Confidential

Tufts UNIVERSITY | School of Dental Medicine

Clinical Evaluation of Kerr SonicFill™ 2 vs 3M ESPE Filtek™ Supreme Ultra Universal Restorative

---

Principal Investigator: Gerard Kugel, DMD, MS, PhD

Co-Investigators: Mabi Singh, DMD, MS
Britta Magnuson, DMD
Yoon H. Kang, DMD, PhD
Matthew Finkelman, PhD
Duong Tran, DDS, MPH, PhD
Ronald Perry, DMD, MS

Study Location: Tufts University School of Dental Medicine
One Kneeland Street
Boston, MA 02111

Sponsor: Kavo Kerr Group

Protocol Version Date: 11/2/2018

I) Introduction

A) Aim/Hypothesis/Objective

The primary objective of this study is to evaluate the clinical performance of a sonic-activated, bulk fill composite, SonicFill™ 2, by comparing it to Filtek™ Supreme Ultra in the following categories[1]:

Esthetic Properties

- Surface luster
- Staining – surface
- Staining – margin
- Color match and translucency
- Esthetic anatomical form

Functional Properties

- Fracture of material and retention
- Marginal adaptation
- Aproximal anatomical form – contact point
- Radiographic examination (when applicable)
- Patient's view

Biological Properties

- Postoperative (hyper-)sensitivity and tooth vitality
- Recurrence of caries, erosion, abfraction
- Tooth integrity (enamel cracks, tooth fractures)
- Adjacent mucosa

The hypothesis to be tested is that the sonic-activated, bulk fill composite, SonicFill™ 2, will have comparable results to the traditional incremental technique composite, Filtek™ Supreme Ultra, in overall clinical acceptability and in all compared categories

II) Background and Rationale

Marginal leakage appears to be an inherent shortcoming of all dental restorations. [2-6] Various techniques have been advocated to enhance the marginal adaptation and reduce the microleakage of composite restorations. Multilayer techniques, in contrast to bulk packing methods, have decreased marginal gap formations. [7,8]The size reduction of the composite material, the diminution of polymerization shrinkage, and the enlargement of the free surface area in relation to the volume are of great importance in this context. [9] When the whole margin area is first filled with an increment, fewer contraction gaps at the margins can be expected.

Traditional, incrementally filled dental composite material has been on the market for many years, and has been proven successful for use in posterior restorations. Traditional composite techniques require small amounts (up to 2mm) of composite be placed at a time and then light cured. This process is pain staking and time consuming. Newer products on the market are bulk fill – allowing increments of up to 5mm to be placed before light curing. Many of these products then require a capping material to be placed over them. The newer SonicFill™ 2 system is a

sonic-activated, bulk fill composite that allows placement of material up to 5mm without the need for a capping layer.[10] The sonic activated technique allows for easy placement and good adaptation of the restoration. This process also shortens the time necessary to complete a restoration, which benefits both the dental practitioner and the dental patient.

Standard of Care at TUSDM clinics
The standard of care in the TUSDM clinics is to place composite following the incremental technique with Filtek™ Supreme Ultra (the resin composite used as a control in this study).

III) Research Plan

A) Experimental Design

This study is a randomized, split-mouth, controlled, examiner-blinded clinical evaluation of Class II restorations using a new bulk-fill composite (SonicFill™ 2) and comparing it to 3M ESPE Filtek™ Supreme Ultra resin composite placed in the traditional incremental technique.

B) Sample Size and Statistical Analysis

Sample size

A sample size calculation was conducted using nQuery Advisor (version 7.0). The calculation determined that with a sample size of n=35 subjects, all 95% confidence intervals will have a margin of error of no more than 16.6%. Up to 44 subjects will be treated to allow for 20% dropout. Up to 100 will be screened to have 35 qualifying subjects complete the study.

Statistical analysis

Tables of descriptive statistics (counts and percentages for categorical variables, means and standard deviations for continuous variables) will be prepared to summarize the demographic characteristics of the patients, the distribution of restorations and baseline data, and to illustrate the recall and data analysis findings. Because the hypothesis of the study does not involve superiority of one technique over another, and comparable results between SonicFill™ 2 and Filtek™ Supreme Ultra are anticipated, confidence intervals will be used rather than p-values. In particular, for each evaluation category, the percentage of times that SonicFill™ 2 outperforms Filtek™ Supreme Ultra, the percentage of times that Filtek™ Supreme Ultra outperform SonicFill™ 2, and the percentage of times with equal performance will be calculated along with 95% confidence intervals. Frequency distributions will also be calculated for each combination of technique and evaluation category, along with 95% confidence intervals. SPSS (Version 22) and R (Version 3.1.2) will be used in the analysis.

Randomization

A computerized randomization scheme will be developed to randomize which teeth will be in the study and which group each tooth will be in. The "sample function" in R version 3.1.2 will be used. Assignment of study teeth and treatment allocation will be recorded in each subject's Case Report Form (CRF).

Blinding
The restoration grading investigator and the subject will be blinded as to which group each restoration is in.

C) Products
All study materials – SonicFill™ 2, SonicFill™ 2 Handpiece and coupler, Optibond XRT, Scotchbond™ Universal and Filtek™ Supreme Ultra resin composite will be provided by Kavo Kerr Group and have received 510(k) clearance from the United States Food and Drug Administration (FDA) as Class II non-significant risk medical devices. All products will be used according to their FDA clearance in this study.

Group	Resin Composite	Bonding Agent
1	SonicFill™ 2	Optibond XRT
2	Filtek™ Supreme Ultra	Scotchbond™ Universal Adhesive

Receipt and usage of the clinical study supplies and products will be documented in the study file. The study materials will be stored in a locked closet/cabinet and will be accessible only to the research team members. Products may be stored at room temperature. The sponsor may request that some supplies be returned at the end of the study.

Restriction in Device Use
The Principal Investigator is responsible for limiting access of the device to participants in this trial and ensuring it is used only as specified in the protocol. The device shall be stored as specified by the sponsor.

SonicFill™ 2[11]

SonicFill™ 2 is, a sonic-activated, bulk fill dental composite system for posterior restorations that requires no additional capping layer. Proprietary sonic activation enables a rapid flow of composite into the cavity for placement and adaptation.

OptiBond XTR[12]

OptiBond XTR self-etch, light-cure universal dental adhesive Universal compatibility enables use for all direct and indirect restorations. The self-etch primer and adhesive in this 2-bottle system brings increased bond strengths to uncut enamel and dentin. OptiBond XTR uses GPDM (glycerophosphoric acid dimethacrylate, an phosphate based adhesive monomer) technology, ternary solvent system, filled adhesive and optimized formulation to produce adhesion for direct and indirect procedures.

Filtek™ Supreme Ultra Universal Restorative**[13]** Filtek™ Supreme Ultra is a Universal Nanocomposite dental restorative material that is visible-light

activated, designed for use in anterior and posterior restorations of any class. This restorative material is available in a wide variety of Dentin, Enamel, Body, Translucent shades, and all shades are radiopaque. Filtek™ Supreme Ultra uses nanofiller technology to give restorations polish retention.

Scotchbond™ Universal Adhesive[14]
Scotchbond™ Universal is a single-bottle adhesive solution for all surfaces, and can be used in total-etch, self-etch or selective-etch mode for both direct and indirect restorations. Scotchbond™ Universal provides consistent bond strength to both moist and dry etched dentin, without additional primer.

D) Subject Characteristics

1) Inclusion Criteria

To be considered eligible for this study, each patient must meet all criteria listed below:

- Is at least 18 years of age
- Is willing to provide voluntary written informed consent
- Is in good medical health and able to tolerate the dental procedures
- Has 1 pair of qualifying molars or premolars that require Class II restorations. Patients with more than 2 cavities may be enrolled but the additional teeth will not be included in the study.
- Restorations must have a buccal to lingual/palatal width equal to or greater than 1/3 the distance from buccal to lingual/palatal cusp tips
- Study teeth must be in occlusal function and must also be in contact with the neighboring tooth on at least one surface
- Study teeth must be vital (i.e., free of clinical signs and symptoms of periapical pathology)

2) Exclusion Criteria

Subjects will be considered ineligible for the study if they meet <u>any</u> criterion listed below:

- Is currently taking part in an evaluation of other dental restorative materials
- Has chronic periodontitis or rampant caries
- Teeth exhibiting clinical signs of periapical pathology
- Teeth with a history of self-reported preoperative pulpal problems
- Women who are pregnant (self-reported). It is standard of care to post-pone routine dental procedures and radiographed until after pregnancy.
- Women who are breast feeding.
- Known allergy to resin composites or local anesthetics.
- An employee of the sponsor or members of their immediate family.
- Condition affecting salivary flow (e.g., salivary gland disorder, Sjögren's Syndrome)
- Any restorative treatment of the teeth involved in the study in the last 12 months.
- Are unwilling or unable to have dental radiographs or photographs taken of their dentition and soft tissues

- Any other condition which is the view of the investigator may affect the ability of a patient to complete the study.

3) Subject Withdrawal/Termination Criteria
   - Subjects who do not comply with the study procedures, such as returning for follow up visits may be withdrawn from the study.
   - Subjects who decide to stop participating in the study will be withdrawn.
   - Subjects who have a clinical pulp exposure during restoration visit will be withdrawn from study and standard of care procedures for pulp exposure and restoration placement will be followed and patient will be advised if they need further treatment and should be seen by a dentist outside the study (such as root canal therapy and/or crown).
   - Subjects who have external procedures or treatments performed on study teeth will be withdrawn from the study. However, if external treatment is only performed on one study tooth, the subject can still participate in the study and the remaining, unaffected study tooth will still be monitored for research purposes.
   - Unanticipated Adverse Device Effect

     The Principal Investigator will determine whether subjects (either withdrawn subjects or subjects completing the study) are in need of additional treatment and/or follow-up observation as a result of participation in this trial (such as if a restoration fails). Additional treatment may be needed for teeth that are not included in this study, but require a restoration. Subjects and/or their insurance will be responsible for the cost of any standard of care follow-up visits or additional treatment that is not part of this study.

E) Assessment

1) Risk

The patient may expect the usual post-operative pain or sensitivity that is typically associated with the standard of care placement of dental restorations, (the risks for both groups is anticipated to be the same and are not greater than standard of care risks), including: tooth pain, bite pain/sensitivity, gingival sensitivity/tenderness/redness, discomfort from the anesthetic, or allergic reaction to the anesthetic. These events are expected to be *localized* and *transient in nature*.

Another potential risk is partial loss, chipping, or fracture of the restoration, trauma to restored or adjacent teeth, or total loss of the restoration. However, the rate of occurrence is anticipated to be very low (no higher than for other restorations).

The risk of radiographs will be kept to a minimum using standard of care procedures (lead apron, digital radiographs, etc.). It is standard of care to have bitewing radiographs annually for caries detection. It is standard of care to have periapical radiographs prior to class II restorations to ensure there are no signs of periapical pathology. These risks are not beyond

standard of care risks. At radiograph time, all female subjects will be questioned regarding pregnancy. Any responding positively at the time of screening will be excluded in accordance with the inclusion/exclusion criteria. If a subject becomes pregnant during the course of the study, radiographs will be delayed until after delivery.

There is the risk of loss of confidentiality to the subject by participating in this study. This risk will be kept to a minimum by following procedures listed under confidentiality section.

2) Benefits
There is no direct medical benefit to the subject for participation in this study.

3) Alternatives
Patients may choose not to participate in the study. A patient may choose to have the procedure completed at the TUSDM or their private dentist at normal clinic fees.

F) Study Procedures

Visit 1 (Approximately 1 hour): Screening
The subjects will be instructed to read the informed consent form (ICF). Subjects will be given ample time to have any questions answered. If a subject decides to participate, he or she will be instructed to sign the ICF. A copy of the ICF will be given to the subject.

Subject will be asked to complete demographic information and a medical history.

An oral exam, including evaluation of oral cavity, soft and hard tissues, will be completed following standard of care procedures in US dentistry using a mouth mirror and dental explorer.

Radiographs (bitewings) will be taken if none exist that are less than 1 year old and of diagnostic quality. It is within standard of care to take radiographs for caries detection if none less than 1 year old exist.

Inclusion/exclusion criteria will be evaluated.

If you are eligible to continue in the study, randomization will occur.

Periapical radiographs will be taken on the randomized teeth (if none exist that are less than 1 year old and of diagnostic quality). It is standard of care to have periapical radiographs prior to class II restorations to ensure there are no signs of periapical pathology.

Visit 2 (May occur same day as Visit 1 and up to 1 month after Visit 1)(1.5-2 hours):Restoration Placement

Medical history will be reviewed and any changes will be noted.

Eligibility and subject withdrawal criteria will be reviewed to ensure the subject still qualifies for the study.

Oral exam will occur as at Visit 1.

Intraoral photographs will be taken (photographs will only be intraoral, no facial photographs will be taken).

Sensitivity will be assessed on randomized teeth. Subjects will be asked if they experience any sensitivity on the randomized teeth. If yes, they will be asked to rate their sensitivity on a scale of 1-100.

Group 1: SonicFill™ 2 Restoration
Local anesthesia will be achieved following standard of care.
Composite shade will be chosen.
Rubber dam or other appropriate isolation will be placed following standard of care.
Tooth will be prepared for restoration following standard of care (using handpieces, burs, hand instruments, etc. as needed). All decay will be removed.
Etching and bonding will be achieved using Optibond XRT following manufacturer's instructions.
Restoration will be placed and cured using SonicFill 2 following manufacturer's instructions.
Finishing and polishing steps will be completed using Axis ProGloss Polishing System.

Group 2: Filtek™ Supreme Ultra:
Local anesthesia will be achieved following standard of care.
Composite shade will be chosen.
Rubber dam or other appropriate isolation will be placed following standard of care.
Tooth will be prepared for restoration following standard of care (using handpieces, burs, hand instruments, etc. as needed). All decay will be removed.
Etching and bonding will be achieved using Scotchbond Universal following manufacturer's instructions.
Restoration will be placed and cured using Filtek™ Supreme Ultra following manufacturer's instructions.

Finishing and polishing steps will be completed using Axis ProGloss Polishing System.

Intraoral photographs will be taken.

Restorations will be evaluated by the grading investigator (an investigator other than who placed the restorations) according to Hickel criteria (Appendix A).[1]

Visit 3 (6 months +/- 1 month after Visit 2) (Approximately 30 mins): Follow-Up

Medical history will be reviewed and any changes will be noted.

Eligibility and subject withdrawal criteria will be reviewed to ensure the subject still qualifies for the study.

Oral exam will occur as at Visit 1.

Restorations will be evaluated by the grading investigator (an investigator other than who placed the restorations) according to Hickel criteria.[1]

Intraoral photographs will be taken.

Visit 4 (1 year +/- 1 month after Visit 2) (Approximately 45 mins): Follow Up

Medical history will be reviewed and any changes will be noted.

Eligibility and subject withdrawal criteria will be reviewed to ensure the subject still qualifies for the study.

Oral exam will occur as at Visit 1.

Radiographs (periapical radiographs) will be taken. It is within standard of care to take radiographs yearly after restoration placement.

Restorations will be evaluated by the grading investigator (an investigator other than who placed the restorations) according to Hickel criteria.[1]

Intraoral photographs will be taken.

Visit 5 (2 years +/- 2 months after Visit 2) (Approximately 1 hour): Follow Up

A new medical history form will be completed by the subject.

Eligibility and subject withdrawal criteria will be reviewed to ensure the subject still qualifies for the study.

Oral exam will occur as at Visit 1.

Radiographs (periapical radiographs) will be taken. It is within standard of care to take radiographs yearly after restoration placement.

Restorations will be evaluated by the grading investigator (an investigator other than who placed the restorations) according to Hickel criteria.[1]

Intraoral photographs will be taken.

Radiographs

All radiographs will be taken digitally following standard of care procedures, including the subject wearing a lead apron. The radiographs used in this study contain no more radiation than would be used in a customary dental procedure. It is within standard of care to take radiographs for caries screening if radiographs that are of diagnostic quality from within the past 1 year do not exist. It is within standard of care to take radiographs yearly for evaluation after restoration placement. Radiographs will be taken at the one-year and two year recalls. In the event an adverse event is suspected, it is clinically necessary, or due to a dental emergency a radiograph may be taken at the time of the AE or emergency, but it is not the norm for this trial.

At radiograph time, all female subjects will be questioned regarding pregnancy. Any responding positively at the time of screening will be excluded in accordance with the inclusion/exclusion criteria. If a subject becomes pregnant during the course of the study, radiographs will be delayed until after delivery. Subjects unwilling or unable to have dental radiographs will be excluded from the study.

Table 1. Subject Timeline

Appointment / Procedures	Visit 1 Screening	Visit 2 Baseline	Visit 3 6 month	Visit 4 1 year	Visit 5 2 year
Informed Consent Form	X				
Demographics	X				
Medical History	X	X	X	X	X
Evaluate eligibility and withdrawal criteria	X	X	X	X	X
Oral Mucosal Tissue Examination	X	X	X	X	X
Radiographs	If needed			X	X
Randomization	X				
Intraoral Photographs		X	X	X	X
Sensitivity Assessment		X			
Restoration Placement		X			
Hickel Criteria Grading		X	X	X	X
Adverse Event Assessment		X	X	X	X
Stipend	X	X	X	X	X

G) Subject Safety

1) Adverse Event Reporting

Any adverse reactions to the treatment provided as part of the study will be fully investigated and recorded, including details of the appropriate clinical action taken, and reported to both the IRB and contact person at Kerr Corporation.

Adverse Events
An adverse event is any untoward or unfavorable medical occurrence in a human subject, including any abnormal physical exam or laboratory finding, symptom, or disease, temporally associated with a subject's participation in the research.

Adverse events will be recorded in source documents and on case report forms. All adverse events and non-serious situations will be recorded, monitored, and reported to the IRB at time of continuing review or at the study's termination if this occurs before the study's next continuing review.

Serious Adverse Events
A serious adverse event is one that results in death, or is life-threatening, or results in hospitalization or prolongation of existing hospitalization, or results in a persistent or significant disability/incapacitation, or results in a

congenital anomaly/birth defect, or may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed above.

Serious adverse events will be recorded in source documents and on case report forms. Serious Adverse Events that meet the criteria of an unanticipated problem will be reported to the IRB within 5 business days following the Reportable New Information Policy. Serious Adverse Events not meeting the criteria for an unanticipated problem will be reported to the IRB at time of continuing review or at the study's termination if this occurs before the study's next continuing review.

Unanticipated Problems
An unanticipated problem is an incident, experience, or outcome that meets all of the following criteria: 1) The nature, severity, or frequency is unexpected for the subject population or research activities as described in the current IRB approved protocol, supporting documents, and the ICF(s); 2) it is related or possibly related to participation in the research; 3) it suggests the research may place the subject or others at a greater risk of harm then was previously recognized.

Unanticipated problems will be recorded in source documents and on case report forms. Unanticipated problems will be reported to the IRB within 5 business days after the PI/study team becomes aware of the problem. A Reportable New Information Form will be submitted to the IRB no later than 5 business days after the PI/study team becomes aware of the problem.

Unanticipated Adverse Device Effects (UADEs)
Unanticipated adverse device effect means any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

UADEs will be documented in source documents and on case report forms as to onset, severity, duration, management, outcome and relatedness to the test device. UADEs will be reported to the IRB within 5 business days after learning of the effect.

H) Ethical Standards
1) Institutional Review Board (IRB) approval will be obtained prior to commencing the study. The Principal Investigator will ensure that this study is conducted in full conformance with the US Federal laws and regulations, as well as the ICH's Good Clinical Practice Guidelines.[15]

I) Subject Participation

1) Screening
   The PI or Co-Is will conduct screening examinations to identify subjects who meet the inclusion / exclusion criteria for enrollment into the study.

2) Informed Consent
   Dr. Kugel and/or his representative will introduce the study.

   Consenting will take place in a private clinic bay area and the patient will be given as much time as he/she needs to consider participation. The participant will be invited to include or exclude any associates (e.g., loved ones) in the consent process.

   Patients will be asked to read the consent form and given ample opportunity to have their questions answered. To avoid coercion, the consenting investigator will read through the copy of the consent form with the participant section by section, making sure the participant understands each section and has an opportunity to ask questions. If at any time the participant indicates s/he is not interested in participation, the meeting will end.

   If after going through the consent form, the participant indicates s/he would like to discuss the study with associates or think about participating, then the meeting will be ended and the participant will be asked to contact the study when s/he makes her decision. If the participant contacts the study in the future for participation, s/he will be invited back to the clinic, and if informed consent is given at that time, study activities will begin then.

   If the participant indicates s/he may be interested in participating after going through the consent form with the investigator, and the investigator determines the participant has the capacity to provide informed consent, the participant will be asked to provide informed consent at that time. Patients will certify their willingness to participate in the study by signing and dating the IRB approved informed consent document. The subject will be given a copy of the consent form.

   If any new finding requires any change to the informed consent form, the subject will be re-consented.

   Non-English speaking subjects will not be enrolled in the study because study staff at this time are not certified, prepared, or trained to translate or communicate in any language other than English. The study budget does not allow for the payment of translation services at this time. There are no direct benefits to this population by participating in this study.

3) Study Location
   Tufts University School of Dental Medicine

4) Personnel
Ongoing communication with the IRB and sponsor – The PI
Obtaining consent – The PI or his representative
Conducting screenings – The PI or Co-Is
Placement of restorations – The PI or Co-Is
Evaluation of restorations – The PI or Co-Is (who did not place restoration)
Maintaining paperwork – The PI and/or study coordinator

5) Anticipated Study Timeline*
- Protocol and ICF Submission to the IRB: September 2016
- Approval by the IRB: October 2016
- Subject Recruitment, Screening, Enrollment and Randomization: June 2017-December 2017
- Placement of Restorations- June 2017-January 2018
- Initial Report- January 2018-February 2018
- Six Months Follow up- December 2017- June 2018
- Six Months Report- July 2018-August 2018
- One year follow up- June 2018-December 2018
- One year Report- January 2019- February 2019
- Two year follow up- June 2019-December 2019
- Final Clinical Study Report- December 2019- January 2020

*this timeline is subject to change depending on completion of study enrollment

6) Payment for Participation
(a) Compensation
Restorations will be provided free of charge. A total stipend of up to $245 in gift-card form will be awarded per subject in the manner as follows: $25 at screening; $50 at baseline; $50 at six month recall; $50 at one year; and $70 at two years. Gift cards to Target will be given. The subject will not receive compensation for any missed recall appointments. Subjects will be responsible for paying all procedural costs not study related, as well as costs incurred after the study expires.

(b) Transportation
No travel reimbursement or transportation costs will be paid. Expenses, such as parking and transportation costs, will be paid by the subject at all times.

(c) Payment and Insurance
Neither the subject, nor their insurance company, will be billed for any study procedures.

(d) Provision for Care in Case of Accident or Injury
In the unlikely event that a study patient becomes ill or is injured as a result of participating in this study and medical care is necessary, such medical care will be provided by a physician chosen by the patient. In the event of a research-related injury, compensation will be determined on a case-by-case basis by KaVo Kerr Group and Tufts University.

7) Study Results
If interested, study results will be presented to a subject upon their request, either in person or via mail according to their preference, upon completion of the study. A log will be kept of the participants who are interested in receiving study results.

8) Confidentiality
To ensure confidentiality of subject information, each subject enrolled in the study will be assigned a unique alphanumeric code. Subjects' files and all study paperwork will be kept in a secure, locked cabinet in a secure room when the documentation is not being reviewed. The information will only be shared between the researchers. Source documents and case report forms will be coded and free of subject names. Photographs will be taken of subject's teeth only (no facials). All HIPAA requirements will be followed. All electronic files will be kept on a password protected computer in a secure, locked office.

(a) Coding
Each will be assigned a subject identification number. Alphanumeric identification numbers will be assigned sequentially. The full subject identification number will consist of the three letters from the subject's initials and their enrollment number. This will be accessible by study personnel only.

(b) Access
Only study personnel will have access to data. Investigators will permit monitoring, audits, and regulatory inspections and will provide direct access to study related documentation.

9) Data Safety Monitoring Plan:
The study will be monitored at appropriate intervals by a trained member of the Kavo Kerr R&D clinical Research group (or qualified designee) by means of visits to the study clinic to evaluate patient charts, study data, and study photographs. Study monitoring visits will involve review of the study status and any issues related to the study. All Informed Consent forms will be reviewed for signatures and dates. Patient charts/records will be reviewed to ensure that all enrolled subjects meet the study inclusion and exclusion criteria. All CRFs will be reviewed for completeness of data entry to ensure that the study protocol is being followed, and to perform source data verification against information contained in the patient charts.

Materials will be checked for adequate storage and sufficient quantity to meet the study needs.

Study personnel will monitor this trial for all safety related issues to determine whether an unreasonable risk to subjects develops. Quality control measures include routine inspection of case report forms, source documents, data tabulations, and tracking of adverse events.

Complaints
Complaint means any written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device. Complaints will be reported in source documents and on case report forms.

10) New Findings
The subject will be informed of any significant new findings discovered during the course of this study that might influence the subject's continuation and participation in the study. Subjects will be told at a study appointment or via telephone of new findings during the study.

Cost of treatment for any new findings will not be covered by the study.

If new findings require revisions to the ICF, the subject will be re-consented.

11) Policy Regarding Replacement of Restorations

All subjects will be pre-screened by the two examiners. Participants will be advised of any dental pathology diagnosed (periapical lesions, caries, periodontal problems, etc) at that time and advised of the specific treatment(s) needed (root canal treatment, restoration, core build-up, periodontal therapy, etc). If any pathology is found, each individual must arrange to have the pathology treated at their own expense. A second examination will be scheduled to assess that treatment before these candidates are considered for inclusion in this study.

If conditions arise in which the subject requires endodontic treatment after the restoration is placed and is within the study duration (two years), the subject will be responsible for any root canal and/or post and core treatment. However, Kavo Ker Group will reimburse the School of Dental Medicine for the cost of the restoration (up to $175 per unit depending on the type of the restoration) which will be credited to the subject towards the cost of his/her new restoration. In order to receive this level of

support, study participants must attend all initial appointments and all recall appointments for the duration of the study, otherwise this policy is voided.

Before any re-treatment is initiated, a second dentist not associated with the study, will be selected by the Investigator in consultation with Kavo Kerr Group. That individual will evaluate the cause of failure and determine the need for a new restoration. The study sponsor or the School of Dental Medicine at Tufts University will not be held responsible for any re-treatment when trauma or injury are determined to be the cause of failure and said failure is unrelated to participation in the study.

I) Record Retention

1) Study Records
The Investigator will maintain all study records and documents during the study period. All paper files and documents will be kept in a locked file cabinet, within a locked room. Electronic records will be kept on a password protected computer and only be accessible to study personnel.

2) Long Term Retention
The investigator will maintain all study records following completion or termination of this study in accordance to state law and institutional policy (at least 7 years after the study is completed or terminated).

K) Reporting

Progress reports on the investigation shall be submitted to the sponsor and the IRB at regular intervals, but in no event less often than yearly. Progress reports to the sponsor should follow baseline, 6 month, 1 year, and 2 year evaluations. A final study report shall be submitted to the sponsor and IRB following termination or completion of the study. Study completion will be defined as completing assessments on the last subject and presentation of final report
Unanticipated problems and adverse events will be reported per the Tufts MC/TUHS IRB Reportable New Information Policy.

The IRB will be notified of any deviations from the protocol in cases of medical emergencies when the change is necessary to eliminate an apparent immediate hazard to the subject

Progress reports on the investigation shall be submitted to the IRB at regular intervals, but in no event less often than yearly, e.g., at continuing review.

L) Protocol Deviations

No protocol changes or deviations will be made without prior agreement by the IRB and the study sponsor unless implemented to prevent an immediate hazard to subjects. All other protocol changes or deviations will be made by a formal amendment subject to IRB approval and with sponsor agreement. All such changes or deviations will be reported to the IRB as they occur and included in the final study report.

M) Study Termination

This study may be terminated for the following reasons:

Discovery of unforeseen risk that could jeopardize the dental/physical well-being of subjects.

Enrollment or recall rates that are not likely to produce sufficient data for evaluation of safety and efficacy

Non-compliance with the clinical investigational plan, the Investigator Agreement, applicable FDA regulations or conditions of approval imposed by the reviewing IRB

Withdrawal of IRB approval

Any other reasons allowed by study agreements/contracts between the sponsor and the institution.

In the event of study termination, the Principal Investigator will determine whether subjects are in need of additional treatment and/or follow-up observation as a result of participation in this trial.

N) Subject Recruitment/Advertising

Investigators may also inform clinic patients about the study.

Investigators may send messages to colleagues via axiUm asking for their help in recruiting eligible subjects.

Likewise, e-mails and/or newsletters that alert the TUSDM community to ongoing studies may include information on this study for recruiting purposes.

Forms of electronic media such as twitter, university websites, Facebook, Craiglist, etc. may also be used to recruit. Print media such as the Metro may also be used.

Study personnel may reach out to individuals that have previously expressed interest in dental research studies using a phone screening script.

All of the forms of recruitment will be submitted for IRB approval prior to use.

A screening interview/questionnaire or screening script will be used for recruitment.

Screen failure data will be retained by PI. Screening ID number and demographic information will be recorded. Identifiable information will not be recorded in the screening log.

O) References

1.) Hickel R, Peschke A, Tyas M, Mjör I, Bayne S, Peters M, Hiller KA, Randall R, Vanherle G, Heintze SD. FDI World Dental Federation: clinical criteria for the evaluation of direct and indirect restorations-update and clinical examples. Clin Oral Investig. 2010 Aug;14(4):349-66. Epub 2010 Jul 14.

2.) Bergenholtz G, Cox CF, Loesche WJ, Syed SA. Bacterial leakage around dental restorations. Its effect on the pulp. J Oral Pathol 1982: 11(6); 439-450

3.) Brannstrom M. communication between the oral cavity and the dental pulp associated with restorative treatment. Oper Dent 1984; 9(2);57-68

4.) Cheung GS. Reducing marginal microleakage of posterior composite resin restorations: A review of clinical techniques. J Prothet Dent 1990;63(3): 286-288.

5.) Eriksen HM, Pears G. In vitro caries related to marginal leagage around composite resin restorations. J Oral Rehabil 1978; 5(1):15-20

6.) Qvist V. Correlation between marginal adaptation of composite restorations and bacterial growth in cavities. Scand J Dent 1980;88:296-300

7.) Navarro Majo JL. Marginal adaptation of posterior resins: Effect of hygroscopic expansion and layer placement technique on Class II and V fillings. Stoma (LISB) 1991;2:47-48.

8.) Saunders WP, Strang R , Ahmad I. effect of composite resin placement and use of an unfilled resin on the microleakage of two dentin bonding agents. AM J Dent 1990;3(4) :153-156

9.) Lutz F, Krejci I, Oldenburg TR. Elimination of polymerization stresses at the margins of posterior composite resin restorations: A new restorative technique. Quint Int 1986;17(12):777-784

10.) Kavo Kerr Group. http://www.kerrdental.com/sonicfill2. Accessed August 10, 2015.

11.) Kavo Kerr Group. http://www.kerrdental.com/kerrdental-composites-sonicfill-2. Accessed August 10, 2015.

12.) Kavo Kerr Group. http://offers.kerrdental.com/optibond-xtr-request-info?utm_campaign=Optibond+XTR&utm_content=ad2&utm_medium=ppc&utm_. Accessed August 10, 2015.

13) 3M ESPE http://www.3m.com/3M/en_US/company-us/all-3m-products/~/filtek-supreme-ultra-Filtek-Supreme-Ultra-Universal-Restorative?N=5002385+3294736391&rt=rud. Accessed March 30, 2017.

14) 3M ESPE http:// ww.3m.com/3M/en_US/company-us/all-3m-products/~/scotchbond-universal-Scotchbond-Universal-Adhesive?N=5002385+3294776545&rt=rud. Accessed March 30, 2017.

15) ICH Topic 6 (R1) Guideline for Good Clinical Practice CPMP/ICH/135/95 July 2002.

Appendix A- Hickel Grading Criteria

	Esthetic Properties					Functional Properties	
	Surface Luster	**Surface Staining**	**Marginal Staining**	**Color Match and Translucency**	**Esthetic anatomical form**	**Fracture of material and retention**	**Marginal adaptation**
1. Clinically excellent/ very good	1. Luster comparable to enamel.	1. No surface staining.	1. No marginal staining.	1. Good color match, no difference in shade and/or translucency.	1. Form is ideal.	1. No fractures /cracks.	1. Harmonious outline, no gaps, no white or discolored lines.
2. Clinically good (after polishing probably very good)	2.1 Slightly dull, not noticeable from speaking distance. 2.2 Some isolated pores.	2. Minor surface staining, easily removable by polishing.	2. Minor marginal staining, easily removable by polishing.	2. Minor deviations in shade and/or translucency.	2. Form is only slightly deviated from the normal.	2. Small hairline crack.	2.1 Marginal gap (<150 µm), white lines. 2.2 Small marginal fracture removable by polishing. 2.3 Slight ditching, slight step/flashes, minor irregularities.
3. Clinically sufficient / satisfactory (minor shortcomings, no unacceptable effects but not adjustable w/o damage to the tooth)	3.1 Dull surface but acceptable if covered with film of saliva. 3.2 Multiple pores on more than one third of surface .	3. Moderate surface staining that may also present on other teeth, not esthetically unacceptable.	3. Moderate marginal staining, not esthetically unacceptable.	3. Distinct deviation but acceptable. Does not affect esthetics: 3.1 more opaque 3.2 more translucent 3.3 darker 3.4 brighter	3. Form deviates from the normal but is esthetically acceptable.	3. Two or more or larger hairline cracks and/or material chip fracture not affecting the marginal integrity or approximal contact.	3.1 Gap <250 µm not removable. 3.2. Several small marginal fractures. 3.3 Major irregularities, ditching or flash,steps.
4. Clinically unsatisfactory (but reparable)	4.1 Rough surface, cannot be masked by saliva film, simple polishing is not sufficient. Further intervention necessary. 4.2 Voids.	4. Unacceptable surface staining on the restoration and major intervention necessary for improvement.	4. Pronounced marginal staining; major intervention necessary for improvement.	4. Localized clinically deviation that can be corrected by repair: 4.1 too opaque 4.2 too translucent 4.3 too dark 4.4 too bright	4. Form is affected and unacceptable esthetically. Intervention/correction is necessary.	4. Material chip fractures which damage marginal quality or approximal contacts. 4.2 Bulk fractures with partial loss (less than half of the restoration).	4.1 Gap >250 µm or dentine/base exposed. 4.2. Severe ditching or marginal fractures. 4.3 Larger irregularities or steps (repair necessary)
5. Clinically poor (replacement necessary)	5. Very rough, unacceptable plaque retentive surface.	5. Severe surface staining and/or subsurface staining, generalized or localized, not accessible for intervention.	5. Deep marginal staining, not accessible for intervention.	5. Unacceptable. Replacement necessary.	5. Form is unsatisfactory and/or lost. Repair not feasible/ reasonable. Replacement needed.	5. (Partial or complete) loss of restoration or multiple fractures.	5.1 Restoration (complete or partial) is loose but in situ. 5.2 Generalized major gaps or irregularities.

	Functional Properties cont.		**Biological Properties**			
	Radiographic examination (when applicable)	**Patient's View**	**Postoperative (hypersensitivity and tooth vitality**	**Recurrence of caries (CAR), erosion, abfraction**	**Tooth integrity (enamel cracks, tooth fractures)**	**Adjacent mucosa**
1. Clinically excellent/ very good	1. No pathology, harmonious transition between restoration and tooth.	1. Entirely satisfied with esthetics and function.	1. No hypersensitivity, normal vitality.	1. No secondary or primary caries.	1. Complete integrity.	1. Healthy mucosa adjacent to restoration.
2. **Clinically good** (after polishing probably very good)	2.1 Acceptable material excess present. 2.2 Positive/ negative step present at margin <150 µm.	2. Satisfied. 2.1 Esthetics. 2.2 Function, e.g., minor roughness	2. Minor hypersensitivity for a limited period of time, normal vitality.	2. Small and localized 1. Demineral-ization 2. Erosion or 3. Abfraction.	2.1 Small Marginal enamel fracture (<150 µm). 2.2 Hairline crack in enamel (<150 µm).	2. Healthy after minor removal of mechanical irritations (plaque, calculus, sharp edges etc.)
3. Clinically sufficient / satisfactory (minor shortcomings, no unacceptable effects but not adjustable w/o damage to the tooth)	3. 1 Marginal gap < 250 µm. 3. 2 Negative steps visible < 250 µm. No adverse effects noticed. 3.3 Poor radiopacity of filling material.	3. Minor criticism but no adverse clinical affects. 3.1 Esthetic shortcomings. 3.2 Some lack of chewing comfort. 3.3 Unpleasant treatment procedure.	3.1 Moderate hypersensitivity. 3.2 Delayed/mild sensitivity; no subjective complaints, no treatment needed.	3. Larger areas of 1.Demineral-ization 2. Erosion or 3. Abrasion/abfraction, dentine not exposed. Only preventive measures necessary.	3.1 Marginal enamel defect <250µm 3.2 Crack <250µm; 3.3 Enamel chipping. 3.4 Multiple cracks compared to control tooth.	3. Alteration of mucosa but no suspicion of causal relationship with restorative material.
4. Clinically unsatisfactory (but reparable)	4.1 Marginal gap >250 µm. 4.2 Material excess accessible but not removable. 4.3 Negative steps >250µm and reparable.	4. Desire for improvement. 4.1. Esthetics 4.2 Function, e.g., tongue irritation. Reshaping of anatomic form or refurbishing is possible.	4.1 Intense hypersensitivity. 4.2 Delayed with minor subjective symptoms. 4.3 No clinical detectable sensitivity. Intervention Necessary but not replacement.	4.1 Caries with cavitation and suspected undermining caries 4.2 Erosion in dentine 4.3 Abrasion/ abfraction in dentine. Localized and accessible can be repaired.	4.1 Major marginal enamel defects; gap >250 µm or dentine or base exposed. 4.2 Large cracks >250 µm, probe penetrates. 4.3. Large enamel chipping or wall fracture	4. Suspected mild allergic, lichenoid or toxic reaction.
5. Clinically poor (replacement necessary)	5.1 Secondary caries, large gaps, large overhangs 5.2 Apical pathology 5.3 Fracture/loss of restoration or tooth.	5. Completely dissatisfied and/or adverse effects, including pain.	5. Intense, acute pulpitis or non vital tooth. Endodontic treatment is necessary and restoration has to be replaced.	5. Deep caries or exposed dentine that is not accessible for repair of restoration.	5. Cusp or tooth fracture.	5. Suspected severe allergic, lichenoid or toxic reaction.