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Polymerization Stress and Gap Formation of Self-adhesive, Bulk-fill and Flowable Composite Resins

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Clinical Relevance

Bulk-fill materials show a similar or better performance than control flowable materials regarding interfacial integrity. However, some self-adhesive composites need improvements to achieve competitive performance.

SUMMARY

Objective: This laboratory study compared the polymerization stress and gap formation of self-adhesive, bulk-fill and control flowable composites. The degree of conversion (DC) and post-gel shrinkage were also assessed.

Methods: Two self-adhesive (Vertise Flow and Fusio Liquid Dentin), two bulk-fill (Tetric N-Flow Bulk-Fill and Filtek Bulk-Fill Flowable Restorative), and two control flowable (Z350 XT Flowable Restorative and Tetric N-Flow) composites were evaluated. Polymerization stress (PS) was determined in a universal testing machine (n=5). Gap formation was evaluated by scanning electron microscopy in class I restorations (n=6). DC was measured by Fourier transform infrared spectroscopy (n=3). Post-gel volumetric shrinkage (VS) was measured using the strain gauge method (n=5). Data were submitted to one-way analysis of variance or a Kruskal-Wallis test (α=0.05).

Results: Vertise Flow and Fusio Liquid Dentin presented the highest interfacial gap (27%±5% and 21%±6%, respectively), which was associated with their highest PS (4.1±0.8 MPa and 3.5±0.6 MPa, respectively) and DC (63%±2% and 60%±2%, respectively) in spite of the lowest VS (1.0%±0.2% and 1.0%±0.3%, respectively). Tetric N-Flow Bulk-Fill and Filtek Bulk-Fill Flowable Restorative presented similar PS (2.9± 0.3 MPa and 2.4±0.2 MPa, respectively) to both control materials. However, the Tetric N-Flow Bulk-Fill showed the lowest gap (7%±2%) and the highest DC (64.3%±0.4%), and the Filtek Bulk-fill presented a marginal gap (17.8%±3.4%) and a DC (54.5%±2.7%) similar to the control materials. The VS values of both bulk-fill materials were similar to those of

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Tetric N-Flow and lower than that of Z350 XT Flowable Restorative.

Conclusions: Bulk-fill composites showed either similar or significantly lower interfacial gaps and PS than the control flowable composites. The self-adhesive composites showed a significantly higher gap percentage and PS than the control and bulk-fill materials.

INTRODUCTION

Despite several improvements in the physical-chemical properties of restorative composites[1-3] and adhesive systems,[4] interfacial integrity remains one of the main limitations of composite restorations.[5] The presence of interfacial gaps at the tooth-restoration interface is usually associated with postoperative hypersensitivity, marginal discoloration, and secondary decay, jeopardizing the longevity of the restorative treatment.[6]

From a clinical standpoint, the simplification of the restorative procedure to make it less time consuming and less prone to error has been the focus of manufacturers and researchers alike.[7-9] The popularity of flowable composites is a clear example of this trend.[10] These materials were developed to facilitate insertion into the cavity preparation, minimizing voids and improving composite adaptation to cavity walls.[11] However, the first available materials showed high volumetric shrinkage,[12] which limited their use to cavity liners or small cavity preparations.[10]

Bulk-fill composites have emerged as a promising technology that allows their placement in a single increment up to 4 mm in thickness.[13,14] These materials were formulated to facilitate light transmission, where their translucency is increased by changing the filler concentration, size, and refractive index[15] or by using photoinitiators as an alternative to camphorquinone.[16]

Additionally, as a strategy to reduce chair-side time, self-adhesive composites were developed to eliminate the need for an adhesive system.[4,9] These materials contain monomers such as GPDM (glycerophosphate dimethacrylate) and 4-MET (4-methacryloxyethyl trimellitic acid), which contain acidic side groups capable of demineralizing dentin and enamel and establishing a chemical bond with the hydroxyapatite.[17,18] As resin infiltration occurs concomitantly with demineralization, the risk of postoperative hypersensitivity is reduced.[9] However, the bond strength of these materials to dental substrates is generally lower than that obtained using an adhesive system.[19,20] Studies have indicated that previous total etching of the tooth or the use of a self-etching adhesive with these materials increases the bond strength,[21,22] but this adds an extra step to the clinical protocol. The presence of an interfacial gap has also been associated with these materials, but the percentage is variable according to studies and composite commercial brand.[23,24]

Despite the clear advantages of these new materials in terms of reducing clinical time, the interfacial integrity of restorations made with bulk-fill and self-adhesive composites is of concern. Interfacial gap length is directly related to the composite polymerization stress.[25] Bulk-fill materials are applied in large volumes and under highly confined conditions (ie, high cavity configurator factor or "C-factor"), and both of these characteristics are associated with the development of increased polymerization stress.[26,27] Few studies have compared bulk-fill and control flowable materials in terms of polymerization stress and gap formation.[28,29] The severity of interfacial gaps has also been shown to be inversely related to bond strength.[30] Therefore, the competition between interfacial bond strength and the polymerization stress of self-adhesive composites could jeopardize interfacial integrity. To our knowledge, there is no available information on polymerization stress and gap formation for this relatively new group of composites.

Based on the factors described in this introduction, the objective of this study was to compare bulk-fill, self-adhesive and control flowable composites in terms of polymerization stress and interfacial integrity. Additionally, degree of conversion (DC) and volumetric shrinkage were tested. The hypothesis of the study was that the bulk-fill (Tetric N-Flow Bulk-Fill and Filtek Bulk-Fill Flowable Restorative) and self-adhesive (Vertise Flow and Fusio Liquid Dentin) composites do not differ from flowable controls (Tetric N-flow and Filtek Z350 XT Flowable Restorative) in terms of polymerization stress and interfacial gap.

METHODS AND MATERIALS

Material Selection

Six flowable restorative composites were evaluated (Table 1). All materials were tested in the A3 shade, except the Tetric N-Flow Bulk-Fill, which was tested in the IVA shade. For all experiments, specimens were photoactivated using a light-emitting diode curing unit at 1200 mW/cm^2 (Radii-Cal, SDI, Baywater, Australia). All composites were irradiated for 25 seconds, with the first 5

Table 1: *Adhesive and Composite Resins Composition*

Materials	Manufacturer	Composition	Filler
Tetric N-Flow Bulk-Fill	Ivoclar Vivadent, Schaan, Liechtenstein	BisGMA, UDMA, barium glass fillers, YbF_3, mixed oxides, silicon dioxide	68.2 wt%/46.4 vol%
Filtek Bulk-Fill Flowable Restorative	3M ESPE, St Paul, MN, USA	UDMA, substituted dimethacrylate (procrylate), BisEMA-6, YbF_3, BisGMA, benzotriazole, TEGDMA, ethyl 4-dimethyl aminobenzoate	64.5 wt%/42.5 vol%
Vertise Flow	Kerr Corp, Orange, CA, USA	GPDM, HEMA, pre-polymerized fillers, barium glass fillers, colloidal silica, YbF_3	70 wt%
Fusio Liquid Dentin	Pentron, Orange, CA, USA	UDMA, TEGDMA, HEMA, 4-MET, amorphous sílica, barium glass silanized, additives.	65 wt%/52 vol%
Tetric N-Flow	IvoclarVivadent, Schaan, Liechtenstein	BisGMA, UDMA, TEGDMA, barium glass fillers, YbF_3, mixed oxides, silicon dioxide.	63.8 wt%
Z350 XT Flowable Restorative	3M ESPE, St Paul, MN, USA	BisGMA, TEGDMA, zircon/silica fillers grouped.	65 wt%/55 vol%
Tetric N-Bond Universal	Ivoclar Vivadent, City, Germany	Methacrylate, ethanol, water, silicon dioxide, initiators and stabilizers.	-
Single Bond Universal	3M ESPE, St Paul, MN, USA	Phosphate monomer MDP, dimethacrylate, HEMA, Vitrebond copolymer , ethanol, water, initiators and silane.	-

Abbreviations: BisGMA, bisphenylglycidyl dimethacrylate; UDMA, diurethane dimethacrylate; BisEMA, ethoxylated bisphenol-A dimethacrylate; TEGDMA, triethylene glycol dumethacrylate; GPDM, glycero-phosphate dimethacrylate; HEMA, hydroxyethyl methacrylate; 4-MET, 4-methacryloyloxyethyl trimellitic acid; MDP, 10-methacryloyloxydecyl dihydrogen phosphate.

seconds ramping irradiance up to 1200 mW/cm^2 according to the device design. For all the variables analyzed, the specimen thickness was 1 mm. The only exception was for the interfacial gap assay, in which the specimen thickness was 3 mm and control and self-adhesive materials required two or more incremental layers, so all the composites were placed and photoactivated according to the manufacturer's instructions, which changed the radiant exposure among the composites, as shown in Table 2. This project was approved by the Ethics Committee on Human Research, and 36 sound molars were supplied by the human tooth bank.

Table 2: *Protocols of Adhesive System and Composite Resin Applications Used for Teeth Restorations, According to the Manufacturer*

Material	Protocol
Single Bond Universal	Active application for 20 seconds Application of air stream for 5 seconds Photoactivation for 25 seconds
Tetric N-Bond Universal	Active application for 20 seconds Application of air stream for 5 seconds Photoactivation for 15 seconds
Filtek Bulk-Fill Flowable Restorative	Insertion of a single 3-mm increment Photoactivation for 25 seconds
Tetric N-Flow Bulk-Fill	Insertion of a single 3-mm increment Photoactivation for 15 seconds
Vertise Flow	Rinsing and drying of preparation walls for 5 seconds Insertion of the first increment (0.5-mm thick) with active application for 20 seconds Photoactivation for 25 seconds Insertion of two consecutive layers and photoactivation for 25 seconds each
Fusio Liquid Dentin	Insertion of a 1.0-mm-thick layer with active application for 20 seconds Photoactivation for 15 seconds Insertion of a 1-mm-thick layer, photoactivated for 15 seconds Insertion of a 1-mm-thick layer, photoactivated for 25 seconds
Z350 XT Flowable Restorative	Insertion of 1.5-mm-thick increments Photoactivation for 15 seconds each
Tetric N-Flow	Insertion of 1.5-mm-thick increments Photoactivation for 15 seconds each

Polymerization Stress

Poly(methyl methacrylate) rods (5-mm diameter, 13- or 28-mm length, FAP Acrílicos, São Paulo, Brazil) were used as bonding substrates to establish a high compliance test. One of the surfaces of the rods was roughened with 600-grit sandpaper and treated with methyl methacrylate monomer before a layer of unfilled resin (Single Bond Universal, 3M ESPE, St Paul, MN, USA), was applied and photoactivated for 15 s. The rods were attached to a universal testing machine (Instron 5565, Instron, Canton, MA, USA). The 13-mm rod was fixed to a stainless steel attachment with a slot allowing for standardized positioning of the light guide in contact with its polished surface (Figure 1). No significant irradiance loss was observed through the acrylic rod. The composite was inserted between the treated surfaces of the rods, with a thickness of 1 mm. An extensometer (model 2630-101, Instron) was coupled to the rods to monitor the specimen's height and control the actuator to keep a constant distance between the rods. The composite was photoactivated through the lower rod, and the shrinkage force was monitored for 5 minutes. Nominal stress was calculated by dividing the maximum load registered by the transverse area of the rods.

Interfacial Gap

The occlusal surfaces of 36 sound human molars were flattened, and class I cylindrical preparations with margins in enamel (5-mm diameter and 3-mm depth) were made using diamond burs (KG Sorensen, Cotia, Brazil) under copious water irrigation. The teeth were restored according to the manufacturers' instructions, as detailed in Table 2. For Z350 XT Flowable Restorative and Filtek Bulk-Fill Flowable Restorative, the Single Bond Universal (3M ESPE) adhesive system was used, whereas Adhesive Tetric N-Bond Universal (Ivoclar Vivadent,Schaan, Liechtenstein) was used for Tetric N-Flow and Tetric N-Flow Bulk-Fill; both were used in the self-etching mode. In each case we used the bonding system from the manufacturer of the resin composite to optimize compatibility between the adhesive system and the composite materials. Additionally, for the self-adhesive composites no acid-etching procedure was conducted at all. The cavity was filled either in a single increment (bulk-fill composites) or two or more increments (control and self-adhesive composites), as shown in Table 2.

After 24 hours in water at 37°C, teeth were sectioned transversely in the buccal-lingual direction through the center of the restoration under constant water irrigation and using a low cutting speed (300 rpm). An impression of the exposed surface was taken using a light consistency polyvinylsiloxane impression material (Panasil initial contact X-Light, Kettenbach GmbH, & Co. KG, Eschenburg, Germany). Epoxy resin was poured into the impressions and allowed to set for 2 hours at room temperature. The epoxy replicas were gold-sputtered and observed under a scanning electron microscope (Jeol Neoscope JCM 5000, JCM, Tokyo, Japan). Images of the entire tooth-restoration interface were taken and combined to allow for gap length measurement, which was recorded as a percentage of the total length of the interface using ImageJ software (Image J 1.52a, National Institutes of Health, Bethesda, MD, USA).

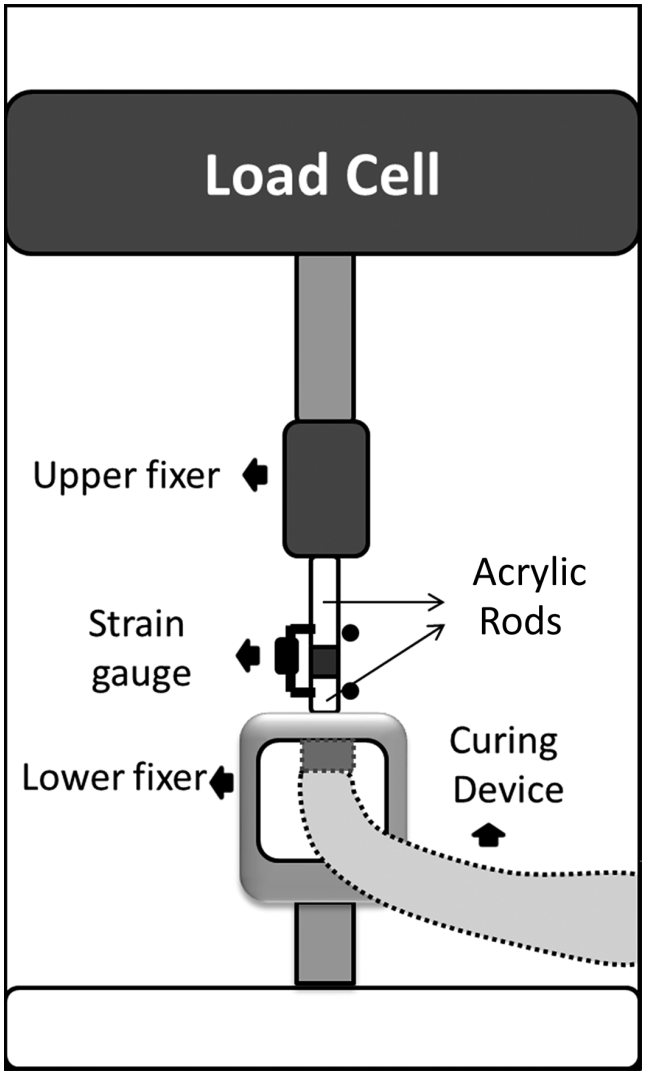

Figure 1. *Diagram of the polymerization stress testing system.*

Table 3: *Means and Standard Deviations of the Polymerization Stress (MPa), Interfacial Gap (%), Volumetric Shrinkage (%), and Degree of Conversion (%), of Bulk-fill, Self-adhesive, and Control Flowable Composite Resins*[a]

Composite Resin	Polymerization Stress (MPa)	Interfacial Gap (%)	Volumetric Ghrinkage (%)	Degree of Conversion (%)
Filtek Bulk-Fill Flowable Restorative	2.3±0.3 C	17.8±3.4 B	1.5±0.3 BC	55.5±2.7 CD
Tetric N-Flow Bulk-Fill	2.8±0.3 BC	6.9±1.9 C	1.8±0.5 BC	64.3±0.4 A
Vertise Flow	3.9±0.7 A	27.1±4.9 A	1.0±0.2 C	62.5±2.1 A
Fusio Liquid Dentin	3.3±0.6 AB	20.9±5.7 AB	1.0±0.3 C	60.1±1.5 AB
Filtek Z350 XT Flowable Restorative	2.7±0.5 BC	17.7±7.1 B	3.5±0.5 A	58.7±0.7 BC
Tetric N-Flow	3.1±0.6 ABC	13.3±4.6 BC	2.1±0.2 B	53.0±2.1 D

[a] *In the same column, the same letters indicate an absence of statistical difference.*

Post-gel Volumetric Shrinkage

Post-gel volumetric shrinkage was measured using a uniaxial strain gauge (n=5). A silicone mold with a 5-mm diameter and 1-mm height was positioned on an extensometer (PA-06-060BA-350-LEN, Excel Sensores, São Paulo, Brazil) and filled with the composite, which was photoactivated for 25 seconds. The strain generated by polymerization shrinkage was monitored for 5 minutes. The materials were considered homogeneous and isotropic, and the recorded data were converted to percentages and multiplied by three to obtain the volumetric shrinkage values.[31]

Degree of Conversion

The DC was determined using attenuated total reflectance Fourier transform infrared spectroscopy (FTIR-ATR, Vertex 70, Bruker Optik, Ettingen, Germany). Thirty-two scans were performed before polymerization and 10 minutes after polymerization in specimens with a 5-mm diameter and 1-mm height (n=3), at a resolution of 6 cm^{-1}. The DC was calculated by the change in the area under the aliphatic carbon double-bond peak (C=C) of 1638 and the carbonyl absorption peak (C=O) of 1730 cm^{-1} of the polymerized material in relation to the nonpolymerized material[32] according to the following formula:

$$DC = \left(Cured_{1638}/Cured_{1730}/Uncured_{1638}/Uncured_{1730}\right) \times 100.$$

Statistical Analysis

Observing the requisites of normality and homoscedasticity, polymerization stress and volumetric shrinkage data were submitted to one-way analysis of variance and the Tukey test. The DC and gap percentage were submitted to Kruskal-Wallis and Student-Newman-Keuls tests. Regression analyses were performed between the interfacial gap and either polymerization stress, DC, or shrinkage. All analyses were performed with a level of significance of 0.05.

RESULTS

The means and standard deviations of polymerization stress, interfacial gap, post-gel volumetric shrinkage, and DC are presented in Table 3. Filtek Bulk-Fill Flowable Restorative developed the lowest polymerization stress, which was statistically lower than those of both self-adhesive composites and similar to that of the Tetric N-flow Bulk-Fill, Filtek Z350 XT Flowable Restorative, and Tetric N-flow. Vertise Flow showed the highest polymerization stress, differing from both the bulk-fill composite and the Z350 XT Flowable Restorative ($p<0.001$).

Tetric N-Flow Bulk-Fill showed the lowest percentage of interfacial gaps, similar to Tetric N-Flow. Vertise Flow had the highest percentage, similar to Fusio Liquid Dentin. Fusio Liquid Dentin showed a similar gap percentage to Z350, Tetric N-flow Bulk-Fill, and Tetric-N-Flow ($p<0.001$).

The Z350 XT Flowable Restorative showed the highest volumetric shrinkage and differed from all groups ($p<0.001$). The shrinkage of both self-adhesive resins was lower than that of the two control flowable composites (Z350 and Tetric N-Flow) and similar to that of the bulk-fill materials. Tetric N-Flow Bulk-Fill and Vertise Flow presented higher conversions than the control materials and Filtek Bulk-Fill Flowable Restorative composite. Tetric N-flow showed the lowest DC, similar to that of Filtek Bulk-Fill Flowable Restorative ($p<0.001$).

The regression analysis between the interfacial gap and polymerization stress involving all six data points did not show a high coefficient ($r=0.43$). However, when Z350 XT Flowable Restorative and Filtek Bulk-Fill Flowable Restorative were excluded, the remaining four composites showed a very good fit

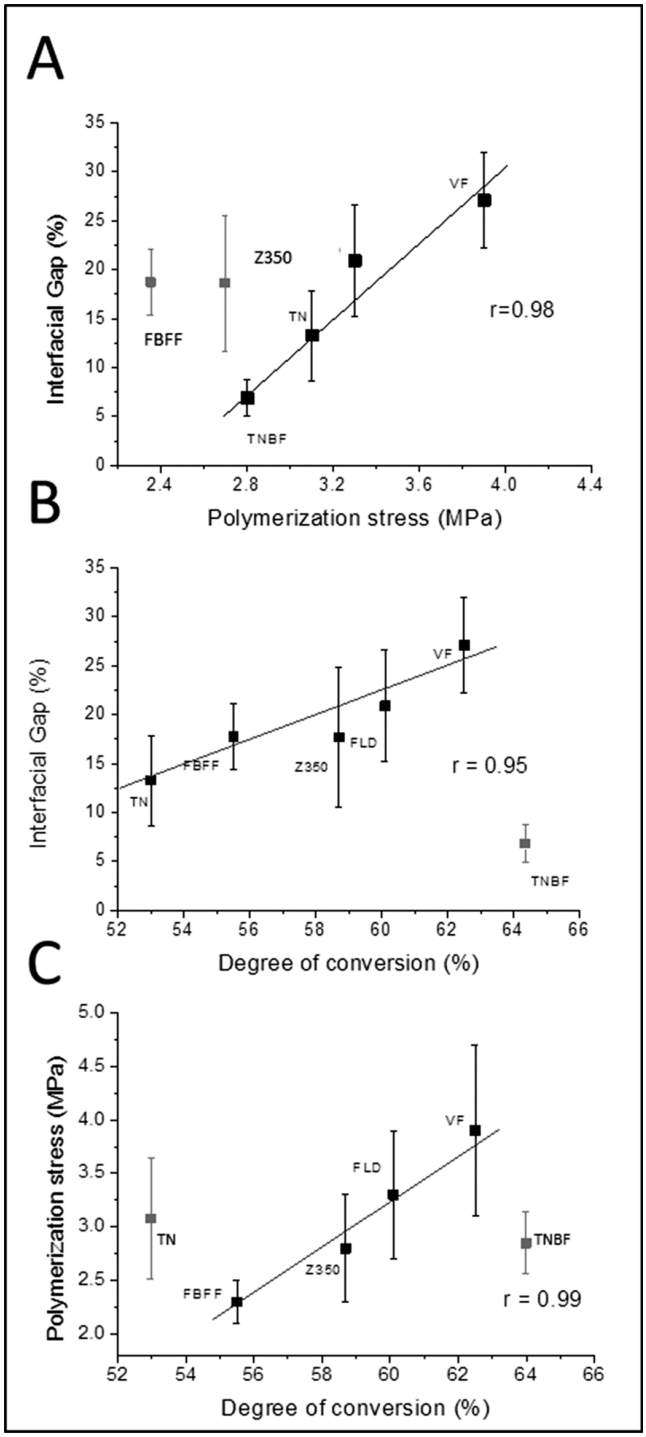

Figure 2. *Correlation analysis between the (A): interfacial gap and polymerization stress, (B): interfacial gap and degree of conversion, and (C): polymerization stress and degree of conversion. FBFF, Filtek Bulk-Fill Flowable Restorative; FLD, Fusio Liquid Dentin; TN, Tetric N-Flow; TNBF, Tetric N-Flow Bulk-Fill; VL, Vertise Flow; Z350, Z350 XT Flowable Restorative.*

with the regression line (r=0.97, Figure 2A). Similar situations occurred between the interfacial gap and DC, where a strong fit was observed after removing Tetric N-Flow Bulk-Fill (r=0.95, Figure 2B), and polymerization stress and DC after both Tetric N-Flow and Tetric N-Flow Bulk-Fill were removed from the regression analysis (r=0.99, Figure 2C). Finally, none of the regressions involving volumetric post-gel shrinkage showed high coefficients.

DISCUSSION

The hypothesis of the study was rejected, as the tested composites presented differences in results for all the evaluated variables. No particular trends were observed when the control and bulk-fill composites were compared. However, Vertise Flow presented higher interfacial gaps and polymerization stress than the other composites.

For marginal gap evaluation, each material was photoactivated according to the manufacturer's instructions, resulting in differences in the radiant exposure received, whereas for polymerization stress, volumetric shrinkage, and DC the same radiant exposure was used for all materials (1200 mW/cm^2 × 25 seconds). Following the manufacturer's instructions looked more important to minimize interfacial failures and reach the best performance of the material when a clinical situation was considered than to standardize the radiant exposure, especially because interfacial gap development can be attributed to several factors related not only to composite resins but also to system adhesives, bonding substrates, and cavity design.[24,25,30,33] In fact, it was observed that when a higher radiant exposure was used, a higher percentage of interfacial gap was observed. This finding should be considered with caution since the materials received different radiant exposure, but also present different composition, and the radiant exposure followed the manufacturer's instructions, so it is the way that clinicians would use the product. Despite differences in curing protocol, a moderate correlation was observed between gap and polymerization stress considering all six composites, and when Z350 XT Flowable Restorative and Filtek Bulk-Fill Flowable Restorative were removed from consideration, the regression coefficient increased to 0.99. Note that although both composites had very similar gap values, these values were much higher than what could be predicted by the regression line based on their polymerization stress values, or even in their radiant exposure. This could be attributed to a lower bond strength of the Single Bond Universal adhesive

used in a self-etching mode.[34] Some studies have demonstrated that the Vertise Flow material presents lower bond strength than both control flowable materials tested in the present study and Fusio Liquid Dentin.[22,23,35,36] Its relatively high filler fraction (70 wt%) results in a high viscosity, and consequently, the wettability of the material on the substrate is impaired. Additionally, the present study showed that Vertise Flow also developed high polymerization stress, which, when associated with the low bond strength, and high radiant exposure would explain its high interfacial gap percentage. A previous study demonstrated that polymerization stress measured in a high compliance system is correlated to the gap formation,[25] even if the gap C-factor is higher than the C-factor of the polymerization stress set up, as in the present study. Also, it has been established that C-factor is significant only in very low compliance systems, which is not the case for a dental cavity.[26,37]

A strong correlation was also observed between the DC and interfacial gap after removing Tetric N-Flow Bulk-Fill and between the DC and polymerization stress after removing Tetric N-Flow Bulk-Fill and Tetric N-Flow. The correlation between the DC and polymerization stress has been previously described in the literature,[37] and it is stronger when the same material is compared with several DC levels.[38] For the Tetric N-Flow Bulk-Fill composite, a low interfacial gap percentage was observed, even with a high DC. The manufacturer notes that this material contains prepolymerized silanized fillers with low elastic modulus as an intrinsic stress relief mechanism. In addition to camphorquinone, the composite contains a photoinitiator (a dibenzoyl germanium derivative) with a higher absorption coefficient, which would explain its high DC.

The necessity of cutting the teeth before doing the replica is a limitation of the technique and can represent some interfacial challenges regarding heating and vibration; in order to minimize that, teeth were sectioned under constant water irrigation and low cutting speed (300 rpm). Also, to minimize bias, the interfacial gap analysis was performed by a single examiner. The range of marginal gap observed in the present study (7%-27%) was similar to the range observed by other researchers studying enamel (5%-17%) and dentin (4%-30%)[29,39,40] that evaluated both high- and low-viscosity materials using the same methodology (scanning electron microscopy analysis). However, Tekce and others[41] observed lower values than those in the present study (4%-6%), but they tested only high-viscosity composites, which could explain the differences observed.

Although some studies have pointed to a direct relation between volumetric shrinkage and polymerization stress[37] or between volumetric shrinkage and interfacial gap,[42] no correlation was observed in the present study. This may be due to the variability in the composition of these commercial materials, which results not only in different shrinkage but also in distinct conversion, elastic modulus, and viscosity. All of these properties interact to influence stress development and gap formation.[43] Both of the self-adhesive composites presented lower shrinkage than the control materials. The type and concentration of monomers in the polymeric matrix and the filler concentration interact to determine the volumetric shrinkage of materials.[43] In spite of the absence of bisphenylglycidyl dimethacrylate (BisGMA), the lower shrinkage of self-adhesive materials can be ascribed to the presence of hydroxyethyl methacrylate (HEMA), a monomethacrylate that is less reactive and generates linear chains, thus reducing the cross-linking density and volumetric shrinkage.[44] The high filler content of the Vertise Flow also contributes to its low shrinkage. The high shrinkage displayed by Z350 XT Flowable Restorative can be explained by the fact that triethylene glycol dumethacrylate (TEGDMA) is the only diluent monomer present in its formulation, whereas in all the other composites, diurethane dimethacrylate (UDMA) or ethoxylated bisphenol-A dimethacrylate (BisEMA) are added to partially or totally replace TEGDMA.[45]

It should be pointed out that the photoactivation mode is an important factor to consider in the present data since it affects all the evaluated properties. The curing unit used in the present study has a 5-second ramp mode until it reaches the maximum irradiance (1200 mW/cm^2); after that the irradiance is kept constant. Studies have shown that the ramp mode is effective to reduce the polymerization stress of composites by extending the pre-gel phase—and consequently marginal gap and post-gel volumetric shrinkage—without compromising the conversion.[46,47]

According to the revealed data and within the limitations of the present study, it should be noted that the bulk-fill materials showed a similar performance to the control materials, and concerns about a higher marginal gap were refuted. However, the self-adhesive composites presented at least a tendency for higher interfacial gaps than the control and bulk-fill materials, which can be associated with their significantly higher polymerization stress values. Therefore, self-adhesive composites should be used

with caution by dentists because they still need to be improved to reach an interfacial integrity similar to that of control or bulk-fill flowable materials.

CONCLUSIONS

The two bulk-fill composites presented polymerization stress similar to that of control composites, but one of them showed a significantly lower marginal gap than one of the control materials. For the two self-adhesive composites, one presented significantly higher polymerization stress than one of the control materials and a significantly larger marginal gap than both control materials. The other self-adhesive material was similar to the control materials in both polymerization stress and marginal gap.

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Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects oversight committee guidelines and policies of the Research Ethics Committee of Ibirapuera University. The approval code issued for this study is CAAE 67796417.7.0000.5597.

Conflict of Interest

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

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