#### **Original Article**

# **Evaluation of the Effect of Porcelain Laminate Thickness on Degree of Conversion of Light Cure and Dual Cure Resin Cements Using FTIR**

#### Maryam Hoorizad Ganjkar<sup>1</sup>, Haleh Heshmat<sup>1</sup>, Reza Hassan Ahangari<sup>2</sup>

<sup>1</sup>, Member of Dental Material Research Centure, Islamic Azad University, Dental Branch, Tehran, Iran Islamic Azad University, Dental Branch, Tehran, Iran.

<sup>2</sup> Postgraduate Student, Dept. of Operative Dentistry, Islamic Azad University, Dental Branch, Tehran, Iran.

# **KEY WORDS**

Resin Cements; Polymerization; Spectroscopy; Fourier Transform Infrared; Ceramics;

# ABSTRACT

**Statement of the Problem:** Increasing the thickness of the veneering porcelain may affect the polymerization of resin cements. Incomplete polymerization of resin cements can lead to compromised quality of restoration and decrease the longevity of indirect restorations.

**Purpose:** This study sought to assess the effect of IPS Empress porcelain thickness on the degree of conversion of light-cure and dual-cure resin cements using Fourier transform infrared spectroscopy.

**Materials and Method:** In this experimental study, IPS Empress porcelain discs (A2 shade) with 10mm diameter and 0.5, 1 and 1.5 mm thicknesses were fabricated. Choice2 (Bisco, USA) and Nexus3 (Kerr, USA) resin cements were light cured through the three porcelain thicknesses in two groups of 3 samples using a LED light-curing unit (LEDemetron II; Kerr, USA). The control group samples were cured individually with no porcelain disc. The degree of conversion of resin cements was determined using FTIR (Bruker; Equinox55, Germany). The data were analyzed using Dunn's test.

**Results:** The degree of conversion (in percent) beneath the 0.5, 1.5 and 2 mm thicknesses of IPS Empress was  $68.67\pm0.88$ ,  $71.06\pm0.94$  and  $72.51\pm0.41$  for Choice2 resin cement and  $69.60\pm2.12$ ,  $69.64\pm1.63$  and  $69.24\pm2.12$  for Nexus3, respectively. Porcelain thickness and type of resin cement had no significant effect on degree of conversion ( $p \ge 0.05$ ).

**Conclusion:** It seems that increasing the porcelain thickness by up to 1.5 mm has no adverse effect on degree of conversion of both dual cure and light cure resin cements evaluated in this study.

**Corresponding Author:** Hassan Ahangari R., N. 4, 10<sup>th</sup> Neyestan, Pasdaran Street, Dental Faculty of Tehran Islamic Azad University, Tehran, Iran. Postal code: 19585/175 Tel: +98-21-22564571 Email: ha\_reza\_ah@ yahoo.com

Cite this article as: Hoorizad Ganjkar M., Heshmat H., Hassan Ahangari R. Evaluation of the Effect of Porcelain Laminate Thickness on Degree of Conversion of Light Cure and Dual Cure resin Cements Using FTIR. J Dent Shiraz Univ Med Sci., 2017 March; 18(1): 30-36.

#### Introduction

Received December 2015;

Accepted March 2016;

Received in revised form February 2016;

Advances in dentistry enable more conservative esthetic dental treatments. Since 1980s, porcelain veneers have been increasingly used for the anterior tooth restorations. With increasing in esthetic features and more predictable bonding techniques, porcelain veneers are now a reliable treatment option. [1] Selection of a suitable luting agent plays an integral role in longevity and esthetics of porcelain veneers. Resin cements have higher flexural, compressive, shear and tensile strengths than other types of cements and increase the retention and fracture resistance of indirect ceramic restorations. [2-9] Appropriate polymerization of these cements is necessary to provide ideal properties and it plays a critical role in achieving an ideal bond between the porcelain and tooth structure. [10-11] Incomplete polymerization

of these cements increases their solubility and degradation at the finish line. The most important advantage of light-cure resin cements is their easy application. However, thickness, opacity, and color shade of the veneer may decrease the light intensity of the transmitted light through the porcelain when luting the restoration with these cements. So, light-cure cements carry the risk of incomplete polymerization. [12-13] To overcome this problem, dual-cure resin cements were introduced. Theoretically, polymerization of dual-cure cements can be initiated by a very low light intensity and continues by delayed chemical reactions; therefore, dual-cure cements benefit from the properties of both light-cure and self-cure cements. [12] However, the degree of conversion (DC) of dual-cure cements depends on the material; in other words, some systems are more dependent on light-activation than others. [14]

The effect of different factors on DC of resin cements beneath the porcelain veneers has been extensively studied. Most previous studies in this regard have used the Knoop or Vickers hardness tests. Although it is believed that hardness is strongly correlated with the DC, [14] more accurate techniques are also available for this purpose which can determine the number of carboncarbon double bonds (C=C) present in resin matrix qualitatively and quantitatively such as nuclear magnetic resonance (NMR), high performance liquid chromatography (HPLC), gel permeation chromatography (CPC), multiple internal reflection (MIR), infrared spectroscopy IR and FTIR spectroscopy. [15-17] It has been shown that light transmission through porcelain can be as little as 2% to 3%, with a porcelain thickness ranging from. 5 to 2 mm. Therefore, increasing the polymerization time may be prudent to ensure adequate polymerization. [18] Cho et al. [19] showed that increasing the e.max Press thickness by up to 1.2mm had no effect on the DC of light-cure resin cements. When using 1.2mm thick porcelain, DC of light-cure cement was significantly higher than that of dual-cure cement. Runnacles et al. [20] indicated that increasing the porcelain thickness by up to one millimeter had no effect on the DC of light-cure resin cements. Palta et al. [21] demonstrated that the light transmittance was decreased with increased material thickness and reported that the ceramic thickness exerted the highest influence on the transmitted irradiance, closely followed by color.

Moraes *et al.* [22] demonstrated that increasing the porcelain thickness decreased the intensity of transmitted light, and light irradiation for an adequate period of time was required to enhance the polymerization of dual-cure resin cements. Nonetheless, increasing the porcelain thickness by up to two millimeters had no effect on the final DC. [22] Kilinc *et al.* [23] showed that the porcelain thickness affected the microhardness of light-cure and dual-cure resin cements more than its color shade. Pazin *et al.* [24] demonstrated that dualcure resin cements required light for initiation of polymerization, and the porcelain thickness was the most important factor responsible for decreased microhardness of dual-cure resin cements. The type of light curing unit, however, had no effect in this regard. [24]

Considering the current controversies in the results of studies and the shortcomings of previous studies and also the growing use of porcelain veneers and lightcure and dual-cure resin cements, this study was aimed to assess the effect of increasing IPS-Empress porcelain thickness on DC of Choice2 light-cure and Nexus3 dual-cure resin cements by using FTIR spectroscopy.

## **Materials and Method**

In this experimental study, porcelain discs were fabricated of A2 shade of IPS Empress ceramic (Ivoclar; Vivadent, Liechtenstein) with 10mm diameter and 0.5, 1 and 1.5mm thicknesses using wax models and the lost-wax technique, based on manufacture instruction cylindrical patterns were made with organic wax (Thowax; Yeti Dentalprodukte, Engen, Germany), invested with phosphate- based material (Esthetic Speed, Ivoclar Vivadent), and heated at 8508 C for 1 h in a ceramic oven (Austromat M; Dekema Dental-Keramiko<sup>°</sup> fen, Freilassing, Germany). The ceramic was then heat pressed into the molds using the EP600 furnace (Ivoclar Vivadent).

Based on the type of cement used (Choice 2 lightcure or Nexus3 dual-cure cements), samples were divided into two groups. Based on the porcelain thickness, each group was divided into four subgroups (including a control group without porcelain). Therefore, 24 samples were divided into eight groups of three (n=3).

To measure the DC (%) using FTIR spectroscopy, uncured resin cement samples were first placed in FTIR in such a way that the red laser beam, which indicates

Material	Brand name	Manufacturing company	Composition	Serial number	
Leucite porcelain	IPS-Empress	Ivoclar, Vivadent, Schaan,	SiO <sub>2</sub> -Al <sub>2</sub> O <sub>3</sub> , K <sub>2</sub> O, Na <sub>2</sub> O <sub>3</sub> , Ce <sub>2</sub> O <sub>2</sub> ,	F68744	
		Liechtenstein	$B_2O_3$ , Cao, BaO, TiO <sub>2</sub>		
Light-cure resin cement	Choice2	Bisco, USA	BIS-GMA, TEG DMA, UDMA	0900011425	
Dual-cure resin cement	Nexus3	Kerr, Orange, USA	Bis-GMA	400004216	
LED	LEDemetron II	Kerr, Orange, USA	-	762004654	
FTIR spectroscopy	Equinox 55	Bruker, Germany	-	-	

 Table 1: Materials used in the study

the path of infrared beam passed right from the center of the sample. The absorption curve of each sample was drawn using the FTIR spectra. (Table 1)

To obtain 50 $\mu$  thickness of resin cements, porcelain discs and a transparent polyethylene film were placed on uncured resin cement and 250mg load was applied on the samples for two minutes. (Figure 1a and 1b) [22] The curing was done by using a LED lightcuring unit (LEDemetron II; Kerr, Orange, CA USA) with a light intensity of 600mW/cm<sup>2</sup> for 40 seconds using an overlapping technique. (Figure 1c) Resin cement samples were fabricated as such beneath the porcelain discs with 0.5, 1 and 1.5mm thicknesses and a control group with no porcelain disc. (Figure 1d) The samples underwent FTIR spectroscopy and the absorption curves were drawn for each sample using FTIR spectra. (Figure 2) The DC of samples was determined using the equation below:

# DC (%) = $[1-(A/B) \times 100]$

Where A was aliphatic absorption of C=C/ aromatic absorption of C=C of polymer and B was aliphatic absorption of C=C/aromatic absorption of C=C of monomer. Aliphatic absorption peak of C=C at 1637cm and aromatic absorption peak of C=C at 1609 cm were considered as internal standards.

## Statistical analysis

The Kruskal Wallis test showed that the data did not have a normal distribution. Thus, the Dunn's test was used for pairwise comparison of porcelain thicknesses. Data were analyzed using SPSS version 11.5 software (Microsoft, IL, USA) and p < 0.05 was considered statistically significant.

# Results

Chocie3 and Nexus3 resin cements before and after light curing were subjected to FTIR spectroscopy. The DC under the 0.5, 1.5 and 2 mm thicknesses of IPS Empress was  $68.67\pm0.88$ ,  $71.06\pm0.94$  and  $72.51\pm0.41$ , respectively for Choice2, which were not significantly different (p> 0.05). (Table 2) These values were  $69.60\pm2.12$ ,  $69.64\pm1.63$  and  $69.24\pm2.12$  for Nexus3 respectively, though not significantly different either (p> 0.05). (Table 3)

**Table 2:** The mean and standard deviation of degree of conversion of Choice 2 resin cement in the experimental and control groups

Degree of Conve	rsion Thickness(mm)	Mean	Standard Deviation	P value
0mm		70.74	±2.32	
0.5mm		68.67	$\pm 0.88$	0.79
1mm		71.06	±0.94	0.79
1.5mm		72.51	±0.41	

The DC of the control groups was  $70.74\pm2.12$  for Choice2 and  $65.38\pm2.25$  for Nexus3; no significant difference was noted in the DC among the experimental and control groups either (*p*> 0.05).



**Figure 1a:** Uncured resin cement and a transparent polyethylene film, **b:** Uncured resin cement and a transparent polyethylene film, **c:** The curing was done by using a LED light-curing unit, **d:** Resin cement samples were fabricated as such beneath the porcelain discs with 0.5, 1 and 1.5mm thicknesses and a control group with no porcelain disc

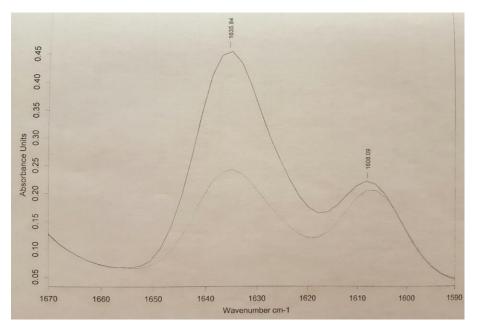


Figure 2: The samples underwent FTIR spectroscopy and the absorption curves were drawn for each sample using FTIR spectra

Table 3: The mean and standard deviation of degree of con-
version of Nexus3 resin cement in the experimental and con-
trol groups

Degree of Con	version Thickness(mm)	Mean	Standard Deviation	P value
0mm		65.38	±2.25	
0.5mm		69.60	±2.12	0.82
1mm		69.64	±1.63	0.82
1.5mm		69.24	±2.12	

#### Discussion

The results of this experimental study showed that increasing the IPS Empress porcelain thickness from 0.5 to 1.5 mm had no significant effect on DC of Choice2 light-cure and Nexus3 dual-cure resin cements. No significant difference was noted in DC of experimental and control groups either.

Light-cure and dual-cure resin cements require optimal lighting for adequate polymerization. [25] In dualcure cements, the chemically cured cement component may compensate for the decreased transmitted light; however, it has been shown that polymerization of the chemical component of dual-cure cements alone cannot yield the maximum DC of monomers. [26-27] Therefore the DC could be influenced by the microstructure of porcelain. [20]

The crystalline phase of ceramic affects the DC of resin cements via light scattering and diffraction. According to De Souza *et al.* [14] the light scattering centers decrease light transmission and subsequently reduce the DC of resin cements and confer an opaque appearance to the porcelain surface. Comparison of the translucency of lithium disilicate glass ceramics and Leucite ceramics revealed that lithium disilicate appeared more opaque due to the orientation of the crystalline phase and DC further decreased in this ceramic compared to Leucite ceramic. [14] Complete polymerization is critical for both these cements because incomplete polymerization of resin cements decreases their mechanical properties, dimensional stability and bond to tooth structure and results in microleakage, decreased biocompatibility, discoloration and post-operative tooth hypersensitivity. [28-30]

IPS-Empress II ceramic can be used for fabrication of different types of indirect restorations such as veneers, inlays, onlays, and crowns. The trend toward natural view for laminate veneers led to introduction of more translucent ceramics. Studies have shown that IPS- Empress II has higher translucency than that of reinforced ceramics such as Procera, In-Ceram Alumina and In-Ceram zirconia. [31-33]

No specific curing time has been recommended for different thicknesses and shades of porcelain by the manufacturers. Generally, 40 seconds of curing with 400 mW/cm<sup>2</sup> light intensity (yielding 16000mJ energy) is sufficient for complete polymerization when light is directly irradiated on the material surface. [34] Evidence shows that the use of higher energy is not directly correlated to the DC. [14] Thus, we also performed 40 seconds of light curing with a light intensity of 600 mW/cm<sup>2</sup> using the overlapping technique. Therefore, all cement areas received maximum light for adequate polymerization. Nonetheless, future studies are required to evaluate the effects of different light curing protocols on polymerization of resin cements.

Öztürk *et al.* [35] assessed the effect of ceramic shade and thickness on the micromechanical properties of light-cure cements beneath the IPS-Empress ceramic using hardness tests. They found that ceramic thickness was more effective on the micromechanical properties of the resin cements than ceramic shade.

In present study, different thickness of ceramic with the same shade was evaluated. In a similar study Cho *et al.* [19] demonstrated that increasing the porcelain thickness by up to 1.2mm had no effect on DC of light-cure resin cements. Using 1.2mm thickness of porcelain, the DC of light-cure cement was found to be significantly higher than that of dual-cure cement, which is in line with the current study.

Runnacles *et al.* [20] showed that increasing the porcelain thickness by up to one millimeter had no effect on the DC. Using 1.5mm thickness of IPS e.max LT ceramics, the DC of cement was found to be significantly lower than that of the control group. The difference between their results and ours may be due to the optical properties of the ceramics used. [20] In a similar study, Yuh *et al.* [13] assessed the DC of light-cure cements beneath the IPS-Empress ceramics using FTIR spectroscopy and concluded that ceramics with 0.5, 1 and 1.5mm thicknesses had no significant effect on DC of resin cements compared to the control group, which is in accordance with our findings. [13]

Moraes *et al.* [22] evaluated the effect of light and duration of curing on DC of dual-cure cements beneath different thicknesses of porcelain using FTIR spectroscopy. They measured the DC of cements beneath 0, 0.7, 1.4 and 2mm thicknesses of porcelain after curing for 40 seconds and one, two, four, six, eight and 10 minutes. They showed that increasing the thickness of porcelain decreased the transmitted light intensity and concluded that adequate duration of light curing is necessary to improve the DC of resin cements. [22]

Kilinc *et al.* [23] evaluated the effect of color shade and thickness of porcelain on polymerization of light-cure and dual-cure resin cements and showed that increasing the ceramic thickness to three millimeters or

higher affected the microhardness of cement, and the microhardness of light-cure resin cements was lower than that of dual-cure cements and the control group. They also confirmed an association between the light intensity and hardness and stated that the porcelain thickness had a greater impact on hardness than the porcelain shade. They measured microhardness in their study, which is a functional method. Moreover, the thickness of cement used was not similar to the clinically ideal thickness of cement. [23]

Pazin *et al.* [24] assessed the effect of porcelain and light curing unit on light transmission through the ceramics and the DC of dual-cure cements. They measured the Knoop hardness number and showed that cements beneath 1.4-2mm ceramics had lower hardness than the control groups of light-cure, self-cure and dualcure cements; these findings are in contrast to the current results. [24] They measured the Knoop hardness number as a function of DC, which is not accurate. Also, the cement thickness was one millimeter, which is different from the clinically ideal cement thickness. [24] In the current study, we tried to simulate the cement thickness in the clinical setting.

#### Conclusion

Within the limitations of this *in vitro* study, the results showed that increasing the IPS Empress porcelain thickness from 0.5 to 1.5mm had no adverse effect on the DC of Choice2 light-cure and Nexus3 dual-cure resin cements. Thus, these cements can be used as luting agents for porcelain veneers with up to 1.5mm thickness; however, discoloration and esthetic complications in the body and margins of the veneers cemented with dual-cure cements in the long-term must be taken into account.

## **Conflict of Interest**

None to declare.

### References

- Rasetto FH, Driscoll CF, von Fraunhofer JA. Effect of light source and time on the polymerization of resin cement through ceramic veneers. J Prosthodont. 2001; 10: 133-139.
- [2] Blatz MB, Sadan A, Martin J, Lang B. In vitro evaluation of shear bond strengths of resin to densely-sintered high-

purity zirconium-oxide ceramic after long-term storage and thermal cycling. J Prosthet Dent. 2004; 91: 356-362.

- [3] Lee IB, An W, Chang J, Um CM. Influence of ceramic thickness and curing mode on the polymerization shrinkage kinetics of dual-cured resin cements. Dent Mater. 2008; 24: 1141-1147.
- [4] Piwowarczyk A, Lauer HC. Mechanical properties of luting cements after water storage. Oper Dent. 2003; 28: 535-542.
- [5] Begazo CC, de Boer HD, Kleverlaan CJ, van Waas MA, Feilzer AJ. Shear bond strength of different types of luting cements to an aluminum oxide-reinforced glass ceramic core material. Dent Mater. 2004; 20: 901-907.
- [6] Piwowarczyk A, Lauer HC, Sorensen JA. The shear bond strength between luting cements and zirconia ceramicsafter two pre-treatments. Oper Dent. 2005; 30: 382-388.
- [7] Sen D, Poyrazoglu E, Tuncelli B. The retentive effects of pre-fabricated posts by luting cements. J Oral Rehabil. 2004; 31: 585-589.
- [8] Behr M, Rosentritt M, Mangelkramer M, Handel G. The influence of different cements on the fracture resistance andmarginal adaptation of all-ceramic and fiber-reinforced crowns. Int J Prosthodont. 2003; 16: 538-542.
- [9] Zidan O, Ferguson GC. The retention of complete crowns prepared with three different tapers andluted with four different cements. J Prosthet Dent. 2003; 89: 565-571.
- [10] Chan KC, Boyer DB. Curing light-activated composite cement through porcelain. J Dent Res. 1989; 68: 476-480.
- [11] Peters AD, Meiers JC. Effect of polymerization mode of a dual-cured resin cement on time-dependent shear bond strength to porcelain. Am J Dent. 1996; 9: 264-268.
- [12] Lee IB, Um CM. Thermal analysis on the cure speed of dual cured resin cements under porcelain inlays. J Oral Rehabil. 2001; 28: 186-197.
- [13] Yuh CS, Kim JH, Kim SJ, Lee YK, Shim JS. Comparison of the degree of conversion of light-cured resin cement in regard to porcelain laminate thickness, light source and curing time using FT-IR. The Journal of Korean Academy of Prosthodontics. 2009; 47: 416-423.
- [14] De Souza G, Braga RR, Cesar PF, Lopes GC. Correlation between clinical performance and degree of conversion of resin cements: a literature review. J Appl Oral Sci. 2015; 23: 358-368.
- [15] Kumbuloglu O, Lassila LV, User A, Vallittu PK. A study of the physical and chemical properties of four resincomposite luting cements. Int J Prosthodont. 2004; 17: 35-

7-363.

- [16] Daronch M, Rueggeberg FA, De Goes MF. Monomer conversion of pre-heated composite. J Dent Res. 2005; 84: 663-667.
- [17] Braga RR, Ferracane JL. Contraction stress related to degree of conversion andreaction kinetics. J Dent Res. 2002; 81: 114-118.
- [18] Craig RG, Powers JM. Restorative dental materials. 12th ed. St.Louis Missouri: Mosby; 2006. p. 493.
- [19] Cho SH, Lopez A, Berzins DW, Prasad S, Ahn KW. Effect of Different Thicknesses of Pressable Ceramic Veneers on Polymerization of Light-cured and Dual-cured Resin Cements. J Contemp Dent Pract. 2015; 16: 347-352.
- [20] Runnacles P, Correr GM, Baratto Filho F, Gonzaga CC, Furuse AY.Degree of Conversion of a Resin Cement Light-Cured Through Ceramic Veneers of Different Thicknesses and Types. Braz Dent J. 2014; 25: 38-42.
- [21] Palta N, Secilmis A, Yazicioglu H. Effect of monolithic zirconia on the degree of conversion of two resin cements analyzed by FT-IR/ATR spectroscopy. J Adhes Sci Technol 2016; 30: 972-982.
- [22] Moraes RR, Brandt WC, Naves LZ, Correr-Sobrinho L, Piva E. Light- and time-dependent polymerization of dualcured resin luting agentbeneath ceramic. Acta Odontol Scand. 2008; 66: 257-261.
- [23] Kilinc E, Antonson SA, Hardigan PC, Kesercioglu A. The effect of ceramic restoration shade and thickness on thepolymerization of light- and dual-cure resin cements. Oper Dent. 2011; 36: 661-669.
- [24] Pazin MC, Moraes RR, Gonçalves LS, Borges GA, Sinhoreti MA, Correr-Sobrinho L. Effects of ceramic thickness and curing unit on light transmission through leucitereinforced material and polymerization of dual-cured luting agent. J Oral Sci. 2008; 50: 131-136.
- [25] Koishi Y, Tanoue N, Atsuta M, Matsumura H. Influence of visible-light exposure on colour stability of current dual- curable luting composites. J Oral Rehabil. 2002; 29: 387-393.
- [26] Caughman WF, Chan DC, Rueggeberg FA. Curing potential of dual-polymerizable resin cements insimulated clinical situations. J Prosthet Dent. 2001; 86: 101-106.
- [27] el-Mowafy OM, Rubo MH, el-Badrawy WA. Hardening of new resin cements cured through a ceramic inlay. Oper Dent. 1999; 24: 38-44.
- [28] Bagis YH, Rueggeberg FA. The effect of post-cure heating on residual, unreacted monomer in a commercial resin c-

omposite. Dent Mater. 2000; 16: 244-247.

- [29] Hosoya Y. Five-year color changes of light-cured resin composites: influence of light-curing times. Dent Mater. 1999; 15: 268-274.
- [30] Janda R, Roulet JF, Latta M, Kaminsky M, Rüttermann S. Effect of exponential polymerization on color stability of resin-based filling materials. Dent Mater. 2007; 23: 696-704.
- [31] Barizon KT, Bergeron C, Vargas MA, Qian F, Cobb DS, Gratton DG, et al. Ceramic materials for porcelain veneers: part II. Effect of material, shade, and thickness on translucency. J Prosthet Dent. 2014; 112: 864-870.
- [32] Heffernan MJ, Aquilino SA, Diaz-Arnold AM, Haselton DR, Stanford CM, Vargas MA. Relative translucency of

six all-ceramic systems. Part I: core materials. J Prosthet Dent. 2002; 88: 4-9.

- [33] Heffernan MJ, Aquilino SA, Diaz-Arnold AM, Haselton DR,Stanford CM, Vargas MA. Relative translucency of six all-ceramic systems. Part II: core and veneer materials. J Prosthet Dent. 2002; 88: 10-15.
- [34] Jung H, Friedl KH, Hiller KA, Haller A, Schmalz G. Curing efficiency of different polymerization methods through ceramicrestorations. Clin Oral Investig. 2001; 5: 156-161.
- [35] Öztürk E, Bolay Ş, Hickel R, Ilie N. Effects of ceramic shade and thickness on the micro-mechanical properties of a light-cured resin cement in different shades. Acta Odontol Scand. 2015; 73: 503-507.