Official Title: NCCL Direct Composite Restoration Performance with Self-Etch and Multimode Adhesives Clinical Trial

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1 - INTRODUCTION

Historically, dental adhesives have been broadly divided into total-etch (TE), etch-and-rinse (ER) and self-etch (SE) adhesives (1–3). Total-etch are considered the gold-standard adhesive systems on enamel bonding rendering the most pronounced etch patterns on cut and uncut enamel.

Self-etching adhesive systems, or "*self-etch"(SE)* as are usually called, were developed in the beginning of years ninety, with main purpose to simplify, even more, the clinical steps comparatively with the available adhesive systems (ER) in the market. SE primers are systems constituted by an acidic primer and a fluid resin and SE adhesives function as all-in-one systems, as a solution that demineralised and impregnates the resin in the demineralised layer, in only one step (1,4,5). SE adhesives use acidic monomers, with different pH values, to demineralise/modify dentin and enamel patterns while, simultaneously, primers/resins infiltrate into demineralised tissues and dentin tubules (6).

Few data exists with respect to mean and long-term observational clinical performance of SE all-in-one adhesive systems (7). However, their clinical use is increasing (8), contributing to this growth the fact of being user-friendlier (shorter application time, less clinical steps), less technique-sensitive (no wet-bonding, simple drying), and the perception that SE adhesives cause less postoperative sensitivity than ER adhesives. This argument is manly supported by their less aggressive (when compared to phosphoric-acid pH value) regarding acidity and, thus more superficially interaction with dentin occurs, leaving tubules largely obstructed with smear layer (6). However, some of those factors are controversial regarding some clinical outputs (9). SE adhesives would result in poorer enamel marginal integrity than TE/ER adhesives, since the integrity and durability of the enamel bond, particularly to uncut enamel, is the weak link for these materials. One-step SE adhesives showed higher bond strengths on ground enamel and no reductions in resin-enamel bonds were observed after 12 months of water storage. Marginal adaptation was significantly better for Clearfil S3 Bond than for Adper Prompt L-Pop, according to *in vitro* findings (10).

More recently, some researchers and dental adhesive manufacturers advocate the selective enamel etching technique, by which phosphoric acid is selectively placed on cut or uncut enamel during 15 seconds and then rinsed. The entire preparation is dried, and a self-etching adhesive system is applied and light-cured (11,12). Some laboratorial

results indicate that intact enamel pre-treatment, by etching with 37% phosphoric acid resulted in longer resin tags and higher depth of penetration of resin tags of the adhesive bond, achieving higher bond strength outputs to intact enamel (13). Pre-etching enamel may enhance the bond strength of SE adhesive systems to values comparable with those found with ER adhesives, which may improve their overall performance in clinical use (12).

The actual bonding performance reached by SE adhesives are widely and some controversially reported, depending on the SE adhesives system characteristics regarding their composition and more specific on functional monomers included in adhesive formulations (3,6,10). According to a systematic review that explore the clinical performance of adhesives, Peumans and colleagues found less favourable clinical performance in the SE bonding strategies compared with an ER protocol. Krithikadatta also performed a review (clinical trials from 2004 to 2010 years) on the clinical effectiveness of contemporary dentin bonding agents and concluded that the clinical performance of different categories of bonding system were comparable (14). However, and according to that author, not all the reviews presented full details regarding their methodology and review/assessment process; different conclusions reached in these studies may be explained by the rigorous selection criteria and robust quality assessment, during clinical practice and restorations clinical performance observation. Recently, a systematic review included studies with low overall risks of bias and reported favourable mean-term (2–3 years) clinical performance for all four bonding strategies regarding restoration retention. The included studies showed wide variation on clinical performance between adhesives with the same bonding strategy/ use mode and, the authors concluded that there was insufficient evidence to make firm recommendations for the use of one adhesive system or bonding strategy over another. The proportion of information obtained from studies with an unclear or high risk of bias was high. Studies with low overall risk of bias found good clinical performance for adhesives with three-step ER (ER-3), two-step ER (ER-2), two-step SE (SE-2) and one-step SE (SE-1) bonding strategies/mode. There is a need for future research on clinical effectiveness of adhesive systems and adhesives mode use, in particular, a better standardisation and reporting of randomised controlled trials and, restorations performance during clinical practice, that allows a more meaningful comparison between adhesives (3).

New “universal” or “Multi-Mode” (MM) adhesives have been introduced in the market and designed to be clinically used by ER or by SE modes. In general, these MM adhesives are more hydrophobic than previous SE products to address permeability issues. The bond strengths to dentin in both, ER and SE, modes are very good. Bond strengths to enamel are reasonable but to ensure long-term durability, the selective-etch technique (etching of enamel only) is recommended for universal adhesives (15).

Multimode one-bottle universal adhesives have been developed recently to make the clinical procedure even more user-friendly. These systems can be used for both direct and indirect restorations (16) and provide the flexibility for the clinician to select and choose the adhesive use mode (ER or SE) according to the clinical and dental hard tissues conditions. From a marketing perspective MM adhesives are highly innovative products offering the clinician the liberty of adapting a single-bottle SE adhesive for use as ER mode or as selective enamel etching (SE-EE) adhesion mode without compromising its bonding effectiveness (17). Controversy remains on, if these versatile adhesives contain technological advances for overcoming challenges associated with previous generations of adhesives or adhesion modes, since the available data mainly is based on in vitro findings. The concept behind these adhesives is novel; hence, only few short/mean-term clinical (16,18–20) and, immediate ultra-morphological and bond strength studies (21–25) have been reported. Some laboratory findings revealed that performance of universal multimode adhesives was shown to be material-dependent (23). Despite being considered user-friendly, acidity adjustment of MM adhesive solutions and incorporation of new functional monomers to promote clinical performance stability over time were the main changes proposed to improve these materials. Perdigao and colleagues observed during 18th month the clinical performance of the MM adhesive, Scotchbond Universal Adhesive (3M ESPE, St Paul, MN, USA) in non-carious cervical lesions (NCCLs) and concluded that, restorations retention with this universal adhesive was not dependent on the bonding strategy. Differences between use modes were detected only for adhesive restorations marginal adaptation, by FDI criteria (World Dental Federation- clinical criteria for direct/indirect restorations evaluation), but not by the USPHS (United States Public Health Service) criteria (16). Controversy remains about the use of MMP inhibitors to control the degradation of dentin-resin interfaces (26). According to the adhesion-decalcification (A-D) concept aggressive demineralization of hard tissues by strong acids results in dissolution of apatite crystallites, decreasing the opportunity to establish chemical bonds between SE

adhesives functional resin monomers (10-MDP- methacryloyloxydecyl dihydrogen phosphate) and apatite crystallites, and the potential for creating nano-layers of calcium precipitates with phosphate resin monomers. However, resin–dentine interfaces created by contemporary MM adhesives containing 10-MDP may not be as immune to degradation as the manufacturers would like (17). Adhesives with MDP (Clearfil SE Bond, Kuraray; Scotchbond Universal, 3M ESPE) in their composition can chemically bond to Ca++ ions and form stable MDP-Ca salts, according to the "adhesion-decalcification" concept, which may be responsible for the good long-term performance of MDP-containing adhesives on dentin, both *in vivo* and *in vitro* outputs. Thus, the enamel selective-etch technique is especially recommended for MDP-containing universal adhesives (15). However, dental adhesives are complex mixtures usually containing several monomers. Yoshida and colleagues investigated the effect of HEMA (2-hydroxyethylmethacrylate) monomer on the chemical interaction of MDP with hydroxyapatite (HAp) by x-ray diffraction (XRD), nuclear magnetic resonance (NMR), and quartz crystal microbalance (QCM). Authors examined the chemical interaction of 5 experimental MDP solutions with increasing concentrations of HEMA. XRD revealed that addition of HEMA inhibits nano-layering at the interface, while NMR confirmed that MDP remained adsorbed onto the HAp surface. QCM confirmed this adsorption of MDP to HAp as well as revealed that, the demineralization rate of HAp by MDP was reduced by HEMA. Thus, the authors concluded that even though the adsorption of MDP to HAp was not hindered, addition of HEMA inhibited interfacial nano-layering so, potential consequences with regard to bond durability necessitate further research (27).

Recently, dentalAEGIS stated Ivoclar Vivadent's Adhese® Universal with VivaPen® as an effective delivery for all etching/adhesive methods; Tysowsky describes the characteristics of the material itself as technique-tolerant and predictable. It forms a stable and homogenous layer that is not sensitive to any application method. "Its hydrophilic solvent, which is acetone-free, provides for optimum wetting of the dentin and enamel, which leads to enhanced infiltration and optimum sealing of the dentinal tubules, preventing microleakage and associated postoperative sensitivity" (28). Although the role of in vitro data to predict clinical performance is increasingly recognised, randomised controlled trials (RCTs) remain the most rigorous study design for assessing the clinical effectiveness of an intervention, a health product or a medical device, especially when they are already commercially available. The majority of

studies investigating the clinical effectiveness of bonding systems use the longevity of restorations in NCCLs as the outcome (3). These are widely available and are normally used in clinical research, for assessment of adhesive systems (26,29) performance and efficacy, because NCCLs present no macro-mechanical retention, they present margins in enamel and/or dentin, and restorations are exposed to high stress during masticatory function (3,17), are located mainly in dentine, facilitating evaluation of the resin–dentine bond which is less stable than the resin–enamel bond (3).

The overarching goal of this RCT is to compare clinical performance at 24th month recall, of two MM adhesives from different manufactures, applied by SE or ER modes, with an SE-all-in-one adhesive (by SE or SE-EE modes) in NCCLs, using both USPHS and FDI criteria.

Objectives and Hypothesis

The purpose is to evaluate/compare clinical effectiveness of dual cure (DC) all-in–one Self-Etch (Futurabond®DC-FBDC) adhesive and the multimode (MM) (FuturabondU® -FBU- and Adhese®Universal –ADU-) adhesives, with or without selective enamel etching, in NCCL restorations, at 24th months follow-up, using Word Dental Federation (FDI) and United States Public Health Services (USPHS) criteria.

The null hypotheses are:

H0 – Bonding to NCCLs with FBDC by Self-Etch mode (FBDC-SE; G1) and MM adhesives by SE mode (MM-SE; G4G6) result in similar (no significant differences) clinical (aesthetic, functional and biologic) behaviour/performance;

H0 – Bonding to NCCLs with FBDC-SE (G1) and MM-SE(G4G6) result in similar restorations (aesthetic, functional and biologic) success rates;

H0 – Bonding to NCCLs with FBDC-SE (G1) and MM-SE (G4G6) adhesives result in similar restoration retention rates;

H0 – Bonding to NCCLs with FBDC by SE and enamel etching mode (FBDC-SE-EE; G2) and MM adhesives by Etch-and-Rinse mode (MM-ER; G3G5) result in similar (no significant differences) clinical (aesthetic, functional and biologic) behaviour/performance;

H0 – Bonding to NCCLs with FBDC-SE-EE (G2) and MM-ER (G3G5) result in similar restorations (aesthetic, functional and biologic) success rates;

H0 – Bonding to NCCLs with FBDC-SE-EE (G2) and MM-ER (G3G5) result in similar restoration retention rates;
H0 – Bonding to NCCLs with FBDC (G1G2) or FBU (G3G4), DC adhesives, and ADU (G5G6) light-curing adhesive, with SE or SE-ER/ER modes result in similar (no significant differences) clinical (aesthetic, functional and biologic) behaviour/performance;
H0 – Bonding to NCCLs with FBDC (G1G2) or FBU (G3G4) and ADU (G5G6) light-curing adhesive, with SE or SE-ER/ER modes result in similar restorations (aesthetic, functional and biologic) success rates;
H0 – Bonding to NCCLs with FBDC (G1G2) or FBU (G3G4) and ADU (G5G6) light-curing adhesive, with SE or SE-ER/ER modes result in similar restoration retention rates;
H0 - FDI or USPHS criteria evaluation outcomes not differ for the same data, at 24th month follow-up.

2 – POPULATION, MATERIALS AND METHODS

2.1- TRIAL DESIGN

The trial design follows the Consolidated Standards of Reporting Trials (CONSORT) statement (30). Prospective, double blind, clinical trial; randomized allocation of NCCL restorations by six adhesion interventional groups (6 arms) for examination of restorations performance.
Study will take place in University [redacted] - [redacted] Dentistry School Clinic. Participants recruitment between November 2015 and April 2016. Restorations estimated to be done until April or May 2016 year.
The study is scheduled to last 24th months. Baseline clinical observation will be done 30 days after placement of adhesion restoration (First data research); a second appointment after 12th months (second data; data not to be included on final report, according to the main purpose and trial hypothesis to study) and the last research evaluation will be at 24th months after baseline (Final data/report). Clinical trial may continue for similar assessment intervals, after 24th months evaluation. This situation requires new analysis according to the clinical and economics conditions, at that time.

2.2- POPULATION AND PARTICIPANT SELECTION

All participants will be informed (Written and verbal Inform Consent, Annex 1) about the trial conditions and purposes, but will not be aware of what tooth will received the adhesion treatment strategy under evaluation. Written informed consent form (Annex 1), according to World Medical Association Declaration of Helsink (31), will be obtained from all participants prior to starting the treatment. University [redacted] Ethics Committee review [redacted] and approved the present protocol. This clinical trial is done according to the European Union law for clinical research and National Law for Clinical Research (Law 21/2014, of 16 April), and was analysed, approved and authorized by the **National Competent Authorities** [redacted]

- **CNPD**, Portuguese Data Protection Authority (Authorization and registry 6430/2015 at 7 July 2015; Case 2536/2015).
- **CEIC**, National Ethics Committee for Clinical Research (N.º 20150305; Approved at 3th August 2015)
- **INFARMED**, National Authority of Medicines and Health Products, IP (N.º EC/011/2015; DPS/DM/450.10.053/2015/0314; Authorization at 4th August 2015)

The decision to participate in this study is voluntary (Annex 1) as well as the decision to refuse participation and decision of withdrawal of the same, at any time of the study respecting all the rights of the patient/participant. Given the purpose of this study, and the fact of existing multiple and several market therapeutic alternative for this type of interventions, the fact of participate in this study will not involve any additional cost, except the one described in the fee schedule of Dentistry School Clinic[redacted]. They will not be granted any incentives or financial benefits (payment of travel or counter-parties) to participate in the trial. The participant has as cost the "restoration of the tooth surface, which of course would have to make even not participating in this investigation, as regulated for the clinical practice. The clinical observations, temporarily established (3 appointments in 24th month) to observe participants and evaluate the research restorations performance, will be free of charge for the participants. All other acts that the participant needs or intends to perform, not included in the protocol of this trial, should meet the same, the fees charges of Dentistry School Clinic-[redacted]. Dental restorations are applied to tooth surfaces requiring intervention/repair for the maintenance of dental structure in oral cavity of the patient. The operator (Dentist and

Associate Professor of [redacted]) inform the patient/participant in all aspects related to the study. Refusal of patient participation, the participant's withdrawal and revocation of consent to participate in this study are rights of the patient/participant, without any consequences or reprisal, and without interference in the relationship between users and teachers/researchers/ University and clinical entities.

Patients with ages of 18 up to 65 years which voluntary come to Dentistry School Clinic of [redacted] will be recruited in the order in which they are report for appointment, thus forming a convenience sample. According to assessed eligibility (inclusion and exclusion) criteria, volunteers will be selected for this study as recommended, by CONSORT guidelines (30). A minimum of 210 restorations will be performed, randomized in order to be allocated to six interventions, named as adhesion intervention groups (Table 1).

In this study will be included participants with clinical diagnosis of tooth structure coronal loss and needs for cervical (vestibular surface) restoration without chemical or bacterial origin, called non-carious cervical lesion (NCCL) located in pre-molars/molars (PM/M) teeth, with cavity dimensions defined in the study design. Therefore, restorations can be made in PM or M teeth; a participant can have up to 16 teeth (8PM + 8M) with NCCL. The number of teeth to restore by participant will be of maximum of 6 and a minimum of one NCCL, within this clinical trial. The allocation of the study arms (G1 to G6) to a particular tooth is randomly allocated, with the information available to the operator/principal investigator in sealed envelopes and previously prepared by the investigator-statistics. The allocation of the study arms (G1, G2, G3, G4, G5, G6) to each tooth by participant is performed randomly, but ensuring that the distribution of the groups is not repeated in the same participant. For this purpose, will be organized by the statistical investigator, 210 envelopes with 35 sequences of 6 study arms, where in each order of 6 groups is randomized.

If the patient has more than six teeth that meet the inclusion criteria, the selection of the PM and M teeth to be included in the clinical trial will be conducted randomly by scenarios randomized by the statistical investigator after participation and contact for the effect (not done a priori, since it is necessary 19448 scenarios prior randomization before observing any patient, whereas the possible teeth to be selected for treatment is between 6 and 16 and the teeth to select from 6).

The participant has as cost the academic/scientific fees, as in usual clinical context of Dentistry School Clinic of [redacted] as "restoration of a tooth surface"/ by tooth to restore (One to six teeth), which of course would have to make even not participating in the investigation, as the Dentistry School Clinic fee scale.

The restorations included in this trial will be evaluated for determine clinical performance from baseline to 24th month by the three calibrated examiners. These observation appointments (three, in two years) as part of the clinical trial will be free of charges for participants. Baseline and 24th month data will be statistically analysing, according to this trial purpose and hypothesis.

2.3- STUDY ADHESION ARMS

Study adhesive NCCLs restorations are randomly distributed to 6 groups (6 arms/interventions), according to adhesive (product) and adhesion mode (SE, ER) of use, as show in table 1.

Table 1 - Control (G1, G2) and study arms/ groups (G3, G4, G5, G6) of NCCL restorations randomized allocated according to adhesion mode and application procedures.

Control and study Groups and NCCL restoration distribution (n)	Adhesives System_Mode	Application Procedures
G1 (Control group) n=35	FBDC_SE	Mixture Liquid 1 into Liquid 2 (1:1 ratio). Apply and rub this homogeneous mixture to enamel and dentine for 20 seconds; Air-blow for 5 seconds; light cure (1000mW/cm2), for 20 seconds.
G2 (Control group) n=35	FBDC, SE with enamel etching (FBDC_SE-EE)	Apply etchant selectively on enamel and leave for 30 seconds. Thoroughly rinse for 1 minute and gently dry. Dentine surface must slightly remain wet. Mixture Liquid 1 into Liquid 2 (1:1 ratio). Apply and rub this homogeneous mixture to enamel and dentine for 20 seconds; Air-blow for 5 seconds; light cure (1000mW/cm2), for 20 seconds.
G3 n=35	FBU_ER	Apply etchant for 30 seconds on enamel and 15 seconds on dentine; Thoroughly rinse for 1 minute and gently dry. Dentine surface remain with silky matt appearance. Apply and rub adhesive for 20 seconds, and air-blow for 5 seconds; light-cured (1000mW/cm2) for 20 seconds.
G4 n=35	FBU_SE	Apply and rub adhesive for 20 seconds, and air-blow for 5 seconds; light-cured (1000mW/cm2) for 20 seconds.
G5 n=35	ADU_ER	Apply etchant for 30 seconds on enamel and 15 seconds on dentine; Thoroughly rinse for 1 minute and gently dry. Dentine surface remain dry. Scrubbed adhesive for at least 20 seconds; Air-blow to disperse adhesive until a glossy, immobile film layer results; Light-cure (1000mW/cm2) for 20 seconds.
G6 n=35	ADU_SE	Scrubbed adhesive for at least 20 seconds; Air-blow to disperse adhesive until a glossy, immobile film layer results; Light-cure (1000mW/cm2) for 20 seconds.

FBDC: Futurabond® DC; FBU: Futurabond® U; ADU: Adhese® Universal; SE: Self-Etch; ER: Etch-and-Rinse

2.4- OPERATOR / EXAMINERS CALIBRATION

For the operator calibration procedure, operator will do one restoration of each group in order to identify all steps involved in the application technique. This procedure will be done three times, with one week, interval. All restorations done by the same calibrated operator. Three experienced and calibrated dentists, not involved with the restoring procedures and therefore blinded to the group assignment, will perform the clinical evaluation. For training purposes, the examiners observed 10 photographs that were representative of each score for each criterion, in 10 cervical restorations (not included in this trial), each one, on two consecutive days. An intra-examiner and inter-examiner agreement will be calculated.

Medical devices composition according to manufactures, Voco and Ivoclar Vivadent safety data sheets for adhesives and products is show in Table 2.

Table 2 - Information regarding Medical devices, Manufacturers, Lot# Number, Composition, adhesives pH value (according to manufactures and medical devices safety data sheet).

Medical Device (manufacture) Lot#Number	**Composition**
Futurabond® DC (FBDC) (Voco, Cuxhaven, Germany) Lot# 1532592	**Liquid 1.** Acidic adhesive monomer*; BIS-GMA (5-10%), 2-HEMA (5-10%); **Liquid 2.** Ethanol (50-100%); Initiator (2.5-5%) ***Mixture.*** organic acids, BIS-GMA, 2-HEMA, TMPTMA, campherchinon, amines (DABE), BHT, catalysts, fluorides and ethanol ***pH-value* 1.5**
Futurabond® U (FBU) (Voco, Cuxhaven, Germany) Lot# 1543141	**Liquid 1.** (2-HEMA) (25-50%); BIS-GMA (25-50%); HEDMA (10-25%); Acidic adhesive monomer (5-10%)*; UDMA (5-10%); catalysts (≤ 2.5%), silica nanoparticles; **Liquid 2.** Ethanol (50-100%); Initiator (2.5-5%); catalysts (≤ 2.5) ***pH-value* 2.3**
Vococid® (Voco, Cuxhaven, Germany) Lot# 152135	35% orthophosphoric acid
Adhese® Universal (ADU) (Ivoclar Vivadent AG, Liechtenstein) Lot# U35131	**Liquid**: 2-HEMA (10-<25%); Bis-GMA (10-<25%); ethanol (10-<25%); 1,10-decandiol dimethacrylate (3-<10%); Methacrylated phosphoric acid ester (3-<10%); campherquinone (1-<2.5%); 2-dimethylaminoethyl methacrylate (1-<2.5%); 2-dimethylaminoethyl methacrylate (0.1-<2.5%). ***pH-value* 2.5-3.0**
Admira® Fusion (Voco, Cuxhaven, Germany) Lot# (Shade A1, A2, A3, A3,5) *1508270, 150827, 1510508, 1509381*	Nano-hybrid ORMOCER®s (organically modified ceramics); large and precondensed molecules of an inorganic matrix with a high degree of cross-linking. 84 % w/w inorganic fillers. Silicon oxide forms the chemical base, not only for the fillers (nanofillers as well as glass ceramics) but also for the resin matrix.

*Acidic adhesive monomer (10-MDP: 10-methacryloyloxydecyl dihydrogen phosphate according to Voco manufacture); Bis-GMA-Bisphenol A glycidil methacrylate; HEMA-hidroxyethil methacrylate; UDMA- Urethane dimethacrylate

2.5- DATA REGISTRY/PROTECTION AND RESTORATIONS PROCEDURES

Photographs (digital data registration) will be carried out by the operator/responsible for research, strictly made to NCCL cavities and restorations as part of this trial. No photographs will be made to identify the patient, including photographs of the patient face or profile. All photographs taken in the context of this study will be "identified" (file name) with a single key (alphanumeric key without any kind of relationship with file number, name, date of birth or other information associated with the participant patient). Only in the registration database (with access to the principal investigator and other team members, with the exception of the statistical investigator for the purposes of observational clinical records) there should be registration/membership of this key with the code-process of patients. The database in question will be lodged in own servers with restricted access levels and well identified. The servers that lodge the photos/ records and the database belong to Dentistry School Clinic [redacted] and are located in datacentre with fully controlled access. This mechanism ensures the concealment of identity of the user (as name and other information identifying the participant) in the photographs and other records file, having access to them only the investigator and research team (except investigator of statistics). This mechanism fulfilled the recommendation and Authorisation of CNPD, Portuguese Data Protection Commission Authority (Authorization and registry 6430/2015 at 7 July 2015; Case 2536/2015).

Appointment and restorative procedures, in accordance with the following steps:

One week, before the Restorative procedure (1st appointment): Inform the patient (Written/Verbal- Anexx-1); Patient signature of informed consent; Fulfilment of the project clinical file (patient identification, general clinical summary, oral clinic examination, oral hygiene state; Annex 2); Dental prophylaxis with fluoride toothpaste and water with a nylon brush. Vitality tests (cold and hot) executed with spray *Endo cool* (ethyl chloride) and warm instrument; Pre-operative sensitivity evaluation by applying air for 10 seconds from a dental syringe placed 2 cm from the tooth surface (16); NCCLs cavities will be evaluated according to the degree (1, 2, 3, 4) of sclerotic dentin (32), cavity dimensions (H-height, W-width, and D-depth) in millimetres (mm) and geometry (evaluated by profile photograph, as Angles Acute (A), Severe (S), Obtuse (O) (16);

1st Appointment-Intervention: Initial intra-oral/cavity surface and tooth digital photography; Teeth anaesthesia with 3% mepivacaine (Scandinibsa, Sintra Business Park, Portugal); Operatory field isolation with cotton rolls and retraction floss (Ultradent). All cavities cleaned with pumice and water in a rubber cup, followed by rinsing and drying. Selection composite colour by shade guide; Adhesive interventions according to G1 to G6 arms assignment. Adhesive systems will be used as SingleDose mode. Composite restorations (AdmiraFusion Universal nano-hybrid composite) with incremental filling technique (two increments maximum), light-cured (LED Unit) with an intensity of 1000mW/cm2, during 40 seconds. Restorations will be finished immediately with diamond disks (OptiDisc® medium 40µm; Kerr) and burns. Polishing performed with diamond-impregnated silicone polishers (Dimanto, Voco, CuxHaven) during 10 seconds. Intra-oral digital photography of the restoration.

2.6- CLINICAL RECALL

Baseline (30 days after restoration), 12th and 24th months Appointments

1 - Intra-oral digital photography of the NCCL restoration;

2- Pos-operative sensitivity evaluation by applying air for 10 seconds from a dental syringe placed 2 cm from the tooth surface (16);

3 – Clinical direct evaluation by 3 calibrated examiners according to FDI (33) (Annex 3) and USPHS (34) (Annex 4);

4º- Data register.

Study variable definition – Clinical/direct observation and performance evaluation acceptance by means of FDI (*FDI World Dental Federation - clinical criteria for the evaluation of direct restorations*) (Adapted from (33) (Annex 3) and USPHS (34) (Annex 4).

2.7- DATA AND STATISTICAL ANALISYS PLAN (SAP)

Data statistical analysis and description according to aims of this trial; Specific program for statistical data analysis (IBM(c) SPSS(c) Statistics vs. 22 or later) will be used.

The changes in parameters clinical performance (paired comparison analysis) by both, FDI and USPHS criteria will be assessed by McNemar or Wilcoxon tests, for both

primary and secondary outcomes, to determine differences between treatments with regard to aesthetic, functional and biological parameters from baseline to 24th month recall (longitudinal assessment). Differences will be considered to be significant at $P<0.05$. Whenever 3 groups will be compared at 24 months' recall, a Kruskal Wallis test will be used and upon significant differences detection, then Mann-Whitney tests considering Bonferroni correction will be used for pairwise group comparisons.

Comparison of FDI and USPHS acceptance (success rate) criteria evaluation outcomes for Esthetic, for Functional and for Biological Parameters, at 24th Month Follow-up, were compared using the chi-square test.

If missing data occurs, that is, if dropouts or non-observed due to loss of retention of the restoration, then the paired comparison will consider for the baseline just the restorations existing at the last moment (24 months).

2.8- OBSERVATIONS REGARDING SAMPLE CALCULATION

It was assumed that the minimum number of adhesive restorations to be held in each of the six arms (G1 to G6) is 35 (210 restorations). The researchers did not have detailed information that allows the estimation of the sample size based on power analysis (the effect of the expected difference to the end of the time considered for the study). Thus, in principle they assumed the rules of thumb, usually considered in research situations where there is no advance information concerning the performance evaluation of these adhesive medical devices available on the market, using this assay. Moreover, when considering a "simple" analysis comparison using a McNemar test (repeated measures) in six groups would be necessary in total, including at least 80 cases (to restore teeth) in the sample. When considering at least 35 restorations by group, researchers are greatly increasing the minimum number stipulated in the aforementioned technique. In addition, clinical studies previously performed on this issue (between 2004 and 2012) relative to the post-market clinical evaluation performance of adhesive products/use mode in NCCLs, in the context of restorative dentistry field, has enabled to measure a minimum of 30 restorations as viable for determining events in a short/mean-term as the clinical performance evaluation of a similar nature of adhesives.

2.9- GOOD CLINICAL PRACTICE FOR CLINICAL RESEARCH

Reporting mechanism of possible adverse incident during the investigation will be held according to Medical Devices (MD) commercially available in the market, so it interprets and assumes the issue as applicable to assumptions in the Portuguese National Law for Clinical Research (Article 22) 21/2014, of 16 April, calling up a mechanism for reporting any incidents inherent to medical devices or resulting from the use of medical devices. In this way, and considering the type of intervention to carry out in this research (restoration of very small extension of NCCL with dental adhesives), the medical devices (Adhesive systems) are not described in the literature and not known records for the occurrence of undesirable incidents, with interpretative effects as Serious or Unexpected “adverse incidents". However, and according to good clinical practice for clinical research, the reporting mechanism of Serious or Unexpected incidents (protocol version FCS-UFP-2014-04-2015-07-19) for this research are approved by CEIC (National Ethics Committee for Clinical Research (N.º 20150305; Approved at 3th August 2015), as followed:

1º - Clinical knowledge of the incident taken by the principal investigator;

2º- Register of occurrence and possible reasons associated with it;

3º- Clear Information to the participant about the serious or unexpected adverse occurrence, providing urgent measures as may be appropriate to safety protect the subjects against any immediate risk or any fact relating to the conduct of the trial.

4º - The investigator notifies the clinical Director and the Sponsor within 24 hours of all serious or unexpected events, and the defects of devices that could have led to a serious adverse event, except those conditions that are identified in the protocol (loss of retention of the adhesive restoration) or in the investigator's brochure as not requiring immediate reporting;

5º- Investigator presents to the sponsor a detailed written report, within five days.

6º - The Sponsor ensure that:

a) All important data regarding serious adverse events related to the clinical trial, which has caused or may cause death or severe deterioration of the health status of participants, users or third parties involved in the study, they are recorded and notified to the National Authorities INFARMED (National Authority of Medicines and Health Products, IP) and CEIC (National Ethics Committee for

Clinical Research), immediately and not more than two days from the moment in which aware of them;

b)- Another type of adverse events, in particular regarding defects of medical devices that could have led to a serious adverse event and new data on any adverse event is recorded and notified National Authorities, INFARMED (National Authority of Medicines and Health Products, IP) and CEIC (National Ethics Committee for Clinical Research), within a period of seven days, starting from the moment they become aware of them. All supervening information considered relevant by the competent authorities will be notified within eight days from the closing date provided for in the preceding paragraph.

7º - The investigator sends to the sponsor, the CEIC and INFARMED any additional information that may be requested.

8º- Sponsor keeps detailed records of all adverse events, which are reported to him, by any investigator.

9º- Other suspected serious and unexpected adverse events are reported by the sponsor to the CEIC, INFARMED and CNPD within 15 days from its notice by the promoter.

Sponsor reports annually to CEIC and INFARMED a list of all suspected serious adverse events, during this period as well as a report on the safety of participants, if applicable. Under the study protocol (Version FCS-UFP-2014-04-2015-07-19), all the possible non-serious adverse events such as, clinical signs or symptoms associated with loss of aesthetic, functional and biological performance of restorations and situations described in the instructions, labelling and safety data sheets of medical devices or even, without incident and security maintenance data of the participants the sponsor notifies the CEIC and INFARMED, only by the final evaluation of this study (24th month of clinical performance), as set forth in article 24th of Law 21/2014 of 16 April, which will include a report of suspicious occurrences and safety records and, if applicable, in the clinical trial in the period evaluation of 24th month. Or annually, if the CEIC advise, even in the absence of adverse events or information, justifying changes to the safety of participants.

3. PROJECT SCHEDULE

Estimation DATES	**Estimation ACTIVITIES**
Initial date- 6 month	Bibliographical research on the subject to approach;
December 2014 – July 2015	Accomplishment of the clinical trial protocol; Order of authorization to the Deontological and Ethical Committee and Scientific Direction of University [redacted] and National Ethics Committee (December 2014). National Data Base Registration (January 2015); Authorization request to National Ethics Committee (CEIC); Infarmed Registration Clinical trials.
September 2015 – May 2016 **(Jun 2016-Nov 2016)**	Sample trial constitution (Participants selection); Clinical evaluation (USPHS and FDI) through calibrate intra-examiner and inter-examiner (First Direct evaluation: Baseline results, 1st month after restoration). Elaboration of database for statistical analysis. **First Baseline Results);**
November 2016 – May 2017	Second Direct evaluation, 12th month after restoration.
November 2017 – May 2018 **(Jun 2018-May 2019)**	Third Direct evaluation, 24th month after restoration. Elaboration of statistical analysis. **-Last Results, 24th month.** Reports to INFARMED, CEIC (Baseline to 24th month follow-up).

4. NECESSITY ESTIMATES

Material/Medical Devices/ Appointments/ Methods/other Needs (description)	Estimated Cost (Euro-€)
Composite to 210 NCCL restorations (Ormofil or other)- Shades A1, A2, A3; Futurabond DC (Voco); Futurabond U (Voco); 4 Ivoclar Vivadent's Adhese® Universal with VivaPen®	300.00€
Availability of a dental equipment, Medical Devices (manual turbine, drills, hand instruments, sculpture instruments) for operatory field isolation, for technical procedures, and evaluation appointments (Digital Photographic machine Canon EOS 20D) in Dentistry School Clinic of [redacted] for attendance and restoration treatments of the patients;	8,400.00€
Operator /Examiners and Coordination Research (Human Resources Time)	5,950.00€
- Logistic Support (clinical document, information to the patient and informed consent forms), Phone calls, internet to contact patient; Administrative work.	600.00 €
- Support of biostatistics department of the [redacted] (database elaboration; data statistical analysis and description according to aims of this trial; Participation on the elaboration/presentation of posters and manuscript- Use of the specific program for statistical data analysis (IBM(c) SPSS(c) Statistics vs. 22.).	1,500.00 €
Observational Trial in clinical Field	**16,750.00€**
Outputs to International Presentations and Manuscripts submissions	

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LINKS:

INFARMED - http://www.infarmed.pt/portal/page/portal/INFARMED/ENGLISH
CEIC - http://www.infarmed.pt/portal/page/portal/CEIC/English
CNPD- https://www.cnpd.pt/english/index_en.htm

ANNEXES

ANNEX 1

Inform Consent Form to Participants

(English translation from Portuguese version)

INFORMED CONSENT FORM TO PARTICIPATE IN [redacted] CLINICAL TRIAL

1.2.1.1.2- Information and Informed Consent

Sponsor: *University* [redacted]

Principal Investigator: [redacted]

Team: [redacted]

Please read the following information carefully. If you feel that something is incorrect or unclear, do not hesitate to ask for more information. If you agree with the proposal we have made, please, sign / date this document.

Title of the study: NCCL Direct Composite Restoration Performance with Self-Etch and Multimode Adhesives Clinical Trial: observational study in clinical field.

Background and Objectives: This clinical trial aims to evaluate the performance of self-etch and universal adhesives (with or without selective acid-enamel etching) by observing (and recording) the clinical behaviour of restorations that will be performed in dental cavities (from non-carious cervical lesions -LCNC) for a period of 2 years using the FDI and USPHS criteria. This essay has not commercial purposes, but academic / scientific objectives, and will be carried out at the [redacted] pedagogical clinic, having as principal investigator and as team, dentists that are [redacted] faculty members.

Study's explanation: In this trial, patients who voluntarily attend PC-[redacted] will be invited to participate, if they present the following conditions: diagnosis and need for restoration of dental cavities (non-retentive, deeper than 1mm, involving enamel and dentin in vital teeth without mobility, the cavo-superficial margin can not involve more than 50% of the enamel) in the cervical area of the vestibular surface (NCCLs), in the premolar / molar teeth. As it was defined in the design of this trial, patients with one of the following conditions can't participate: Less than 20 teeth in the oral cavity, Non-vital Tooth, Advanced Periodontal disease, Patient unavailability to return to follow-up visits, Simultaneous participation in another current clinical trial, medical history, psychiatric or pharmacotherapy likely to compromise the protocol, Pregnancy, Allergies and / or idiosyncratic responses to the products constituents, Patient under fixed orthodontic treatment, Teeth prepared for fixed prosthetic rehabilitation treatments, Teeth or support structures with pulpal injury, periodontal surgery in the previous 3 months, severe bruxism, extremely poor oral hygiene or if the patient voluntarily refuses to participate in the trial. The number of teeth to be restored per participant will be a maximum of 6 and a minimum of 1, as part of the clinical trial. There is a random distribution of the restorative procedures to be done in each tooth, with the information being available only to the main investigator / operator in sealed and previously prepared envelopes. The participant has the usual cost of academic / scientific fees, as it is determined on the clinical protocol of the CP[redacted], regarding the "restoration of a dental surface" / per tooth to be restored (1 to 6 teeth), which of course they would have to pay, even if they were not participating in the investigation, according to the fee schedule of [redacted].

[redacted]

Benefits of the Study: [redacted]

Risks associated with the Study [redacted]

Conditions and funding: [redacted]

This clinical trial has academic and scientific scope and is sponsor by [redacted]. The technical and material procedures used are financially supported by university [redacted]. There is no conflict of interest. This study was approved by the Ethics Committee for Clinical Research (CEIC), and authorised by Infarmed and by the National Commission for Data Protection (CNPD).

Confidentiality and anonymity: [redacted] The mechanism ensures the confidentiality of data and concealment of the participant's identification (in particular the name and other data that identifies the participant), and only the investigator and the research team have access to them. [redacted]

Thank you very much, for your participation!

Contact [redacted]: [redacted]

-o-o-o-o-o-o-o-o-o-o-o-o-o-o-o-o-o-o-o-o-o-

According to the Declaration of Helsinkia (2013) I was informed and clarified, by oral and written way, about the study in which I will participate. I declare that I have understood the descriptions and explanations provided, that I have been given the opportunity to put the doubts and issues that I considered important, and I give my consent to be a participant in this clinical trail. I am conscious that I may withdraw from this investigation at any time, and the refusal to participate, the withdrawal, or the consents´s withdrawal to participate in this study, are rights that assist me, without any consequence or reprisal, and without interference in my relationship with the teachers / researchers / entity. I have become aware that my decision to participate in this clinical trial is voluntary and that participation will not entail any additional cost besides the one that is described in the University [redacted] fee schedule. The operator (Dentist, Professor and Researcher of [redacted]) informed me about all aspects related to the study. In this way, I accept to participate in this trial and allow the data usage that I voluntarily provide, trusting that they will only be used for this research and the guarantees of confidentiality and anonymity given by the researcher.

Porto, ___of _____of 201_ **Participant's signature: _____**

Porto, ___of _____of 201_ **Dentist/investigator signature: _____**

THIS DOCUMENT HAS TWO PAGES AND TWO COPIES WERE MADE: ONE IS GIVEN TO THE RESEARCHER AND THE OTHER IS FOR THE PERSON WHO CONSENTS

ANNEX 2

Participants/Restorations Clinical/Research File

PATIENT IDENTIFICATION
Name_____
Age (years) _____ Birth date_____
Date _____ [redacted] Code of patient_____

Register of 1ª Appointment

1- GENERAL CLINICAL EXAMINATION (Summary)

	YES	NOT	WHICH?
•SISTEMIC PATHOLOGY			
•PHARMOTERAPHY			
• TABAGYC HABITS			
•ALLERGIES			

2- HYGIENE STATUS Good ☐ Reasonable ☐ Insufficient ☐

3- VITALITY AND SENSIBILITY TEST

Vitaliy Test	**Tooth Number**	**Pre-operative**		**1st Month**		**12th Months**		**24th Months**	
		Yes	No	Yes	No	Yes	No	Yes	No
Cold									
Heat									
AIR									
Cold									
Heat									
AIR									
Cold									
Heat									
AIR									
Cold									
Heat									
AIR									
Cold									
Heat									
AIR									
Cold									
Heat									
AIR									

4- DENTIN SCLEROSIS/ 5 - CAVITY DIMENTIONS (HWD) /6 – GEOMETRY
_____ / H-_____W-_____D-_____/_____

Date	**NCCL Nº**	**Randomized allocated Group treatments**	**Material**
		1-	
		2-	
		3-	
		4-	
		5-	
		6-	

[redacted] Code of patient_____

NCCL Number	FDI Criteria_ _ - / /							
	A) ESTHETIC PROPERTIES			B) FUNCTIONAL PROPERTIES		C) BIOLOGICAL PROPERTIES		
	1. Surface Luster	2. Surface Staining	3. Colour stability and translucency	4. Fractures and retention	5. Marginal Adaptation	6. Postoperative Hipersesibility, tooth vitality	7. Recurrence of Caries	8. Tooth integrity (enamel cracks)

NCCL Number	USPHS Criteria_ - / /							
	A) ESTHETIC PROPERTIES			B) FUNCTIONAL PROPERTIES		C) BIOLOGICAL PROPERTIES		
	Surface Staining	Marginal Discoloration	Color Match	Retention	Marginal Integrity (Adaptation)	Postoperative Sensitivity	Secondary Caries	Gingival Bleeding

[redacted] Code of patient_____

DENTIN SCLEROSIS CLINICAL SCALE (adapted from (32)

Category	**Criteria**
1	No sclerosis present; dentin is light yellowish or whitish, with little discoloration; dentin is opaque, with little translucency or transparency
2	More sclerosis than in category 1 but less than halfway between categories 1 and 4
3	Less sclerosis than in category 4 but more than halfway between categories 1 and 4
4	Significant sclerosis present; dentin is dark yellow or even discolored (brownish); glassy appearance, with significant translucency or transparency evident

CAVITY DIMENTIONS (adapted from (16))

CAVITY DIMENSIONS (HWD)(mm)	Height	Width	Depth
Cavity dimensions in millimetres (mm)			

CAVITY GEOMETRY CRITERIA (adapted from (16))

Category	**Criteria evaluated by profile photograph**
Acute (A)	< 45º
Severe (S)	45º- 90º
Obtuse (O)	> 90º

ANNEX 3
WORLD DENTAL FEDERATION (FDI) CRITERIA

A) ESTHETIC PROPERTIES	1. Surface Luster	2. Staining margin	3. Colour stability and translucency
1. Clinically excellent/ very good	1.1 Luster comparable to enamel	2.1 No surface staining	3.1 Good colour match no diference in shade and translucency.
2. Clinically good (after correction, very good)	1.2 Slightly dull, not noticeable from speaking distance.	2.2 Minor staining, easily removable.	3.2 Minor deviations
3. Clinically sufficient/ satisfactory (minor shortcomings with no adverse effects but not adjustable without damage to the tooth)	1.3 Dull surface but acceptable if covered with film of saliva.	2.3.Moderate surface staining, also present on other teeth, not aesthetically unaccetable.	3.3 Clear deviation but acceptable. Does not affect aesthetics: 3.3.1.more opaque 3.3.2.more translucent 3.3.3 darker 3.3.4 brighter
4. Clinically unsatisfactory (repair for prophylactic reasons)	1.4 Rough surface, cannot be masked by saliva film, simple polishing is not sufficient. Further intervention necessary.	2.4 Surface staining present on the restoration and is unacceptable; major intervention necessary for improvement	3.4 (Localised) clinically unsatisfactory but can be corrected by repair 3.4.1 too opaque 3.4.2 too translucent 3.4.3 too dark 3.4.4 too bright
5. Clinically poor (replacement necessary)	1.5. Quite rough, unacceptable plaque retentive surface.	2.5 Severe staining and/or subsurface staining (generalized or localized); not accessible for intervention	3.5 Unacceptable. Replacement necessary.
Acceptable or not acceptable (n, %, and reasons) Adapted from (33)			

B) FUNCTIONAL PROPERTIES	4. Fractures and Retention	5. Marginal Adaptation
1. Clinically excellent/ very good	4.1Restoration retained, no fractures/cracks.	5.1 Harmonious outline, no gaps, no discoloration.
2. Clinically good (after correction, very good)	4.2. Small hairline crack	5.2.1 Marginal gap (50 µm) 5.2.2 Small marginal fracture removable by polishing.
3. Clinically sufficient/ satisfactory (minor shortcomings with no adverse effects but not adjustable without damage to the tooth)	4.3. Two or more or larger hairline cracks and/or chipping(not affecting the marginal integrity or proximal contact.	5.3.1 Gap< 150 µm not removable 5.3.2 Severe small enamel or dentin fractures
4. Clinically unsatisfactory (repair for prophylactic reasons)	4.4 Chipping fractures which damage marginal quality or proximal contacts; bulk fractures with or without partial loss(less than half of the restoration)	5.4.1 Gap> 250 µm or dentine exposed 5.4.2 Chip fracture damaging margins 5.4.3 Notable enamel or dentine wall fracture
5. Clinically poor (replacement necessary)	4.5. Parcial or complete loss of restoration	5.5 Filling is loose but in situ.
Acceptable or not acceptable (n, %, and reasons) Adapted from (33)		

c) BIOLOGICAL PROPERTIES	6. Postoperative Hipersesibility, tooth vitality	7. Recurrence of Caries, erosion, abfraction	8. Tooth integrity (enamel cracks)
1. Clinically excellent/ very good	6.1 No hipersensitivity, normal vitality	7.1 No secondary or primary caries	8.1 Complete integrity.
2. Clinically good (after correction, very good)	6.2 Low hipersensitivity for a limited period of time, normal vitality.	7.2 Very small and localized 1. Demineralization 2. Erosion or 3. Abfraction. No operative treatment required	8.2.1 Small margin enamel(<150 µm) 13.2.2 Hairline crack in enamel (<150 µm not probable)
3. Clinically sufficient/ satisfactory (minor shortcomings with no adverse effects but not adjustable without damage to the tooth)	6.3.1 Premature/slightly more intense 6.3.2 Delayed/weak sensitivity; no subjective complaints, no treatment needed.	7.3.Larger areas of 1.Desmineralisation 2.Erosion 3. Abrasion/abfraction in dentine Localized and acessible and can be repaired	8.3.1 Enamel split(<250 µm) 8.3.2 Crack < 250 µm, no adverse effects.
4. Clinically unsatisfactory (repair for prophylactic reasons)	6.4.1 Premature/very intense 6.4.2 Extremely delayed/weak with subjective complaints 6.4.3 Negative sensitivity intervention necessary but not replacement	7.4.1Caries with cavitation 7.4.2 Erosion in dentine 7.4.3 Abrasion/abfraction in dentine Localized and accessible and can be repaired	8.4.1 Major enamel split (gap>250 µm or dentine or base exposed) 8.4.2 Crack>250 µm (probe penetrates).
5. Clinically poor (replacement necessary)	6.5 Very intense, acute pulpitis or no vital.Endodontic treatment is necessary and restoration has to be replaced.	7.5 Deep secondary caries or exposed dentine that is not accessible for repair of restoration.	8.5 Cusp or tooth fracture.
Acceptable or not acceptable (n, %, and reasons) Adapted from (33)			

ANNEX 4

USPHS (MODIFIED U.S. PUBLIC HEALTH SERVICE) CRITERIA
Used for Clinical Evaluation

RYGE´S (MODIFIED U.S. PUBLIC HEALTH SERVICE) CRITERIA FOR RESTAURATION EVALUATION †		
PARAMETER	**CRITERIA**	**RYGE SCORE***
ESTHETICS	**Surface Staining**	**Alfa (α):** No staining in the restoration and/or the tooth **Bravo (*B*):** Slight staining in the restoration and/or the tooth **Charlie (χ):** The staining penetrated in the restoration and/or the tooth in a pulpar direction
	Marginal Discoloration	**Alfa (α):** No discoloration along the margin between the restoration and adjacent tooth **Bravo (*B*):** Slight discoloration along the margin between the restoration and the adjacent tooth (removable, usually localized) **Charlie (χ):** Deep staining cannot be polished away
	Color Match	**Alfa (α)*:** Restoration matches the adjacent tooth structure in color and translucency **Bravo (*B*)*:** Light mismatch in color, shade or translucency between the restoration and the adjacent tooth **Charlie (χ)*:** The mismatch in color and translucency is outside the acceptable range of tooth color and translucency
FUNCTIONAL	**Retention**	**Alfa (α):** Retained **Bravo (*B*):** Partially retained **Charlie (χ):** Missing
	Marginal Integrity (Adaptation)	**Alfa (α):** No visible evidence of crevice along the margin **Bravo (*B*):** Visible evidence of a crevice along the margin into which the explorer will penetrate **Charlie (χ):** Dentin or the base is exposed **Delta (δ)*:** Restoration is fractured, mobile or missing
BIOLOGICAL	**Postoperative Sensitivity**	**A:** No evidence of postoperative sensitivity **B:** Experience of postoperative sensitivity
	Secondary Caries	**A*:** No evidence of caries **B*:** Evidence of caries along the margin of the restoration
	Gingival Bleeding	**A:** No evidence of gingival bleeding adjacent to Class II restoration **B:** Evidence of gingival bleeding adjacent to Class II restoration
*Alfa (α): Clinically excellent/ very good; highest degree of clinical acceptance. Bravo (*B*): Clinically satisfactory and Charlie (χ): Clinically unsatisfactory, but repairable; lower degrees of clinical acceptability. Delta (δ): Clinically bad, without repair; Restoration clinically unacceptable. A: No evidence of pathology present. B: Presence of pathology, related to restoration. † Source: Adapted from (34)		