

Repair Techniques in CAD/CAM System Ceramics: a Literature Review

Técnicas de Reparo em Cerâmicas do Sistema CAD/CAM; uma Revisão de Literatura

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Abstract

Currently, CAD / CAM systems have been increasingly used in Dentistry, however due to the characteristic of the technique, since it is milled from a ceramic block, some flaws, such as fractures, become a challenge after the piece is cemented. To avoid the complete replacement of the part, the technique through intraoral repair of the fractured region is ideal for these cases. There are several protocols for this technique, this study aims to review the literature regarding the techniques and protocols for ceramic repair of the CAD / CAM system. A literature review was carried out on the Pubmed database using the terms Ceramic repair, Adhesive and Composite resin searching for studies published in the period from 2000 to 2020. 104 articles were found, after reading 32 articles were selected because they presented a greater correlation with the present study. There was unanimity among the authors about the importance of a surface treatment on the ceramic to be repaired, 70% of them still indicated the roughness with drills and conditioning with hydrofluoric acid due to the ease of the technique and good result. The combination of several surface treatments in the same region to be repaired produces better tensile strength. The use of the silane agent in a separate step presents better bonding strength results when compared to the universal type adhesive system with silane incorporated in the formula.

Keywords: Repair. Ceramics. Adhesive. Composite Resins.

Resumo

Atualmente os sistemas CAD/CAM tem sido cada vez mais utilizados na Odontologia, porém devido a característica da técnica, já que é fresada a partir de um bloco cerâmico, algumas falhas, como fraturas, se tornam um desafio após a peça ser cimentada. Para evitar a completa substituição da peça a técnica através de reparo intraoral da região fraturada é ideal para esses casos. Existem diversos protocolos para esta técnica, este estudo tem por objetivo uma revisão de literatura quanto às técnicas e protocolos de reparo em cerâmica do sistema CAD/CAM. Foi realizada uma revisão de literatura no indexador Pubmed database utilizando os termos Ceramic repair, Adhesive e Composite resin buscando estudos publicados no período de 2000 a 2020. Foram encontrados 104 artigos, após leitura 32 artigos foram selecionados pois apresentavam maior correlação com o presente estudo. Foi unanimidade entre os autores acerca da importância de um tratamento de superfície na cerâmica a ser reparada, 70% deles ainda indicaram a asperização com brocas e condicionamento com ácido fluorídrico pela facilidade da técnica e bom resultado. A associação de vários tratamentos de superfície na mesma região a ser reparada produz melhor resistência a tração. O uso do agente silano em etapa separada apresenta melhores resultados de resistência de união quando comparado ao sistema adesivo do tipo universal com silano incorporado na fórmula.

Palavras-chave: Cerâmicas. Adesivos. Resinas Compostas.

1 Introduction

Dental ceramics are indirect restorative materials, they have properties that mimic dental dentin and enamel. They are biocompatible materials with low thermal conductivity, electrical, chemical stability, do not absorb oral fluids, with minimal plaque retention in addition to longevity^{1,2}. Its characteristics justify its great use in Dentistry for situations of replacement of the lost dental structure in both anterior and posterior teeth.

The technology has provided more agility and precision in rehabilitating treatment with the use of the computer-aided design (CAD) and computer-aided manufacturing (CAM) of ceramics parts, minimizing the external interference inherent to the conventional manufacturing technique^{3,4}.

Clinical failures in rehabilitations performed with ceramic parts can occur, and fracture is the main problem, which may have several causes such as occlusion, failure in the laboratory or professional technique. Because the use of ceramics in rehabilitations is increasingly frequent, fractures have been increasingly frequent after rehabilitation⁵. A fractured piece generates esthetic and functional dissatisfaction⁵. This fracture can be corrected by the complete replacement of the fractured part or by the execution of a composite resin repair that is made more agile by the direct technique, reduces clinical time and costs⁶.

Direct repairs require treatment of the fractured surface, followed by the application of a silane agent, application of an adhesive and composite resin¹. Surface treatment

for repair can be mechanical by spraying with drill bits or abrasion with aluminum oxide, chemical through acids at different concentrations and application times that aim to cause microporosities and/or union agents such as silane and adhesives that are responsible for the chemical union between the part and the composite resin⁷.

This study aims to perform a literature review on the techniques and protocols of direct repair with resin composed of dental ceramics made with the CAD/CAM system, with the aim of elucidating this information to the clinician and contributing to the decision making in these cases. Among its characteristics, ceramics present biocompatibility, color stability, low thermal conduction, low plate accumulation, abrasion resistance, besides promoting an excellent esthetic⁸. Since the appearance of the first porcelain tooth until the present day, the technological advance provided the development of several ceramic systems in dentistry, these new systems try to overcome the fragility characteristics due to low mechanical resistance when submitted to stress, which compromises their clinical performance in some aspects⁹.

Resistance to fracture of the ceramic crowns is based on several factors, such as compliance with the indication of each ceramic type according to the region to be rehabilitated, adequate dental preparation, thorough laboratory execution, adequate coping thickness, cementation type and careful

occlusal adjustment¹⁰. Thus, its physical-chemical advance is of paramount importance through clinical and laboratory research with the objective of combining esthetic properties with resistance values that ensure its longevity.

2 Development

2.1 Methodology

The literature review was performed using the Pubmed database indexer with the crossing of the terms *Ceramic repair, Adhesive, Composite resin* in texts published from 2000 to 2020.

Articles published in Portuguese and English, in vitro studies, clinical studies and literature reviews were included, articles that fit the proposed theme. It was considered that this CAD/CAM technique is recent and the repair technique in these ceramics, in this sense, it was opted for articles published in the last two decades for inclusion.

Articles were excluded from repair in other types of ceramics than the CAD/CAM system, articles that were from the CAD/CAM system not using composite resins.

104 articles were found, after reading the title and abstract, following the inclusion and exclusion criteria, 21 articles were selected because they presented a greater correlation with the present study.

Table 1 - Selection of articles

Articles	Study	Ceramic Type	Acid Conditioning	Silaniz.	Adhesive	Recommended Method
2003 Blatz	Review	Silica and Alumina	Silica: Hydrofluoric acid 9.5% by 2' to 3'	Yes	Conventional adhesive	Cond. Ác. hydrofluoric
2009 Hammond	In vitro	Feldspathic, Leute and Dyssilicate	Hydrofluoric acid 5% by 2'		Conventional adhesive	Cond. Hydrofluoric Acid + Blasting
2009 Ozcan	In vitro	Feldspathic reinforced with alumina	Hydrofluoric acid + silane + adhesive	Yes	Conventional adhesive	Silane + Adhesive
Necklaces 2013	In vitro	Lithium disilicate	Hydrofluoric acid 9.5% 20 sec	Yes	Conventional adhesive	Cond. Hydrofluoric acid +silane
2014 Aboushelib	In vitro	Lithium disilicate	Hydrofluoric acid 9.5%	Yes	Conventional adhesive	Hydrofluoric acid + silane + adhesive
2014 Santos	In vitro	Feldsalon	Ác.hydrofluoric 5% / Ác.hydrofluoric 10%		Conventional adhesive	Ac hydrofluoric 10%
2015 Duzyol	In vitro	Lithium disilicate and Feldspar	Hydrofluoric acid 5%	Yes	Universal adhesive	Lithium disilicate: Fluorideric acid
2015 Elsaka	In vitro	Hybrid ceramics	Hydrofluoric acid 9.5% 20 sec	Yes	Conventional and universal adhesive	Hydrofluoric acid + silane + conventional adhesive
2015 Kalra	In vitro	Metalloceramic	Phosphoric acid 40%; 37% and 8%	Yes	Conventional and universal adhesive	Phosphoric at 40%
2015 Walsh and Ghallab,	In vitro	Lithium disilicate and nano ceramic resin	-	Yes	Conventional and universal adhesive	Silane + conventional adhesive
2015 Wiegand	In vitro	PMMA (high density polymers)	-	Yes	Conventional adhesive	Silanization
2016 Campos et al.	In vitro	Hybrid ceramics and feldspathic ceramics	Hydrofluoric acid 10% for 60sec + phosphoric ace 37% for 60sec;	Yes	Conventional adhesive	Cond. Hydrofluoric ACID 10%

To be continued...

Articles	Study	Ceramic Type	Acid Conditioning	Silaniz.	Adhesive	Recommended Method
Gungor et al., 2016	In vitro	Hybrid ceramics	Hydrofluoric ACID 9% for 60 sec	Yes	-	Asperization with drills
Loomans 2016	Literature Review	Metalloceramics and Zirconia	Hydrofluoric ACE 5% or 9% for 20 sec to 90 sec	Yes	Conventional adhesive	Combined surface treatment
2016 Ustun	In vitro	IPS and.max CAD, Vita Suprinity, Vita Enamic, Ultimate Lava	Phosphoric acid at 40% and a. 37%	Yes	Conventional and universal adhesive	Similar results in the strength of the
2017 Carraba et al.	In vitro	Feldspathic ceramics	Hydrofluoric ACID 9% per 120 sec		Conventional and universal adhesive	Cond.Ác. Hydrofluoric
2017 Loomans	In vitro	Hybrid ceramics	Hydrofluoric ACID 9.6%	Yes	Conventional adhesive	Surface treatment + jet abrasion and silanization.

Source: Research data.

2.2 Ceramics repair

The repairs in ceramics are classified as indirect and direct, the first one requires a laboratory phase, which after the preparation, are cemented in the fractured region. Direct repair is made by the incremental insertion of composite resin directly in the patient's mouth after preparation of the fractured surface¹¹.

Direct repair with composite resin aims at not completely replacing the restoration, with the aim of reducing clinical time, dental structure wear and financial cost⁷; in addition to increasing longevity, maintaining esthetics and function¹². Disadvantages should be considered, since the resin presents a higher risk of wear and staining, which may compromise esthetics and adaptation over time¹³.

Knowledge of the microstructure of ceramic materials and their behavior in relation to different surface treatment techniques is of great importance in determining the appropriate protocol of adhesive cementation and which can be taken into consideration when direct repair is to be performed in ceramics restorations¹⁴.

2.3 Surfaces treatment

The surface treatments create irregularities on the surface to be repaired which improves the bonding resistance of resins composed of *CAD/CAM blocks* of hybrid, resin and zirconia-reinforced lithium silicate materials in repair^{15,16}.

Several techniques have been suggested in the literature as effective for producing adequate micromechanical or chemical retention to promote interaction with compound resins^{5,17} such as: 1- surface blasting with Al_2O_3 ¹⁸, 2- silicate¹⁹, 3 - Spraying with drill bits, 4 - Conditioning with hydrofluoric acids^{18,19}, 5 - silanization²⁰ and 6 - Universal adhesive systems²⁰.

The blasting or abrasion aluminum oxide (35 to 250 μ m), modify the surface for a high bonding and consequent increase in the joining resistance between composite resin and ceramic. Despite the efficacy of the technique is infeasible due to the risk of damage to adjacent oral structures and teeth, as well as biosafety impairment, since the patient can aspirate oxide particles²¹.

In silicatization, the surface is abrasive with aluminum trioxide and particles modified with silica. Silica-coated alumina, particles are firmly incorporated into the porcelain surface as a result of blasting pressure. The silica-modified surfaces are chemically more reactive to resin composites than to silane bonding agents^{21,22}, but this procedure is more suitable for acid-resistant ceramics with low silica content⁷, which is not the case for lithium-dissipate ceramics. Similarly to the aluminum oxide technique, there are risks due to the presence of particles of sand suspended in the air, making application in the direct repair technique impossible.

Silane is a bonding agent used after conditioning with hydrofluoric acid and is intended to increase resistance to binding force, it has a better result than the application of the bonding agent in isolation. The use of hydrofluoric acid for intraoral repair procedures may also be dangerous for adjacent tissues, so the clinical procedure of this stage requires much more caution for its intraoral application²².

Studies have shown good results in direct repairs and agree on the need for treatment of fractured surface, following the application of silane, adhesive and composite resin⁵. They also corroborate that the clinical success of a repair of ceramic restorations with light-cured resin is dependent on an effective mechanical and chemical bonding between these two materials, which is achieved by surface preparation followed by the application of the silane agent and the adhesive^{13,23}.

The clinical success of ceramic repairs has the quality and durability directly related to the adhesion between the composite resin and the ceramic and in order to have an adequate retention between these two materials, the micromechanical treatment of this surface must be done⁷, ensuring stability in the bonding between ceramics and the composite resin⁵.

In a study comparing surface treatment techniques, they report that spraying with diamond tip for eight seconds, blasting with Al_2O_3 for 10 seconds or spraying with COJET for 10s followed by silane application 60 seconds, presented similar bonding resistance values. Because they have similar results, diamond tip spraying becomes an excellent option

for practicality and low costs for execution, since blasting with particles requires a specific apparatus and material not available in every dental practice¹⁶.

In a study Loomans et al.²⁴ demonstrated that the use of hydrofluoric acid conditioning was effective to increase adherence of LAVA ULTIMATE repair to compound resins, however this effect was not observed after thermal cycling. It was observed that for the group without aging, the bonding resistance was intermediate, but after aging *in situ*, the bonding resistance of group HF10% was the one that obtained the lowest statistical value, the acid dissolves the particles of ceramic glass or composite resins resulting in higher surface roughness²⁴.

Sismanoglu et al.²⁵ assessing the micro tensile binding force of CAD-CAM composite resins submitted to simulated repair procedures, they found that all surface treatments (conditioning with 9% hydrofluoric acid, blasting with aluminum oxide and silicatization) effectively improved the strength values of the micro tensile repair bonding compared to the control group (without surface treatment)²⁵.

2.4 Bonding agents

Different adhesive techniques are used in Dentistry for the intra-oral repair of ceramics, with several surface pretreatment protocols and adhesive systems¹⁵. The bonding agents are used after surface preparation to increase strength⁹.

The chemical bonding of the ceramic surface with the composite resin is achieved with the application of the silane agent, a bifunctional monomer that contains a silanol group that reacts with ceramic surfaces and a methacrylate group that copolymerizes with the composites organic matrix, this characteristic increases the adhesion between the composite and the ceramics resins^{15,17,21}.

Currently, within the adhesive formulations available on the market, there is the group of universal adhesive agents that present silane in their composition and promise to maximize the chemical bonding between ceramics and resin, which can replace the need for a separate silanization step^{26,27}.

The comparison between conventional adhesives and universal type adhesives, which have in their composition the silane agent, it aims to determine whether it is necessary to apply a silane coupling agent prior to the use of a universal adhesive containing silane or the sole use of a universal adhesive and the prior application of a silane coupling agent would not provide an advantage in the binding force or contact angle value²⁸.

The published results are still scarce, but point out that signaling as an additional step can be used to improve the chemical-mechanical bonding of ceramics and resin, especially those rich in glass, this reinforces the inefficiency of silane incorporated in the universal adhesive²⁷ and the need for silanization as an additional step in the different protocols of surface pretreatment²⁶. To bind to glass-rich ceramics, the conditioning with hydrofluoric acid followed by silanization

is the standard binding protocol and it is observed that the universal adhesive containing silane is less effective and less stable in composite resin and lithium disilicate²⁷.

Wille et al.²⁹ analyzed the bonding resistance of the composite resin to the ceramic of lithium disilicate and zirconium, using Monobond etch & Prime as conditioning agents of the surface of these ceramics and compared with hydrofluoric acid followed by silane and found bonding resistance values for lithium disilicate ceramics comparable to hydrofluoric acid, in surface analysis they also presented alterations in the topography of these ceramics. In zirconia ceramics, bonding resistance values were significantly lower when compared to hydrofluoric acid and after storage in water for 30 days, all specimens presented reduced bonding resistance values²⁹.

The bonding resistance between the resinous VarioLink esthetic cement and lithium disilicate ceramic (e.max) by the CAD/CAM system was analyzed by Guimaraes et al.³⁰ and subjected the samples to different surface treatments and found the combination of hydrofluoric acid 10% and silane with better bonding resistance values and the group treated with hydrofluoric acid and universal adhesive presented the lowest values of bonding resistance, besides predominance in adhesive failures³⁰. Whereas the study by Sismanoglu et al.²⁵, which evaluated the binding strength of CAD-CAM composite resins submitted to repair procedures using various treatments of universal surfaces and adhesives, found that universal adhesive containing silane presented increased binding strength, and recommends the application of universal adhesive after surface treatment to increase resistance to repair²⁵.

3 Conclusion

Surface treatment has a positive influence on the repair of ceramics, regardless of the type of ceramics being worked and the association of various treatments in the same repair produces higher tensile strength values. The use of the silane agent in a separate step presents better bonding strength results when compared to the universal type adhesive system with silane incorporated in the formula.

References

1. Hickel R, Brühaver K, Ilie N. Repair of restorations-criteria for decision making and clinical recommendations. *Dent Mater* 2013;29(1):28-50. doi: 10.1016/j.dental.2012.07.006
2. Mallineni SK, Nuvvula S, Matinlinna JP, Yiu CK, King NM. Biocompatibility of various dental materials in contemporary dentistry: a narrative insight. *J Investig Clin Dent* 2013;4(1):9-19. doi: 10.1111/j.2041-1626.2012.00140.x
3. Bahr N, Keul C, Edelhoff D, Eichberger M, Roos M, Gernet W, et al. Effect of different adhesives combined with two resin composite cements on shear bond strength to polymeric CAD/CAM materials. *Dent Mater J* 2013;32(3):492-501. doi: 10.4012/dmj.2012-329
4. Hsu K-W, Shen Y-F, Wei P-C. Compatible CAD-CAM

- titanium abutments for posterior single-implant tooth replacement: a retrospective case series. *J Prosthet Dent* 2017;117(3):363-
5. Ozcan M. Evaluation of alternative intra-oral repair techniques for fractured ceramic-fused-to-metal restorations. *J Oral Rehabil* 2003;30(2):194-203. doi: 10.1016/j.prosdent.2016.07.023
 6. Hakimaneh SMR, Shayegh SS, Ghavami-Lahiji M, Chokr A, Moraditalab A. Effect of Silane Heat Treatment by Laser on the Bond Strength of a Repair Composite to Feldspathic Porcelain. *J Prosthodont* 2020;29(1):49-55. doi: 10.1111/jopr.12762.
 7. Kumchai H, Juntavee P, Sun AF, Nathanson D. Comparing the repair of veneered zirconia crowns with ceramic or composite resin: an in vitro study. *Dent J (Basel)* 2020;8(2):37. doi: 10.3390/dj8020037.
 8. Haselton DR, Diaz-Arnold AM, Hillis SL. Clinical assessment of high-strength all-ceramic crowns. *J Prosthetic Dent* 2000;83(4):396-401. doi.org/10.1016/S0022-3913(00)70033-3.
 9. Anusavice KJ, Jadaan OM, Esquivel-Upshaw JF. Time-dependent fracture probability of bilayer, lithium-disilicate-based, glass-ceramic, molar crowns as a function of core/veneer thickness ratio and load orientation. *Dent Mat* 2013;29(11):1132-8. doi: doi.org/10.1016/j.dental.2013.08.206.
 10. Figueiredo RJA, Andrade AKM, Duarte RM, Medeiro e Silva FDSC. Otimizando a estética por meio de reanatomizações em dentes conóides. *RGO* 2008;56(3):333-6.
 11. Galiatsatos AA. An indirect repair technique for fractured metal-ceramic restorations: a clinical report. *J Prosthetic Dent* 2005;93(4):321-3. doi: doi.org/10.1016/j.prosdent.2004.12.018.
 12. Blatz MB, Sadan A, Kern M. Resin-ceramic bonding: a review of the literature. *J Prosthet Dent* 2003;89(3):268-74. doi: 10.1067/mps.2003.50.
 13. Hammond BD, Swift JR, Edward J, Brackett WW. Intraoral repair of fractured ceramic restorations. *J Esthetic Restorative Dent* 2009;21(4):275-84.
 14. Gul P, Altınok-Uygun L. Repair bond strength of resin composite to three aged CAD/CAM blocks using different repair systems. *J Adv Prosthodont* 2020;12(3):131-9. doi: 10.4047/jap.2020.12.3.131.
 15. Elsaka SE. Repair bond strength of resin composite to a novel CAD/CAM hybrid ceramic using different repair systems. *Dent Mat J* 2015;34(2):161-7.
 16. Veríssimo AH, Duarte Moura DM, Oliveira Dal Piva AM, Bottino MA, Fátima Dantas de Almeida L, Fonte Porto Carreiro A, et al. Effect of different repair methods on the bond strength of resin composite to CAD/CAM materials and microorganisms adhesion: an in situ study. *J Dent* 2020;93:103266. doi: 10.1016/j.jdent.2019.103266.
 17. Raposo LHA, Neiva NA, Silva GR, Carlo HL, Mota AS, Prado CJ, et al. Ceramic restoration repair: report of two cases. *J Appl Oral Sci* 2009;17(2):140-4.
 18. Gourav R, Ariga P, Jain AR, Philip JM. Effect of four different surface treatments on shear bond strength of three porcelain repair systems: an in vitro study. *J Conserv Dent* 2013;16(3):208-12. doi:10.4103/0972-0707.111315.
 19. Colares RCR, Neri JR, Souza AMB, Pontes KMF, Mendonça JS, Santiago SL. Effect of surface pretreatments on the microtensile bond strength of lithium-disilicate ceramic repaired with composite resin. *Braz Dent J* 2013;24(4):349-52. doi: https://doi.org/10.1590/0103-6440201301960.
 20. Matinlinna JP and Vallittu PK. Bonding of resin composites to etchable ceramic surfaces – an insight review of the chemical aspects on surface conditioning. *J Rehab* 2007(34):622-30. doi: 10.1111/j.1365-2842.2005.01569.x
 21. Mutlu Ö, Valandro LF, Amaral R, Leite F, Bottino MA. Bond strength durability of a resin composite on a reinforced ceramic using various repair systems. *Dent Mater* 2009;25(12):1477-83.
 22. Duzyol M, Sagsoz O, Sagsoz NP, Akgul N, Yildiz M. The effect of surface treatments on the bond strength between CAD/CAM blocks and composite resin. *J Prosthodont* 2016;25(6):466-71.
 23. Paranhos MP, Burnett LH Jr, Magne P. Effect Of Nd:YAG laser and CO2 laser treatment on the resin bond strength to zirconia ceramic. *Quintessence Int* 2011;42(1):79-89.
 24. Loomans B, Opdam N, Attin T, Bartlett D, Edelhoff D, Frankenberger R, et al. Severe tooth wear: european consensus statement on management guidelines. *J Adhes Dent* 2017;19:111-9. doi: 10.3290/j.jad.a38102.
 25. Sismanoglu S, Yildirim-Bilmez Z, Erten-Taysi A, Ercal P. Influence of different surface treatments and universal adhesives on the repair of CAD-CAM composite resins: An in vitro study *J Prosthet Dent* 2020;S0022-3913(20)30166-9. doi:10.1016/j.prosdent.2020.02.029.
 26. Zaghoul H, Elkassas DW, Haridy MF. Effect of incorporation of silane in the bonding agent on the repair potential of machinable esthetic blocks. *Eur J Dent* 2014;8(1):44-52.
 27. Yoshihara K, Nagaokab N, Sonodac A, Maruod Y, Makitac Y, Okiharac T, et al. Effectiveness and stability of silane coupling agente incorporated in ‘universal’ adhesives. *Dent Mater* 2016;32(10):1218-25. doi: 10.1016/j.dental.2016.07.002
 28. Sattabanasuk V, Charnchairer P, Punsukumtana L, Burrow MF. Effects of mechanical and chemical surface treatments on the resin-glass ceramic adhesion properties. *J Invest Clin Dent* 2017;8(3). doi: 10.1111/jicd.12220
 29. 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):491-6. doi: 10.3290/j.jad.a39545.
 30. Guimarães HAB, Cardoso PC, Decurcio RA, Monteiro LJE, Almeida LN, Martins, WM, et al. Simplified surface treatments for ceramic cementation: use of universal adhesive and self-etching ceramic primer. *Int J Biomat* 2018. doi: https://doi.org/10.1155/2018/2598073.