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Comparison of shear bond strength of two veneering ceramics to zirconia

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ABSTRACT

Background: Chip-off fracture of veneering porcelain has been described as the most frequent reason for the failure of zirconia-based fixed partial dentures. The purpose of this study was to evaluate the shear bond strength (SBS) of two commercial zirconia core ceramics to their corresponding veneering ceramics.

Materials and Methods: Zirconia disks with 7-mm diameter and 3-mm height were prepared (Cercon and Biodenta systems) and veneered with recommended layering ceramics (Cercon ceram and 2 in 1 ceramic, respectively) (n = 10). The disks were polished with diamond paste and airborne-particle abraded before layering. The specimens were mounted in a T-shaped metal holder using autopolymerized acrylic resin and stored in 37°C distilled water for one week, after which they were subjected to thermal cycling. SBS of zirconia core to veneering ceramic was measured using a universal testing machine and failure modes were determined microscopically. Data were analyzed using t test ($\alpha < 0.05$).

Results: Mean (±SD) SBS values were 27.19(±3.43) and 28.22(±4.08) MPa for Cercon and Biodenta systems, respectively, with no significant difference. Biodenta system showed more adhesive failure compared to more combined (adhesive and cohesive) failures in Cercon system.

Conclusion: Within the limitations of this study it can be concluded that SBS of Biodenta and Cercon specimens were nearly the same, but the fracture mode of these two systems were different. Since Biodenta fracture pattern was predominantly adhesive, it seems that maybe Biodenta porcelain was stronger than Cercon porcelain where as its adhesive bond was weaker.

Key Words: Failure mode, shear bond strength, veneering ceramic, zirconia

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INTRODUCTION

The porcelain fused to metal technique has been known as a reliable choice of treatment for fixed partial dentures (FPD) for almost four decades now, still representing the gold standard.[1-3] However, with the increasing interest in esthetic dentistry and the question of some dental metals and alloys being biocompatible or not, the development of other alternatives to metallic ceramic dental restorations has advanced.[4] In the early 1990s, yttrium oxide partially stabilized tetragonal zirconia polycrystal (Y-TZP) was introduced to dentistry as a core material for all-ceramic restorations and has been made available through the CAD/CAM technique. Y-TZP has proved to be superior in mechanical properties compared with other all-ceramic systems (flexural strength of 900-1200 MP a,[5,6] and fracture toughness of 9-10 MP a.m1/2[7]) due to a transformation toughening mechanism.

Long-term clinical results for zirconia all-ceramic restorations are not available at the present time. In short[8] and medium-term studies[9-11] the Y-TZP core ceramic had a high stability as a framework material.

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There have been no fractures of the zirconia framework reported to date.[10-12] However, delamination or minor chip-off fracture of veneering porcelain has been described as the most frequent reason for the failures of zirconia FPDs. The incidence of veneer fractures in zirconia FPDs was significantly higher compared with those in metal-ceramic FPDs.[12] Therefore, the bond between core and veneer or the veneer material itself is one of the weaknesses in layered zirconia-based restorations and plays a crucial role in their long-term success.[13]

Chip-off fracture rates of 15% after 24 months,[9] 25% after 31 months,[11] 15.2% after 60 months[14] and 8% and 13% after 36-38 months, were observed respectively.[10] A review of the literature for FPDs with metal framework, however, revealed either no fracture of the veneering ceramic[15] or substantially lower fracture rates ranging from 2.7 up to 5.5% for observation periods from 10 to 15 years.[16,17] The cause of fracture of veneering ceramics on zirconia all-ceramic cores was reported to be multifactorial in clinical applications. Restoration geometry such as lack of proper veneering ceramic support, inadequate framework design and thickness of the ceramic layers seem to play a decisive role.[10] Moreover, direction, magnitude and frequency of the applied load other than the size and location of occlusal contact areas can lead to failures of the veneering ceramic.[11] Bond strength is determined by a series of factors including strength of the chemical bonds, mechanical interlocking, type and concentration of defects at the interface, wetting properties, and the degree of compressive stress in the veneering layer due to a difference in the coefficients of thermal expansion between zirconia and the veneering ceramic.[18-20]

Since the mechanical integrity and adhesion of the veneering ceramic to the ceramic substructure have proven to be key factors for the successful performance of veneer/core bilayered restorations, the initial bond strength and their reliability after thermocycling obtained from *in vitro* investigations can provide useful information for the behavior and predictability of Y-TZP all-ceramic systems in clinical application.[11]

The purpose of this study was to evaluate the shear bond strength (SBS) of two commercial zirconia core ceramics to their corresponding veneering ceramics and microscopic characteristics of bond failure at fracture surface.

MATERIALS AND METHODS

Two types of zirconia-based ceramics were selected for this experimental study: Biodenta (Biodenta Swiss AG, Bernek, Switzerland) and Cercon (Degudent, Hanau, Germany). With each zirconia system, 10 disk-shaped specimens of 7-mm diameter and 3-mm height were fabricated. Presintered zirconium oxide blocks were milled according to the manufacturers' instructions. Then, they were cleaned, dried, and sintered according to the suggested firing schedules [Table 1]. The bonding surfaces of zirconia core specimens were polished with diamond paste (Lach Diamant, Hanau, Germany) to obtain standardized surface roughness of 3 μm. Then, airborne particle abrasion was applied on the bonding surfaces with 110-μm aluminum oxide (Al_2O_3) particles (Hasenfratz, Assling, Germany) for 15 seconds at 3 bar pressure and at 10-mm distance from the surface. Finally, the specimens were ultrasonically cleaned in 96% isopropyl alcohol for 3 minutes and steam-cleaned for 15 seconds. The specimens of Biodenta and Cercon zirconia systems were veneered with their manufacturer-recommended veneering ceramics, 2 in 1 ceramic (Biodenta Swiss AG, Bernek, Switzerland) and Cercon Ceram (Degudent, Hanau, Germany), respectively [Table 2]. Using a specially designed, separable stainless steel mold, a prepared zirconia disk specimen was placed in the mold where clearance of 5-mm diameter and 3-mm height was available above the core material for condensing the veneer ceramic. The veneering procedure was performed using the manual layering technique. First, two liner layers of porcelain were applied and fired independently, then the dentin porcelain was condensed using the vibration blotting technique, fired and finally a glaze firing was performed according to the manufacturer's instructions. By means of an autopolymerized acrylic resin (Meliodent, Heraeus Kulzer GmbH, Hanau, Germany), each specimen was embedded at the center of a T-shaped metal holder, with the core-veneer interface positioned at the top level of the holder [Figure 1]. All specimens were stored in distilled water at 37°C for 1 week. and then thermal cycled for 5000 cycles, 5°-55°C with a 30-s dwell time.

Then, these metal holders were mounted in universal testing machine (Type LFM-L, Walter+Bai AG, Löhningen, Switzerland). Specimens were tightened and stabilized to ensure that the 1-mm thick edge of the shearing device was in contact with the core

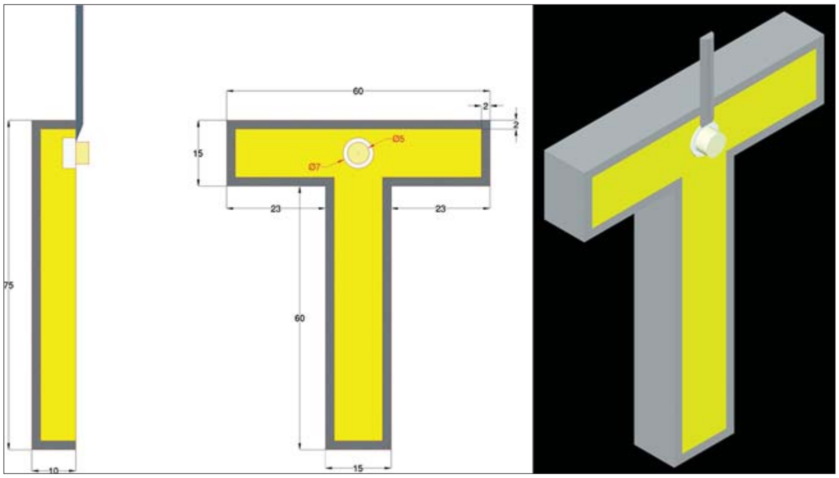

Figure 1: Illustration of shear bond strength test setup and specimen preparation

Table 1: Zirconia systems evaluated in this study and their firing schedules

Core material	Manufacturer	Lot number	Sintering temperature (°C)	Sintering time (hour)
Biodenta	Biodenta Swiss AG, Bernek, Switzerland	800427	1450	6
Cercon	Degudent, Hanau, Germany	18010888	1350	6

Table 2: Chemical composition and mechanical properties of the core and veneering materials (CTE, coefficient of thermal expansion) according to the manufacturers' information

Manufacture	Material	Composition	CTE($\times 10^{-6}$/K)
Biodenta	Zirconia	ZrO_2, Al_2O_3, Y_2O_3	9.8
2 in 1 ceram	Liner	SiO_2, ZrO_2, Al_2O_3, B_2O_3, K_2O, Na_2O, SrO, CeO_2, P_2O_5, SnO_2, ZnO, CaO, Li_2O, F	8.5
	Dentin	SiO_2, ZrO_2, Al_2O_3, B_2O_3, K_2O, Na_2O, SrO, CeO_2, P_2O_5, SnO_2, ZnO, CaO, Li2O, F	10
Cercon	Zirconia	ZrO_2, Y_2O_3, Hf O_2, SiO_2, Al_2O_3	10.5
Cercon ceram	Liner	SiO_2, Al_2O_3, K_2O, Na_2O,	9.5
	Dentin	SiO_2, Al_2O_3, K_2O, Na_2O and silicate glasses	9.5

surface and was positioned as close as possible to the veneer-core interface. Shear load was applied at a crosshead speed of 0.5 mm/min until fracture occurred. The ultimate load to failure was recorded in Newton (N). The average SBS (MPa) was calculated by dividing the load (N) at which failure occurred by the bonding area (mm^2) as follows:

Shear stress (MPa) = Load (N)/19.625 (mm^2);

These data were used to calculate the mean failure load and standard deviation for each group. The fractured surfaces were visually analyzed with a stereomicroscope (MBX–10, N9116734, St Petersburg, Russia) to determine the failure modes of specimens. Failure modes were classified as follows: cohesive fracture within the veneer, adhesive fracture between the core and veneer, or a combination of both. *t*-test was used to analyze the differences in SBS between zirconia ceramics and their veneering ceramics. An alpha-level of 0.05 was used for all statistical analyses, which were performed using statistical software (SPSS 15.0; SPSS, Inc, Chicago, IL).

RESULTS

Table 3 summarizes the mean values and standard deviations of SBS for the tested zirconia ceramics and veneering ceramics and presents the fracture analysis results in percentage. T-test revealed that there is no significant difference between two groups ($P = 0.551$). Upon examination under the stereomicroscope (×36), the Biodenta group exhibited mostly adhesive failures [Figure 2]; whereas, the Cercon group showed mixed cohesive/adhesive failures [Figure 3].

DISCUSSION

Bond strength measurement of metal ceramic systems was standardized by the International Organization of Standardization through the Schwickerath crack initiation test (three point bending test) and the mean debonding strength/crack initiation strength should be greater than 25 MPa to meet the ISO requirement.[21-23]

Table 3: Summary of shear bond strength values in MPa and failure modes in percentage (%)

Core material	N	Veneering ceramic	Min	Max	Mean	Std. Deviation	Failure modes
Biodenta	10	2 in 1ceram	22.27	36.40	28.22	4.08	20% combined 80% adhesive
Cercon	10	Cercon ceram	22.28	34.49	27.19	3.43	90% combined 10% cohesive

Figure 2: Adhesive failure

Figure 3: Combined (adhesive and cohesive) failure

Due to the brittleness of all-ceramic core materials this test setup cannot be applied to all-ceramic multilayered system.[24] An adequate standardized test set-up and a minimum required bond strength for bi-layered all-ceramic materials has not been determine yet.[25] Few articles have utilized various bond strength test methods for all-ceramic core and veneering ceramic, such as the SBS test,[25-31] three and four point loading test,[32] biaxial flexure strength test,[19] and the microtensile bond strength test.[27,33-35] However, each test has a common limitation which is the difficulty in determining the core-veneer bond strength from applied force at failure on the sample in the specific test setup. In this study, the SBS test method was selected because of its simplicity, such as the ease of specimen preparation, simple test protocol and the ability to rank different products according to bond strength values. But the SBS test has some disadvantages; such as high standard deviations, occurrence of nonuniform interfacial stresses, and the influence from specimen geometry. Therefore, the standardization of specimen preparation, cross-sectional surface area and rate of loading application are important for improving the clinical usefulness of SBS test.[30] In metal-ceramic systems, excessive stresses arising from coefficient of thermal expansion (CTE) mismatch may be compensated to some extent by plastic or elastic deformation of the metallic framework.[36] However, unlike metals, the zirconia framework has a higher rigidity and this feature causes more destructive stress to be formed in the veneer layer of zirconia-based restorations.[37] In some studies, the SBS between metal alloys and porcelain has been found to range from 26.4 to 96.80 MPa.[22,28,38,39] For core-veneered all-ceramic restorations, previous investigations indicated that the core-veneer bond strength ranged from 9.4 MPa to 42 MPa.[25,26,28-31,33-35,40] Mean SBS values obtained in the present study were 27.19 and 28.22 for Cercon and Biodenta groups, respectively, confirming the findings of previous studies.

Mean SBS value of Cercon zirconia to Cercon Ceram has been reported to be 20.19 MPa by Ozkurt *et al*.,[29] 25.43 MPa by Choi *et al*.[30] and 9.4 MPa by Guess *et al*.[28] In our study this value was higher than the previous studies. In a study by Aboushelib *et al*.,[35] Cercon Ceram Express (press-on veneering ceramic) exhibited a bond strength value of 37.9 MPa with the Cercon framework, which was higher than the 27.19 MPa obtained in this study and the values of SBS in previous studies for Cercon Ceram (layering veneer ceramic). Maybe, a key reason for this difference in bond strength lays in the use of press-on veneering ceramic versus the layering veneer ceramic. We could not find any studies evaluating the mechanical properties of Biodenta Zirconia System.

In the present study, specimens of Biodenta group revealed predominantly adhesive failure between the zirconia cores and their veneering ceramics, but in Cercon Group, the most failure pattern was combined. Adhesive failure does not occur in the presence of a good bond between compatible ceramic core and veneering materials,[25] so it seems that the cohesive strength of Biodenta ceramics was higher than the bond strength between Biodenta zirconia and the veneering ceramic. In Cercon group the weakest link was the veneering ceramic. Some studies showed that the bond strength of veneering ceramics to zirconia core seems to be higher than the SBS of the ceramic itself. In SBS tests with zirconia/veneering ceramic composites, adhesive failures were the least failure modes seen in these studies,[25,30,31,33] whereas others claimed that the SBS of veneering ceramics were higher than SBS between core and veneering ceramics and the failure mode observed was mainly combined as adhesive at the interface and cohesive in the veneering ceramic.[28,34,41,42]

Ozkurt *et al.* showed 80% adhesive and 20% combined failure modes for Cercon zirconia ceramics in their study, and Guess *et al.* showed that the intrinsic SBS of Cercon Ceram S (33.6 MPa) was significantly higher than the SBS between Cercon zirconia core and its corresponding ceramic (9.4 MPa) which was not consistent with the findings of our study. We could not find any studies about Biodenta zirconia system. In order to compare the strength of the adherence zone and the mechanical properties of the veneering ceramic, determination of the intrinsic SBS of the veneering ceramic is recommended in future studies.

In the present study, all the test specimens were stored in distilled water at 37°C for one week before testing and thermal cycling was also performed for each specimen, which is important in the simulation of clinical conditions, but some critical aspects must be taken into account when using an *in vitro* method to estimate the clinical performance of materials. First, *in-vitro* information cannot be used as a direct, straightforward prediction for the clinical situation. Secondly, large variations exist in *in vitro* test results.[43] The specimens investigated do not represent clinical shape conditions of dental restorations, but provide a geometry that permits SBS measurement. This was another limitation of our study.

CONCLUSIONS

Within the limitations of the current study it can be concluded that (1) SBS of veneering porcelain to zirconia core for both Cercon and Biodenta systems did not show significant difference and (2) failure mode for Biodenta system was mostly adhesive while it was mostly combined (adhesive and cohesive) for Cercon system.

REFERENCES

1. Tan K, Pjetursson BE, Lang NP, Chan ES. A systematic review of the survival and complication rates of fixed partial dentures (FPDs) after an observation period of at least 5 years. Clin Oral Implants Res 2004;15:654-66.
2. Scurria MS, Bader JD, Shugars DA. Meta-analysis of fixed partial denture survival: Prostheses and abutments. J Prosthet Dent 1998;79:459-64.
3. Creugers NH, Kayser AF, van't Hof MA. A meta-analysis of durability data on conventional fixed bridges. Community Dent Oral Epidemiol 1994;22:448-52.
4. Raigrodski AJ. Contemporary materials and technologies for all-ceramic fixed partial dentures: A review of the literature. J Prosthet Dent 2004;92:557-62.
5. Tinschert J, Natt G, Hassenpflug S, Spiekermann H. Status of current CAD/CAM technology in dental medicine. Int J Comput Dent 2004;7:25-45.
6. Filser F, Kocher P, Weibel F, Luthy H, Scharer P, Gauckler LJ. Reliability and strength of all-ceramic dental restorations fabricated by direct ceramic machining (DCM). Int J Comput Dent 2001;4:89-106.
7. Christel P, Meunier A, Heller M, Torre JP, Peille CN. Mechanical properties and short-term *in-vivo* evaluation of yttrium-oxide-partially-stabilized zirconia. J Biomed Mater Res 1989;23:45-61.
8. Sturzenegger B, Fehér A, Lüthy H, Schumacher M, Loeffel O, Filser F, *et al.* Clinical study of zirconium oxide bridges in the posterior segments fabricated with the DCM system. Schweiz Monatsschr Zahnmed 2000;110:131-9.
9. Vult von Steyern P, Carlson P, Nilner K. All-ceramic fixed partial dentures designed according to the DC-Zirkon technique. A 2-year clinical study. J Oral Rehabil 2005;32:180-7.
10. Sailer I, Fehér A, Filser F, Lüthy H, Gauckler LJ, Schärer P, *et al.* Prospective clinical study of zirconia posterior fixed partial dentures: 3-year follow-up. Quintessence Int 2006;37:685-93.
11. Raigrodski AJ, Chiche GJ, Potiket N, Hochstedler JL, Mohamed SE, Billiot S, *et al.* The efficacy of posterior three-unit zirconium-oxide-based ceramic fixed partial dental prostheses: A prospective clinical pilot study. J Prosthet Dent 2006;96:237-44.
12. Sailer I, Pjetursson BE, Zwahlen M, Hammerle CH. A systematic review of the survival and complication rates of all-ceramic and metal-ceramic reconstructions after an observation period of at least 3 years. Part II: Fixed dental prostheses. Clin Oral Implants Res 2007;18 (Suppl 3):86-96.
13. Guazzato M, Proos K, Sara G, Swain MV. Strength, reliability, and mode of fracture of bilayered porcelain/core ceramics. Int J Prosthodont 2004;17:142-9.
14. Sailer I, Feher A, Filser F, Gauckler LJ, Luthy H, Hammerle CH.

Five-year clinical results of zirconia frameworks for posterior fixed partial dentures. Int J Prosthodont 2007;20:383-8.
15. Walter M, Reppel PD, Boning K, Freesmeyer WB. Six-year follow-up of titanium and high-gold porcelain-fused-to-metal fixed partial dentures. J Oral Rehabil 1999;26:91-6.
16. Coornaert J, Adriaens P, De Boever J. Long-term clinical study of porcelain-fused-to-gold restorations. J Prosthet Dent 1984;51:338-42.
17. Valderhaug J. A 15-year clinical evaluation of fixed prosthodontics. Acta Odontol Scand 1991;49:35-40.
18. al-Shehri SA, Mohammed H, Wilson CA. Influence of lamination on the flexural strength of a dental castable glass ceramic. J Prosthet Dent 1996;76:23-8.
19. Isgro G, Pallav P, van der Zel JM, Feilzer AJ. The influence of the veneering porcelain and different surface treatments on the biaxial flexural strength of a heat-pressed ceramic. J Prosthet Dent 2003;90:465-73.
20. De Jager N, Pallav P, Feilzer AJ. The influence of design parameters on the FEA-determined stress distribution in CAD-CAM produced all-ceramic dental crowns. Dent Mater 2005;21:242-51.
21. ISO 9693 Metal-ceramic bond characterization (Schwickerath crack initiation test). Geneva, Switzerland: International Organization for Standardization; 1999.
22. Akova T, Ucar Y, Tukay A, Balkaya MC, Brantley WA. Comparison of the bond strength of laser-sintered and cast base metal dental alloys to porcelain. Dent Mater 2008;24:1400-4.
23. Craig RG, Powers JM. Restorative dental material. 11 ed. St. Louis: Mosby; 2002.
24. Albakry M, Guazzato M, Swain MV. Fracture toughness and hardness evaluation of three pressable all-ceramic dental materials. J Dent 2003;31:181-8.
25. Al-Dohan HM, Yaman P, Dennison JB, Razzoog ME, Lang BR. Shear strength of core-veneer interface in bi-layered ceramics. J Prosthet Dent 2004;91:349-55.
26. Dundar M, Ozcan M, Comlekoglu E, Gungor MA, Artunc C. Bond strengths of veneering ceramics to reinforced ceramic core materials. Int J Prosthodont 2005;18:71-2.
27. Dundar M, Ozcan M, Gokce B, Comlekoglu E, Leite F, Valandro LF. Comparison of two bond strength testing methodologies for bilayered all-ceramics. Dent Mater 2007;23:630-6.
28. Guess PC, Kulis A, Witkowski S, Wolkewitz M, Zhang Y, Strub JR. Shear bond strengths between different zirconia cores and veneering ceramics and their susceptibility to thermocycling. Dent Mater 2008;24:1556-67.
29. Ozkurt Z, Kazazoglu E, Unal A. *In vitro* evaluation of shear bond strength of veneering ceramics to zirconia. Dent Mater J 2010;29:138-46.
30. Choi BK, Han JS, Yang JH, Lee JB, Kim SH. Shear bond strength of veneering porcelain to zirconia and metal cores. J Adv Prosthodont 2009;1:129-35.
31. Fischer J, Grohmann P, Stawarczyk B. Effect of zirconia surface treatments on the shear strength of zirconia/veneering ceramic composites. Dent Mater J 2008;27:448-54.
32. White SN, Miklus VG, McLaren EA, Lang LA, Caputo AA. Flexural strength of a layered zirconia and porcelain dental all-ceramic system. J Prosthet Dent 2005;94:125-31.
33. Aboushelib MN, de Jager N, Kleverlaan CJ, Feilzer AJ. Microtensile bond strength of different components of core veneered all-ceramic restorations. Dent Mater 2005;21:984-91.
34. Aboushelib MN, Kleverlaan CJ, Feilzer AJ. Microtensile bond strength of different components of core veneered all-ceramic restorations. Part II: Zirconia veneering ceramics. Dent Mater 2006;22:857-63.
35. Aboushelib MN, Kleverlaan CJ, Feilzer AJ. Microtensile bond strength of different components of core veneered all-ceramic restorations. Part 3: double veneer technique. J Prosthodont 2008;17:9-13.
36. Anusavice KJ, Carroll JE. Effect of incompatibility stress on the fit of metal-ceramic crowns. J Dent Res 1987;66:1341-5.
37. Fischer J, Stawarczyk B, Hammerle CH. Flexural strength of veneering ceramics for zirconia. J Dent 2008;36:316-21.
38. Ashkanani HM, Raigrodski AJ, Flinn BD, Heindl H, Mancl LA. Flexural and shear strengths of ZrO2 and a high-noble alloy bonded to their corresponding porcelains. J Prosthet Dent 2008;100:274-84.
39. Joias RM, Tango RN, Junho de Araujo JE, Junho de Araujo MA, Ferreira Anzaloni Saavedra Gde S, Paes-Junior TJ, *et al.* Shear bond strength of a ceramic to Co-Cr alloys. J Prosthet Dent 2008;99:54-9.
40. Fischer J, Stawarczyk B, Sailer I, Hammerle CH. Shear bond strength between veneering ceramics and ceria-stabilized zirconia/alumina. J Prosthet Dent 2010;103:267-74.
41. Studart AR, Filser F, Kocher P, Luthy H, Gauckler LJ. Mechanical and fracture behavior of veneer-framework composites for all-ceramic dental bridges. Dent Mater 2007;23:115-23.
42. Kim B, Zhang Y, Pines M, Thompson VP. Fracture of porcelain-veneered structures in fatigue. J Dent Res 2007;86:142-6.
43. Hadavi F, Hey JH, Ambrose ER, Louie PW, Shinkewski DJ. The effect of dentin primer on the shear bond strength between composite resin and enamel. Oper Dent 1993;18:61-5.

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