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Kiara Serafini Dapieve

# TEMPOS DE APLICAÇÃO DE UM PRIMER AUTOCONDICIONANTE: EFEITOS NA ADESÃO E NO COMPORTAMENTO À FADIGA DE UMA CERÂMICA DE DISSILICATO DE LÍTIO

Santa Maria, RS
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Dissertação de mestrado apresentada ao Programa de Pós-Graduação em Ciências Odontológicas da Universidade Federal de Santa Maria (UFSM), como requisito para a obtenção do título de **Mestre em Ciências Odontológicas com ênfase em Prótese Dentária.**

Orientador: Prof. Dr. Luiz Felipe Valandro

Coorientadora: Prof.ª Dra. Andressa Borin Venturini

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**Aprovado em 09 de março de 2020:**

**Luiz Felipe Valandro, Prof. Dr. (UFSM)**
(Orientador/Presidente)

**Iana Lamadrid Aurélio, Prof.ª Dra. (UFSM)**

**Luís Felipe Guilardi, Prof. Dr. (UFSM)**

Santa Maria, RS
2020

*Com amor,*

*aos meus pais Valmor e Graciele*

*e ao meu irmão Guilherme.*

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*"Porque a felicidade exige esforço. Ela se origina dos problemas. A alegria não brota do chão como margaridas e arco-íris. Satisfação e propósito genuínos, sérios e duradouros devem ser conquistados pela escolha e pela maneira como conduzimos nossas batalhas" Mark Manson*

# RESUMO

## EFEITO DE DIFERENTES TEMPOS DE UM PRIMER CERÂMICO AUTOCONDICIONANTE NA ADESÃO E NO COMPORTAMENTO À FADIGA DE UMA CERÂMICA DE DISSILICATO DE LÍTIO

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ORIENTADOR: Luiz Felipe Valandro
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A presente dissertação é composta por dois estudos. O estudo 1 teve como objetivo avaliar o efeito de diferentes tempos de condicionamento do primer cerâmico (E&P, Monobond Etch & Prime) na durabilidade da resistência de união ao microcisalhamento (µSBS) entre uma cerâmica de dissilicato de lítio e um cimento resinoso. As amostras de cerâmica foram submetidas à simulação em laboratório da usinagem pelo *Computer-aided design/Computer-aided manufacturing* (CAD/CAM) e alocadas aleatoriamente considerando: "tratamento de superfície" - ácido fluorídrico 5% e silano (HF5+SIL) ou E&P (20s+40s; 20s+2min; 20s+5min; 20s+10min); e "condição de envelhecimento": curto prazo (testados 24 h após a cimentação) ou longo prazo (armazenados por 180 dias + 12.000 ciclos térmicos). Assim, cilindros de cimento resinoso foram confeccionados, submetidos ao teste de µSBS e o padrão de falha foi determinado. A curto prazo, todos os grupos apresentaram resistência de união estatisticamente semelhantes (22,42 – 25,06 MPa). No entanto, apenas os grupos E&P20s+40s (19,25 MPa) e E&P20s+5min (21,51 MPa) mantiveram uma resistência adesiva estável a longo prazo, na qual este último foi estatisticamente superior ao HF5+SIL (17,05 MPa). A maioria das falhas foram predominantemente adesivas. Portanto, o uso do primer cerâmico mostra-se uma alternativa viável ao condicionamento com ácido fluorídrico 5% e silano, promovendo uma resistência de união estável para aplicação passiva de 40 s ou 5 min. O estudo 2 teve como objetivo avaliar o efeito do aumento de tempo da aplicação passiva do primer cerâmico no desempenho à fadiga de restaurações simplificadas de dissilicato de lítio cimentadas adesivamente. Discos (Ø= 10mm; espessura= 1,0mm) de cerâmica foram submetidos ao mesmo processo de simulação CAD/CAM e alocados segundo: "tratamento de superfície" - PRIMER, somente aplicação de silano; HF5+PRIMER, ácido fluorídrico 5% e silano; E&P20s+40s e E&P20s+5min, condicionamento com E&P durante 20 s de aplicação ativa seguida de 40 s ou 5 min de aplicação passiva, respectivamente; e "condição de envelhecimento" - *baseline*, testes realizados após 24 h até 5 dias da cimentação; ou envelhecidos, armazenamento por 90 dias + 12.000 ciclos térmicos. A cimentação adesiva foi realizada sobre discos de resina epóxi (Ø= 10 mm; espessura= 2 mm) e os conjuntos cimentados foram submetidos ao teste de fadiga pela abordagem *stepstress* (carga inicial de 200 N; incremento de carga de 50 N a cada 10.000 ciclos; 20 Hz). Na condição *baseline*, os tratamentos de superfície apresentaram desempenho semelhante à fadiga, com exceção do grupo E&P20s+5min (940,0 N; 123.000), que apresentou valor superior ao PRIMER (786,7 N; 92.333). Quando envelhecido, o grupo PRIMER apresentou pior desempenho à fadiga (480,8 N; 31.154) em comparação aos outros grupos (810,0 – 840,0 N; 97.000 – 103.000 ciclos). Além disso, o tratamento com PRIMER apresentou desempenho instável à fadiga após envelhecimento. Assim, condicionar a superfície da cerâmica é necessário para um desempenho estável em fadiga de restaurações de dissilicato de lítio cimentadas adesivamente. Ademais, o primer cerâmico E&P promoveu desempenho semelhante à fadiga comparado ao tratamento com ácido fluorídrico 5% e agente de união, mas o aumento passivo no tempo de condicionamento não melhorou o comportamento à fadiga.

**Palavras-chave:** Análise de sobrevida. CAD/CAM. Cerâmica vítrea. Microcisalhamento. Resistência de união. Tratamentos de superfície.

# ABSTRACT

## EFFECT OF DIFFERENT TIMES OF A SELF-ETCHING CERAMIC PRIMER ON THE ADHESION AND FATIGUE BEHAVIOR OF A LITHIUM DISILICATE CERAMIC

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PROMOTER: Luiz Felipe Valandro
CO-PROMOTER: Andressa Borin Venturini

This dissertation is composed of two studies. Study 1 aimed to evaluate the effect of different etching times of the ceramic primer (E&P, Monobond Etch & Prime) on the durability of the microshear bond strength (µSBS) between a lithium disilicate ceramic and a resin cement. The ceramic samples were subjected to an in-lab simulation of Computer-aided design/Computer-aided manufacturing (CAD/CAM) milling and randomly allocated considering: "surface treatment" - 5% hydrofluoric acid and silane (HF5 + SIL) or E&P (20s+40s; 20s+2min; 20s+5min; 20s+10min); and "aging condition": short-term (tested 24 h after bonding) or long-term (stored for 180 days + 12,000 thermal cycles). Thereby, resin cement cylinders were built, submitted to the µSBS test and the failure pattern was determined. In the short-term, all groups presented statistically similar bond strength (22.42 – 25.06 MPa). However, only the E&P20s+40s (19.25 MPa) and E&P20s+5min (21.51 MPa) groups maintained a stable long-term bond strength, in which the latter was statistically higher than HF5+SIL (17.05 MPa). Most failures were predominantly adhesive. Thus, the use of ceramic primer is a viable alternative to conditioning with 5% hydrofluoric acid and silane, providing a stable bond strength for passive application of 40 s or 5 min. Study 2 aimed to evaluate the effect of increased time of passive application of ceramic primer on the fatigue performance of adhesively cemented lithium disilicate simplified restorations. Ceramic discs (Ø= 10mm; thickness= 1.0mm) were submitted to the same CAD/CAM simulation process and allocated according to: "surface treatment" - PRIMER, coupling agent application only; HF5 + PRIMER, 5% hydrofluoric acid and coupling agent; E&P20s+40s and E&P20s+5min, etching with E&P for 20 s of active application followed by 40 s or 5 min of passive application, respectively; and "aging condition" - baseline, tests performed after 24 h within 5 days of cementation; or aged, storage for 90 days of storage + 12,000 thermal cycles. The adhesive cementation was performed onto epoxy resin discs (Ø= 10 mm; thickness= 2 mm) and the cemented assemblies were submitted to the fatigue test by step-stress approach (initial load of 200 N; step-size of 50 N for each 10,000 cycles; 20 Hz). In the baseline condition, the surface treatments presented similar fatigue performance, except for E&P20s+5min group (940.0 N; 123,000), which presented higher value than PRIMER (786.7 N; 92,333). When aged, the PRIMER group had worst fatigue performance (480.8 N; 31,154) compared to the other groups (810.0 – 840.0 N; 97,000 – 103,000 cycles). In addition, treatment with PRIMER showed unstable fatigue performance after aging. Thus, etching the ceramic surface is required for stable fatigue performance of adhesively cemented lithium disilicate restorations. In addition, the E&P ceramic primer promoted similar fatigue performance compared to the treatment with 5% hydrofluoric acid and coupling agent, but the passive increase in etching time did not improve the fatigue behavior.


**Key words:** Bond strength. CAD/CAM. Glass ceramic. Microshear. Surface treatments. Survival analysis.

**SUMÁRIO**

# 1. INTRODUÇÃO GERAL

Para atender à crescente demanda por restaurações estéticas e duradouras, o dissilicato de lítio se destaca entre as cerâmicas odontológicas frente a associação de características mecânicas e ópticas (SPITZNAGEL; BOLDT; GIERTHMUEHLEN, 2018; LUCIANO et al., 2019). A microestrutura da cerâmica a base de dissilicato de lítio consiste em aproximadamente 70% de volume de cristais alongados e intertravados que reforçam a matriz vítrea, fato potencialmente responsável pelo aumento da resistência à flexão (aproximadamente 400 MPa) (GUESS et al., 2011; ZOGHEIB et al., 2011; KRUZIC et al., 2018).

Ao mesmo tempo, com a modernização no processamento e na fabricação das restaurações indiretas após a introdução dos sistemas de desenho e manufatura assistida por computador (*Computer-aided design/Computer-aided manufacturing* - CAD/CAM), a aplicação da odontologia digital para materiais cerâmicos tem se destacado (BLATZ; CONEJO, 2019; EDELHOFF et al., 2019) em função da facilidade e padronização do processo de fabricação (SPITZNAGEL; BOLDT; GIERTHMUEHLEN, 2018) e da otimização da confiabilidade estrutural do material (TINSCHERT et al., 2000). Nesse contexto, coroas monolíticas de dissilicato de lítio fabricadas com auxílio dos sistemas CAD/CAM apresentaram taxas satisfatórias de sobrevida clínica: 100% após 2 anos (AKIN; TOKSAVUL; TOMAN, 2015; SEYDLER; SCHMITTER, 2015) e 83,5% após 10 anos (RAUCH et al. 2018).

Para o alcance do sucesso clínico das restaurações cerâmicas necessita-se, principalmente, de uma adequada e longeva união entre cerâmica, cimento e substrato dentário, bem como um material cerâmico provido de características mecânicas que o tornem resistentes às condições orais a que são submetidos (GUESS et al., 2009; MANSO et al., 2011; BLATZ; VONDERHEIDE; CONEJO, 2018). Nesse sentido, os cimentos resinosos são considerados padrão-ouro para a cimentação adesiva e, consequente, reforço e retenção de restaurações a base de sílica (PEUTZFELDT; SAHAFI; FLURY, 2011; BLATZ; VONDERHEIDE; CONEJO, 2018; JOHNSON et al., 2018; SOUSA et al., 2019). Esse efeito de fortalecimento pode ocorrer devido à formação de uma camada híbrida entre a cerâmica e os agentes cimentantes a base de resina, resultante da penetração do cimento resinosos na superfície condicionada da cerâmica (FLEMING et al., 2006; SPAZZIN et al., 2016).

A cimentação adesiva requer etapas de pré-tratamento na superfície interna das restaurações (BLATZ; VONDERHEIDE; CONEJO, 2018), para que uma ligação íntima seja alcançada entre a superfície cerâmica e o agente cimentante (FLEMING et al., 2006). Para as cerâmicas vítreas, como o dissilicato de lítio, o protocolo clássico de tratamento de superfície é a aplicação do ácido fluorídrico e de um agente de união contendo silano (HORN, 1983; BRENTEL et al., 2007; BLATZ; VONDERHEIDE; CONEJO, 2018). O condicionamento com ácido fluorídrico ataca seletivamente a porção vítrea das cerâmicas, expõe óxidos de sílica ($SiO_2$) e, consequentemente, promove alterações topográficas superficiais (intertravamento mecânico) para a retenção micromecânica a materiais resinosos. O agente de união atua quimicamente neste conjunto (MATINLINNA; LUNG; TSOI, 2018), através da interação das moléculas bifuncionais, as quais participam das ligações siloxanas entre a sílica contida na matriz vítrea cerâmica e a matriz orgânica do cimento resinoso (DELLA BONA; SHEN; ANUSAVICE, 2004).

Embora o protocolo com a aplicação de ácido fluorídrico possa efetivamente melhorar a adesão entre as cerâmicas vítreas aos cimentos resinosos (BRENTEL et al., 2007), seu efeito sobre a resistência das cerâmicas ainda é controverso e limítrofe. Estudos relatam que o condicionamento com ácido fluorídrico da cerâmica de dissilicato de lítio em um tempo maior que o recomendado resulta em impactos deletérios na resistência flexural (ZOGHEIB et al., 2011; XIAOPING; DONGFENG; SILIKAS, 2014). Além disso, o ácido fluorídrico pode ser altamente tóxico e corrosivo. As manifestações adversas decorrentes da utilização desse ácido dependem da concentração utilizada e do tempo de contato com a pele e mucosas, e mesmo em baixas concentrações (em torno de 5%, DENNERLEIN et al., 2016), como comummente empregado na Odontologia, podem causar queimaduras e necrose tecidual (OZCAN; ALLAHBEICKARAGHI; DÜNDAR, 2012; CARPENA, BALLARIN, 2014; WANG et al., 2014).

Com o intuito de simplificar a técnica de cimentação adesiva e diminuir a exposição de cirurgiões-dentistas e pacientes ao ácido fluorídrico, um produto alternativo ao condicionamento com ácido fluorídrico foi proposto para o tratamento de superfície das cerâmicas vítreas. O Monobond Etch & Prime (E&P, Ivoclar Vivadent) é um primer cerâmico autocondicionante de frasco único composto de polifluoreto de amônio (componente ácido), um sistema de silano à base de metacrilato de trimetoxipropil, solventes (álcoois e água) e um pigmento proporcionando visibilidade na aplicação com aspecto de cor verde (SCIENTIFIC DOCUMENTATION, IVOCLAR VIVADENT). A ação físico-química desse primer cerâmico permite o condicionamento e a silanização das superfícies cerâmicas em apenas um passo. Logo, esta técnica simplificada para adesão pode diminuir o potencial tóxico de risco à saúde e, além disso, evitar o efeito de enfraquecimento da cerâmica vítrea por ser um tratamento menos agressivo em comparação ao ácido fluorídrico.

Como o E&P é um produto introduzido recentemente no mercado odontológico a literatura que discorre a respeito desse primer cerâmico e cerâmicas vítreas ainda é limitada. Para desfechos de resistência de união, alguns estudos (WILLE; LEHMANN; KERN, 2017; TRIBST et al., 2018; LYANN et al., 2019; MURILLO-GÓMEZ; DE GOES, 2019) mostraram que o protocolo clássico de condicionamento (ácido fluorídrico + agente de união contendo silano) e o primer cerâmico apresentaram resultados semelhantes estatisticamente, enquanto outros (GUIMARÃES et al., 2018; LOPES et al., 2018; PRADO et al., 2018) indicaram que o protocolo clássico apresentou melhores valores de resistência adesiva. Nesse contexto, é importante ressaltar que o tempo padrão de condicionamento com o primer cerâmico E&P nos estudos citados anteriormente foi de 60 segundos (20 segundos de aplicação ativa, acrescido de 40 segundos de aplicação passiva), tempo recomendado pelo fabricante. Apenas um estudo avaliou a variação do tempo de aplicação do E&P no desfecho de adesão (CARDENAS et al., 2019).

Assim como nos estudos que avaliam diferentes tempos de condicionamento com ácido fluorídrico (ZOGHEIB et al., 2011; XIAOPING; DONGFENG; SILIKAS, 2014; PUPPIN-RONTANI et al., 2017; WONG et al., 2017), o tempo de aplicação do primer cerâmico pode ser modificado na tentativa de melhorar a adesão e o desempenho mecânico da cerâmica de dissilicato de lítio. Essa variação de tempo afeta a introdução de defeitos de superfície, que pode ter consequências dicotômicas: i) pode ser positivo quando defeitos adicionais produzidos por um tempo de condicionamento mais longo são preenchidos por cimento resinoso, gerando uma distribuição uniforme de tensões no material de suporte (MAY et al. , 2012); ii) pode ter efeitos negativos, quando o número/tamanho/forma dos defeitos dificultar a penetração do cimento resinoso, prejudicando a interface de união, induzindo mecanismos de crescimento lento de trincas e baixo desempenho mecânico (ANUSAVICE; HOJJATIE, 1992).

Como os materiais cerâmicos odontológicos tem por objetivo final estarem em função na cavidade oral, salienta-se a importância do conhecimento do mecanismo que leva a falha das restaurações. WISKOTT; NICHOLLS; BELSER, (1995) reportaram que a falha mecânica das restaurações dentárias é decorrente da fadiga, sendo este um mecanismo definido pela degradação de um componente estrutural sob a influência de estresse mecânico, químico ou biológico - e na maioria dos casos - uma combinação deles (KELLY et al., 2017). Assim, ressalta-se a relevância de estudos *in vitro* para prever a vida útil de materiais cerâmicos e orientar as escolhas clínicas no que diz respeito aos tratamentos de superfícies para promover adesão químico-mecânica entre cerâmica/cimento/substratos. Além disso, é inexistente a literatura que aborda a aplicação do primer cerâmico E&P e o aumento do tempo de aplicação passiva como tratamento de superfície para cerâmicas vítreas no contexto de fadiga (SCHERER et al., 2018; SCHESTATSKY et al., 2019, TRIBST et al., 2019).

Levando em consideração os fatores acima citados, a avaliação de diferentes tempos de condicionamento com o primer cerâmico E&P na resistência adesiva e no comportamento à fadiga de uma cerâmica de dissilicato de lítio é um pressuposto pertinente, uma vez que esses desfechos influenciam diretamente o sucesso clínico de restaurações cerâmicas. Considerando o contexto exposto, a presente dissertação está fragmentada em 2 artigos:

**ARTIGO 1:** *Distinct etching times of a one-step ceramic primer: effect on the resin bond strength durability to a CAD/CAM lithium disilicate glass-ceramic*. Com o objetivo de avaliar o efeito de diferentes tempos de condicionamento do primer cerâmico E&P na resistência de união ao microcisalhamento a curto e longo prazo entre um cimento resinoso e uma cerâmica de dissilicato de lítio submetida à simulação da superfície CAD/CAM.

**ARTIGO 2:** *One-step ceramic primer as surface conditioner: effect on the load-bearing capacity under fatigue of bonded lithium disilicate ceramic simplified restorations*. Com o objetivo de avaliar o efeito do aumento do tempo de condicionamento do primer cerâmico E&P em comparação ao protocolo clássico (ácido fluorídrico e agente de união contendo silano) no desempenho em fadiga a curto e longo-prazo de restaurações de dissilicato de lítio cimentadas adesivamente em um substrato análogo de dentina.

## 2. ARTIGO 1:

Este artigo está submetido ao periódico *Journal of Adhesive Dentistry, Elsevier,* ISSN: 1461-5185 (print); 1757-9988 (online). Fator de impacto: 1.875, Qualis CAPES A2. As normas para publicação estão descritas no Anexo A.

# Distinct etching times of a one-step ceramic primer: effect on the resin bond strength durability to a CAD/CAM lithium disilicate glass-ceramic

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**Running title**: Ceramic etching-primer and lithium disilicate adhesion to resin cement.

**Abstract**

*Purpose:* To evaluate different etching times of a self-etching ceramic primer on microshear (μSBS) bond strength between a resin cement and a lithium disilicate ceramic.

*Materials and Methods:* Ceramic slices were subjected to an in-lab simulation of CAD/CAM milling and randomly allocated into 10 groups (n=35), considering: "surface treatment" – 5% hydrofluoric acid and silane (HF5+SIL) or ceramic etching primer (Monobond Etch & Prime, E&P) for 20s of active application, followed by different times of passive application: 40s; 2min; 5min; or 10min; and "aging" – short-term, tests running 24h after bonding; or long-term, water storage for 180 days+12,000 thermal cycles. Resin cement cylinders were built and μSBS tests were run in a universal testing machine. The failure pattern was categorized and complementary analysis by SEM (scanning electron microscopy) and AFM (atomic force microscopy) were performed.

*Results:* The groups showed statistically similar bond strength in the short-term condition (range from 22.42 to 25.06 MPa). However, only the E&P 20s+40s (19.25 MPa) and E&P 20s+5min (21.51 MPa) maintained stable bond strength in the long-term, in which the latter was statistically superior to HF5+SIL (17.05 MPa). The failure pattern was predominantly adhesive. The increased application time of the ceramic primer promoted progressive topographical changes and the fractal dimension analysis showed that the most complex surface characteristics were observed in the E&P 20s+10min group.

*Conclusion:* The use of self-etching ceramic primer shows to be an alternative to the classical conditioning with HF plus silane, promoting stable bond strength when maintained reacting passively for 40s or 5min.

**Keywords:** Adhesion. CAD/CAM. Fractal Dimension. Glass ceramic. Surface treatments. Topographical changes.

**INTRODUCTION**

Lithium disilicate is a synthetic glass ceramic reinforced by lithium oxide ($Li_2O$) crystal.[13] It has been considered as an acid-sensitive ceramic, with the most recommended protocol for enhanced adhesion being hydrofluoric acid (HF) etching[16,28] followed by the application of a silane coupling agent[19]. Hydrofluoric acid dissolves the glass matrix by reacting with the silicon dioxide, exposing the crystalline microstructure and creating surface roughness for micromechanical interlocking.[4,22,37,27] Meanwhile, the silane has a chemical function and binds with the organic matrix of the resin cement (activated by light curing), and with the inorganic matrix of the ceramics (through the siloxane linkages).[4,23]

Even though HF etching can effectively improve the bond strength between glass ceramics and resin cements, it is a dangerous, toxic and highly corrosive inorganic acid.[8,42] HF at high concentrations (>50%) can cause severe morbidity and death,[3,24] although at low concentrations (about 5%) it may already pose a risk to the human body.[10] In addition, studies have reported that surface treatment with HF etching increases ceramic roughness by the presence of pores, which in turn may act as sources of crack initiation and lead to a weakening effect on the mechanical properties of glass ceramics.[1,39]

Consequently, alternative etching methods for glass ceramics have been proposed, such as the self-etching ceramic primer (E&P; Monobond Etch & Prime, Ivoclar Vivadent). Monobond Etch & Prime is a one-step technique composed of an ammonium polyfluoride (mild etchant) silane system based on trimethoxypropyl metacrylate, solvents and a pigment.[34] Studies have demonstrated promising results for E&P, but hydrofluoric acid etching plus silane application still showed superior bond strength when the E&P manufacturer's protocol was used;[11,15,18,29] this protocol entails an active application for 20 s, allowing the material to react for another 40 s. However, some studies have reported similar bond strength values in comparing these two surface conditioning techniques.[43,20,38,26]

Still in this sense, one study[7] recently evaluated the use of different E&P protocols and the bond strength of lithium disilicate and feldspathic ceramics and compared them to the HF + silane protocol. They varied the active application time between 5 to 60 s (20 s as recommended by the manufacturer) and the passive application (primer maintained to react) between 20 and 40 s (40 s as recommended by the manufacturer). They noticed better bond results for lithium disilicate ceramics when using the ceramic etching primer under active application for 60 s and maintained to react for 40 s, thus corroborating a potential benefit of increasing the exposure time to such agent in comparison to the manufacturer's protocol (as mentioned). Despite this, they did not evaluate the resin bond stability, and consequently the real potential of this simplified one-step technique still needs to be evaluated by subjecting the adhered interfaces to long-term aging.[7] Thus, new studies exploring this research field and different protocols of E&P application are still encouraged to better clarify and understand this thematic.

When evaluating topographic changes, HF promotes a deeper and more aggressive etching pattern compared to E&P in the time recommended by the manufacturer[43,29]. The topographical pattern achieved by E&P is more superficially deep, showing apparently less micromechanical retention with smaller glassy dissolution and without crystal exposition.[15,32,25] Thus, an increase in E&P exposure time could optimize the generated topographical changes and promote better or closer micromechanical behavior to that observed with HF. Furthermore, laboratorial studies usually evaluate the adhesive performance of surface treatments in polished samples, and as expressed herein topographical features are fundamental for the observed adhesion mechanism; therefore, it becomes important to attempt to mimic such a scenario in order to acquire more reliable data.[31]

Finally, this study aimed to evaluate the effect of different etching times of E&P primer on the short- and long-term (aging) microshear (μSBS) bond strength between a resin cement and lithium disilicate ceramic submitted to CAD/CAM milling simulation. The tested hypotheses were: 1) the ceramic surface treatments will promote similar bond strength; 2) aging will deleteriously impact the bond strength.

## MATERIAL AND METHODS

The general description of the materials used in the present study, the manufacturers, composition, and batch numbers are listed in Table 1. A schematic drawing representing the steps from specimens manufacturing, ceramic surface treatment and microshear bond strength testing is presented in Figure 1.

### Sample Preparation

Lithium disilicate glass ceramic blocks for CAD/CAM (IPS e.max CAD LT A2/C16, Ivoclar Vivadent, Amherst, USA) were sectioned into rectangular slices (16mm x 9mm x 2mm) using a diamond disc at low-speed under water-cooling in a cutting machine (Isomet 1000, Buehler, Lake Bluff, USA). They were polished (EcoMet/AutoMet 250, Buehler, Lake Bluff, USA) using #400-, #600-, and #1200-grit silicon carbide papers (SiC) for 30 s each to produce standardized polished surfaces (Table 2).

As the machining process introduces a complex network of events (such as defects, higher roughness) in the cementation surface of ceramic restorations,[12] we considered a similar protocol to CAD/CAM processing. Thus, all ceramic samples were submitted to an in-Lab simulation of the CAD/CAM milling roughness by using a standardized size (100 mm × 50 mm) of #60 grit SiC paper for each slice, which were marked (axes x and y) with a marking pen and submitted to manual grinding with humidified SiC papers by a single trained operator (KSD).[31] The manual grinding was performed applying light finger pressure for 15 s on each axis (x and y). After simulating the milling roughness (Fig. 2), the ceramic slices were crystallized according to the manufacturer's instructions (840°C, 7 min vacuum, Vacumat 6000 MP, VITA Zahnfabrik, Bad Sackingen, Germany).

The mean roughness values of all ceramic surfaces were measured after the polishing procedures, in-Lab simulation of the CAD/CAM milling roughness and crystallization. Six measurements were performed on each specimen (axes x and y).[31] The parameters of average roughness (Ra) and mean distance between the five higher peaks and valleys (Rz) were obtained through a roughness tester (Mitutoyo SJ-410, Kanagawa, Japan) according to ISO 4287.[17] The roughness parameters achieved by the in-Lab simulation (Table 2) were similar to the one generated by CAD/CAM machining (Mean, Standard Deviation: Ra= 1.84, 0.18; Rz= 11.07, 1.00).[12]

Next, the ceramic slices were embedded in PVC cylinders (Krona, Joinville, Brazil) with self-curing acrylic resin (JET Clássico; Campo Lindo Paulista, Brazil), leaving the simulated milled surface free to perform the surface treatments. Then, all the specimens were cleaned in an ultrasonic bath (1440 D, Odontobras, Ind. and Com. Equip. Med. Odonto. LTDA, Ribeirão Preto, Brazil) with isopropyl alcohol for 5 min.

**Study design and surface treatments**

The specimens were randomly allocated (https://www.randomizer.org/) into 10 groups according to the factors "surface treatment" and "aging condition" (Table 3).

For the HF5 + SIL group, 5% hydrofluoric acid (IPS Ceramic Etching Gel, Ivoclar Vivadent, Schaan, Liechtenstein) was applied with a microbrush for 20 s, removed with air-water spray for 30 s and air dried for 30 s. A silane solution (Monobond Plus, Ivoclar Vivadent, Schaan, Liechtenstein) was rubbed on the ceramic surface with a microbrush for 15 s and left to react for 45 s, as recommended by the manufacturer.

For the E&P groups, self-etching ceramic primer (E&P, Monobond Etch & Prime, Ivoclar Vivadent, Schaan, Liechtenstein) was rubbed on the ceramic surface with a microbrush for 20 s and left to react by a specific time according to each group: 40 s (E&P 20s + 40s - time recommended by the manufacturer), 2 min (E&P 20s + 2min), 5 min (E&P 20s + 5min) and 10 min (E&P 20s + 10min). One product reapplication was performed for the E&P 20s + 5min (in the time of 2.5 min), and two reapplications were performed in the E&P 20s + 10min (in the time of 3.3 min and 6.7 min). This product reapplication was based on a previous pilot study, in which it was observed that the product evaporated over time. This reapplication process was passive without agitating it, in which the product was maintained to react on the ceramic until the time set for each group. The product was washed with air-water spray for 30 s and air dried for 30 s only at the end of the time determined for each E&P group, i.e., the ceramic was not washed after each reapplication.

After the surface treatments, all specimens were cleaned in an ultrasonic bath with distilled water to remove precipitates for up to 5 min, as recommended by the manufacturer.

**Cementation procedure**

Seven starch tubes (1.2 mm internal diameter; 1.0 mm high; Isabela, M. Dias Branco S.A. Indústria e Comércio de Alimentos, São Caetano do Sul, Brazil) were positioned over each treated surface and fixed with stick wax (Lysanda, São Paulo, Brazil),[36] with a total of thirty-five (n= 35) resin cement cylinders for each condition. A dual cure resin cement (Multilink Automix, Ivoclar Vivadent) was carefully applied inside each tube with a digital spacer (#25, Densply Maillefer; Ballaigues, Switzerland) and condensed with a resin instrument (Golgran - Millennium Titanium Resin N$^{o}$.9, São Caetano do Sul, Brazil), according to the methodology of Prado et al.[29] The resin cement was light-cured (1200 mW/cm2, Radii-Cal, SDI, Bayswater, Australia) for 40 s. The starch tubes were carefully removed with a dental explorer (#5, Hu-Friedy) after 24 h of storage in distilled water (37°C) to obtain the cement cylinders (sample unit). The specimens were individually assessed using an optical microscope (Stereo Discovery V20, Carl Zeiss, Gottingen, Germany) at 40× magnification to identify any failure (e.g. bubbles, porosity) at the adhesive interface. The specimen was excluded and replaced if any irregularities or gaps were observed at the adhesive interface. The specimens were subsequently allocated according to the aging conditions according to the next section.

**Aging conditions**

The specimens of each surface treatment were randomly assigned into two aging conditions: “short-term” - specimens were submitted to microshear bond strength tests after storage in distilled water at 37°C  for 24 h; “long-term” samples under aging condition were subjected to thermocycling (12,000 cycles - baths of 30 s within 5 to 55°C, transfer time of 5 s [2,41]; Nova Ética, São Paulo, Brazil) and storage in distilled water at 37°C for 180 days before testing.

## Microshear Bond Strength Test (μSBS)

The embedded ceramic was placed in a test device coupled to a universal testing machine (EMIC DL-2000, São José dos Pinhais, Brazil) and the test was performed using the *wire-loop* method (stainless steel wire, Ø= 30 μm). The thin stainless-steel wire loop was positioned as close as possible to the adhesive interface and a constant load at a crosshead speed of 1.0 mm/min was applied until failure occurred. The bond strength was calculated according to the formula: R= F/A; where "R" is the strength (MPa), "F" is the load required for failure of the specimen (N) and "A" is the interface area of the specimen (1.13 mm²).

## Failure analysis

The fracture pattern was determined under a stereomicroscope (Stereo Discovery V20, Carl Zeiss, Gottingen, Germany), and classified into two types: 1) predominantly adhesive failure at the interfacial region between the resin cement and ceramic (adhesive - adhesive areas of up to 50% were considered); 2) cohesive failure at the cement (cohesive cem - cohesive areas from 50% were considered). Representative specimens (n= 1) were sputter-coated with gold and evaluated under scanning electron microscopy (SEM - Vega3, Tescan, Brno, Czech Republic) in order to observe the failure pattern.

## Topographic analysis

### *Surface-etching Pattern in Field Emission Scanning Electron Microscopy (FE-SEM)*

Specimens of each group (n= 1) were evaluated under field emission scanning electron microscopy (FE-SEM, Sigma 300 VP, Carl Zeiss, England) at 1000× and 30000× magnifications in order to observe the surface alterations of the treated ceramic surfaces.

### *Evaluation of the Fractal Dimension under Atomic Force Microscopy (AFM)*

Fractal dimension (FD) data is a mathematical tool which provides a new way of explaining the complexity of the topographic pattern of the treated ceramic surface. The fractal dimension was computed by the box count method (BC). The BC approach is a technique for estimating the FD of an image for its simplicity and automation, and is based on the linear interpolation of pixels in the AFM topography image. The FD result is a non-integer number between 2 and 3, and the closer it is to 3, the more complex the topography is.[30,14,33]

For the analysis, one sample of each experimental group (n= 1) was submitted to AFM analysis (Park Systems NX10 equipment, Suwon, Korea). It was performed through the non-contact mode and conducted using a reflective aluminum backside-coated highly-doped monolithic silicon probe (Nanosensors PPP-NCHR, Neuchâtel, Switzerland). All measurements were done under ambient conditions at room temperature of 21 ± 5°C and a relative humidity of 55 ± 10% with a scanning rate of 0.7 Hz. Samples were imaged over areas of 10 x 10 µm. AFM data analysis was performed using Park XEI software (version 4.3.4Build22.RTM1): the FD was carried out at five different regions of each sample (5 samples, with 5 regions under analysis each one - the average of the measurements was obtained for each sample).

**Statistical Analysis**

The resin cement cylinder was used as the experimental unit for the bond strength data analysis. Two-Way ANOVA and post-hoc Bonferroni test (α= 0.05) were performed to compare results from short- and long-term aging conditions and to compare data among the different groups. Pre-test and cohesive failures were excluded from the statistical analysis, since those failures did not represent the real bond strength between materials. The statistical analyses were performed by SPSS 21 statistical software (IBM, Chicago, IL, USA).

**RESULTS**

RESULTS

Considering the bond strength data obtained in aged conditions at HF5 + SIL and E&P 20s + 5min groups, a power analyses of 96.17% was detected with confidence interval of 95% (http://openepi.com/Power/PowerMean.htm). Two-Way ANOVA revealed significant influence of “surface treatment” (p= 0.0049, F= 3.81) and “aging” (p= 0.0000, F= 75.63) factors. The interaction between the factors “aging x surface treatment” was not statistically significant (p= 0.3341, F= 1.15).

In comparing the treatments, there was no statistical difference among the groups in the short-term condition (range from 22.42 to 25.06 MPa), whereas the E&P 20s + 5min group (21.51 MPa) presented higher values in the long-term condition than the HF5 + SIL (17.05 MPa) (Table 4). No significant decrease in bond strength was observed in either the E&P 20s + 40s and E&P 20s + 5min groups after aging, while the adhesive interface of other groups was degraded by thermocycling and long-term water storage (Table 4). Regarding the failure analysis, all groups showed predominantly adhesive failures (Table 4, Fig. 3).

Treatment with hydrofluoric acid (HF5 + SIL group) resulted in an irregular topographic pattern with larger voids, meanwhile the protocol recommended by the manufacturer of the self-etching ceramic primer (E&P 20s + 40s) showed less pronounced surface alterations. However, the increase in E&P etching time exhibited intensified surface micro-morphological alterations (Fig. 4), in which the fractal dimension analysis corroborated that the E&P 20s + 10min presented the most complex surface pattern (Table 5).

## DISCUSSION

Although short-term bond strength was statistically similar among the tested conditions, the E&P 20s + 5min group promoted higher long-term bond strength than the conventional surface treatment with hydrofluoric acid and silane application, rejecting the first hypothesis. Only the E&P 20s + 40s and 20s + 5min groups promoted stable bond strength (no statistically significant decrease in bond strength after aging). Therefore, the second hypothesis was partially accepted.

Representative micrographs clearly demonstrate that the different treatments promoted defects with distinct shapes and depths (Fig. 4, Table 5). Less pronounced topographical changes were observed with the ceramic primer using the manufacturer’s instructions (E&P 20s + 40s) compared to those induced by hydrofluoric acid, which is corroborated by the literature.[43,15,32,25] However, increasing the application time of the E&P substantially changed the surface topography, exposing lithium disilicate crystals and resulting in micro- and nano-morphological changes (porosity) in the ceramic structure to promote interlocking effects.[7] When the defects become deeper and more aggressive (as promoted by the HF5 + SIL and E&P 20s + 10min protocols) and the surface topography becomes more complex (corroborated by higher fractal dimension), the hypothesis is that the cement is not able to completely fill these defects, which in turn provided greater susceptibility for degradation, and this would be the reason for the decreased bond strength in such groups after aging.

It is important that the cementing agent, such as resin cement, fills in the defects created by the etching agent (HF or ceramic primer) so that the ceramic structural reinforcement and proper adhesion are observed. Greater surface defects produced by aggressive etching protocols may favor micromechanical interlocking with the resin cement, as long as the resin cement can penetrate those irregularities.[40] In this sense, cement viscosity can also influence this process.[4,35] Therefore, bonding between two materials not only depends on the size of the irregularities (amount of dissolved glass phase), but also on the ability of cements to infiltrate them.[35,9] It should be noted that there must be a balance between the topographic changes favorable for adhesion: number of irregularities and the creation of defects with a shape which can be filled by the cementing agent. Finally, we emphasize that studies exploring the impact of different viscosities of the resin cement on such outcomes are highly demanded.

It is further important to mention that the ultimate goal of good adhesion in dental materials is to produce an interface that is strong and long-lasting.[22] Although there is difficulty in mimicking oral cavity aging in vitro, studies have reported the thermal cycling (5ºC/55ºC, 1 min)[4] and storage at 37ºC (simulated mouth temperature) as valid methods for aging the adhesive interface,[21] which were performed in the present study. Even though some tested groups significantly reduced bond strength after the aging protocols, only surface treatments with self-etching ceramic primer reacting for 40 s and 5 min maintained stable bonding performance. In this sense, we also highlight the better performance of the E&P 20s + 5min protocol over the HF5 + SIL in such a scenario, which is an important finding since hydrofluoric acid is also a hazardous substance. Thus, our data clearly show findings which corroborate the promising use of E&P as a substitute to HF in lithium disilicate ceramics.

Finally, one of the main factors to promote enhanced adhesion to ceramics is the topographic alteration generated by the surface treatment. When considering a monolithic restoration manufactured with a glass ceramic such as lithium disilicate, the topography produced by CAD/CAM systems can also influence the evaluated outcomes. This important factor is rarely explored by in vitro studies. Moreover, as the cost of a machined ceramic is still high, we chose to make the process feasible and simulate the machined surface based on an in vitro study (Fig. 2).[31] It is interesting to note that the roughness parameters produced by the in-Lab simulation of the present study (Table 2; Ra= 1.44 ±0.1; Rz= 9.38 ±0.6) were close to that found in a study with CAD/CAM machined ceramics (Ra= 1.84 ±0.2; Rz= 11.07 ±1.0).[12] There may undeniably be differences in the shape, size and quantity of the defects produced, which could still be considered a study limitation.

Thus, our data corroborates that the self-etching ceramic primer (characterized as an all-in-one approach) depicts promising results for bond strength to glass ceramics, in addition to being less toxic.[29,32] However, restorations are clinically challenged by cyclic loading and environmental issues, such as saliva immersion and exposure to foods and beverages with varying pH, chemicals and temperatures.[37] In this sense, the current findings should be considered with caution, since in vitro studies have inherent limitations to simulate the clinical conditions.

## CONCLUSION

Based on the findings of this in vitro study, the following conclusions may be drawn:

- The treatment of the lithium disilicate ceramic with self-etching ceramic primer showed similar or even better (for E&P 20s + 5min group) long-term bonding results to resin cement in comparison to the classic hydrofluoric acid and silane protocol, corroborating it as an alternative and promoting a benefit of less toxicity.
- The use of E&P 20s + 40s or 5 min were the only protocols which showed stable adhesion after aging by water storage and thermocycling.
- Increasing the application time of the ceramic primer produced a progressive topographic change, improving bonding performance upon 5 min of passive exposure.

## CLINICAL RELEVANCE

The one-step ceramic primer used as a glass-ceramic conditioner proved to be an alternative to HF etching plus silane application for resin bond improvements to the lithium disilicate glass-ceramic, associating smooth topographical alterations (micromechanical bond) and chemical bond activation.

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**REFERENCES**


1. Addison O, Marquis PM, Fleming GJ. The impact of hydrofluoric acid surface treatments on the performance of a porcelain laminate restorative material. Dent Mater. 2007 Apr;23(4):461-8.
2. Andreatta Filho OD, Araújo MAJ, Bottino MA, Nishioka RS, Menezes MMM. Study of thermocycling effect on the bond strength between an aluminous ceramic and a resin cement. J Appl Oral Sci 2005; 13:53-57.
3. Bartlett D. Dermal exposure to hydrofluoric acid causing significant systemic toxicity. J Emerg Nurs. 2004 Aug;30(4):371-3.
4. Blatz MB, Sadan A, Kern M. Resin-ceramic bonding: a review of the literature. J Prosthet Dent. 2003 Mar;89(3):268-74.
5. Blumer L, Schmidli F, Weiger R, Fischer J. A systematic approach to standardize artificial aging of resin composite cements. Dent Mater. 2015 Jul;31(7):855-63.
6. Buzio R, Boragno C, Biscarini F, Buatier de Mongeot F, Valbusa U. The contact mechanics of fractal surfaces. Nat Mater. 2003 Apr;2(4):233-6.
7. Cardenas AFM, Quintero-Calderon AS, Siqueira FSF, Campos VS, Wendlinger M, Pulido-Mora CA, Masson-Palacios MJ, Sarmiento-Delgado ML, Loguercio AD. Do Different Application Modes Improve the Bonding Performance of Self-etching Ceramic Primer to Lithium Disilicate and Feldspathic Ceramics? J Adhes Dent. 2019;21(4):319-327.
8. Carpena G, Ballarin A. Hydrofluoric Acid – Simple Things You May Do Not Know About Something You Are So Habituated To Use. Odovtos Int J Dental SC. 2014; 16:15-23.
9. Colombo LDA, Murillo-Gómez F, De Goes MF. Bond Strength of CAD/CAM Restorative Materials Treated with Different Surface Etching Protocols. J Adhes Dent. 2019;21(4):307-317.
10. Dennerlein K, Kiesewetter F, Kilo S, Jäger T, Göen T, Korinth G, Drexler H. Dermal absorption and skin damage following hydrofluoric acid exposure in an ex vivo human skin model. Toxicol Lett. 2016 Apr 25; 248:25-33.
11. El-Damanhoury HM, Gaintantzopoulou MD. Self-etching ceramic primer versus hydrofluoric acid etching: Etching efficacy and bonding performance. J Prosthodont Res. 2018 Jan;62(1):75-83.
12. Fraga S, Amaral M, Bottino MA, Valandro LF, Kleverlaan CJ, May LG. Impact of machining on the flexural fatigue strength of glass and polycrystalline CAD/CAM ceramics. Dent Mater. 2017 Nov;33(11):1286-1297.
13. Gracis S, Thompson VP, Ferencz JL, Silva NR, Bonfante EA. A new classification system for all-ceramic and ceramic-like restorative materials. Int J Prosthodont. 2015 May-Jun;28(3):227-35.
14. Griggs JA. Using fractal geometry to examine failed implants and prostheses. Dent Mater. 2018 Dec;34(12):1748-1755.
15. Guimarães HAB, Cardoso PC, Decurcio RA, Monteiro LJE, de Almeida LN, Martins WF, Magalhães APR. Simplified Surface Treatments for Ceramic Cementation: Use of Universal Adhesive and Self-Etching Ceramic Primer. Int J Biomater. 2018 Dec 31; 2018:2598073.
16. Horn, H.R. Porcelain laminate veneers bonded to etched enamel. In: __. Phillips RW editor. Symposium on Dental Material. Dental Clinics of North America, 1983. v.27, p.671-684
17. ISO 4287. Geometrical product specifications (GPS) – Surface texture: Profile method – Terms, definitions and surface texture parameters. International Organization for Standardization, Geneva; 1997.
18. Lopes GC, Perdigão J, Baptista D, Ballarin A. Does a Self-Etching Ceramic Primer Improve Bonding to Lithium Disilicate Ceramics? Bond Strengths and FESEM Analyses. Oper Dent. 2018 Aug 14.
19. Lung CY, Matinlinna JP. Aspects of silane coupling agents and surface conditioning in dentistry: an overview. Dent Mater. 2012 May;28(5):467-77.
20. Lyann SK, Takagaki T, Nikaido T, Uo M, Ikeda M, Sadr A, Tagami J. Effect of Different Surface Treatments on the Tensile Bond Strength to Lithium Disilicate Glass Ceramics. J Adhes Dent. 2018;20(3):261-268.
21. Mair L, Padipatvuthikul P. Variables related to materials and preparing for bond strength testing irrespective of the test protocol. Dent Mater. 2010 Feb;26(2): e17-23.
22. Marshall SJ, Bayne SC, Baier R, Tomsia AP, Marshall GW. A review of adhesion science. Dent Mater. 2010 Feb;26(2): e11-6.

23. Matinlinna JP, Lung CYK, Tsoi JKH. Silane adhesion mechanism in dental applications and surface treatments: A review. Dent Mater. 2018 Jan;34(1):13-28.
24. McKee D, Thoma A, Bailey K, Fish J. A review of hydrofluoric acid burn management. Plast Surg (Oakv). 2014 Summer;22(2):95-8.
25. Moreno MBP, Murillo-Gómez F, de Goes MF. Physicochemical and morphological characterization of a glass ceramic treated with different ceramic primers and post-silanization protocols. Dent Mater. 2019 Aug;35(8):1073-1081.
26. Murillo-Gómez F, De Goes MF. Bonding effectiveness of tooth-colored materials to resin cement provided by self-etching silane primer after short- and long-term storage. J Prosthet Dent. 2019 Apr;121(4): 713.e1-713.e8.
27. Murillo-Gómez F, Palma-Dibb RG, De Goes MF. Effect of acid etching on tridimensional microstructure of etchable CAD/CAM materials. Dent Mater. 2018 Jun;34(6):944-955.
28. Ozcan M, Vallittu PK. Effect of surface conditioning methods on the bond strength of luting cement to ceramics. Dent Mater. 2003;19(8):725–31.
29. Prado M, Prochnow C, Marchionatti AME, Baldissara P, Valandro LF, Wandscher VF. Ceramic Surface Treatment with a Single-component Primer: Resin Adhesion to Glass Ceramics. J Adhes Dent. 2018;20(2):99-105.
30. Prochnow C, Venturini AB, Guilardi LF, Pereira GKR, Burgo TAL, Bottino MC, Kleverlaan CJ, Valandro LF. Hydrofluoric acid concentrations: Effect on the cyclic load-to-failure of machined lithium disilicate restorations. Dent Mater. 2018 Sep;34(9): e255-e263.
31. Rodrigues CDS, Guilardi LF, Follak AC, Prochnow C, May LG, Valandro LF. Internal adjustments decrease the fatigue failure load of bonded simplified lithium disilicate restorations. Dent Mater. 2018 Sep;34(9): e225-e235.
32. Scherer MM, Prochnow C, Venturini AB, Pereira GKR, Burgo TAL, Rippe MP, Valandro LF. Fatigue failure load of an adhesively-cemented lithium disilicate glass-ceramic: Conventional ceramic etching vs etch & prime one-step primer. Dent Mater. 2018 Aug;34(8):1134-1143.
33. Schestatsky R, Zucuni CP, Venturini AB, de Lima Burgo TA, Bacchi A, Valandro LF, Rocha Pereira GK. CAD-CAM milled versus pressed lithium-disilicate monolithic crowns adhesively cemented after distinct surface treatments: Fatigue performance and ceramic surface characteristics. J Mech Behav Biomed Mater. 2019 Jun; 94:144-154.
34. Scientific Documentation – Monobond Etch & Prime. Ivoclar Vivadent, 2015.
35. Sundfeld D, Palialol ARM, Fugolin APP, Ambrosano GMB, Correr-Sobrinho L, Martins LRM, Pfeifer CS. The effect of hydrofluoric acid and resin cement formulation on the bond strength to lithium disilicate ceramic. Braz Oral Res. 2018 May 24;32: e43.
36. Tedesco TK, Montagner AF, Skupien JA, Soares FZ, Susin AH, Rocha RO. Starch tubing: an alternative method to build up microshear bond test specimens. J Adhes Dent. 2013 Aug;15(4):311-5.
37. Tian T, Tsoi JK, Matinlinna JP, Burrow MF. Aspects of bonding between resin luting cements and glass ceramic materials. Dent Mater. 2014 Jul;30(7): e147-62.
38. Tribst J, Anami LC, Özcan M, Bottino MA, Melo RM, Saavedra G. Self-etching Primers vs Acid Conditioning: Impact on Bond Strength Between Ceramics and Resin Cement. Oper Dent. 2018 Jul/Aug;43(4):372-379.
39. Venturini AB, Prochnow C, May LG, Bottino MC, Felipe Valandro L. Influence of hydrofluoric acid concentration on the flexural strength of a feldspathic ceramic. J Mech Behav Biomed Mater. 2015 Aug; 48:241-248.
40. Venturini AB, Prochnow C, May LG, Kleverlaan CJ, Valandro LF. Fatigue failure load of feldspathic ceramic crowns after hydrofluoric acid etching at different concentrations. J Prosthet Dent. 2018 Feb;119(2):278-285.
41. Venturini AB, Prochnow C, Rambo D, Gundel A, Valandro LF. Effect of hydrofluoric acid concentration on resin adhesion to a feldspathic ceramic. J Adhes Dent 2015; 17:313- 20.
42. Wang X, Zhang Y, Ni L, You C, Ye C, Jiang R, Liu L, Liu J, Han C. A review of treatment strategies for hydrofluoric acid burns: current status and future prospects. Burns. 2014 Dec;40(8):1447-57.
43. Wille S, Lehmann F, Kern M. Durability of Resin Bonding to Lithium Disilicate and Zirconia Ceramic using a Self-etching Primer. J Adhes Dent. 2017;19(6):491-496.

## TABLES

**Table 1.** Description of materials, commercial name, manufacturer, composition and batch number.

| Material | Commercial name/manufacturer | Composition | Batch number |
|---|---|---|---|
| Lithium disilicate glass ceramic | IPS e.Max CAD, Ivoclar Vivadent, Amherst, USA | SiO2, Li2O, K2O, P2O5, ZrO2, ZnO, other and colouring oxides | W31404 |
| Silane coupling agent | Monobond Plus, Ivoclar Vivadent, Schaan, Liechtenstein | Alcohol solution of silane methacrylate, phosphoric acidmethacrylate and sulphide methacrylate | W10892 |
| 5% Hydrofluoric acid | IPS Ceramic Etching Gel, Ivoclar Vivadent, Schaan, Liechtenstein | < 5% hydrofluoric acid (HF) | W14921 |
| Self-etching ceramic primer | Monobond Etch & Prime, Ivoclar Vivadent, Schaan, Liechtenstein | Ammonium polyfluoride, silane system based on trimethoxypropyl methacrylate, alcohols, water and colorant | W06855 |
| Dual cure resin cement | Multilink Automix, Ivoclar Vivadent, Schaan, Liechtenstein | Silicate glass, ytterbium trifluoride, highly dispersed silica, catalysts and stabilizer, pigments | W07285 |

*The chemical composition is described according to the manufacturers' information.

**Table 2.** Mean and standard deviation from roughness analysis after polishing and in-lab simulation of CAD/CAM milling surface.

| Group | After polishing | | After in-lab simulation of CAD/CAM milling surface | |
|---|---|---|---|---|
| | Ra | Rz | Ra | Rz |
| HF5 + SIL | 0.15 (0.05)[a] | 1.21 (0.45)[a] | 1.46 (0.14)[a] | 9.50 (0.80)[a] |
| E&P 20s + 40s | 0.12 (0.04)[a] | 0.97 (0.23)[a] | 1.41 (0.11)[a] | 9.23 (0.56)[a] |
| E&P 20s + 2min | 0.12 (0.04)[a] | 1.05 (0.28)[a] | 1.46 (0.10)[a] | 9.48 (0.63)[a] |
| E&P 20s + 5min | 0.13 (0.04)[a] | 1.25 (0.31)[a] | 1.46 (0.10)[a] | 9.47 (0.66)[a] |
| E&P 20s + 10min | 0.14 (0.11)[a] | 1.01 (0.27)[a] | 1.41 (0.07)[a] | 9.23 (0.49)[a] |

*The same superscript letters indicate no significant differences (One-way ANOVA and Bonferroni's test; $\alpha$= 5%).

**The roughness parameters achieved by the in-Lab simulation were similar to the one generated by CAD/CAM machining (Mean, Standard Deviation: Ra= 1.84, 0.18; Rz= 11.07, 1.00).[12]

**Table 3.** Experimental design.

| Group codes | Surface treatment | Aging condition |
|---|---|---|
| HF5 + SIL | 5% HF etching for 20 s + silane application† | Short-term* |
| | | Long-term** |
| E&P 20s + 40s | 20 s of active application waiting 40 s for reaction† | Short-term |
| | | Long-term |
| E&P 20s + 2min | 20 s of active application waiting 2 min for reaction | Short-term |
| | | Long-term |
| E&P 20s + 5min | 20 s of active application waiting 5 min for reaction | Short-term |
| | | Long-term |
| E&P 20s + 10min | 20 s of active application waiting 10 min for reaction | Short-term |
| | | Long-term |

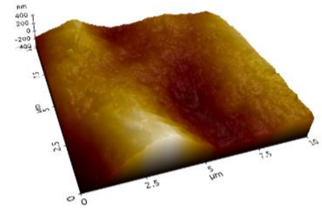
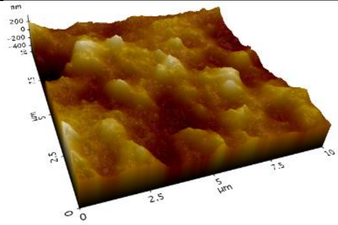
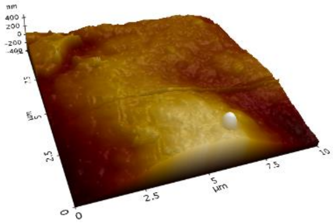
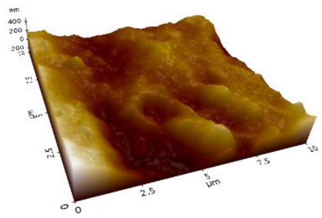
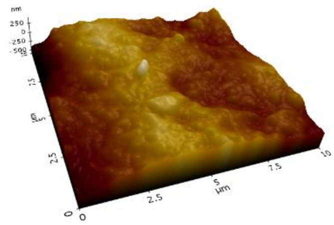
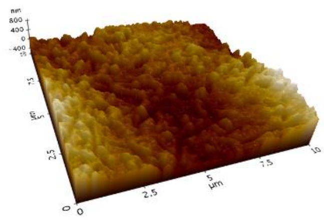
* 24 hours at 37ºC of storage in distilled water before testing;
** 180 days of storage in distilled water + thermocycling: 12,000 cycles between 5 and 55 ºC with a dwell time of 30 s and a transfer time of 5 s;
† recommended by the manufacturer.

**Table 4.** Microshear bond strength (mean and standard deviation) in MPa, total samples tested, total samples of pre-tested failures (PTF – pre-test failures, specimens detached during thermocycling or storage) and types of failure evaluated after the bond strength tests (predominantly adhesive failure; cohesive failure at the cement).

| Treatment | μSBS | | Samples tested before/after aging/PTF | Type of failure | | | |
|---|---|---|---|---|---|---|---|
| | | | | Adhesive | | Cohesive-cem | |
| | Short-term | Long-term | | Short-term | Long-term | Short-term | Long-term |
| HF5 + SIL | 23.18 (4.3)$^{Aa}$ | 17.05 (5.1)$^{Bb}$ | 35/35/0 | 35 (100%) | 35 (100%) | 0 (0%) | 0 (0%) |
| E&P 20s + 40s | 22.42 (5.5)$^{Aa}$ | 19.25 (4.7)$^{ABa}$ | 35/34/1 | 33 (94,3%) | 31 (91,2%) | 2 (5,7%) | 3 (8,8%) |
| E&P 20s + 2min | 24.22 (5.2)$^{Aa}$ | 19.04 (4.7)$^{ABb}$ | 35/35/0 | 35 (100%) | 32 (91,4%) | 0 (0%) | 3 (8,6%) |
| E&P 20s + 5min | 25.06 (4.3)$^{Aa}$ | 21.51 (4.9)$^{Aa}$ | 35/35/0 | 32 (91,4%) | 33 (94,3%) | 3 (8,6%) | 2 (5,7%) |
| E&P 20s + 10min | 24.49 (4.1)$^{Aa}$ | 18.87 (6.3)$^{ABb}$ | 35/34/1 | 33 (94,3%) | 33 (97,0%) | 2 (5,7%) | 1 (3,0%) |

* Capital letters in each column indicate statistical differences depicted by two-way ANOVA and Bonferroni post-hoc test; α= 5% (different surface treatments on same aging condition).
** Small letters in each line indicate statistical differences depicted by two-way ANOVA and Bonferroni post-hoc test; α= 5% (same surface treatment compared at baseline Vs aging conditions).

**Table 5.** Mean, standard deviation and representative topographic images from AFM analysis considering fractal dimension.

| Treatment | Fractal Dimension** | AFM topographic images |
|---|---|---|
| Without etching* | 2.13 (0.06) |  |
| HF5 + SIL | 2.18 (0.05) |  |
| E&P 20s + 40s | 2.11 (0.03) |  |
| E&P 20s+ 2min | 2.13 (0.02) |  |
| E&P 20s+ 5min | 2.11 (0.01) |  |
| E&P 20s+ 10min | 2.26 (0.06) |  |

* The specimen was only submitted to in-lab simulation with #60-grit silicon carbide paper.
**No statistical analysis was performed for this analysis, because an increase of 10% in the fractal dimension causes the surface stiffness to decrease by more than one order of magnitude in solid surfaces[6].

# FIGURES

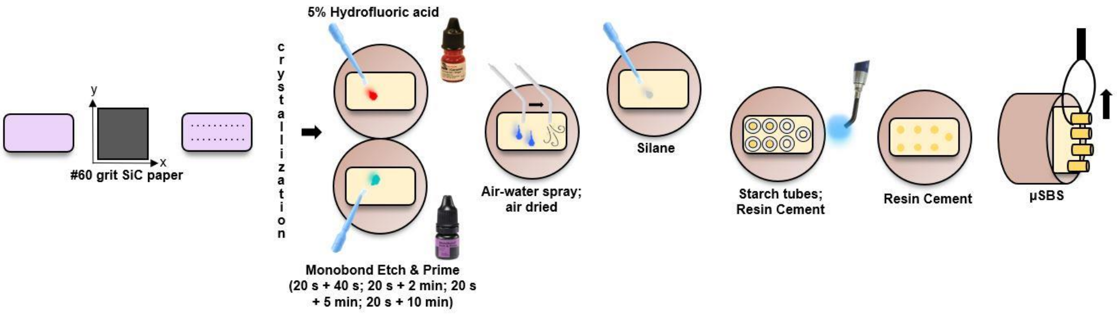



**Figure 1.** Schematic drawing representing the steps of the ceramic surface treatment.

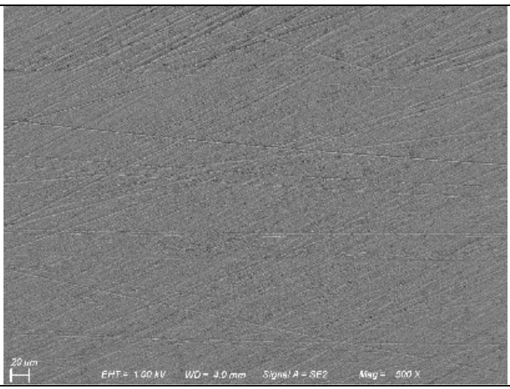
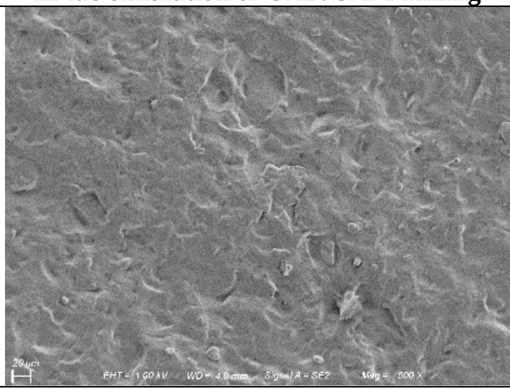
| Polished | In-lab simulation of CAD/CAM milling |
|---|---|
|  |  |

**Figure 2.** Micrographs (500× magnification) of the cross section of: lithium disilicate ceramic in crystallized stage depicting a smoother and homogeneous surface after polishing, and the same lithium disilicate surface with defects created after CAD/CAM milling simulation, which is more heterogeneous.

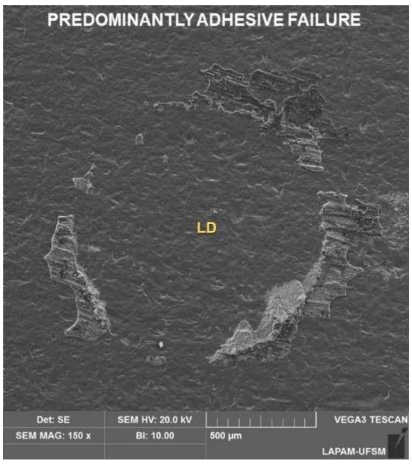
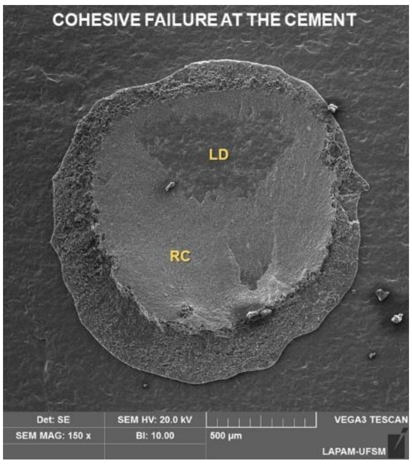
| | |
|---|---|
|  |  |
| LD: Lithium Disilicate ceramic;<br>RC: Resin Cement | |

**Figure 3.** Representative SEM images of microshear tested specimens under 150× magnification in defined failure patterns.

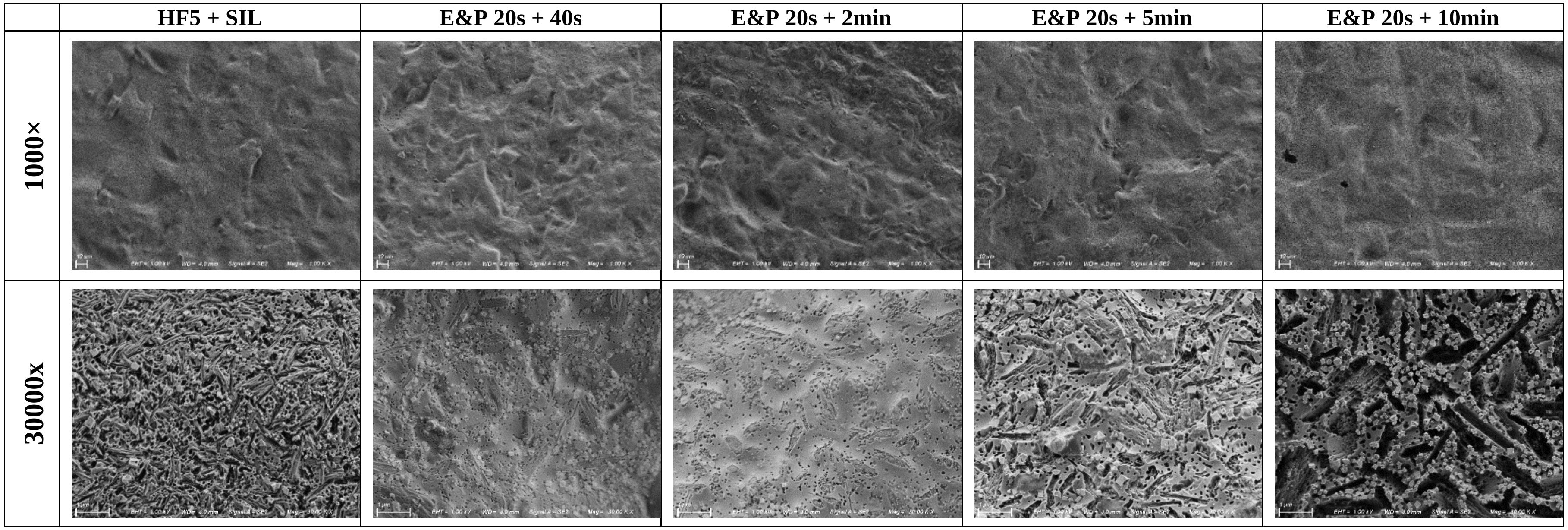



**Figure 4.** The micrographs represent the topographic characteristics after each surface treatment. The HF5 + SIL group had an irregular topographic pattern with deeper defects compared to the E&P 20s + 40s group, which had a shallower pattern. The increase in E&P passive application time (2 min; 5 min; 10 min) led to the dissolution of the slightly larger vitreous matrix with the increasing development of micro porosities, which promoted more intense topographic changes.

**3. ARTIGO 2:**

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# One-step ceramic primer as surface conditioner: effect on the load-bearing capacity under fatigue of bonded lithium disilicate ceramic simplified restorations

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**Running title**: Ceramic primer on the fatigue performance of lithium disilicate.

**Abstract**

The aim of the study was to evaluate the effect of a ceramic primer and its increased passive application on the fatigue performance of adhesively cemented lithium disilicate simplified restorations. Ceramic discs (Ø= 10mm; thickness= 1.0mm) were submitted to an in-lab simulation of CAD/CAM milling and allocated into 8 groups (n= 15), considering 2 factors: “surface treatment” – PRIMER, only coupling agent application (Monobond N); HF5+PRIMER, 5% hydrofluoric acid and coupling agent; E&P 20s+40s and E&P 20s+5min, ceramic etching/priming (Monobond Etch & Prime, E&P) for 20 s of active application followed by 40 s or 5 min of passive application, respectively; and “aging condition”– baseline, storage for 24 h to 5 days; aged, storage for 90 days + 12,000 thermal cycles. Adhesive cementation (Multilink N) was performed onto epoxy discs (Ø= 10mm; thickness= 2mm), and the cemented assemblies were subjected to step-stress fatigue tests (initial load of 200 N; step-size of 50 N; 10,000 cycles per step; 20 Hz). The results showed that the groups had similar fatigue performance in the baseline condition (except for E&P 20s+5min: 940.0 N; 123,000 cycles > PRIMER: 786.7 N; 92,333 cycles). When aged, the PRIMER group presented the worst fatigue performance (480.8 N; 31,154 cycles) compared to the other groups (810.0–840.0 N; 97,000–103,000 cycles). In addition, only the PRIMER treatment showed unstable fatigue performance (baseline > aged). Therefore, ceramic surface treatment promoting micromechanical interlocking and chemical bonds is mandatory for stable fatigue performance of adhesively cemented lithium disilicate restorations. The one-step ceramic primer/conditioner promoted similar fatigue performance to the 5% hydrofluoric acid + coupling agent, but increased E&P etching time did not improve the fatigue behavior.

**Keywords:** Computer Aided Design/Computer Aided Machining. Etching. Topographical changes. Mechanical phenomena. Survival Probability. Weibull Analysis.

**Highlights**

- Etching is required for proper mechanical behavior of lithium disilicate restorations.
- One-step ceramic primer is an alternative to hydrofluoric acid etching + coupling agent.
- Increased etching time of one-step ceramic primer does not improve fatigue behavior.

## 1. Introduction

Successful adhesion among ceramic, cement, and substrate requires a bonding mechanism which associates micro-mechanical interlocking and chemical bonding (Manso et al., 2011; Blatz et al., 2018). In this context, adhesive cementation with resin cement is the gold standard for providing reinforcement and retaining silica-based restorations (Peutzfeldt et al., 2011; Blatz et al., 2018; Johnson et al., 2018; Sousa et al., 2019). The strengthening effect of resin-based luting agents can occur due to the formation of a ceramic-resin hybrid layer resulting from the resin interpenetrating onto the etched ceramic surface (Fleming et al., 2006; Spazzin et al., 2016). Thus, the fracture resistance of ceramic restorations increases when the adhesion mechanism occurs (May et al., 2012), as it improves stress transmission through the bonded interface, consequently enhancing the clinical survival of these restorations (Malament and Socranski, 2001).

Resin bonding requires multiple pre-treatment steps on the intaglio surface of the restoration (Blatz et al., 2018) to achieve an intimate bond between the ceramic surface and the luting agent (Fleming et al., 2006). In contrast, hydrofluoric acid (HF) etching and silane coupling agent application is the classic surface treatment protocol for a glass ceramic (based on feldspathic, leucite enhanced and lithium disilicate) (Blatz et al., 2003; Blatz et al., 2018). HF promotes surface alterations (mechanical interlocking) for the micro-retention of resin cements and silane chemically acts in this set (Horn, 1983; Dimitriadi et al., 2018; Matinlinna et al., 2018). Although HF acid can effectively improve the bond strength between glass-ceramics and resin cement (Brentel et al., 2007), this acid can be toxic and may trigger acute and chronic symptoms in the human body (Kirkpatrick et al., 1995; Ozcan et al., 2012). Moreover, an over-etched ceramic surface can lead to deleterious effects on the flexural strength of lithium disilicate ceramics, mainly as a result of the increase in surface defect population (Zogheib et al., 2011; Xiaoping et al., 2014).

Nowadays, a one-step self-etching ceramic primer (E&P, Monobond Etch & Prime, Ivoclar Vivadent) has been proposed as an alternative to HF etching to treat glass ceramic surfaces. According to the manufacturer, this primer is less harmful and requires shorter clinical time due to less application steps compared to the conventional protocol (HF etching plus coupling agent). Still in this sense, the E&P promotes a physicochemical conditioning through a mild etchant (ammonium polyfloride) and a trimethoxypropyl metracrylate for silanization, resulting in a reduced number of defects on the ceramic surface due to the more superficial alterations than those produced by HF etching, which might favor better fatigue performance (Tribst et al., 2019). However, the few existing studies evaluating fatigue performance showed similar results comparing the etching with hydrofluoric acid plus coupling agent to the treatment with E&P (Schestatsky et al., 2019), or superior fatigue behavior of the hydrofluoric acid plus coupling agent (Scherer et al., 2018). It is important to clarify that the aforementioned studies evaluated the etching time of the E&P as recommended by the manufacturer (20 s of active application and 40 s of passive).

In addition to studies on HF etching time (Zogheib et al., 2011; Xiaoping et al., 2014; Puppin-Rontani et al., 2017; Wong et al., 2017), the application time of one-step self-etching ceramic primer may be changed in an attempt to improve and ensure the best mechanical performance (bond and mechanical improvements) of lithium disilicate restorations. This time variation affects the introduction of surface defects, which might have dichotomic consequences, such as: i) it might be positive when additional defects produced by a longer etching time are filled in with resin cement, inducting better stress distribution to the support material, and consequently reducing the probability for failure (May et al., 2012); ii) it will have negative effects when the number/size/shape of the defects make it difficult for the resin cement to penetrate the defects, thus impairing bonding, inducing slow crack growth mechanisms and poor mechanical performance (Anusavice and Hojjatie, 1992).

Taking into consideration the toxicity of hydrofluoric acid and the absence of studies evaluating the increased of E&P ceramic primer application time on the fatigue behavior of simplified lithium disilicate restorations, this study aimed to answer two main questions: i) Does the one-step ceramic primer promote similar or better fatigue behavior of the glass-ceramic restorations than the treatment with hydrofluoric acid etching plus coupling agent? ii) Does the longer conditioning time of the one-step ceramic primer improve the fatigue performance of the restorations?

Therefore, the present study aims to evaluate the effect of increased etching time of E&P one-step ceramic primer compared to the classical protocol (hydrofluoric acid plus coupling agent) on the short and long-term fatigue performance of lithium disilicate glass-ceramic restorations adhesively cemented onto a dentin analogue substrate. The assumed hypotheses are: (1) the increased etching time of E&P will promote similar fatigue behavior among the proposed conditionings; and (2) fatigue performance will be influenced by aging.

## 2. Material and Methods

### 2.1. Materials and study design

The general description of the materials used in the present study, their manufacturers, composition, and batch numbers are listed in Table 1.

This study was designed in 8 study groups, considering 2 factors (n= 15) (Table 2):

i. "Ceramic surface treatment" in 4 levels: PRIMER – only coupling agent application; HF5 + PRIMER – 5% hydrofluoric acid etching and coupling agent application; E&P 20s + 40s and E&P 20s + 5min – ceramic etching/priming (E&P, Monobond Etch & Prime) for 20 s of active application followed by 40 s or 5 min of passive application, respectively;

ii. "Aging condition" in 2 levels: baseline – tests after 24 h until 5 days from the cementation; or aged – water storage for 90 days + 12,000 thermal cycles levels before testing.

**2.2. Specimen assembly description and sample preparation**

The simplified test assembly employed in the present study has been widely used in the literature (Chen et al., 2014; Prochnow et al., 2018; Scherer et al., 2018). It consists of a simplified occlusal restoration for a posterior tooth represented by a lithium disilicate disc with a final diameter of 10 mm (average occlusal table of a first molar, Ferrario et al., 1999), which is adhesively cemented onto a glass fiber reinforced epoxy resin disc as a dentin analogue substrate with the same diameter of the ceramic disc.

**2.2.1. Preparation of dentin analogue discs**

The dentin substrate was represented by an epoxy resin disc (thickness= 2.0mm; Ø= 10mm). These discs were produced from epoxy resin plates (150 × 350 × 2.0 mm; Carbotec GmbH & Co. KG, Königs Wusterhausen, Germany), which were shaped into cylinders using a diamond drill (internal diameter= 10 mm; Diamant Boart, Brussels, Belgium) coupled to a bench drill (SBE 1010 Plus, Metabo; Nürtingen, Germany) under refrigeration. The discs were manually polished on both sides after cutting with grit silicon carbide papers (SiC, #400- and #1200-grit) and cleaned in an ultrasonic bath (distilled water; 5 min).

**2.2.2. Preparation of ceramic discs**

Lithium disilicate glass ceramic blocks for CAD/CAM (IPS e.max CAD, Ivoclar Vivadent, Schaan, Liechtenstein) were shaped into cylinders using a diamond drill (Ø = 10 mm; Diamant Boart; Brussels, Belgium) in a drilling machine (SBE 1010 Plus, Metabo; Nürtingen, Germany) under refrigeration. The cylinders were cut (Isomet 1000, Buehler, Lake Bluff, USA) under water cooling, resulting in 120 discs. They were polished with manual pressure in a polishing machine (EcoMet/AutoMet 250, Buehler) on both surfaces with #120-, #400, and #1200-grit SiC papers to achieve a thickness of 1.0 mm and standardize the surfaces.

**2.2.2.1. In-lab simulation of CAD/CAM milling roughness**

After polishing, the ceramic discs were subjected to an in-lab simulation of the CAD/CAM milling roughness, since machining process introduces defects and promotes a higher roughness in the cementation surface of the ceramic restorations (Fraga et al., 2017). A standardized size (100 mm × 50 mm) of #60 grit SiC paper was used for each slice. The ceramics discs were marked (axes x and y) with a marking pen and submitted to manual grinding with humidified SiC papers by a single trained operator (Rodrigues et al., 2018). The manual grinding was performed applying light digital pressure for 15 s on each axis (x and y). After the milling simulation, the ceramic slices were crystallized (Vacumat 6000 MP, VITA Zahnfabrik, Bad Sackingen, Germany) according to the manufacturer's instructions, and the roughness values of all cementation ceramic surfaces were measured to compare them to those generated by CAD/CAM machining (Fraga et al., 2017), as well as to certify that all groups received similar roughness prior to the surface treatments investigated herein. Next, six measurements were performed for each specimen (axes x and y) on a profilometer (Mitutoyo SJ-410, Mitutoyo Corporation, Kawasaki, Japan), and the average of each specimen was used for statistical analysis. The roughness parameters achieved by the in-lab simulation before ceramic surface treatment for Ra (µm) and Rz (µm) were respectively (mean ± standard deviation): PRIMER: 1.75 ± 0.40; 10.44 ± 1.17; HF5 + PRIMER: 1.67 ± 0.15; 10.65 ± 0.81; E&P 20s + 40s: 1.65 ± 0.16; 10.48 ± 0.83; E&P 20s + 5min: 1.60 ± 0.15; 10.19 ± 0.83. The roughness means were statistically similar (one-way ANOVA test, $\alpha$= 5%), being compatible to the one generated by CAD/CAM machining (Ra: 1.84 ± 0.18; Rz: 11.07 ± 1.00) obtained by Fraga et al. (2017). The specimens were subsequently cleaned in an ultrasonic bath (1440 D, Odontobras, Ind. and Com. Equip. Med. Odonto. LTDA, Ribeirão Preto, Brazil) with isopropyl alcohol for 5 min.

### 2.3. Ceramic surface treatments

After the in-lab simulation of CAD/CAM milling and crystallization, the intaglio ceramic surfaces received one of the following surface treatments (Table 2):

**PRIMER group:** an alcohol solution of silane methacrylate, phosphoric acid methacrylate and sulphide methacrylate coupling agent (Monobond N, Ivoclar Vivadent) was rubbed over the ceramic surface with a microbrush for 15 s and left to react for 45 s (for a total of 60 s), as recommended by the manufacturer.

**HF5 + PRIMER group:** 5% hydrofluoric acid (IPS Ceramic Etching Gel, Ivoclar Vivadent) was applied with a microbrush for 20 s, removed with air-water spray for 30 s and air dried for 30 s, and then the aforementioned coupling agent was applied as previously described for the PRIMER group.

**E&P groups:** a ceramic self-etching primer (E&P, Monobond Etch & Prime, Ivoclar Vivadent) was rubbed on the ceramic surface with a microbrush for 20 s actively and then left to react for 40 s (E&P 20s + 40s group, being the time recommended by the manufacturer), or 5 min (experimental time: E&P 20s + 5min group). It is emphasized that one drop had to be dispensed/reapplied at the time of 2:30 min in order to allow 5 min of passive exposure to the agent and to counteract its volatilization. The product was removed with air-water spray for 30 s and air dried for 30 s in all E&P groups.

All discs were subjected to an ultrasonic cleaning (distilled water for 5 min) after the ceramic surface treatments (i.e. before coupling agent application for PRIMER and HF + PRIMER groups, after etching in one-step for E&P group).

**2.4. Cementation procedure**

The cementation surface of dentin analogue discs was etched with 10% hydrofluoric acid (Condac Porcelana, FGM, Joinville, Brazil) for 1 min, followed by rinsing with air-water spray (30 s), air spray (30 s) and ultrasonic cleaning (5 min) with distilled water. Next, Multilink Primers A and B (Ivoclar Vivadent, Schaan, Liechtenstein), a dentinal primer recommended for dual-curing resin cement (Multilink N, Ivoclar Vivadent), were mixed in a 1:1 ratio, scrubbed onto the epoxy surface (30 s), and air-dried until a thin layer was obtained. The resin cement was manipulated according to the manufacturer’s instructions and applied onto the treated surfaces of the ceramic discs. Each ceramic disc was adhesively cemented to an epoxy disc under a constant load of 2.5 N for 10 min. The resin cement excesses were subsequently removed and the assemblies were light-cured (Radiical LED curing light, SDI, Bayswater, Australia) for five exposures of 20 s each (one in each direction of 5 positions: 0°, 90°, 180°, 270°, and on top).

**2.5. Aging conditions**

The cemented assemblies of each condition were randomly assigned into two following conditions, based on a previous study (Scherer et al., 2018): “**baseline**” – the samples were tested under fatigue after storage in distilled water at 37°C for approximately 24 h until 5 days, featuring a short-term situation; or “**aging condition**” – the samples were subjected to thermocycling (Nova Ética, São Paulo, Brazil) - 12,000 cycles (Andreatta Filho et al., 2005), 30 s baths at 5 and 55°C, transfer time of 5 s; and storage in distilled water at 37°C for 90 days before testing procedures, representing a long-term situation.

**2.6. Step-stress fatigue test**

The cemented assemblies (n= 15) were tested using the step-stress fatigue test approach according to previous studies (Dapieve et al., 2018; Schestatsky et al., 2019) in an electric machine (Instron ElectroPuls E3000, Instron, Norwood, USA). Cyclic loads were applied with a 40 mm diameter stainless-steel hemispheric piston (Kelly et al., 2010; Prochnow et al., 2018) under distilled water at a frequency of 20 Hz. An adhesive tape (110 µm) was placed on the occlusal surface of the restoration and a thin sheet of a non-rigid material (cellophane, 2.50 µm) was placed between the piston and the ceramic surface to reduce contact stress concentration (Kelly, 1999). An initial load of 200 N for 5000 cycles was performed to accommodate piston/specimen relation. Then, incremental steps of 50 N for 10,000 cycles starting from 400 N were applied until the failure (fracture or radial cracks) of the sample. The specimens were checked for cracks at the end of each step by light oblique transillumination (Dibner and Kelly, 2016). The evaluated outcome was radial crack or fracture, and therefore if this failure were found the sample was categorized as 'failed', and the fatigue test of this sample ended. The corresponding failure data (load and number of cycles to failure) of each sample were recorded for statistical analysis.

### 2.7. Fractographic analysis

All the specimens were inspected by stereomicroscope (Discovery V20, Carl Zeiss, Gottingen, Germany) after the fatigue test and representative samples (n= 1) were selected from each condition, in which the ceramic fragments were detached to access the origin of the defects. The fragments were then ultrasonically cleaned with 78% isopropyl alcohol (5 min), air-dried, gold-sputtered and analyzed under scanning electron microscopy (SEM - Vega3, Tescan, Czech Republic) at 200× and 1,000× magnifications to determine the crack origin characteristics.

### 2.8. Topographic analysis

Additional ceramic samples were produced to be inspected regarding the topographical changes, microstructure features and alterations after the surface treatments (n= 1), being that no coupling agent was applied for it, i.e., the surface in the PRIMER group was maintained as simulated CAD/CAM milling roughness. The samples for the analysis were cleaned in an ultrasonic bath with 78% isopropyl alcohol (5 min), air-dried and analyzed by Field Emission Scanning Electron Microscopy (FE-SEM, Sigma 300 VP, Carl Zeiss, Cambridge, England) at 500× and 20,000× magnifications. No alloy sputtering was necessary prior to FE-SEM analysis.

### 2.9. Cementation interface analysis

Additional sets of three layers (treated ceramic – resin cement – treated ceramic, n= 1) were produced based on previous studies (Spazzin et al., 2017; Coelho et al., 2019) for each surface treatment condition tested to inspect the morphology of the adhesive interfaces, the defects introduced by the treatments and the filling of these defects by resin cement. To do so, two ceramic discs of the same condition were adhesively cemented after performing the ceramic surface treatments, according to item 2.3. After storage (distilled water – 24 h), they were transversely sectioned in a cutting machine (Isomet 1000, Buehler). Then, the cross-sectional was mirror-polished (EcoMet/AutoMet 250, Buehler) using #600-, #1200-, and #2000-grit SiC papers, cleaned in an ultrasonic bath with 78% isopropyl alcohol (5 min) and air dried to be analyzed by Field Emission Scanning Electron Microscopy (FE-SEM, Sigma 300 VP, Carl Zeiss) at 10,000× magnification. No alloy sputtering was performed prior to FE-SEM analysis.

**2.10. Data analysis**

A statistical software program (IBM SPSS Software; IBM, Armonk, NY, USA) was used with a significance level of 0.05. Data distribution of fatigue failure load (FFL) in Newton and the number of cycles for failure (CFF) was accessed by the Shapiro-Wilk and Levene tests. Thus, a two-way ANOVA and post-hoc Tukey's test was executed to analyze the influence of the "surface treatment" and "aging" factors, as well as the interaction of both, and for comparing the surface treatments in the baseline and aging conditions. A survival analysis was also performed using the Kaplan Meier and Mantel-Cox (Log Rank) tests, and the survival probability was tabulated for each step of the test.

Additionally, FFL and CFF data were submitted to Weibull analysis using the Super SMITH Weibull 4.0k-32 software program (Wes Fulton, Torrance, United States) under the maximum likelihood method to obtain the Weibull modulus of each condition. The Weibull modulus is used as a measure for the distribution of the values, which is a way to statistically access the mechanical reliability of a condition/parameter.

Fractographic, topographic and cementation interface analyses were qualitatively analyzed.

**3. Results**

Two-way ANOVA and Tukey's post-hoc test of FFL and CFF data revealed significant influence of the "surface treatment" ($p = 0.000$, $F = 27.167$) and "aging" ($p = 0.000$, $F = 28.764$) factors, as well as the interaction of both "aging x surface treatment" ($p = 0.000$, $F = 8.770$). In comparing the groups at baseline conditions, the surface treatments had no statistically significant difference except for the E&P 20s + 5min group (940.0 N; 123,000 cycles) compared to the PRIMER group (786.7 N; 92,333 cycles). In comparing the aging groups, the PRIMER presented the worst fatigue performance, while the other treatments showed no difference. Only the PRIMER group degraded when analyzing the fatigue stability (baseline Vs aging for each surface treatment), highlighting a dramatic decrease: 38.9% for FFL and 63.3% for CFF (Table 3).

The Weibull analysis showed greater mechanical structural reliability (Weibull modulus) using E&P 20s + 5min in comparison to only PRIMER application after aging, while there was no statistically significant difference among the tested groups in the baseline condition (Table 4).

Furthermore, the survival analysis corroborates the aforementioned fatigue findings: the PRIMER groups samples failed earlier (lower survival rates), while the other surface treatments lasted longer until failure (higher survival rates) (Table 5).

The fractographic analysis showed that failures (fracture or radial crack) originated from the defects of the cement-ceramic interface (Fig. 1). Topographic images demonstrated the potential of surface treatments to promote surface alterations (glassy matrix removal and pull out of lithium disilicate crystals) at different intensities, where a higher number of defects were observed after the etching by the HF5 + PRIMER and E&P 20s + 5min groups (Fig. 2). In addition, FE-SEM revealed unfilled areas at the cementation interface with all the distinct topographic patterns introduced by the surface treatments. Also, the HF promoted deeper defects than the E&P treatments in the cementation interface analysis, in which shallower defects were observed with the increased exposure time to E&P (Fig. 3).

## 4. Discussion

The present study demonstrated that the fatigue behavior at baseline condition had no statistical difference, exception when comparing PRIMER and E&P 20s þ 5min groups. Differently, at aging condition, the PRIMER group had the worst behavior compared to other groups, which behaved similarly. Thus, the first hypothesis has to be rejected. When evaluating the fatigue stability (baseline Vs aging) for each treatment, it notes that only the FFL and CFF of the PRIMER group degraded after aging, while the fatigue performance of the other surface treatments kept unaltered after aging. Thus, the second hypothesis was accepted.

As already known, the longevity of dental ceramics mainly depends on the adhesion durability among the substrate and the load-bearing capacity under fatigue of the restoration/assembly, in particular when performing minimally invasive preparations, i.e., restorations depending on adhesion (laminates, inlays, onlays) (Morimoto et al., 2016). Chemical and physical surface treatments have been proposed altogether for adhesion improvements in glass-ceramics, i.e. treatments for surface alterations (micromechanical bond mechanism), such as acid etchant, and for chemical activation (bond promoters) to adhere ceramic and resinous materials via siloxane bonds (Manso et al., 2011). The present study agrees with this premise, as it showed that it was not possible to promote stable fatigue performance of restorations under intermittent cyclical loading and wet environment if only a chemical mechanism is applied (coupling agent application only – PRIMER group).

The dual bonding mechanisms to etched and silane primed glass-ceramic surfaces are important due to the contribution of each individual treatment (Dimitriadi et al., 2019). Acid etching promotes the surface alterations necessary to resin cement infiltration (micro-mechanical interlocking) and enhances chemical interactions among substrates (Horn, 1983; Dimitriadi et al., 2018; Matinlinna et al., 2018). Dental silane primers (including Monobond N) are composed by the ɣ-methacryloxypropyl trimethoxysilane silanols (MPTMS), solvents (acetone/water), acidic and phosphate monomers. When this silane is applied on a hydrated surface, the pH become acidic, and a low pH (e.g. pH values ≅ 2.5) may strongly accelerate hydrolysis by increasing silanol condensation (Heikkinen et al. 2013; Dimitriadi et al., 2018), which could impair the system's performance, which is corroborated by the present study (Table 3, Table 5 – accelerated degradation observed by PRIMER group). Thus, the silane component should be applied in an environment that is not strongly acidic (pH ≅ 4 - van Ooij, 2005; Dimitriadi et al., 2018), which will reduce silanol condensation and creates a thin branched hydrophobic surface layer that will decrease hydrolysis (Matinlinna and Vallittu, 2007; Moreno et al., 2019) and, consequently, optimize the long-term fatigue performance of the restorative system (Scherer et al., 2018; Tribst et al., 2019).

Meanwhile, E&P ceramic primer is composed by ammonium polyfluoride (mild etchant) and a trimethoxypropyl metacrylate component (silane). Thus, the mechanism of action of this system is based on topographical changes (triggered by the first component) followed by intensive water rinsing, which should eliminate all polyfluoride reminiscent and set off the reaction between the silane component. Then, the silane component will be reduced to a thin layer of chemically reactive surface responsible for the stability of adhesion (Moreno et al., 2019) and fatigue performance corroborated in the herein presented data.

Although there are surface topographic changes produced by the In-lab simulation of CAD/CAM milling roughness in the present study, only the coupling agent was not able to promote long-term fatigue performance without a previous etching step (such as HF or E&P etching for silica-based ceramics). This assumption is corroborated by the smallest Weibull modulus and the high percentage of decrease in fatigue failure load (38.9%) and cycles for failure (66.3%) when comparing PRIMER group at the baseline and aging conditions (Table 3, Table 4, Table 5). The main reasons for this worse fatigue behavior include adhesion involving the high instability and hydrolytic degradation of bonds in the interfacial layer, which depends on the coupling agent molecular structure, concentration, pH, temperature and humidity, among others (Lung and Matinlinna, 2012; Matinlinna et al., 2018). Thus, it has to be highlighted that the topographical changes promoted by hydrofluoric acid etching (group HF5 + PRIMER) or the one-step ceramic conditioner primer (E&P 20s + 40s or E&P 20s + 5min) of the intaglio surface are key for bond improvements, in addition to chemical bonds, as the bond strength is dependent on the quantity and quality of defects introduced through surface conditioning (Fleming et al., 2006).

Representative images of FE-SEM (Fig. 2, Fig. 3) demonstrated smoother topographic changes when using the one-step conditioner primer following the manufacturer's instructions (E&P 20s + 40s) compared to classical hydrofluoric acid conditioning, according to previous literature

(Scherer et al., 2018; Moreno et al., 2019). On the other hand, it is possible to observe substantial changes in this topography by increasing the time of E&P application, since a larger amount of lithium disilicate crystals was exposed (Fig. 2). In this sense, the E&P 20s + 5min group seems to present shallower defects when observing the cementation interface analysis (Fig. 3) due to the more homogeneous aspect of the interface, but these characteristics did not deleteriously impact the evaluated mechanical properties (Table 3, Table 4, Table 5).

Moreover, it is important to state that the interfacial relationship (ceramic-cement) is crucial for the restoration performance, since it is the region with the highest concentration of tensile stresses (May et al., 2012); this is also observed by the fractography analysis (Fig. 1), which shows that all cracks started from defects in the cementation surface. Therefore, the defects produced by surface treatments play a strong role in inducing cracking, unless these defects are filled/healed by resin cement, promoting a strengthening effect by the ceramic (Fleming et al., 2006; Spazzin et al., 2017). Furthermore, it is important that the intimate contact between the ceramic and the cementing agent occurs, which should form a continuous and homogeneous interface, once the presence of unfilled porosity or irregularities can concentrate stresses and reduce the overall stress/load-bearing capacity (Spazzin et al., 2017; Bacchi et al., 2018). In this sense, it can be observed that all evaluated conditions presented bubbles and defects, which were not filled in by resin cement in the cementation interface analysis performed in the present study (Fig. 3). Thus, resin-based systems presenting different filling potentials from the one used in the present study could change the performance observed herein.

While some authors corroborate the similar or even better mechanical performance of E&P when compared to HF etching plus coupling agent (Schestatsky et al., 2019; Tribst et al., 2019), Scherer and collaborators (2018) reported superiority by the classical protocol. Even though it is a very similar methodology, this difference can be explained by the in-lab simulation of CAD/CAM milling surface roughness which occurred in the present study. The topographic changes generated by this in-lab simulation are observed in the roughness parameters identified in the methodology session and in the PRIMER group micrographs (Fig. 2, Fig. 3). Therefore, while in-lab simulation is not sufficient to create a suitable micromechanical interlocking, it can influence the surface topographic pattern generated by conditioning.

Finally, we have to state that our study has some limitations, such as using an in-lab simulation of CAD/CAM milling roughness instead of real CAD/CAM milled restorations and the fatigue evaluation of simplified restorations. Nevertheless, our findings contribute to clarifying an important clinical issue: the chemical and mechanical bonds (as promoted by hydrofluoric acid + coupling agent or one-step ceramic conditioner primer tested by us) are a must for fatigue improvements of glass ceramic lithium disilicate restorations apart from the topography changes promoted by machining.

**5. Conclusion**

- The chemical and mechanical bonds promoted by etching/priming treatments are necessary to promote higher fatigue performance of adhesively cemented lithium disilicate glass-ceramic restorations.
- The one-step ceramic etching/priming agent demonstrated to be a suitable and promising surface treatment of the evaluated glass-ceramic in terms of its fatigue performance tested herein.
- The increased etching time of the one-step ceramic etching/priming agent did not improve the fatigue performance of glass-ceramic restorations, being a protocol not feasible.

**CRediT authorship contribution statement**

**Kiara Serafini Dapieve:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualization, Writing - original draft, Writing - review & editing.

**Renan Vaz Machry:** Data curation, Writing - review & editing.

**Rafaela Oliveira Pilecco:** Data curation, Writing - review & editing.

**Cornelis Johannes Kleverlaan:** Conceptualization, Supervision, Writing - review & editing.

**Gabriel Kalil Rocha Pereira:** Conceptualization, Formal analysis, Investigation, Methodology, Visualization, Writing - review & editing.

**Andressa Borin Venturini:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing - review & editing.

**Luiz Felipe Valandro:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources Software, Supervision, Validation, Visualization, Writing - review & editing.

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**REFERENCES**

1. Andreatta Filho OD, Araújo MA, Bottino MA, Nishioka RS, Menezes MM. Study of thermocycling effect on the bond strength between an aluminous ceramic and a resin cement. J Appl Oral Sci. 2005 Mar;13(1):53-7.

2. Anusavice KJ, Hojjatie B. Tensile stress in glass-ceramic crowns: effect of flaws and cementation voids. Int J Prosthodont. 1992 Jul-Aug;5(4):351-8.

3. Bacchi A, Spazzin AO, de Oliveira GR, Pfeifer C, Cesar PF. Resin cements formulated with thio-urethanes can strengthen porcelain and increase bond strength to ceramics. J Dent. 2018 Jun; 73:50-56. doi: 10.1016/j.jdent.2018.04.002.

4. Blatz MB, Sadan A, Kern M. Resin-ceramic bonding: a review of the literature. J Prosthet Dent. 2003 Mar;89(3):26874.

5. Blatz MB, Vonderheide M, Conejo J. The Effect of Resin Bonding on Long-Term Success of High-Strength Ceramics. J Dent Res. 2018 Feb;97(2):132-139. doi: 10.1177/0022034517729134.

6. Brentel AS, Özcan M, Valandro LF, Alarça LG, Amaral R, Bottino MA. Microtensile bond strength of a resin cement to feldpathic ceramic after different etching and silanization regimens in dry and aged conditions. Dent Mater. 2007;23(11):1323-31.

7. Chen C, Trindade FZ, de Jager N, Kleverlaan CJ, Feilzer AJ. The fracture resistance of a CAD/CAM Resin Nano Ceramic (RNC) and a CAD ceramic at different thicknesses. Dent Mater. 2014 Sep;30(9):954-62. doi: 10.1016/j.dental.2014.05.018.

8. Coelho NF, Barbon FJ, Machado RG, Boscato N, Moraes RR. Response of composite resins to preheating and the resulting strengthening of luted feldspar ceramic. Dent Mater. 2019 Oct;35(10):1430-1438. doi: 10.1016/j.dental.2019.07.021.

9. Dapieve KS, Guilardi LSF, Silvestri T, Rippe MP, Pereira GKR, Valandro LF. Mechanical performance of Y-TZP monolithic ceramic after grinding and aging: survival estimates and fatigue strength. J Mech Behav Biomed Mater. 2018 Nov; 87:288-295. doi: 10.1016/j.jmbbm.2018.07.041.14.

10. Dibner AC, Kelly JR. Fatigue strength of bilayered ceramics under cyclic loading as a function of core veneer thickness ratios. J Prosthet Dent. 2016 Mar;115(3):335-40. doi: 10.1016/j.prosdent.2015.09.017.

11. Dimitriadi M, Panagiotopoulou A, Pelecanou M, Yannakopoulou K, Eliades G. Stability and reactivity of γ-MPTMS silane in some commercial primer and adhesive formulations. Dent Mater. 2018 Aug;34(8):1089-1101. doi: 10.1016/j.dental.2018.05.006.

12. Dimitriadi M, Zafiropoulou M, Zinelis S, Silikas N, Eliades G. Silane reactivity and resin bond strength to lithium disilicate ceramic surfaces. Dent Mater. 2019 Aug;35(8):1082-1094. doi: 10.1016/j.dental.2019.05.002.

13. Ferrario VF, Sforza C, Tartaglia GM, Colombo A, Serrao G. Size and shape of the human first permanent molar: a Fourier analysis of the occlusal and equatorial outlines. Am J Phys Anthropol. 1999 Mar;108(3):281-94.

14. Fleming GJ, Maguire FR, Bhamra G, Burke FM, Marquis PM. The strengthening mechanism of resin cements on porcelain surfaces. J Dent Res. 2006 Mar;85(3):272-6.

15. Fraga S, Amaral M, Bottino MA, Valandro LF, Kleverlaan CJ, May LG. Impact of machining on the flexural fatigue strength of glass and polycrystalline CAD/CAM ceramics. Dent Mater. 2017 Nov;33(11):1286-1297. doi: 10.1016/j.dental.2017.07.019.

16. Heikkinen TT, Matinlinna JP, Vallittu PK, Lassila LV. Long term water storage deteriorates bonding of composite resin to alumina and zirconia short communication. Open Dent J. 2013 Sep 30; 7:123-5. doi: 10.2174/1874210601307010123.

17. Horn HR. Porcelain laminate veneers bonded to etched enamel In:__. Phillips RW editor. Symposium on Dental Material. Dental Clinics of North America, 1983. v.27, p.671-684.

18. Johnson GH, Lepe X, Patterson A, Schäfer O. Simplified cementation of lithium disilicate crowns: Retention with various adhesive resin cement combinations. J Prosthet Dent. 2018 May;119(5):826-832. doi: 10.1016/j.prosdent.2017.07.012.

19. Kelly JR, Rungruanganunt P, Hunter B, Vailati F. Development of a clinically validated bulk failure test for ceramic crowns. J Prosthet Dent. 2010 Oct;104(4):228-38. doi: 10.1016/S0022-3913(10)60129-1.

20. Kelly JR. Clinically relevant approach to failure testing of all-ceramic restorations. J Prosthet Dent. 1999 Jun;81(6):652-61.

21. Kirkpatrick JJ, Enion DS, Burd DA. Hydrofluoric acid burns: a review. Burns. 1995 Nov;21(7):483-93.

22. Lung CY, Matinlinna JP. Aspects of silane coupling agents and surface conditioning in dentistry: an overview. Dent Mater. 2012 May;28(5):467-77. doi: 10.1016/j.dental.2012.02.009.

23. Malament KA, Socranski SS. Survival of Dicor glass-ceramic dental restorations over 16 years. Part III. effect of luting agent and tooth or tooth-substitute core structure. Journal of Prosthetic Dentistry 2001; 86:511–9.

24. Manso AP, Silva NR, Bonfante EA, Pegoraro TA, Dias RA, Carvalho RM. Cements and adhesives for all-ceramic restorations. Dent Clin North Am. 2011 Apr;55(2):311-32. doi: 10.1016/j.cden.2011.01.011.
25. Matinlinna JP, Vallittu PK. Bonding of resin composites to etchable ceramic surfaces – an insight review of the chemical aspects on surface conditioning. J Oral Rehabil. 2007;34:622-30. doi:10.1111/j.1365-2842.2005.01569.x.
26. Matinlinna JP, Lung CYK, Tsoi JKH. Silane adhesion mechanism in dental applications and surface treatments: A review. Dent Mater. 2018 Jan;34(1):13-28. doi: 10.1016/j.dental.2017.09.002.
27. May LG, Kelly JR, Bottino MA, Hill T. Effects of cement thickness and bonding on the failure loads of CAD/CAM ceramic crowns: multi-physics FEA modeling and monotonic testing. Dent Mater. 2012 Aug;28(8):e99-109. doi: 10.1016/j.dental.2012.04.033.
28. Moreno MBP, Murillo-Gómez F, de Goes MF. Physicochemical and morphological characterization of a glass ceramic treated with different ceramic primers and post-silanization protocols. Dent Mater. 2019 Aug;35(8):1073-1081. doi: 10.1016/j.dental.2019.05.003.
29. Morimoto S, Rebello de Sampaio FB, Braga MM, Sesma N, Özcan M. Survival Rate of Resin and Ceramic Inlays, Onlays, and Overlays: A Systematic Review and Meta-analysis. J Dent Res. 2016 Aug;95(9):985-94. doi: 10.1177/0022034516652848.
30. Ozcan, M, Allahbeickaraghi, A, Dundar, M. Possible hazardous effects of hydrofluoric acid and recommendations for treatment approach: a review. Clin Oral Investig. 2012 Feb;16(1):15-23. doi: 10.1007/s00784-011-0636-6.
31. Peutzfeldt A, Sahafi A, Flury S. Bonding of restorative materials to dentin with various luting agents. Oper Dent. 2011 May-Jun;36(3):266-73. doi: 10.2341/10-236-L.
32. Prochnow C, Pereira GKR, Venturini AB, Scherer MM, Rippe MP, Bottino MC, Kleverlaan CJ, Valandro LF. How does hydrofluoric acid etching affect the cyclic load-to-failure of lithium disilicate restorations? J Mech Behav Biomed Mater. 2018 Nov; 87:306-311. doi: 10.1016/j.jmbbm.2018.07.040.
33. Puppin-Rontani J, Sundfeld D, Costa AR, Correr AB, Puppin-Rontani RM, Borges GA, Sinhoreti M, Correr-Sobrinho L. Effect of Hydrofluoric Acid Concentration and Etching Time on Bond Strength to Lithium Disilicate Glass Ceramic. Oper Dent. 2017 Nov/Dec;42(6):606-615. doi: 10.2341/16-215-L.
34. Rodrigues CDS, Guilardi LF, Follak AC, Prochnow C, May LG, Valandro LF. Internal adjustments decrease the fatigue failure load of bonded simplified lithium disilicate restorations. Dent Mater. 2018 Sep;34(9): e225-e235. doi: 10.1016/j.dental.2018.05.015.
35. Scherer MM, Prochnow C, Venturini AB, Pereira GKR, Burgo TAL, Rippe MP, Valandro LF. Fatigue failure load of an adhesively-cemented lithium disilicate glass-ceramic: Conventional ceramic etching vs etch & prime one-step primer. Dent Mater. 2018 Aug;34(8):1134-1143. doi: 10.1016/j.dental.2018.04.012.15
36. Schestatsky R, Zucuni CP, Venturini AB, de Lima Burgo TA, Bacchi A, Valandro LF, Rocha Pereira GK. CAD-CAM milled versus pressed lithium-disilicate monolithic crowns adhesively cemented after distinct surface treatments: Fatigue performance and ceramic surface characteristics. J Mech Behav Biomed Mater. 2019 Jun; 94:144-154. doi: 10.1016/j.jmbbm.2019.03.005.
37. Sousa SJL, Poubel DLDN, Rezende LVML, Almeida FT, de Toledo IP, Garcia FCP. Early clinical performance of resin cements in glass-ceramic posterior restorations in adult vital teeth: A systematic review and meta-analysis. J Prosthet Dent. 2019 Apr 11. pii: S0022-3913(18)31176-4. doi: 10.1016/j.prosdent.2018.12.006.
38. Spazzin AO, Bacchi A, Alessandretti R, Santos MB, Basso GR, Griggs J, Moraes RR. Ceramic strengthening by tuning the elastic moduli of resin-based luting agents. Dent Mater. 2017 Mar;33(3):358-366. doi:10.1016/j.dental.2017.01.002.
39. Spazzin AO, Guarda GB, Oliveira-Ogliari A, Leal FB, Correr-Sobrinho L, Moraes RR. Strengthening of Porcelain Provided by Resin Cements and Flowable Composites. Oper Dent. 2016 Mar-Apr;41(2):179-88. doi: 10.2341/15-025-L.
40. Tribst JPM, Monteiro JB, Venturini AB, Pereira GKR, Bottino MA, Melo RM, Valandro LF. Fatigue Failure Load of Resin-bonded Simplified Lithium Disilicate Glass-Ceramic Restorations: Effect of Ceramic Conditioning Methods. J Adhes Dent. 2019;21(4):373-381. doi: 10.3290/j.jad.a43000.
41. van Ooij WJ. Silanes and metal pretreatments. In: Packman ED, editor. Handbook of adhesion. 2nd ed. Chichester, UK: John Wiley & Sons; 2005. p. 463–6.
42. Wong ACH, Tian T, Tsoi JKH, Burrow MF, Matinlinna JP. Aspects of adhesion tests on resin-glass ceramic bonding. Dent Mater. 2017 Sep;33(9):1045-1055. doi: 10.1016/j.dental.2017.06.013.
43. Xiaoping L, Dongfeng R, Silikas N. Effect of etching time and resin bond on the flexural strength of IPS e.max Press glass ceramic. Dent Mater. 2014 Dec;30(12):e330-6. doi: 10.1016/j.dental.2014.08.373.
44. Zogheib LV, Bona AD, Kimpara ET, McCabe JF. Effect of hydrofluoric acid etching duration on the roughness and flexural strength of a lithium disilicate-based glass ceramic. Braz Dent J. 2011;22(1):45-50.

# TABLES

**Table 1.** Description of materials, commercial name, manufacturer, composition and batch number.

| Material | Commercial name/manufacturer | Composition | Batch number |
|---|---|---|---|
| Lithium disilicate glass ceramic | IPS e.Max CAD, Ivoclar Vivadent, Schaan, Liechtenstein | $SiO_2$, $Li_2O$, $K_2O$, $P_2O_5$, $ZrO_2$, ZnO, other and colouring oxides | W93126 |
| Ceramic primer coupling agent | Monobond Plus, Ivoclar Vivadent | Alcohol solution of silane methacrylate, phosphoric acid methacrylate and sulphide methacrylate | W90329 |
| 5% hydrofluoric acid | IPS Ceramic Etching Gel, Ivoclar Vivadent | < 5% hydrofluoric acid | W14921 |
| 10% hydrofluoric acid | Condac Porcelana, FGM, Joinville, Brazil | < 10% hydrofluoric acid | W140319 |
| Self-etching ceramic primer | Monobond Etch & Prime, Ivoclar Vivadent | Ammonium polyfluoride, silane system based on trimethoxypropyl methacrylate, alcohols, water and colorant | W40212 |
| Dual cure resin cement | Multilink N, Ivoclar Vivadent | Silicate glass, ytterbium trifluoride, highly dispersed silica, catalysts and stabiliser, pigments | W44613 |
| Primer | Multilink Primer (A and B), Ivoclar Vivadent | Primer A: water, initiators; primer B: phosphonic acid acrylate, hydroxyethyl methacrylate, methacrylate mod. polyacrylic acid, stabilizer | Primer A: W89775 Primer B: W92311 |
| Epoxy resin | Carbotec GmbH & Co. KG, Königs Wusterhausen, Germany | Continuous filament woven fiberglass bonded with epoxy resin | - |

*The chemical composition is described according to the manufacturers' information.

**Table 2.** Experimental design.

| Group | Surface treatment | Aging condition |
|---|---|---|
| PRIMER | Coupling agent application | Baseline* Aging** |
| HF5 + PRIMER | 5% HF acid etching for 20 seconds + coupling agent application | Baseline Aging |
| E&P 20s + 40s | 20 seconds of active application and 40 seconds of react*** | Baseline Aging |
| E&P 20s + 5min | 20 seconds of active application and 5 minutes of react | Baseline Aging |

* 1 up to 5 days of water distilled storage (37 ◦C) before testing;
**90 days of storage in distilled water + thermocycling: 12,000 cycles between 5 and 55 ºC with a dwell time of 30 s and a transfer time of 5 s;
***recommended by the manufacturer.

**Table 3.** Mean fatigue failure load (FFL) in Newton, number of cycles for failure (CFF) with respective standard deviation (SD) and the percentage of decrease comparing the baseline condition to aging in both outcomes.

| Groups | FFL | | | CFF | | |
|---|---|---|---|---|---|---|
| | Baseline | Aging | | Baseline | Aging | |
| | Mean (SD) | Mean (SD) | % of mean FFL decrease (Baseline / aging) | Mean (SD) | Mean (SD) | % of mean CFF decrease (baseline / aging) |
| **PRIMER** | 786.67 (213.36) $^{B}$ | 480.77 (90.23) $^{C}$ | 38.9% | 92,333 (42,673) $^{B}$ | 31,154 (18,046) $^{C}$ | 66.3% |
| **HF5 + PRIMER** | 830.00 (127.90) $^{AB}$ | 810.00 (82.81) $^{AB}$ | 2.4% | 101,000 (25,579) $^{AB}$ | 97,000 (16,562) $^{AB}$ | 4% |
| **E&P 20s + 40s** | 880.00 (106.57) $^{AB}$ | 840.00 (96.73) $^{AB}$ | 4.5% | 111,000 (21,314) $^{AB}$ | 103,000 (19,346) $^{AB}$ | 7.2% |
| **E&P 20s + 5min** | 940.00 (98.56) $^{A}$ | 840.00 (54.12) $^{AB}$ | 10.6% | 123,000 (19,712) $^{A}$ | 103,000 (10,823) $^{AB}$ | 16.3% |

* Different uppercase letters indicate statistical differences based on Two-Way ANOVA and Tukey's post-hoc test.

**Table 4.** Weibull modulus for fatigue failure load (FFL) and cycles for failure (CFF).

| Groups | FFL | | CFF | |
|---|---|---|---|---|
| | Baseline | Aging | Baseline | Aging |
| | Weibull modulus (CI) | Weibull modulus (CI) | Weibull modulus (CI) | Weibull modulus (CI) |
| **PRIMER** | 4.67 (2.93 – 6.93) $^{A}$ | 5.30 (3.43 – 7.48) $^{B}$ | 2.40 (1.49 – 3.60) $^{B}$ | 1.94 (1.24 – 2.79) $^{B}$ |
| **HF5 + PRIMER** | 7.91 (5.08 – 11.43) $^{A}$ | 9.87 (6.57 – 13.69) $^{AB}$ | 4.78 (3.05 – 6.94) $^{AB}$ | 6.12 (4.06 – 8.52) $^{A}$ |
| **E&P 20s + 40s** | 8.74 (5.78 – 12.22) $^{A}$ | 10.51 (6.75 – 15.18) $^{AB}$ | 5.66 (3.73 – 7.95) $^{A}$ | 6.47 (4.14 – 9.40) $^{A}$ |
| **E&P 20s + 5min** | 10.45 (6.93 – 14.47) $^{A}$ | 16.24 (10.71 – 22.80) $^{A}$ | 6.99 (4.61 – 9.73) $^{A}$ | 10.14 (6.67 – 14.26) $^{A}$ |

* Different uppercase letters indicate statistical differences based on maximum-likelihood estimations for Weibull analysis.

**Table 5.** Survival rates – probability of specimens to exceed the respective fatigue failure load (FFL) and number of cycles for failure (CFF) step without crack propagation, and its respective standard error values.

| Surface treatment | Aging condition | FFL (N) / CFF | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **200 / 5,000** | **400 / 15,000** | **450 / 25,000** | **500 / 35,000** | **550 / 45,000** | **600 / 55,000** | **650 / 65,000** | **700 / 75,000** | **750 / 85,000** | **800 / 95,000** | **850 / 105,000** | **900 / 115,000** | **950 / 125,000** | **1000 / 135,000** | **1050 / 145,000** | **1100 / 155,000** | **1150 / 165,000** |
| **PRIMER** | **Baseline** | 1 | 0.93 (0.06) | 0.87 (0.09) | 0.87 (0.09) | 0.80 (0.10) | 0.73 (0.11) | 0.67 (0.12) | 0.67 (0.12) | 0.53 (0.13) | 0.53 (0.13) | 0.47 (0.13) | 0.40 (0.13) | 0.13 (0.09) | 0.13 (0.09) | 0.0 | - | - |
| | **Aging** | 1 | 0.69 (0.13) | 0.39 (0.14) | 0.23 (0.12) | 0.15 (0.10) | 0.08 (0.07) | 0.08 (0.07) | 0.0 | - | - | - | - | - | - | - | - | - |
| **HF5 + PRIMER** | **Baseline** | 1 | 1 | 1 | 1 | 0.93 (0.06) | 0.93 (0.06) | 0.93 (0.06) | 0.80 (0.10) | 0.73 (0.11) | 0.47 (0.13) | 0.33 (0.12) | 0.27 (0.11) | 0.20 (0.10) | 0.0 | - | - | - |
| | **Aging** | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0.87 (0.09) | 0.60 (0.13) | 0.40 (0.13) | 0.20 (0.10) | 0.07 (0.06) | 0.07 (0.06) | 0.0 | - | - | - |
| **E&P 20s + 40s** | **Baseline** | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0.93 (0.06) | 0.80 (0.10) | 0.80 (0.10) | 0.47 (0.13) | 0.27 (0.11) | 0.13 (0.08) | 0.13 (0.08) | 0.07 (0.06) | 0.0 | - |
| | **Aging** | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0.87 (0.09) | 0.60 (0.13) | 0.60 (0.13) | 0.53 (0.13) | 0.13 (0.09) | 0.07 (0.06) | 0.0 | - | - | - |
| **E&P 20s + 5min** | **Baseline** | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0.93 (0.06) | 0.93 (0.06) | 0.93 (0.06) | 0.87 (0.08) | 0.60 (0.13) | 0.27 (0.11) | 0.13 (0.09) | 0.07 (0.06) | 0.07 (0.06) | 0.0 |
| | **Aging** | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 0.93 (0.06) | 0.53 (0.13) | 0.27 (0.11) | 0.07 (0.06) | 0.0 | - | - | - | - |

* Kaplan Meier and Mantel-Cox tests.
** The symbol '-' indicates absence of specimens being submitted to the respective category.

# FIGURES

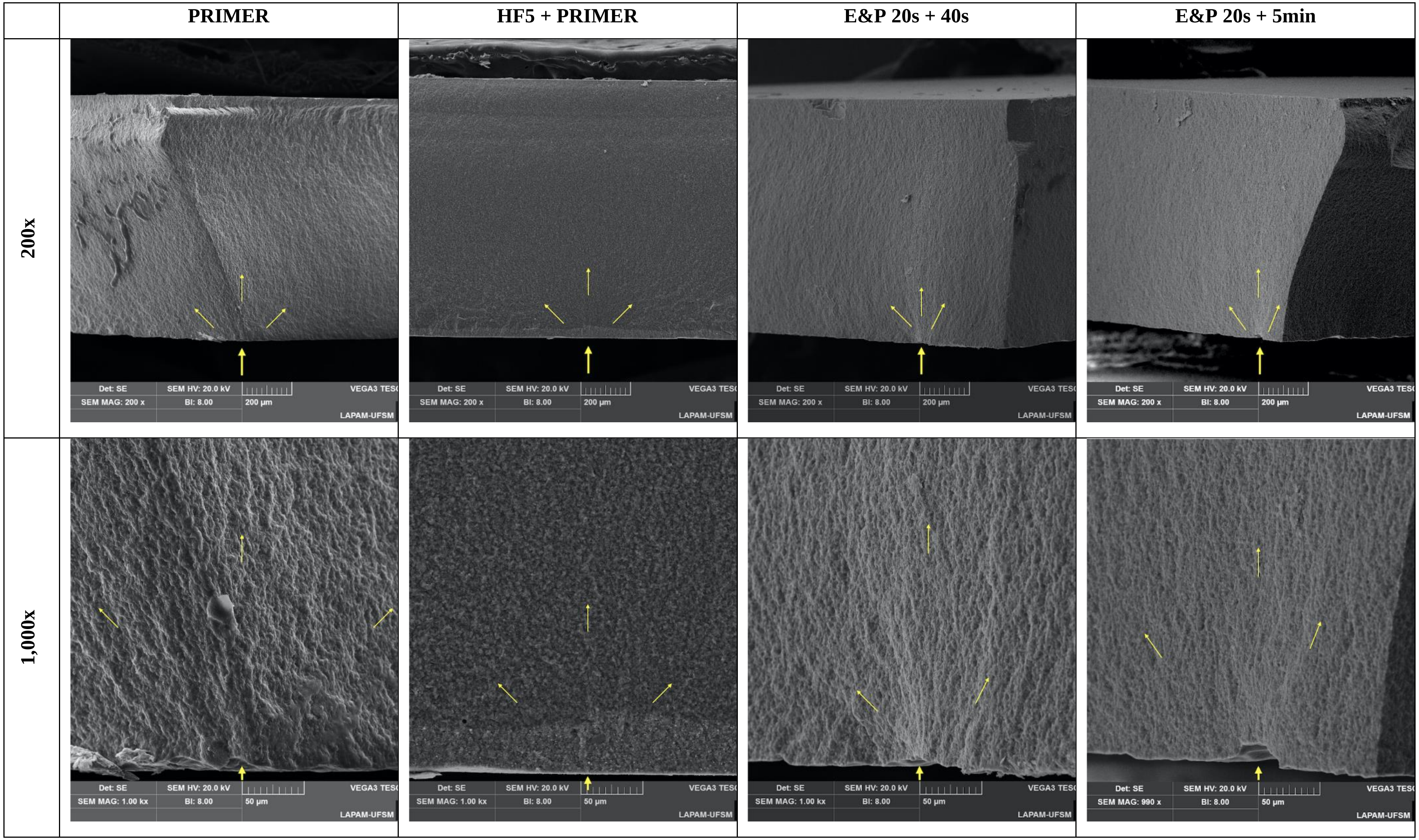


**Figure 1.** Micrographs (200× – top; 1,000× – bottom) obtained by SEM illustrating that all failures originated at cementation surface from defects present at the ceramic surface, pointed by yellow arrows, and then propagated to the opposite side (oclusal/top surface), where it notices the compression curl.

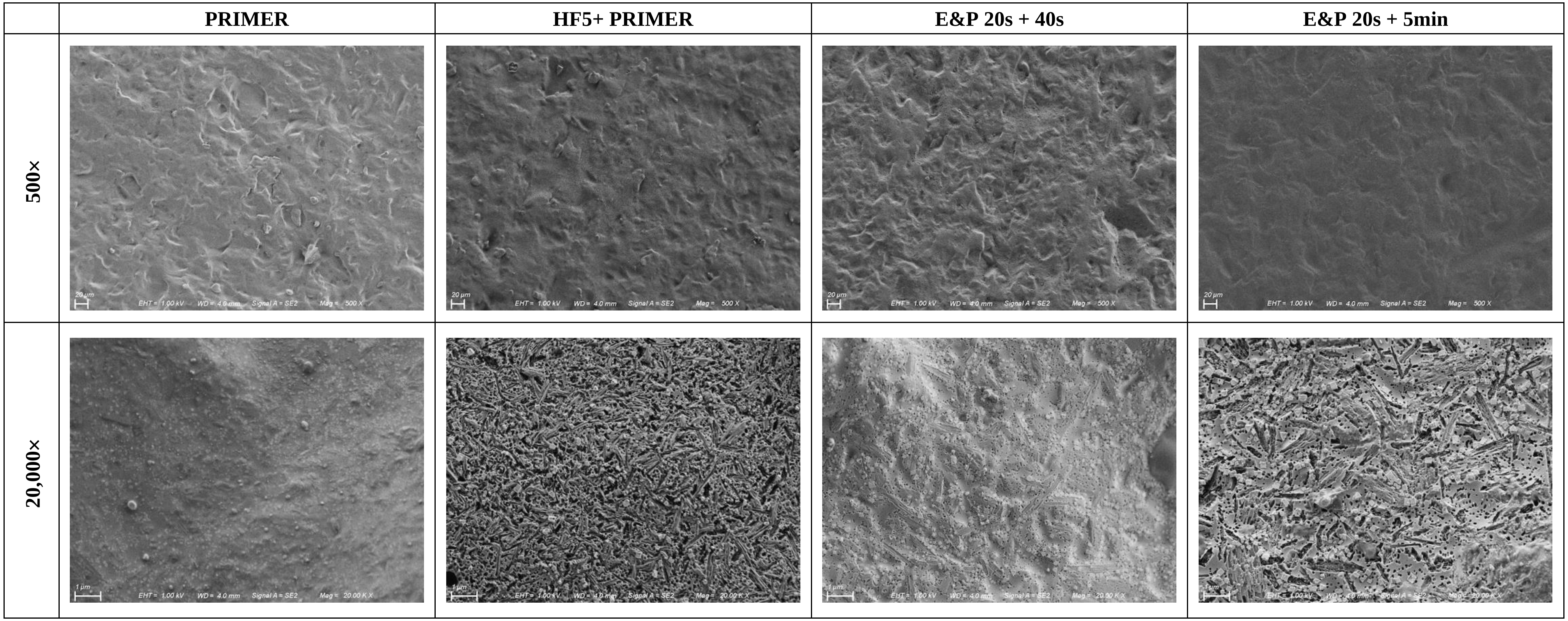


**Figure 2.** Topographic images (500× – top, 20,000× – bottom) obtained at FE-SEM analysis. It becomes clear the potential of the surface treatments on promote glass matrix dissolution in different intensities (higher at HF5+PRIMER and E&P 20s+5min), exposing crystallographic intergranular regions that will enable micromechanical interlocking, as also enhance the posterior chemical interaction with resin cement.

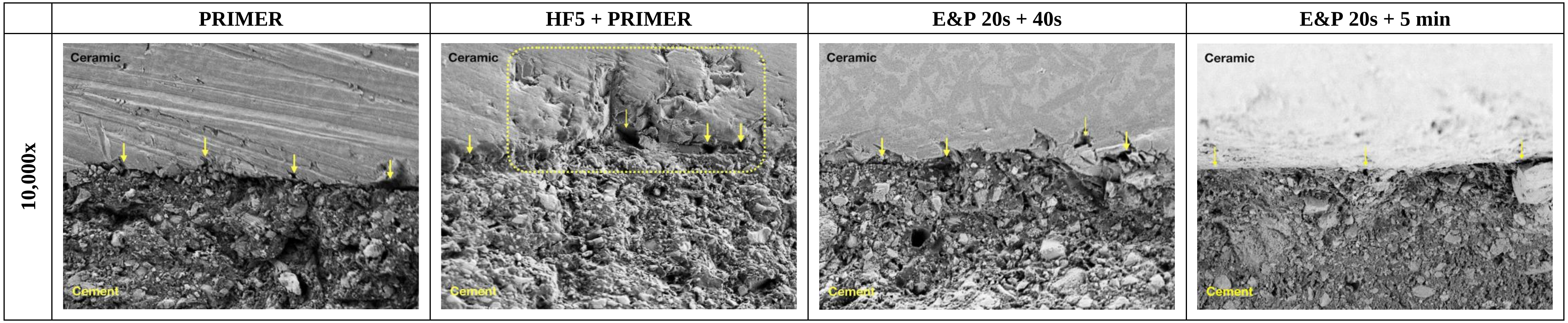


**Figure 3.** Micrographs (10,000×) obtained by FE-SEM illustrating the intaglio surface between the ceramic and the cement, where it notices the presence of unfilled areas (pointed by yellow arrows) between these substrates in all conditions explored. The surface treatments (HF5 + PRIMER and E&P) introduces different patterns of defects, since HF promotes deeper defects than E&P and the increased exposure time to E&P leads to the presence of shallower defects.

# 4. DISCUSSÃO GERAL

As restaurações de dissilicato de lítio são consideradas ácido sensíveis e tem como protocolo clássico, prévio à cimentação adesiva, o condicionamento com ácido fluorídrico e a aplicação de um agente de união que contenha silano (BRENTEL et al., 2007; BLATZ; VONDERHEIDE; CONEJO, 2018; MATINLINNA; LUNG; TSOI, 2018). Devido à toxicidade do ácido fluorídrico (OZCAN; ALLAHBEICKARAGHI; DÜNDAR, 2012; CARPENA; BALLARIN, 2014; WANG et al., 2014; DENNERLEIN et al., 2016), um primer cerâmico autocondicionante e de frasco único tem sido proposto, no qual o fabricante recomenda 20 segundos de aplicação ativa, acrescido de 40 segundos de aplicação passiva. Sabe-se a aplicação de um agente condicionante (em tempo e concentração adequados) altera a topografia de superfície das cerâmicas vítreas e, consequentemente, pode influenciar positivamente os desfechos de resistência de união e fadiga (SCHERER et al, 2018; MURILLO-GÓMEZ; DE GOES, 2019). Assim, a presente dissertação se propôs a avaliar diferentes tempos de aplicação de um primer cerâmico autocondicionante na resistência adesiva e no comportamento à fadiga de uma cerâmica de dissilicato de lítio.

Em um primeiro momento, objetivou-se avaliar a adesão entre uma cerâmica de dissilicato de lítio e um cimento resinoso frente a diferentes tempos de aplicação de um primer cerâmico (*Distinct etching times of a one-step ceramic primer: effect on the resin bond strength durability to a CAD/CAM lithium disilicate glass-ceramic*). Neste estudo, o grupo do primer cerâmico com 5 minutos de aplicação passiva (E&P 20s + 5min) apresentou maior resistência adesiva a longo-prazo (após 180 dias de armazenamento e termociclagem) comparado ao tratamento clássico (aplicação de ácido fluorídrico e agente de união contendo silano). Esse resultado é importante visto que alguns autores relataram que o tratamento com ácido fluorídrico seguido do agente de união contendo silano apresentava melhor resistência adesiva do que a aplicação do primer cerâmico no tempo recomendado pelo fabricante (GUIMARÃES et al., 2018; LOPES et al., 2018; PRADO et al., 2018). Ainda em relação à adesão, o protocolo com tempo aumentado do grupo E&P 20s + 5 min foi semelhante ao protocolo recomendado pelo fabricante (E&P 20s + 40s), tanto na condição de curto quanto de longo-prazo, sendo ambos os tratamentos estáveis após envelhecimento.

Além disso, destaca-se a relevância de avaliar a influência do tempo aumentado da aplicação do primer cerâmico em um contexto mais complexo (conjunto cimentado e submetido a cargas cíclicas e intermitentes), uma vez que cenários diferentes podem repercutir de forma distinta. Assim, o artigo "*One-step ceramic primer as surface conditioner:effect on the load-*

*bearing capacity under fatigue of bonded lithium disilicate ceramic simplified restorations*" teve como proposta avaliar o efeito do aumento do tempo de aplicação de um primer cerâmico no desempenho à fadiga de restaurações simplificadas de dissilicato de lítio cimentadas adesivamente a um substrato análogo de dentina.

Os resultados mostraram que, sob fadiga, a aplicação de um tempo aumentado do primer cerâmico (20 segundos de aplicação ativa acrescido 5 minutos de aplicação passiva, E&P 20s + 5min) foi semelhante ao protocolo clássico de tratamento de superfície (ácido fluorídrico mais agente de união contendo silano, HF5 + PRIMER) e ao tempo recomendado pelo fabricante do primer cerâmico (E&P 20s + 40s), sendo superior apenas ao tratamento com a aplicação de agente de união contendo silano (PRIMER). Na condição envelhecida, deve-se salientar que todos os tratamentos de superfície foram semelhantes e estáveis, exceto ao grupo com a aplicação do agente de união contendo silano (PRIMER), que apresentou o pior desempenho mecânico à fadiga.

O alto decréscimo de carga para falha em fadiga e número de ciclos para falha do grupo PRIMER destaca que, em um contexto de fadiga, a adesão promovida apenas pelo agente de união é dramaticamente suscetível à degradação hidrolítica (LUNG; MATINLINNA, 2012; MATINLINNA; LUNG; TSOI, 2018). E que, embora existam alterações topográficas superficiais produzidas pela simulação da usinagem dos sistemas CAD/CAM, ainda se demonstra a necessidade de uma etapa de condicionamento prévio para promover uma adequada retenção micromecânica. Assim, deve-se destacar que as alterações topográficas promovidas pelo condicionamento com ácido fluorídrico ou pelo primer cerâmico na superfície interna da restauração são indispensáveis para um desempenho estável em fadiga das restaurações de cerâmica dissilicato de lítio.

Outro aspecto fundamental é que a presença de porosidades ou irregularidades na interface de cimentação, ou seja, áreas não preenchidas pelo cimento resinoso, podem concentrar tensões tração e reduzir a capacidade do material em suportar cargas (SPAZZIN et al., 2017; BACCHI et al., 2018). Em face da importância do contato íntimo entre a cerâmica e o cimento e que vise uma interface contínua e homogênea, a alteração gerada pela usinagem também pode influenciar o desfecho avaliado, visto que introduz defeitos na mesma superfície interna em que é realizado o tratamento de superfície. Entretanto, como o custo da usinagem ainda é consideravelmente alto, optou-se por viabilizar o processo e simular a superfície usinada com base em um estudo *in vitro* (RODRIGUES et al., 2018). Nesse sentido, os artigos que compõem a presente dissertação realizaram uma simulação da usinagem promovida pelo sistema CAD/CAM por meio de uma metodologia simplificada com o auxílio de lixas de água (granulação #60), sendo que os parâmetros de rugosidade (Ra e Rz) produzidos pela simulação CAD/CAM foram semelhantes ao encontrado na literatura (FRAGA et al., 2017) para ambos os estudos.

Como limitações da presente dissertação, pode-se mencionar a avaliação de apenas uma cerâmica (dissilicato de lítio), o uso de geometrias de teste simplificadas e a ausência da avaliação de fatores característicos da cavidade bucal, como saliva e variação de pH. Em face disso, os achados atuais devem ser considerados apenas para a cerâmica testada e com cautela, uma vez que estudos in vitro têm limitações inerentes à metodologia.

# 5. CONSIDERAÇÕES FINAIS

Com base nas investigações científicas apresentadas nos artigos, pode-se concluir que, para os contextos de resistência de união e à fadiga, o primer cerâmico autocondicionante com o tempo recomendado pelo fabricante (aplicação ativa de 20 segundos, seguido por aplicação passiva de 40 segundos) entre uma cerâmica de dissilicato de lítio e cimento resinoso é uma alternativa ao condicionamento clássico (ácido fluorídrico seguido de aplicação de agente de união contendo silano), visto que associa mecanismos de adesão micromecânicos e químicos.

Além disso, o aumento do tempo de condicionamento com o primer cerâmico autocondicionante foi benéfico no desfecho de resistência de união até 5 minutos de aplicação passiva, mas não melhorou o desempenho à fadiga das restaurações simplificadas testadas. Por fim, destaca-se que nossas descobertas contribuem para esclarecer uma importante questão clínica: os mecanismos químicos e micromecânicos (promovidas pelo ácido fluorídrico + agente de união contendo silano ou primer cerâmico) são essenciais para a longevidade em fadiga de restaurações simplificadas de dissilicato de lítio.

## 6. REFERÊNCIAS


1. ABOUSHELIB, M. N.; SLEEM, D. Microtensile bond strength of lithium disilicate ceramics to resin adhesives. **J Adhes Dent.** Dec;16(6):547-52, 2014.

2. AKIN, A.; TOKSAVUL S.; TOMAN, M. Clinical marginal and internal adaptation of maxillary anterior single all-ceramic crowns and 2-year randomized controlled clinical trial. **J Prosthodont.** 24(5):345-50, 2015.

3. ANUSAVICE, K. J.; HOJJATIE, B. Tensile stress in glass-ceramic crowns: effect of flaws and cementation voids. **Int. J. Prosthodont.** 5 (4), 351–358, 1992.

4. BACCHI, A. et al. Resin cements formulated with thio-urethanes can strengthen porcelain and increase bond strength to ceramics. **J Dent.** Jun; 73:50-56, 2018.

5. BLATZ, M. B.; CONEJO, J. The Current State of Chairside Digital Dentistry and Materials. **Dent Clin North Am.** 63(2):175-197, 2019.

6. BLATZ, M. B.; VONDERHEIDE, M.; CONEJO, J. The Effect of Resin Bonding on Long-Term Success of High-Strength Ceramics. **J Dent Res.** 97(2):132-139, 2018.

7. BRENTEL, A. S. et al. Microtensile bond strength of a resin cement to feldspathic ceramic after different etching and silanization regimens in dry and aged conditions. **Dent Mater.** 23(11):1323-31, 2007.

8. CARDENAS, A. F. M. et al. Do Different Application Modes Improve the Bonding Performance of Self-etching Ceramic Primer to Lithium Disilicate and Feldspathic Ceramics? **J Adhes Dent**. 21(4):319-327, 2019.

9. CARPENA, G.; BALLARIN A. Hydrofluoric Acid – Simple Things You May Do Not Know About Something You Are So Habituated To Use. **Odovtos Int J Dental SC**. 16:15-23, 2014.

10. DELLA BONA, A. SHEN, C. ANUSAVICE, K. J. Work of adhesion of resin on treated lithia disilicate-based ceramic. **Dent Mater.** 20(4):338-44, 2004.

11. DENNERLEIN, K. et al. Dermal absorption and skin damage following hydrofluoric acid exposure in an ex vivo human skin model. **Toxicol Lett.** 25;248:25-33, 2016.

12. EDELHOFF, D. et al. Advances in materials and concepts in fixed prosthodontics: a selection of possible treatment modalities**. Br Dent J.** 226(10):739-748, 2019.

13. FLEMING, G. J. et al. The strengthening mechanism of resin cements on porcelain surfaces. **J Dent Res**. 85(3):272-6, 2006.

14. FRAGA, S. et al. Impact of machining on the flexural fatigue strength of glass and polycrystalline CAD/CAM ceramics. **Dent Mater.** Nov;33(11):1286-1297, 2017.

15. GUESS, P. C. et al. All-ceramic partial coverage restorations - midterm results of a 5-year prospective clinical splitmouth study. **J Dent.** 37(8):627-37, 2009.

16. GUESS, P. C. et al. All-Ceramic Systems: Laboratory and Clinical Performance. **Dent Clin North Am.** 55(2):333-52, 2011.

17. GUIMARÃES, H. A. B. et al. Simplified Surface Treatments for Ceramic Cementation: Use of Universal Adhesive and Self-Etching Ceramic Primer. **Int J Biomater.** v.2018, id-2598073, 2018.

18. HORN, H. R. Porcelain laminate veneers bonded to etched enamel In:__. Phillips RW editor. Symposium on Dental Material. **Dent Clin North Am.** v.27, p.671-684, 1983.

19. JOHNSON, G. H. et al. Simplified cementation of lithium disilicate crowns: Retention with various adhesive resin cement combinations. **J Prosthet Dent.** 119(5):826-832, 2018.

20. KELLY, J. R. et al. ADM guidance-ceramics: Fatigue principles and testing. **Dent Mater**. 33(11):1192-1204, 2017.

21. KRUZIC, J. J. et al. Recent advances in understanding the fatigue and wear behavior of dental composites and ceramics. **J Mech Behav Biomed Mater**. 88:504-533, 2018.

22. LOPES, G. C. et al. Does a Self-Etching Ceramic Primer Improve Bonding to Lithium Disilicate Ceramics? Bond Strengths and FESEM Analyses. **Oper Dent**. V.44, n.2, p.210-218, 2018.

23. LUCIANO, M. et al. Lithium disilicate posterior overlays: clinical and biomechanical features. **Clin Oral Investig**. Jun 14, 2019.

24. LUNG, C. Y.; MATINLINNA, JP. Aspects of silane coupling agents and surface conditioning in dentistry: an overview. **Dent Mater.** May;28(5):467-77, 2012.

25. LYANN, S. K. et al. Efficacy of Various Surface Treatments on the Bonding Performance of Saliva-contaminated Lithium-Disilicate Ceramics. **J Adhes Dent**. 21(1):51-58, 2019.

26. MANSO, A. P. et al. Cements and adhesives for all-ceramic restorations. **Dent Clin North Am.** 55(2):311-32, 2011.

27. MATINLINNA, J. P.; LUNG, C. Y. K.; TSOI, J. K. H. Silane adhesion mechanism in dental applications and surface treatments: A review. **Dent Mater**. 34(1):13-28, 2018.

28. MAY, L. G. et al. Effects of cement thickness and bonding on the failure loads of CAD/CAM ceramic crowns: multi-physics FEA modeling and monotonic testing. **Dent Mater.** 28(8): e99-109, 2012.

29. MURILLO-GÓMEZ, F.; DE GOES, M. F. Bonding effectiveness of tooth-colored materials to resin cement provided by self-etching silane primer after short- and long-term storage. **J Prosthet Dent.** 121(4): 713.e1-713.e8, 2019.

30. OZCAN, M. ALLAHBEICKARAGHI, A. DUNDAR, M. Possible hazardous effects of hydrofluoric acid and recommendations for treatment approach: a review. **Clin Oral Investig.** Feb;16(1):15-23, 2012.

31. PEUTZFELDT, A.; SAHAFI, A.; FLURY, S. Bonding of restorative materials to dentin with various luting agents. **Oper Dent.** 36(3):266-73, 2011.

32. PRADO, M. et al. Ceramic Surface Treatment with a Single-component Primer: Resin Adhesion to Glass Ceramics. **J Adhes Dent**. 20(2):99-105, 2018.

33. PUPPIN-RONTANI, J. et al. Effect of Hydrofluoric Acid Concentration and Etching Time on Bond Strength to Lithium Disilicate Glass Ceramic. **Oper Dent.** 42(6):606-615, 2017.

34. RAUCH, A. et al. Clinical survival of chair-side generated monolithic lithium disilicate crowns:10-year results. **Clin Oral Investig**. 22(4):1763-1769, 2018.

35. RODRIGUES, C. D. S. et al. Internal adjustments decrease the fatigue failure load of bonded simplified lithium disilicate restorations. **Dent Mater.** Sep;34(9): e225-e235, 2018.

36. SCHERER, M. M. et al. Fatigue failure load of an adhesively-cemented lithium disilicate glass-ceramic: Conventional ceramic etching vs etch & prime one-step primer. **Dent Mater.** 34(8):1134-1143, 2018.

37. SCHESTATSKY, R. et al. CAD-CAM milled versus pressed lithium-disilicate monolithic crowns adhesively cemented after distinct surface treatments: Fatigue performance and ceramic surface characteristics. **J Mech Behav Biomed Mater**. 94:144-154, 2019.

38. SCIENTIFIC DOCUMENTATION – Monobond Etch & Prime. Ivoclar Vivadent, 2015.

39. SEYDLER, B.; SCHMITTER, M. Clinical performance of two different CAD/CAM-fabricated ceramic crowns: 2-year results. **J Prosthet Dent**. 114(2):212–216, 2015.

40. SOUSA, S. J. L. et al. Early clinical performance of resin cements in glass-ceramic posterior restorations in adult vital teeth: A systematic review and meta-analysis. **J Prosthet Dent.** pii: S0022-3913(18)31176-4, 2019.

41. SPAZZIN, A. O. et al. Ceramic strengthening by tuning the elastic moduli of resin-based luting agents. **Dent Mater**. Mar;33(3):358-366, 2017.

42. SPAZZIN, A. O. et al. Strengthening of Porcelain Provided by Resin Cements and Flowable Composites. **Oper Dent**. 41(2):179-88, 2016.

43. SPITZNAGEL, F. A.; BOLDT, J.; GIERTHMUEHLEN, P. C. CAD/CAM Ceramic Restorative Materials for Natural Teeth. **J Dent Res.** 97(10):1082-1091, 2018.

44. TINSCHERT, J. et al. Structural reliability of alumina-, feldspar-, leucite-, mica- and zirconia-based ceramics. **J Dent.** Sep;28(7):529-35, 2000.

45. TRIBST, J. et al. Self-etching Primers vs Acid Conditioning: Impact on Bond Strength Between Ceramics and Resin Cement. **Oper Dent.** 43(4):372-379, 2018.

46. TRIBST, J. P. M. et al. Fatigue Failure Load of Resin-bonded Simplified Lithium Disilicate Glass-Ceramic Restorations: Effect of Ceramic Conditioning Methods. **J Adhes Dent**. 21(4):373-381, 2019.

47. WANG, X. et al. A review of treatment strategies for hydrofluoric acid burns: current status and future prospects. **Burns**. 40(8):1447-57, 2014.

48. WILLE, S.; LEHMANN, F.; KERN, M. Durability of Resin Bonding to Lithium Disilicate and Zirconia Ceramic using a Self-etching Primer. **J Adhes Dent**. 19(6):491-496, 2017.

49. WISKOTT, H. W. A.; NICHOLLS, J. I.; BELSER, U. C. Stress fatigue: basic principles and prosthodontic implications. **Int J Prosthodont**. 8:105-116, 1995.

50. WONG, A. C. H. et al. Aspects of adhesion tests on resin-glass ceramic bonding. **Dent Mater**. 33(9):1045-1055, 2017.

51. XIAOPING, L.; DONGFENG, R.; SILIKAS, N. Effect of etching time and resin bond on the flexural strength of IPS e.max Press glass ceramic. **Dent Mater.** 30(12): e330-6, 2014.

52. ZOGHEIB, L. V. et al. Effect of hydrofluoric acid etching duration on the roughness and flexural strength of a lithium disilicate-based glass ceramic. **Braz Dent J.** 22(1):45-50, 2011.

# ANEXO A – NORMAS PARA PUBLICAÇÃO NO PERIÓDICO *JOURNAL OF ADHESIVE DENTISTRY*

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1. Clinical and basic science research reports – based on original research in adhesive dentistry and related topics.
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Examples: 'as demonstrated (Allan, 2000a, 2000b, 1999; Allan and Jones, 1999). Kramer et al. (2010) have recently shown ....'
*List:* References should be arranged first alphabetically and then further sorted chronologically if necessary. More than one reference from the same author(s) in the same year must be identified by the letters 'a', 'b', 'c', etc., placed after the year of publication.
*Examples:*
Reference to a journal publication:
Van der Geer, J., Hanraads, J.A.J., Lupton, R.A., 2010. The art of writing a scientific article. J. Sci. Commun. 163, 51–59.
Reference to a book:
Strunk Jr., W., White, E.B., 2000. The Elements of Style, fourth ed. Longman, New York.
Reference to a chapter in an edited book:
Mettam, G.R., Adams, L.B., 2009. How to prepare an electronic version of your article, in: Jones, B.S., Smith , R.Z. (Eds.), Introduction to the Electronic Age. E-Publishing Inc., New York, pp. 281–304.
Reference to a website:
Cancer Research UK, 1975. Cancer statistics reports for the UK. http://www.cancerresearchuk.org/ aboutcancer/statistics/cancerstatsreport/ (accessed 13 March 2003).
Reference to a dataset: [dataset] Oguro, M., Imahiro, S., Saito, S., Nakashizuka, T., 2015. Mortality data for Japan
ese oak wilt disease and surrounding forest compositions. Mendeley Data, v1. https://doi.org/10.17632/ xwj98nb39r.1. Journal abbreviations source Journal names should be abbreviated according to the List of Title Word Abbreviations.

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