"Clinical Performance of an Incrementally Placed Highly Filled Composite, an Incrementally Placed Flowable Composite, and a Bulk Filled Composite in Class II Restorations"

Protocol February 12, 2020 (1/9/19 modification)

NCT02889835

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Introduction and Review of the Literature

Flowable composites were first introduced to the dental profession in the 1990's.[1] The handling characteristics and syringe delivery system of flowable composites remove some of the challenges encountered with placing composite resin in small to medium size tooth preparations since the small tips allow the filling material to be syringed placed. Early flowable composite resins were produced by reducing filler content or increasing the diluent monomers in the composite formulation to increase flow[2]. A comparison of the filler content of these earlier flowable formulations were reported to be 20 to 25% less than that of the universal composite materials[1]. Unfortunately by reducing the reinforcing filler particles the mechanical properties of flowable composites are compromised[1,2].

Filler content influences the polymerization shrinkage of resin composites. Since filler particles, unlike resin, do not contract during polymerization, increased filler content will decrease the polymerization shrinkage of composite resins. In studies of experimental composites filled with varying concentrations of filler particles, filler concentration was inversely correlated to shrinkage and shrinkage stress.[3,4] As flowable composite resin improved new resin monomers were produced further reducing shrinkage and shrinkage stress.[3] Commercially available materials have demonstrated that composites with lower filler content have higher volumetric shrinkage[5-7], shrinkage stress[6,7] and shrinkage strain[8] than more highly filled materials. However volumetric shrinkage was not correlated to shrinkage stress for a series of commercially available flowable composites.[7] This surprising data was explained by the reduced modulus of elasticity which allows flowable composites to compensate for shrinkage due to flow prior to polymerization.[5] The clinical repercussion of polymerization shrinkage is tooth-composite marginal opening, possibly leading to leakage under a restoration. In a vitro study Bonilla et al reported increased leakage under flowable composite occlusal restorations compared to highly-filled composites.[9]

Early flowable composites, with reduced filler content, had less flexural strength than higher filled conventional composite filling materials raising concerns about increased bulk fracture of flowable composite resin restorations. Using an experimental composite made by increasing hybrid filler content up to 65.2vol% and nanoparticle filler content up to 40wt% produced increased flexural strength.[10,11] A comparative study of 72 commercially available composites showed that flowable resins with higher filler load (up to 60vol%) had increased flexural strength.[12] However when the flexural strength between commercially available flowable composites and their universal counterparts were compared the flowable materials had higher flexural strength. Upon closer examination it was discovered that many of the flowable composites had higher filler concentration than the corresponding universal material.[13,14] Two studies examining fracture properties determined that flowable materials showed similar fracture strength as highly-filled materials.[15,16]

The wear resistance of flowable composites compared to universal composites is controversial. Older materials had lower wear resistance however there is a strong trend toward higher filler loading and increased wear resistance in currently marketed flowable materials. Filler particles protect the weaker resin matrix during abrasive wear.[17] Experimentally filled composites with micro-filers have shown increased wear at concentrations below 48vol% in one study while concentrations between 0-60wt% showed no difference in wear in another.[18,19] Lim et al in an in vitro study reported increasing nano-filler concentration up to 35vol% improved wear resistance.[20]

In vitro wear studies of commercially available composites have generally shown more wear on flowable composites than highly-filled materials if the filler concentrations in both materials is similar.[16,21] One study reported less wear on flowable composites, however, the flowable composites had higher filler concentration than the comparative universal composites.[14]

A summary of laboratory data suggests that some flowable composites have greater polymerization shrinkage, increased wear and comparable flexural strength and fracture properties compared with universal composites. Because some physical properties are lower than conventional composites, flowable composites have been used clinically for restorations with minimal occlusal loading, such as liners, small Class I and II cavities and Class V lesions. A clinical trial of small Class I restorations restored with 2 flowable composites demonstrated that marginal discoloration and marginal adaption worsened 3 years after baseline. However as these materials have developed their clinical performance has improved. Gallo et al have shown that the presence of secondary caries, anatomical form, retention, polishability, and color match of the flowable restorations did not significantly change over the three year period.[22,23] A 2-year clinical trial compared conventional and flowable composites in Class II restorations and observed no difference between the materials.[24] One 3-year and three 2-year clinical trials compared conventional and flowable composites in cervical lesions for marginal discoloration, marginal adaptation, secondary caries, surface texture, color match, and anatomic form.[25-28] No difference was discovered between materials in any study except a clinical comparing restorations for non-carious cervical restorations. One of these reported that the conventional material had superior marginal adaptation.[25]

Traditionally composite resin restorations have been placed in 2 mm increments. These increments are added to fill the cavity due to the limited depth of cure that the restoring composite had. Recently a bulk placed flowable resin composite (Filtek Bulk Fill Flowable Restorative, 3M ESPE) has been developed and marketed with a curing system that will allow fewer increments to be placed to restore the cavity. This composite resin has a 4mm depth of cure which allows fewer larger increments to be placed which shortens the tie needed to restore the tooth. Wear of the composite resin is an important property for the clinical success for dental composites especially for very large restorations with heavy occlusal contacts and is especially for patients with heavy or abnormal occlusal function. [2,3]

In vitro wear testing methods are used to measure wear and predict in vivo wear of composites. These methods are reliable and more cost effective than in vivo trials and allow quantitative measurement of wear.[36,37] From data produced from in vitro wear resistance testing, the 3M Bulk Filled Flowable material has adequate wear resistance to be placed in a class II load bearing area.

Table 1: *In vitro* wear of bulk placed composite resins

Materials	Type	Volume/(mm3)
Venus Bulk Fill-Flowable/Heraeus Kulzer	Flowable/nano-hybrid	$0.024\pm0.004^{A,F}$
Filtek Bulk Fill/3M ESPE		$0.012\pm0.001^{B,C}$

Tetric Evo Ceram BulkFill/Ivoclar	Nano-hybrid	0.011±0.002[C]
SureFil High Density Posterior Restorative (HDR)/Dentsply	Packable	0.007±0.001[D]
SureFil SDR Flow/Dentsply	Flowable	0.04±0.01[E]
Sonic Fill/Kerr	Packable/nano-hybrid/sonically activated delivery	0.02±0.004[F]
Quixx Posterior Restorative	Packable	0.02±0.006
Z100/3M ESPE/(Control)	Packable/microhybrid	0.004±0.001[G]

Studies in the past suggest that highly filled microhybrid composites may have greater wear resistance for contact-supporting posterior restorations than flowable microfilled resins. 39,40 However current generation flowable composites have higher filler content and demonstrate higher wear resistance than early flowable resins and even some conventional bulk filled materials (Table 1).[41-43]

Experimental Design and Methods:

This clinical trial will compare three techniques using three materials (one for each technique) for restoring class II preparations. The purpose of this clinical trial is to evaluate the effectiveness of a flowable resin composite (Filtek Supreme Ultra Flowable Restorative, filler content: 65 wt% and 46 vol%) used in Class II restorations compared to a conventional highly filled composite resin (Filtek Supreme Ultra, filler content: 72.5 wt% and 55.6 vol%) and Filtek Bulk Fill in class II restorations. This is a randomized prospective single-center, single-blinded, clinical trial 36 months in duration. We propose using one bonding agent (Scotchbond Universal, 3M ESPE) for this study with a total etch technique (the enamel and the dentin are etched). Success with Scotchbond Universal, using the total etch technique was 100% in a 2 year[44] and 98% a three year[45] clinical study.

Purpose: This study will examine the clinical success of 3 composite resins, a conventional composite (Filtek Supreme Ultra Universal Restorative, 3M ESPE) placed in 2 mm increments, a flowable composite resin (3M ESPE, Filtek Supreme Ultra Flowable, a flowable composite placed in 2mm increments) and a bulk placed and cured composite (Filtek Bulk Fill Flowable Restorative, 3M ESPE). All composite resin restorations will be placed using a single adhesive Scotchbond Universal in a three year clinical trial.

Objective: The objective of this study is to evaluate the clinical efficacy of these three restorative materials placed in class II posterior restorations using Scotchbond Universal adhesive. To accomplish this goal we will place **50 class II** composite resin restorations for each material and evaluate them in accordance with the ADA and FDI criteria.

Specific Aims

1. Place and 50 composite resins of each composite in Class II cavity preparations, evaluate the resin composite restorations used in the three techniques at baseline, 6 months, 1 year, 2 years, and 3 years, using specific criteria (Attachment 2).
2.

Specific Aim: To place three commercially available resin composites in Class II cavity preparations, evaluate the resin composite restorations at baseline, 6 months, 1 year, 2 and 3years using specific criteria (direct and indirect).

Materials:

Filtek Supreme Ultra Universal, 3M ESPE, placed and cured in 2 mm increments, Filtek Supreme Ultra Flowable a flowable composite resin placed and cured in 2 mm increments, and Filtek Bulk Fill Flowable a composite placed and cured in 4 mm increments will be used in this study. All restorations will be placed with an adhesive, Scotchbond Universal, using a total etch technique. **All composites and the adhesive used in this study are in use in the US dental market at this time and are commercially available (3M ESPE website).**

Duration of the Investigation:

36 months

Number of Restorations:

At least 40 restorations are needed at 36-month recall. Our experience at the UAB – School of Dentistry Clinical Research area with dropouts over a 36-month period is about 10%. Fifty restorations will be placed to ensure ample restorations at the 36-month recall.

Class of Restorations:

Restorations will be placed in separate preparations in Class II in upper and lower jaw molars. All teeth will have natural teeth or crown and bridgework as antagonists. For the clinical evaluation of the resin, specific criteria (Attachment 2). will be used to evaluate, directly and indirectly.

Distribution of Restorations:

Sets of three restorations, one of each composite will be placed per patient for evaluation. If needed by the subject two sets of class restorations may be placed.

Patient Population:

Patients for this investigation will be selected from patients of the Dental School at the University of Alabama at Birmingham (UAB) and from those recruited from advertisements placed in newspaper ads. Approximately 50 subjects ranging in age from 19 to 90 years will be recruited for this study. The estimated subject number depends upon the number of restorations placed per subject. Pregnant women will not be included in this study.

Inclusion Criteria:

- must have given written informed consent to participate in the trial
- must need at least three posterior dental fillings
- replacement restorations due to caries or an esthetic replacement with or without caries are acceptable.
- must be available for the required post-operative follow-up visits
- restorations must be in contact with opposing natural or crowned teeth with at least at least one occlusal contact in habitual closure
- Class II restorations must have at least one proximal contact
- all restorations must Class II with a proximal contact with a natural or artificial tooth

Subjects may be excluded from this study if they:

- have severe medical complications (organ transplants, long term antibiotic or steroid treatment, cancer or immunocompromised) and disabilities who may not be able to tolerate the time required to complete the restorations or to provide adequate oral hygiene
- have xerostomia either by taking medications known to produce xerostomia or those with radiation induced or Sjogren's syndrome patients
- have chronic periodontitis, rampant caries or poor oral hygiene which may require extraction of the teeth to be restored
- are unavailable for long term recall
- cannot tolerate the rubber dam required for isolation of the tooth during preparation and restoration.
- do not meet all inclusion criteria
- present with any systemic or local disorders that contra-indicate the dental procedures included in this study
- have an unstable occlusion
- have severe bruxing or clenching or in need of TMJ related therapy
- have teeth with periapical pathology or expected pulp exposures
- have teeth that are non-vital or that exhibit signs of pulpal pathology
- are pregnant.

Screening:

Each subject will be screened for compliance with the inclusion/exclusion criteria specified above. After the risks and benefits are explained to the subject, they will be asked if they understand and any questions they have will be answered. They will then be asked to give written informed consent and provided a copy of the consent form.

Risks to the Patient:

Patients will wear lead aprons as a protective measure during the radiographic procedure to minimize risk. Patient data will be monitored and if, during the course of the study, it becomes apparent that the restorative material is significantly poorer than other currently marketed materials, the patient will be informed and if needed the restorations replaced.

Consent:

Consent for this study will be obtained prior to the initial examination and the initiation of any portion of the study. The PI or Co-investigator will explain the consent to the patient and answer questions they may have. The consent forms and all records associated with this study will be maintained in the clinical research office (Room 611) in the Clinical Research Clinic (three locked doors to enter) to ensure the records are confidential. Each subject will provide written consent to participate in this study in accordance with Federal regulations (21 CFR Parts 50 and 56).

Materials

Composite resins	Shades	% Filler	Filler type
Filtek Supreme Ultra Flowable		65 weight % and 46 volume %	0.1 to 5.0 microns ytterbium trifluoride, a non-agglomerated/non-aggregated surface modified 20 nm silica filler, on-agglomerated/non-aggregated surface modified 75 nm silica filler, and a surface modified aggregated zirconia/silica cluster filler (comprised of 20 nm silica and 4 to 11 nm zirconia particles). The aggregate has an average cluster size of 0.6 to 10 microns.
Filtek Supreme Ultra Universal Restorative		78.5% weight and 63.3 % by volume	a non-agglomerated/non-aggregated surface modified 20 nm silica filler, on-agglomerated/non-aggregated surface modified 75 nm silica filler, and a surface modified aggregated zirconia/silica cluster filler (comprised of 20 nm silica and 4 to 11 nm zirconia particles). The aggregate has an average cluster size of 0.6 to 10 microns.
Filtek Bulk Fill Flowable Restorative	A1, A2, A3. B1 and C2 shades.	64.5 % weight or 42.5 % volume %	20 nm silica and 4-11 nm zirconia, aggregated zirconia/silica clusters and 100nm ytterbium trifluoride filler

Materials and Methods:

Digital images will be made to document the restoration size and placement at each step. Teeth will be cleaned with pumice and water to remove surface stains, a shade selected and the teeth to be restored will be isolated with a rubber dam. Filtek Supreme Ultra and Filtek Supreme Ultra Flowable, will be placed inserted in 2 mm increments and lighted cure using a LED curing light with output of 1000-2000mW/cm^2 which will be monitored to ensure irradiance greater than 1000mW/cm^2 throughout the trial. Filtek Supreme Ultra will also be placed and cured in 2mm increments body, enamel will be cured for 10 seconds while dentin, A6B and B 5B will be cured for 20 seconds. These will be compared with each other and to Filtek Bulk Fill placed in 4 increments and cured for 10 seconds. All restored teeth will be in occlusion and at least one proximal surface of each class II restorations will be in proximal contact with an adjacent tooth. Cavity preparations will be prepared for all restorations following rubber dam isolation unless it is not possible due to abnormal anatomic considerations.

Cavity Preparation Design

Each proximal surface to be prepared will be pre-wedged with wooden wedges. Restorations must have a buccal to lingual width no greater than 1/3 the distance from buccal to lingual/palatal cusp tips. All prepared margins will be placed ninety degrees to the external tooth surface. Any tooth with a pulpal exposure will be excluded from the study. Any cavity preparations judged to be within 1mm of pulpal tissue either clinically or radiographically may be lined with Vitrebond (3M ESPE) a glass ionomer liner. A light cured, universal bonding agent Scotchbond Universal (3M ESPE, St Paul, MN) will be used for the restorations. Each composite will be placed per manufacturer directions. Composi-Tight (Garrison Dental) or Trident sectional matrices will be used with class 2 restorations. However at the choice of the operator a Tofflemire circumferential matrix may be used. The composite will be photoinitiated with a light with an output of at least 1000 mW/cm^2. The two resin composites (Flowable and Filtek Supreme Ultra will be placed using an incremental fill technique, beginning with a 2 mm initial increment in the gingival floor, and completing the restoration with 2 mm increments. The bulk fill will be placed and cured in 4 mm increments. Four clinicians will insert fifty restorations. Carbide finishing burs will be used to remove gross excess, followed by finishing strips and disks (Sof-Lex, 3M, St Paul, MN), and the Sof Lex Diamond Polishing System. All polishing will be done at slow speed with water spray. After removing the rubber dam, adjusting the occlusion and polishing the restoration a digital image with the articulating paper marks on the tooth will be made. An conventional impression of the restoration will be taken with PVS impression material (Imprint 4) in a full arch or quadrant tray.

Each restoration will be evaluated directly and indirectly at baseline (one week after restoration placement), at 6 months, 1, 2 and 3 years. The direct clinical evaluations will be made using a modification of the USPHS and FDI guidelines. Each restoration will be evaluated for proximal contact, marginal discoloration, secondary caries, loss of anatomical form, and marginal adaptation, surface condition and post operative sensitivity. Digital images will be used to document marginal staining and color match of the composite restoration to the tooth. A visual analog scale will be used to evaluate the sensitivity of the restoration by placing a cotton pellet soaked with skin refrigerant for three seconds. The subject will mark their response on a calibrated

line (10mm) where 1 represents no pain and 10 represents the worse pain possible like major surgery, childbirth etc.

Evaluators will be trained and calibrated. Preclinical sessions will train clinicians by preparing and restoring at least two extracted teeth mounted in stone. A clinical training session will train clinicians to conduct the evaluations during sessions using patients with similar restorations placed in a previous clinical trial. Scores for each evaluator will be compared to other evaluators and inter-evaluator comparisons made. The trained evaluators will independently evaluate each restoration in our clinical study and a forced consensus obtained if necessary. Those who evaluate the restorations must not evaluate the restorations they placed. Additional training will also be obtained by the e-calib tool.

Data Analysis:

The categorized clinical assessment data (color, marginal discoloration, secondary caries, anatomic form, marginal adaptation) will be summarized by computing percentages for each category and used to describe trends noted in the performance of the groups. In the analysis of categorical data of staining, marginal integrity, proximal contact, recurrent caries, retention, anatomical form and marginal adaptation, the frequency distribution over various categories will be calculated and reported. A sample size of 50 restorations is not based on a statistical plan, but rather on guidelines put forth by the American Dental Association for obtaining approval as an amalgam replacement for posterior restorations. The guidelines specifically call for an evaluation of a minimum of 40 restorations in a minimum of 20 subjects at 18 months. The basis for sample size is based by taking subject attrition into account over the 36 month clinical evaluation. All enrolled subjects, defined as those who have at least one experimental composite resin restoration - will be evaluated for safety of the composite.

Restoration survival at thirty-six months will be assessed using Kaplan-Meier survival analysis and Log Rank (Mantel-Cox) test for equality. The three groups will compared with Kruskal-Wallis H test (mean rank scores, chi-square values, degrees of freedom, and p-values) for each FDI criteria at the thirty-six month recall using SPSS software (Microsoft).

Criteria for evaluation:

Modified USPHA and FDI criteria will be used to assess individual restorations. Silicone impressions will be made at each recall to measure the marginal integrity and loss of anatomical form of each restoration.

SUMMARY

Subjects that are from 19-90 years old will be eligible for this study. Patients with health problems, who cannot tolerate the dental appointment, will be excluded. Signs advertising the study will be posted in the dental school and in the local newspaper. Up to 2 sets of three dental fillings for each patient will be filled with these materials in moderate sized cavities. The patient's teeth will be restored by using a local anesthetic and a rubber sheet (rubber dam) placed over the prepared teeth to isolate the cavities from the patient's saliva. The cavities will be prepared using currently accepted procedures, an impression or digital scan made of the preparation and the resin composite filling material will be placed after applying an etchant and adhesive to the cavity. The filling materials will be placed in increments according to the instructions for use. To ensure that the material is set or hardened sufficiently, the curing light (Elipar Deep Cure S, 3M ESPE) that activates the polymerization reactions of the filling material. The light will be routinely checked to verify it meets the curing specifications noted in the composite instructions for use. The biting surface of the restoration will be adjusted so that the patient's teeth function the same as before the procedure. The restoration will be polished and an impression and digital scan of the completed filling will be made to record the filling at that point with and without occlusal biting markings. A trained dentist will examine the patient's fillings at 1 week, 6 months, 1, 2, and 3 years after placement of the filling. At each recall appointment, discoloration and decay at the margin of the restoration, wear of the biting surface, presence of defects such as gaps at the margin, amount of contact between adjacent teeth, and color matching with natural teeth will be recorded as scores according to an accepted clinical rating system. For each category in the evaluation, percentages of alpha (perfect) scores will be tabulated. Video images of the procedure to document the filling placement for at least one patient will be made