]

Adhesion to phosphoric acid etched enamel is no longer a concern for dentists due to its clinically proven durability,[4-6,31,35,37-40] however, durability of self-etch adhesives in heavily loaded Classes I and II is still not clinically proven, whereas in cervical lesions, medium-term results are promising.[12,21,22,41,42] Knowledge about adhesion to dentin is different; the self-etch approach - at least with two steps - seems to be the most promising way to get durable bonds beside multi-step etch-and-rinse systems.[30,31,35,40,43,44] Comparing enamel and dentin as adhesive substrates still reveals dentin to be the weaker substrate due its tubular structure and intrinsic wetness which leads to permeability problems with all-in-one self-etch adhesives.[27,31,33-35,44-47]

More or less all degradation processes found for dental biomaterials are related to fatigue.[10,37,48-55] Especially with resin-based composites, fatigue is not only a matter of loss of adhesive performance over time (adhesive fatigue) but also of bulk fatigue (fracture) and surface fatigue (wear). For resin composites, two fatigue phenomena (adhesive fatigue leading to recurrent caries and bulk fatigue leading to fractures) are responsible for the vast majority of clinical failures observed during clinical long-term trials.[6,7,11,16,56] Wear is in most of the cases less clinically relevant because worn resin composites may still be clinically serviceable, however, loss of anatomic form over time may lead to occlusal interferences.[10,57-59] Research in restorative dentistry is, since decades, focused on predicting clinical issues in the lab.[60] Of course, clinical long-term trials remain the ultimate instrument for thoroughly evaluating dental biomaterials. However, the main problem with clinical trials is that when they give

valuable results after several years of observation time, the adhesive and/or resin composite may no longer be on the market.

Therefore, preclinical *in vitro* investigations are very important, however, it is contradictorily reported in the literature whether these tests are able to reliably predict clinical behavior. So the aim of this paper was to investigate this particular question with a special focus on marginal integrity, bulk fatigue (fracture), and surface fatigue (wear).

Materials and Methods

Publications in dental and biomaterial journals with dental materials since 1990 were retrieved in PubMed, MedLine, Dimdi, and Embase. Search key words were: margin, gap, marginal integrity, marginal adaptation, enamel margin, dentin margin, marginal quality, fracture, chipping, bulk fracture, abrasion, and wear. We only chose papers dealing with resin composites. Congress abstracts were completely ignored. Top cited papers were retrieved from www.scopus.com in order to prioritize publications that were frequently referred to[39]. As indicator for top cited papers, the frequency of citations per year (CPA) was set >5.

Results

An overview of top cited papers dealing with marginal integrity, fatigue, and wear of bonded restorations is displayed in Tables 6.1-6.3.

Marginal quality

Papers reporting direct comparisons between in vitro and in vivo results are scarce in the literature in the field of adhesive dentistry. However, several evaluations of marginal integrity from the preclinical point of view exist as do a few papers focusing on marginal adaptation in vivo. Marginal integrity papers *in vitro* repeatedly report a superior performance of etch-and-rinse adhesives in enamel bonding,[16,18,19,22,31,35,36,39,40,48,61,62] however, again there are contradictory reports of Hannig *et al.* claiming self-etch adhesives being an alternative to phosphoric acid even in stress-bearing cavities.[63,64] For dentin bonding, Frankenberger and Tay

reported equal results for etch-and-rinse adhesives and two-step self-etch adhesives in dentin margins of Class II cavities after thermomechanical loading, and significantly worse results when all-in-one adhesives were used for bonding of resin composites in vitro.[35]

Abdalla and Davidson directly compared *in vitro* and *in vivo* applied resin composite restorations in Class II cavities with less microleakage in the laboratory.[65] Two papers of our group investigated the resin composites Ariston pHc and Solitaire both in vitro and in vivo. In the in vitro part, both restoratives exhibited some shortcomings,[36] however, these previously reported materials properties led to catastrophic outcomes in vitro with mean survival times for both materials of 2.4 years.[66] Frankenberger *et al*. also compared the same materials in vitro and in vivo with respect to marginal adaptation of Class I resin composite resotrations in molars.[39] Here, some minor differences were noticed between the in vitro and the in vivo situation, however, the rankings regarding the adhesive's performances were the same, revealing superior results for etch-and-rinse adhesives when compared to self-etch adhesives.[39] And among the self-etch adhesives, two-step self-etch adhesives were more effective than one-step self etch adhesives.[39] Another publication observed marginal quality for Grandio and Tetric Ceram restorations both in vitro and in vivo over 6 years.[4] Also here, in vitro and in vivo results for marginal quality were similar until the 6-year recall with a combined 6-year water storage/thermomechanical loading scenario.[4] Heintze *et al*. compared results of clinical studies with bonded Class V resin composite restorations with two different in vitro stressing regimens for a variety of 37 adhesives.[44] They concluded that the systematic analysis of the correlation between laboratory data of marginal adaptation and the outcome of clinical trials of Class V restorations revealed that the correlation was weak and only present if studies were compared which used the same composite for the *in vitro* and *in vivo* evaluation.[44]

Bulk fatigue / fracture behavior

Regarding the fatigue behavior related to flexural strength, some studies evaluated the flexural fatigue behavior in terms of a so-called flexural fatigue limit (FFL).[48,49,67-79] The flexural fatigue limits (FFL) of the composite materials were determined for 10^5

cycles under equivalent test conditions at a frequency of 0.5 Hz (n = 25). The "staircase" approach was used for fatigue evaluation.[70] For every cycle the stress alternated between 1 MPa and the maximum stress. Tests were conducted sequentially, with the maximum applied stress in each succeeding test being increased or decreased by a fixed increment of stress, according to whether the previous test resulted in failure or not. The first specimen was tested at approximately 50% of the initial flexural strength value. As the data are cumulated around the mean stress, the number of specimens required is less than with other methods. The mean flexural fatigue limit (FFL) is determined using Eq. 1 and standard deviation, using Eq. 2, respectively:

$$FFL = X_0 + d\left(\frac{\sum in_i}{\sum n_i} \pm 0.5\right) \quad (1)$$

$$SD = 1.62d\left(\frac{\sum n_i \sum i^2 n_i - \left(\sum in_i\right)^2}{\left(\sum n_i\right)^2} + 0.029\right) \quad (2)$$

X_0 is the lowest stress level considered in the analysis and d is the fixed stress increment. To determine the FFL, the analysis of the data was based on the least frequent event (failures versus nonfailures). In Eq. 1 a negative sign was used when the analysis was based on failures. The lowest stress level considered was designated as $i = 0$, the next as $i = 1$, and so on, and n_i was the number of failures or non-failures at the given stress level. Turssi *et al.* evaluated FFLs of microfill versus nanfilled resin composite with equal to worse outcome for the nanomaterials.[80] Abe *et al.* compared an array of resin composites with results having been inferior for most of the packable resin composites under investigation.[81] Lohbauer et al. evaluated the FFL behavior of different resin composites for posterior use and concluded that high initial flexural strengths do not automatically mean high FFLs.[77,78] In a direct in vitro - in vivo comparison of resin-based materials regarding FFL and clinical outcome, the low FFL for the resin composite Solitaire led to unacceptably high fracture rates in vivo, so the authors concluded that FFL >30 MPa is the critical threshold value for bulk fatigue in order to withstand masticatory forces and clinical fatigue life over time.[66,77,78]

Surface contact fatigue/clinical wear

Early abrasion studies during the first stages of resin composite testing were cast analyses according to some scales such as the Leinfelder scale allowing estimates of clinical wear in terms of calibrated casts in 50 µm steps.[1,52,53,82-88] Compared to preclinical screenings where normally only the test material is abraded,[54,55,89,90] clinical wear measurements in restorative dentistry always deal with enamel and restorative materials and an exact determination of reference points is only possible with demanding 3D laser devices.[57-59,91-93] Due to the expensive tool and sophisticated software issues, very few 3D laser scan studies dealing with clinical wear phenomena are available in the literature, reporting wear rates after 3 years of clinical service of ~80 µm.[91,92]

Discussion

In vitro research on dental adhesive biomaterials is necessary, because a) special experimental research questions would never pass an ethics committee and b) not every adhesive and/or resin-based composite can be the subject of randomized prospective clinical trials because these are time-consuming and expensive. Nevertheless, it is still not fully understood whether and what we can really simulate in the lab and where major shortcomings are. So, the objective of this paper was to clarify the question "Is clinical performance of dental biomaterials predictable in the lab?". Roulet thought about this topic years ago indicating that in vitro research suffers from interpretation problems and even in vivo studies always reveal significant limitations.[94]

Today, there are still only a handful of studies directly comparing in vitro with in vivo results from the same workgroup. Abdalla and Davidson published the first "Comparison of the marginal integrity of in vitro and in vivo Class II composite restorations" being unique so far. This investigation dealt with microleakage in laboratory and ex vivo specimens.[65] Whereas only 40% of in vitro specimens revealed microleakage after mechanical loading, 100% of in vivo restorations exhibited microleakage.[65] Therefore, the authors concluded that laboratory studies may not be able to completely predict clinical behavior of adhesive junctions in the oral cavity.[65]

Clinical studies are mainly peformed in Classes V or II cavities being the latter the most difficult to obtain. Major advantages of clinical trials in Class V cavities were referred to as non-existing macromechanical retention, considerable amounts of dentin margins, probably less influence of the particular resin composite, and easy judgement of retention vs. retention loss.[20-22,43,44,62] However, the main problem in adhesive dentistry is not retention of Class V restorations, it is still to prove whether bonded resin compositess are able to fully replace amalgam in stress-bearing posterior cavities. However, disadvantages of Classes I and II are that retention is often provided by undermining dentin decay and subsequent undercuts, and less presence of clinically judgeable dentin margins.[4,6,9] So marginal quality assessments in posteror stress-bearing resin composite restorations may be less suitable to investigate adhesives alone compared to non-carious Class V restorations, however, clinical importance facing millions of stress-bearing posterior resin composite restorations is great.[6]

Opdam *et al.* reported marginal integrity and postoperative sensitivity in Class II restorations in vivo finding that etch-and-rinse adhesives showed good results in enamel bonding and self-etch adhesives produced less postoperative hypersensitivity.[17] When clinical staining is related to inferior or loss of enamel bonding durability, and postoperative hypersensitivities are linked to inferior or loss of dentin bonding quality, this was predictable from laboratory investigations.[39]

Four recent publications of our workgroup aimed to evaluate resin composites and their corresponding adhesives in both aspects, *in vitro* and *in vivo*.[4,36,39,66] Frankenberger *et al.* reported in vitro performance of resin composites by means of microtensile bond strenghts to enamel and dentin, flexural fatigue behavior, and wear behavior. The resin composites Ariston pHc and Solitaire were different from contemporary resin composites, i.e. Ariston exhibited significantly less adhesion, Solitaire revealed an inferior flexural fatigue limit.[36] Krämer et al. reported clinical findings of identical materials demonstrating catastrophic clinical outcome with several bulk fractures of Solitaire, and even more failures of Ariston restorations caused by postoperative hypersensitivities and enamel fractures.[66] Frankenberger *et al.* compared different classes of adhesives in vitro and in vivo with identical enamel bonding rankings for the different bonding approaches.[39] The same was true for a recent publication showing 6-year results in vitro and in vivo with again similar

outcomes over time.[4] So in all cases, clinical performance of resin composites in Classes I and II cavities was predictable from laboratory results, especially significant differences between etch-and-rinse adhesives and self-etch adhesives in enamel bonding durability. So even the results of Heintze et al.[43,44] actually match the outcome of our workgroup where always the same resin composites were used *in vitro* and *in vivo* which may have contributed to the more consistent values.[4,39]

All these findings clearly reflect that marginal quality prediction is possible from laboratory studies, however, marginal integrity is only one among several crucial factors for clinical outcome with bonded tooth-colored materials. A high amount of gaps after thermomechanical challenge in vitro increases the probability of the same scenario *in vivo*. However, this does not necessarily lead to recurrent decay because the presence of marginal gaps *in vivo* does not necessarily lead to secondary caries. One ultimate question is still unclear: when e.g. resin composite restoration achieves good results in an in vitro marginal quality assessment, it is rather predicable that its clinical marginal quality will not cause significant problems. On the other hand, can we conclude this also from the other side of the scale? Probably not. We still do not know below which percentage of gap-free margin it is not safe to use the material combination also clinically.

The final reason in favor of in vitro research regarding marginal quality is that many studies focus on experimental questions that would never pass an ethics committee for a clinical trial. In these cases *in vitro* studies are the only way, giving important tendencies for clinical application of dental biomaterials. Among all in vitro approaches to predict clinical outcome, thermomechanical loading and subsequent marginal analysis is the closest scenario to the clinical situation, however, it is almost as intricate as a clinical trial.

As the frequency of citations as well as the presence of top cited papers clearly reflects, flexural fatigue behavior of dental biomaterials receives far less attention. However, a few top papers indicate that flexural fatigue behavior of dental biomaterials is closely related to clinical outcome in terms of fracture behavior.[36,48,49,66,67,70,71,95] Compared to the multiple questions about marginal quality, FFL measurements in vitro are able to exactly define a kind of lower borderline at ~30 MPa flexural fatigue limit, because below that level clinically much more fractures were observed.[66] On the other hand, there are still not enough clinical data

proving that higher and higher initial and fatigue values for flexural strength automatically lead to less fractures observed in clinical recalls after several years of clinical service.[96]

Wear is an important consequence of occlusal interactions.[10,16,91,97,98] If not controlled, wear could lead to poor masticatory function with a concomitant reduction in quality of life.[99-102] However, for most of the investigated resin-based composites this is simply not the case.[10,16,91,97,98] Compared with other modes of in vitro testing of dental biomaterials, preclinical wear simulation is the most sophisticated branch.[52,53,86,98,103,104] Clinical wear is a very complex scenario being influenced by several factors such as pH, contact-free abrasion, occlusal contact fatigue, and antagonist structure and material.[52,53,86,98,103,104] Most of the in vitro regimens are only able to mimic one of these several co-factors. Analyzed as an array, many different wear simulation scenarios could finally result in an appropriate estimation of clinical wear.[52,53,86,98,103,104] Also here it is clearly visible in Table 6.3 that the scientific importance of wear investigations decreased during the last decade and top cited papers are scarce. 3D laserscans are the ultimate instrument to evaluate clinical wear, however, there is an urgent need for more clinical data with different restoratives.[98]

In times of ranking publications according to their journal impact factor (JIF), citations are an important tool in order to judge the importance of individual papers in the literarure. High JIF regularly result from frequently cited papers. As performed before with a substantial amount of citations, the authors again decided to include this aspect by focussing on frequently cited papers being indicated by CPA (citations per anno; Tables 6.1-6.3). For the top cited paper published by Van Meerbeek *et al.* this means that this single publication receives an individual or "true" impact factor of 50 compared to the journal impact factor of ~3 meaning that the importance of the paper exceeds the importance of the journal by means of 16. Although citation rankings and measurement are always criticized to be somewhat subjective, it is the only way to judge or rank scientific outcome. The same is true for the journal impact factor, i.e. it may not be an optimum tool for author evaluations, however, is there a better alternative? So finally, the inclusion of top cited papers is of at least some relevance and should not be underestimated.

Conclusions

Clinical marginal quality is predictable from in vitro adhesive fatigue investigations with thermomechanical loading, but it is not possible to determine a cut off for clinically successful marginal quality. Flexural fatigue can be appropriately determined in the lab as well, having been successful in defining lower borderlines for additional clinical safety. To compare in vitro and in vivo results according to wear phenomena, valid in vivo results are too seldom. Altogether, it has to be taken into account that the described co-factors are only a few among several important aspects in restorative dentistry, i.e. overall clinical performance is not predictable from fatigue aspects alone.

Year	Author	Title	Citations per year (CPA)
2003	Van Meerbeek et al.[13]	Adhesion to enamel and dentin: Current status and future challenges	50.9
1997	Mehl at al.[23]	Physical properties and gap formation of light-cured composites with and without softstart polymerization	14.5
1995	Feilzer et al.[24]	Influence of light intensity on polymerization shrinkage and integrity of restoration-cavity interface	12.1
2005	Frankenberger & Tay[35]	Self-etch vs etch-and-rinse adhesives: effect of thermo-mechanical fatigue loading on marginal quality of bonded resin composite restorations	10.8
1990	Kemp-Scholte et al.[41]	Complete marginal seal of Class V resin composite restorations effected by increased flexibility	10.3
1999	Hannig et al.[63]	Self-etching primer vs. phosphoric acid: an alternative concept for composite-to-enamel bonding	10.0
2000	Peumans et al. [25]	Porcelain veneers: A review of the literature	9.0
2000	Frankenberger et al.[45]	Technique sensitivity of dentin bonding: Effect of application mistakes on bond strength and marginal adaptation	8.6
1998	Opdam et al.[17]	Marginal integrity and postoperative hypersensitivity in Class II resin composite restorations in vivo	6.8
2007	Heintze[43]	Systematic reviews: I. The correlation between laboratory tests on marginal quality and bond strength. II. The correlation between marginal quality and clinical outcome	6.0
2000	Frankenberger et al.[2]	Leucite-reinforced glass ceramic inlays and onlays after six years: clinical behavior	6.0
1990	Kemp-Scholte & Davidson[60]	Marginal integrity related to bond strength and strain capacity of composite resin restorative systems	5.8
2007	Frankenberger et al. [39]	Marginal integrity: Is the clinical performance of bonded restorations predictable in vitro?	5.7

Table 6.1: Top cited papers (CPA >5) regarding marginal adaptation of resin composites.

Year	Author	Title	Citations per year (CPA)
1997	Gladys et al.[95]	Comparative physico-mechanical characterization of new hybrid restorative materials with conventional glass-ionomer and resin composite restorative materials	11.4
2003	Drummond et al.[73]	Static and cyclic loading of fiber-reinforced dental resin	8.9
2005	Lohbauer et al.[78]	The effect of different light-curing units on fatigue behavior and degree of conversion of a resin composite	5.6

Table 6.2: Top cited papers (CPA >5) regarding bulk fatigue behavior of resin composites.

Year	Author	Title	Citations per year (CPA)
1998	Bayne et al.[99]	A characterization of first-generation flowable composites	11.3
2005	Sarrett et al.[101]	Clinical challenges and the relevance of materials testing for posterior composite restorations	9.6
1996	Mair et al.[100]	Wear: Mechanisms, manifestations and measurement. Report of a workshop	7.4
2005	Turssi et al.[102]	Filler features and their effects on wear and degree of conversion of particulate dental resin composites	7.4

Table 6.3: Top cited papers (CPA >5) regarding surface fatigue / wear of resin composites.

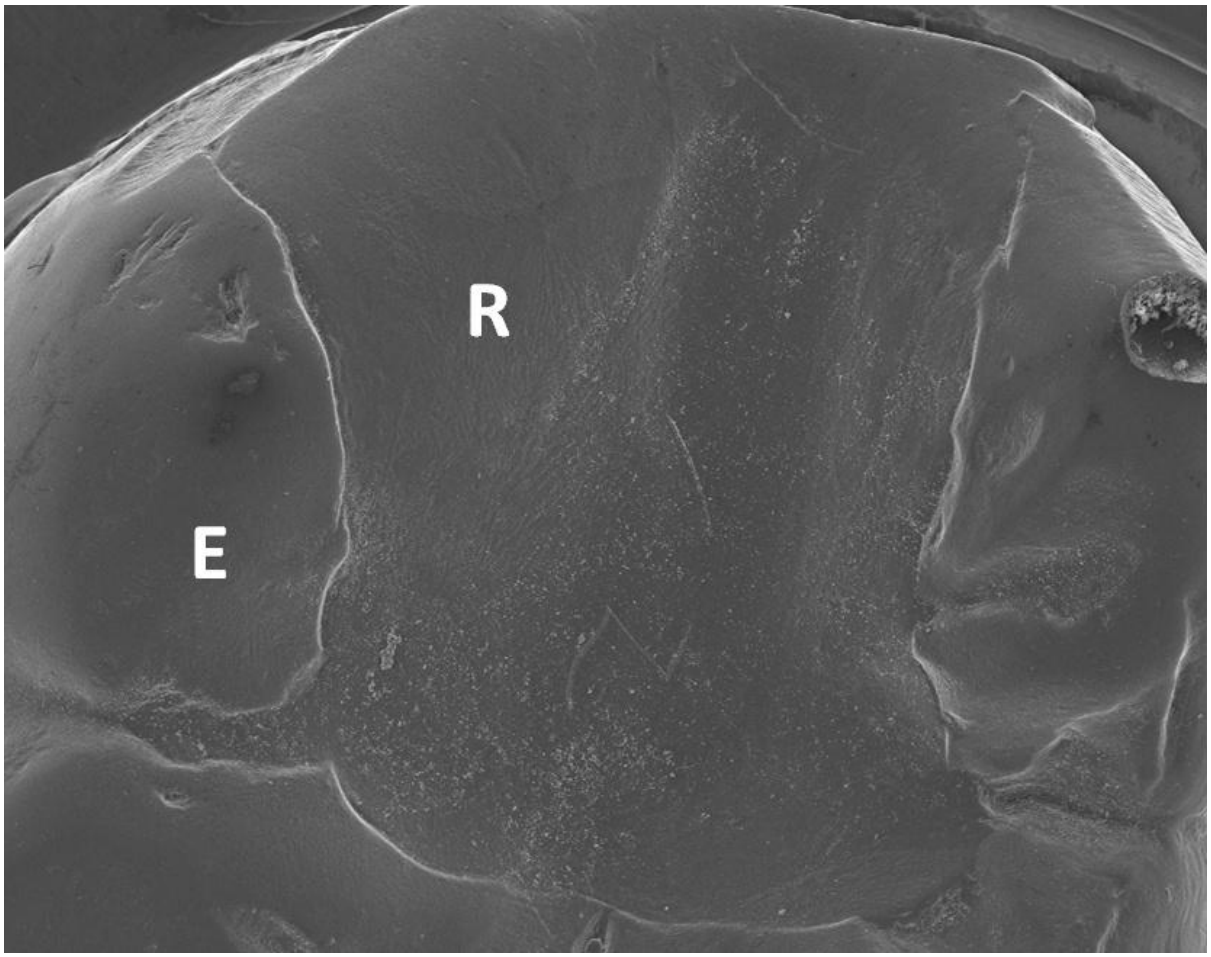

Figure 6.1: Biodegradation of a resin composite restoration in a lower first molar after 6 years of clinical service. R: Resin composite. E: Enamel. Clinical wear is clearly visible around the occulsal margins. Gap formation does not play a major role in this case.[4]

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