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Blue-Light Transmittance of Esthetic Monolithic CAD/CAM Materials With Respect to Their Composition, Thickness, and Curing Conditions

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Clinical Relevance

The amount of light passing through VITA ENAMIC restorations is reduced and less light-sensitive dual-curing cements should be used for cementation.

SUMMARY

Determining the amount of blue light (360-540nm) passing through nine monolithic computer-aided design/computer-aided manufacturing (CAD/CAM) materials depends on material thickness, initial irradiance, and the distance between the curing unit and the specimen's surface. A total of 180 specimens of two thicknesses (1 mm and 2 mm, n=10/subgroup) were fabricated from TelioCAD, VITA CAD-Temp (VCT), experimental nanocomposite, LAVA Ultimate (LU), VITA ENAMIC (VE), VITA MarkII (VM), IPS EmpressCAD (IEC), IPS e.maxCAD (IEM), and CELTRA DUO (CD). The irradiance passing through the CAD/CAM materials and thicknesses was measured using a light-emitting-diode curing unit with standard-power, high-power, and plasma modes by means of a USB4000 spectrometer. The curing unit was placed directly on the specimen's surface at 2- and 4-mm distances from the specimen's surface. Data were analyzed using a multivariate analysis and one-way analysis of variance with the *post hoc* Scheffé test ($p<0.05$). The highest transmitted irradiance was measured for VM and LU, followed by VCT and IEC, while the lowest values showed VE, followed by IEM and CD. The highest transmitted irradiance was recorded by exposing the material to the plasma mode, followed by the high- and standard-power modes. The measured irradiance was

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decreased by increasing the specimen's thickness from 1 to 2 mm. Fewer differences were measured when the curing unit was placed at 0 or 2 mm from the specimen's surface, and the irradiance passing through the specimens was lower at a distance of 4 mm.

INTRODUCTION

There is a range of polymer-, composite-, or ceramic-based esthetic monolithic computer-aided design/computer-aided manufacturing (CAD/CAM) materials presently available on the market. Dentists can process these materials using CAD/CAM technology in minutes while the patient is seated in the chair. Industrially prefabricated CAD/CAM materials appear to be more structurally reliable for dental applications than materials that are manually processed under dental laboratory conditions. Polymeric-based CAD/CAM materials showed significantly higher mechanical properties compared to conventional temporaries[1-5] and can be used for long-term restorations.[6] Standard monolithic CAD/CAM materials for permanent restorations contain lithium disilicate glass ceramics,[7-9] feldspathic silicate ceramics,[10] and feldspar-based leucite-reinforced glass ceramics[11,12] but also newly developed materials, such as a resin-based block nanocomposite,[13] an experimental isofiller resin-based composite with "nano additives,"[14] and a novel interpenetrating network ceramic (VITA ENAMIC).[15-18] Similarly, a zirconia-reinforced lithium silicate ceramic (CELTRA DUO) offers the opportunity for a permanent restoration. Since the latter materials are quite new, there is little scientific knowledge about them.

In addition to the particular restorative material, the esthetics of a CAD/CAM restoration also depends on the chosen luting cement. Traditional cements, such as glass ionomer and zinc phosphate, are usually very opaque and can therefore distort the color of the esthetic restoration. Esthetic glass-ceramic restorations also demonstrated better long-term clinical stability when cemented with resin composite cements rather than traditional cements.[19,20] An *in vitro* study also reported on the increase of fracture resistance of adhesive-luted crowns compared to traditionally cemented ones.[21] Esthetic restorative materials with lower mechanical properties require reinforcement by adhesive cementation.[21-23] Dual-cure resin adhesive composite cements are often used for these indications. An advantage of these resin composite cements is that they can cure both chemically (autocuring) and via visible-light activation. Such resin composite cements include a catalyst paste with a chemical activator (benzoyl peroxide) and a base paste containing blue-light–cured resin cement as well as an amine responsible for the beginning of the autocuring reaction.[24,25] After mixing both pastes and with a supply of light, the polymerization takes place through physical (photo) and chemical (redox) activation.[24] The working time is controlled by inhibitors of the autocure reaction or by the amount of activators in the polymerization.[26] Nevertheless, when not properly photoactivated, dual-cure resin cements may present reduced degrees of conversion.[27-29] This in turn leads to lower mechanical properties, such as hardness[25] and flexural and compressive strength,[25,30] and higher solubility.[31] Studies have also shown that the absence of light negatively influences the long-term bond strength.[32,33] The impact of light on the polymerization process of dual-cure luting resin composite cements is material dependent.[34] Light-cured resin cements and, in particular, resin composites have thus become an important part of modern, minimally invasive treatment.[35] These resin composites consist of a single paste with a visible-light activation of a photosensitive component (eg, camphorquinone) and an amine. The visible light activates the photosensitive initiator to generate a short-lived excited-state species that complexes with the tertiary amine to promote a sequential electron and proton transfer that creates the active initiating radicalable to start the polymerization.[24]

Direct resin composites are densely filled with inorganic particles and therefore provide high mechanical properties. However, increasing filler parts in resin composites also enhances viscosity, which could reduce the ease of clinical application. Options to improve the rheological behavior by using ultrasonics[36] or preheating[37-39] are of primary interest to the clinician.

Along with improvements of the mechanical properties, cementation using light-luting resin composites has several benefits in clinical applications. Light-cured resin composites have long working times, with the polymerization beginning immediately after the exposure of the material to light.[33]

Many resin composites indicate a high sensitivity to the additional occurrence of blue light, which significantly affects their mechanical properties.[34] The amount of light passing through restoration materials and the translucency of the materials are thus essential elements of cementation with dual-

Table 1: *Product Name, Abbreviation, Material Type, Lot Number, and Color of CAD/CAM Materials Evaluated*

Material (Abbreviation)	Manufacturer	Material Type	Lot Number	Color
Telio CAD (TC)	Ivoclar Vivadent, Schaan, Liechtenstein	PMMA	N73354	LT A2
VITA CAD-Temp (VCT)	VITA Zahnfabrik, Bad Säckingen, Germany	PMMA	CE 0124	2M2
Experimental nanocomposite (TEC)	Ivoclar Vivadent	Resin composite	28923	HT A2
LAVA Ultimate (LU)	3M ESPE, Seefeld, Germany	Resin composite	N372985	HT A2
VITA ENAMIC (VE)	VITA Zahnfabrik	Hybrid ceramic	33000	3M2
VITA Mark II (VM)	VITA Zahnfabrik	Feldspar ceramic	N502353	A2
IPS Empress CAD (IEC)	Ivoclar Vivadent	Leucite glass ceramic.	R39335	LT A2
IPS e.max CAD (IEM)	Ivoclar Vivadent	Lithium disilicate glass ceramic	R37085	LT A2
CELTRA Duo (CD)	DeguDent, Hanau, Germany	Zirconia-reinforced lithium silicate	18015733	LT A2

curing resin composite cements. A previous study investigated the amount of blue light passing through differently colored zirconia ceramics and recommended the use of less light-sensitive dual-cured cements for restorations thicker than 1.5 mm in light-shaded zirconia and 0.5 mm in darker-shaded zirconia.[40]

This study investigated the amount of blue light passing through nine CAD/CAM monolithic materials. Four hypotheses were tested: 1) different CAD/CAM materials, 2) material thickness, 3) curing unit distance to the specimen, and 4) initial irradiance level (curing modes) show no impact on the transmitted irradiance through the CAD/CAM materials.

METHODS AND MATERIALS

Nine different CAD/CAM monolithic materials were selected: TelioCAD (TC; PMMA based; Ivoclar Vivadent, Schaan, Liechtenstein), VITA CAD-Temp (VCT; PMMA based and 10% filled with prepolymers; VITA Zahnfabrik, Bad Säckingen, Germany), experimental nanocomposite (TEC; filled composite; Ivoclar Vivadent) LAVA Ultimate (LU; filled composite; 3M ESPE, Seefeld, Germany), VITA ENAMIC (VE; interpenetrating network ceramic; VITA Zahnfabrik), VITA Mark II (VM; feldspar ceramic; VITA Zahnfabrik), IPS EmpressCAD (IEC; leucite glass ceramic; Ivoclar Vivadent), IPS e.max CAD (IEM; lithium disilicate glass ceramic; Ivoclar Vivadent), and CELTRA DUO (CD; zirconia-reinforced lithium silicate ZLS; DeguDent, Hanau, Germany) (Table 1). CAD/CAM blocks were cut using a low-speed diamond saw in 1- and 2-mm-thick slices (n=10) (Well 3241, Well Diamantdrahtsägen, Mannheim, Germany) under water cooling.

All specimens were polished up to 1 μm with a diamond suspension (Struers, Ballerup, Denmark) and then ultrasonically cleaned for 5 minutes in distilled water. The final dimensions of all specimens were $10 \times 10 \times 1$ mm $\pm$ 0.05 and 10×10 mm $\times 2 \pm$ 0.05 mm.

The analysis of the irradiance passing through the CAD/CAM materials was performed using the blue-violet light-emitting-diode polymerizing unit (VALO, Ultradent, South Jordan, UT, USA) on a laboratory-grade National Institute of Standards and Technology–referenced USB4000 Spectrometer (MARC System, Bluelight Analytics Inc, Halifax, NS, Canada) (n=10). The miniature fiber-optic USB4000 spectrometer uses a 3648-element Toshiba linear charge-coupled-device array detector and high-speed electronics. The spectrometer was spectroradiometrically calibrated using Ocean Optics' NIST-traceable light source (300-1050 nm) (Figure 1). The system uses a CC3-UV Cosine Corrector to collect radiation over a 180-degree field of view, thus mitigating the effects of optical interference associated with light collection sampling geometry.

The irradiance (wavelength ranged from 360 to 540 nm) passing through the nine different CAD/CAM materials and material thicknesses (1 and 2 mm) was measured at the bottom of the specimens at a velocity of 16 records per second. The sensor was triggered at 20 mW. The curing unit was placed directly on the specimen's surface as well as 2 and 4 mm away from the specimen's surface. Three curing modes were examined (standard-power, high-power, and plasma modes), resulting in 180 measurements (2 material thicknesses $\times$ 3 exposure modes $\times$ 3 distances $\times$ 10 specimens) for each ceramic.

Additionally, one randomly selected specimen for each material was analyzed in a scanning electron microscope (SEM; Supra 55 VP, Zeiss, Jena, Germany). For this, the VM and IEC were etched for 60 seconds and IEM and CD for 30 seconds with 9% hydrofluoric acid (Ultradent, lot B6X7B). The specimens were then ultrasonically cleaned and subsequently gold sputtered for 20 seconds. Surface

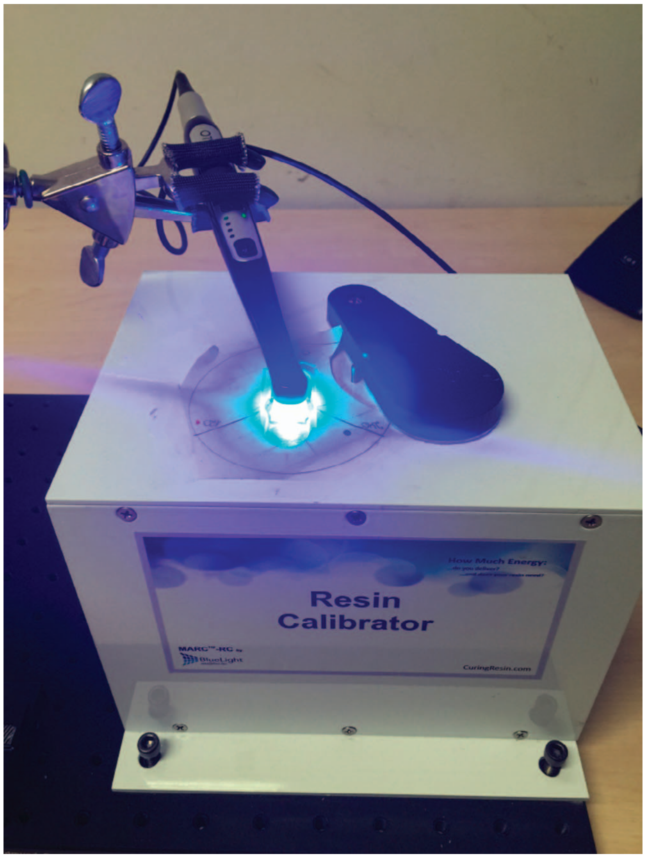

Figure 1. *Testing apparatus.*

topography analyses were performed using an inLens detector at 10 kV with a working distance of 4.5-6.0 mm.

A multivariate analysis (general linear model) assessed the effect of the material, material thickness (1 and 2 mm), distance from the surface (0, 2, and 4 mm), and curing mode (standard-power, high-power, and plasma modes) on the irradiance passing through the CAD/CAM materials. The statistical comparisons between the groups were performed using one-way analysis of variance followed by the *post hoc* Scheffé test; *p*-values smaller than 5% were considered statistically significant (SPSS, version 22.0, SPSS Inc, Chicago, IL, USA).

RESULTS

The greatest influence on the transmitted irradiance was exerted by the curing mode ($\eta_P^2 = 0.991$), closely followed by specimen thickness ($\eta_P^2 = 0.989$), CAD/CAM material ($\eta_P^2 = 0.966$), and distance from the specimen's surface ($\eta_P^2 = 0.904$). All binary combinations of these parameters were also significant ($p<0.05$).

The highest significant values for transmitted irradiance were measured for the materials VM and LU, followed by VCT and IEC, while the lowest significant values were for VE, followed by IEM and CD (Figures 2 through 4). Detailed information about the significant differences between the tested CAD/CAM materials is presented in Table 2.

Among the three tested curing regimens, the highest significant irradiance was recorded by exposing the CAD/CAM material to the plasma mode, followed by the high- and standard-power modes ($p<0.05$). The irradiance measured at 0-mm distance was 3416. ± 8.3 mW/cm^2 for the plasma mode, 1766 ± 0.1 mW/cm^2 for the high-power mode, and 1178 ± 0.5 mW/cm^2 for the standard-power mode. Following the same sequence, an increase in irradiance was identified at 2-mm distance (3797 ± 87.6 mW/cm^2, 1939 ± 3.2 mW/cm^2, and 1272 ± 24.5 mW/cm^2, respectively), and the lowest irradiances were measured at 4-mm distance from the specimen surface (2606 ± 6.6 mW/cm^2, 1346 ± 3.7 mW/cm^2, and 1002 ± 18.0 mW/cm^2).

The transmitted irradiance decreased significantly by increasing the specimen's thickness from 1 to 2 mm ($p<0.05$). Fewer differences were measured when the curing unit was placed at 0 or 2 mm from the specimen's surface, and the irradiance passing through the specimens was lower at a distance of 4 mm ($p<0.05$). SEM pictures of the microstructure of all tested CAD/CAM materials are presented in Figure 5.

DISCUSSION

Tooth-colored monolithic CAD/CAM materials seem to be suitable materials for dental applications; however, a cementation method using resin composite cements remains a key factor in ensuring long-lasting survival and success rates. Previous investigations have shown that the mechanical properties of dual-cure luting cements,[34] as well as the bond strength to dental ceramics, are positively influenced by the amount of light reaching the cements.[41,42]

In general, the highest transmitted irradiance was measured at the bottom of the feldspathic ceramic VM and the resin composite LU in the present study. The lowest values were measured for a hybrid ceramic VE followed by both lithium disilicate ceramics IEM and CD. The first null hypothesis, that the different CAD/CAM materials show no impact on the irradiance through the material, is rejected. It is worth noting that 60.8%-84.0% of the initial irradiance reaching the material surface is

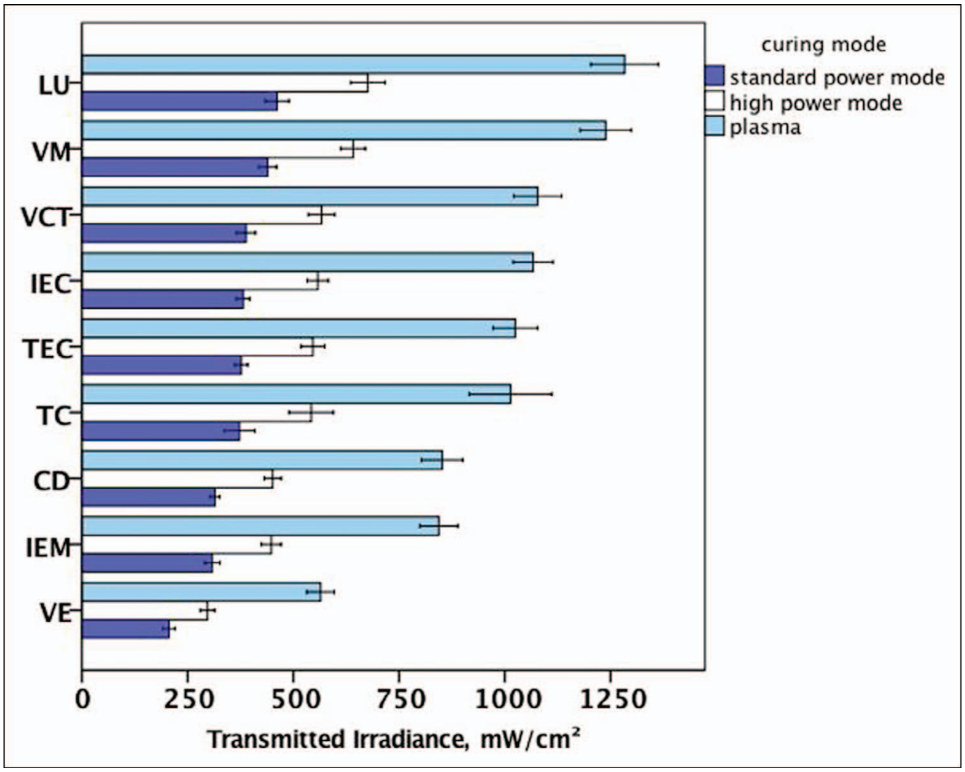

Figure 2. *Transmitted irradiance as a function of material and initial irradiance in 1-mm-thick specimens. The curing unit was positioned directly on the specimen surface.*

lost in passing 1-mm-thick increments of the analyzed materials, and this range changes to 80.6% –95.5% for 2-mm-thick specimens. Within one material, this value is influenced in only a minor way by the level of the initial irradiance. The analyzed materials might be grouped into four categories with respect to this behavior in descending order of their translucency: 1) LU and VM

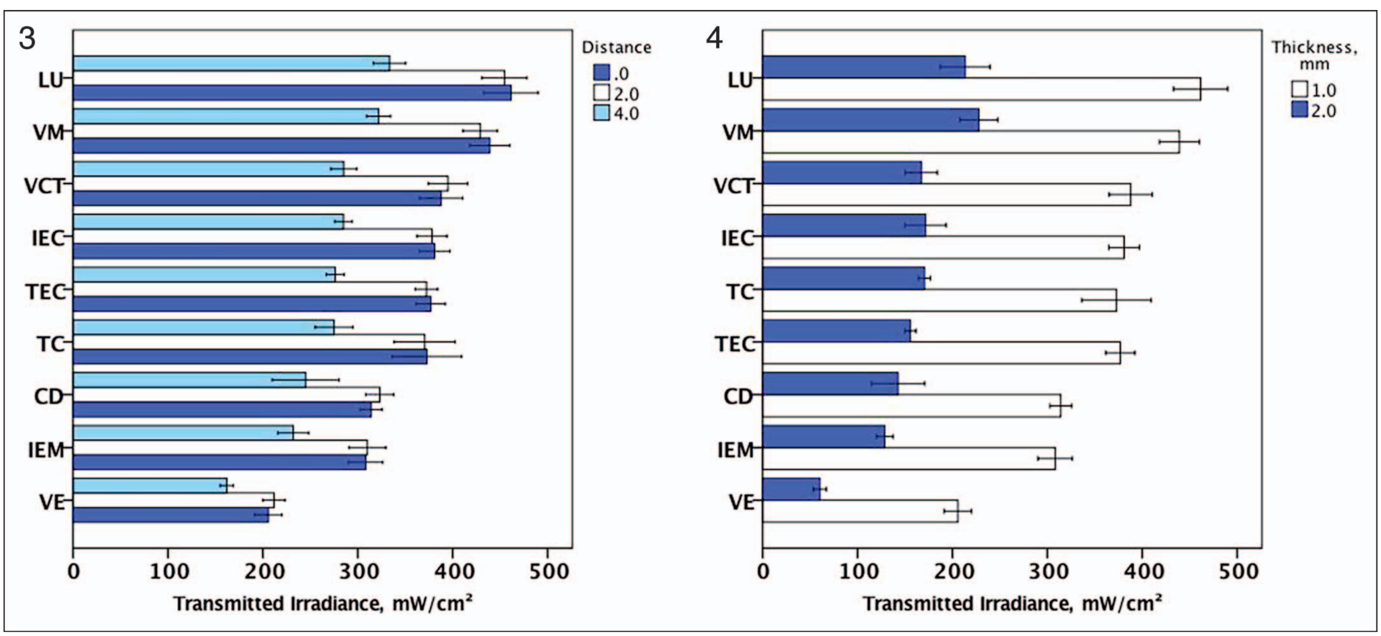

Figure 3. *Effect of distance between light curing and material surface (standard curing mode, 1-mm-thick specimens)*
Figure 4. *Transmitted irradiance as a function of material type and thickness. The curing unit (standard curing mode) was positioned directly on the specimen surface*

Table 2: *Descriptive Statistics for All Tested CAD/CAM Materials With Respect to Material Thickness, Curing Modus, and Distance Between Specimens and Light Unit*

CAD/CAM Material	Distance Between Specimens and Light Unit					
	0 mm		2 mm		4 mm	
	Thickness of CAD/CAM Material		Thickness of CAD/CAM Material		Thickness of CAD/CAM Material	
	1 mm Mean (SD)	2 mm Mean (SD)	1 mm Mean (SD)	2 mm Mean (SD)	1 mm Mean (SD)	2 mm Mean (SD)
Standard-power mode						
TC	373 (18.3) C	171 (3.1) D	371 (16.1) C	168 (3.9) C	275 (9.9) C	129 (2.1) DE
VCT	388 (11.4) C	167 (8.5) D	395 (10.3) D	163 (7.0) C	285 (6.8) C	126 (4.4)* DE
TEC	377 (7.7) C	156 (2.9) CD	372 (5.9) C	155 (4.5)* C	276 (4.8) C	120 (2.6) CD
LU	462 (14.3) E	213 (13.1) E	455 (11.9) F	204 (10.7) D	333 (8.6) D	157 (8.4) F
VE	206 (7.3) A	60 (3.5) A	212 (5.9) A	62 (5.0) A	162 (3.5) A	50 (2.0) A
VM	439 (10.6) D	228 (10.0) E	429 (9.1) E	219 (7.6)* E	322 (6.3) D	178 (4.3) G
IEC	381 (8.1) C	172 (10.9) D	378 (7.9) CD	167 (11.8) C	285 (4.6) C	132 (7.4)* E
IEM	308 (9.1) B	129 (4.4) B	310 (9.7) B	127 (4.9) B	232 (8.3)* B	102 (3.7) B
CD	314 (5.7) B	143 (14.1) BC	323 (7.3) B	139 (10.2) B	245 (17.7) B	111 (7.1) BC
High-power mode						
TC	542 (26.3) C	243 (3.2) DE	537 (23.8) C	236 (3.5) C	397 (13.8) C	183 (3.3) CD
VCT	567 (15.7) C	241 (11.5) DE	575 (15.0) CD	237 (9.4) C	414 (11.0) C	181 (7.4) CD
TEC	546 (13.9)* C	221 (5.8) CD	540 (6.2) C	220 (6.4) C	399 (6.1) C	171 (4.3) C
LU	676 (20.2) E	307 (20.1) F	666 (11.1) E	294 (15.4) D	486 (10.3) D	226 (12.2) E
VE	297 (8.5) A	84 (4.0) A	307 (8.0) A	86 (5.1) A	233 (5.9) A	69 (2.3) A
VM	641 (14.5) D	330 (13.2) F	609 (60.9) D	317 (12.6)* F	473 (9.8) E	257 (6.9) F
IEC	558 (12.5) C	246 (17.7) E	554 (11.7) C	241 (17.7)* C	417 (7.2) C	190 (13.4) D
IEM	448 (11.7) B	183 (5.4) B	450 (14.7) B	181 (5.5) B	338 (12.4) B	140 (5.0) B
CD	451 (10.0) B	200 (18.4) BC	466 (7.7) B	199 (15.0) B	355 (27.9) B	155 (11.1) B
Plasma mode						
TC	1014 (48.7) C	441 (8.3) DE	1007 (44.3) C	431 (8.4) DE	744 (30.2) C	333 (5.9) DE
VCT	1078 (28.3) D	452 (21.4) E	1100 (29.2) E	441 (20.1) DE	793 (20.4) D	340 (13.8) DE
TEC	1025 (26.3) CD	406 (9.9) CD	1017 (13.6) CD	405 (13.3) CD	753 (9.4) CD	315 (7.5) CD
LU	1283 (40.0) E	564 (39.6) F	1261 (38.7) G	543 (33.5) G	922 (19.6) E	418 (22.4) G
VE	546 (16.3) A	155 (7.7) A	582 (14.2) A	158 (10.5) A	443 (9.7) A	125 (5.6) A
VM	1239 (30.2) E	625 (26.5) G	1204 (24.0) F	605 (22.5) G	909 (19.1) E	485 (14.9) G
IEC	1067 (23.6) CD	466 (35.9) E	1064 (22.4) DE	455 (37.2) E	797 (12.7) D	359 (29.7) E
IEM	844 (22.6) B	339 (10.3) B	850 (27.7)* B	336 (10.0) B	636 (21.7)* B	263 (8.5) B
CD	852 (24.4) B	371 (35.3) BC	879 (27.1) B	370 (30.1) BC	672 (59.4)* B	291 (20.7) BC

** Significant differences between the different CAD/CAM materials within one material thickness, cutting modus, and distance between specimens and light unit are marked with different letters.*

(60.8%-62.7% initial irradiance loss when passing 1-mm-thick increments and 80.6%-81.9% when passing 2-mm-thick increments); 2) VCT, IED, TEC, and TC (67.1%-68.3% and 85.8%-86.8 %, respectively); 3) CD and IEM (73.3%-78.8% and 87.9%-89%); and 4) VE (82.5% and 94.9%).

The translucency of ceramic materials and thus the transmitted irradiance are dependent on the crystalline structure, grain size, and pigments as well as the number, size, and distribution of defects and porosity.[43,44] In this study, lithium disilicate glass-ceramic IEM and lithium silicate glass-ceramic CD showed significantly lower transmitted irradiance values than the leucite-reinforced ceramic Empress CAD or feldspathic ceramic VM. A previous study reported higher translucency values for leucite-reinforced IEC than for lithium disilicate glass ceramics and explained this as a result of the different microstructures, with less dense crystals in the leucite-reinforced ceramic than in the lithium disilicate ceramic.[45] These results were confirmed in this study. Lithium disilicate crystals are needle shaped and randomly oriented, representing about two-thirds of the glass-ceramic volume.[46] The

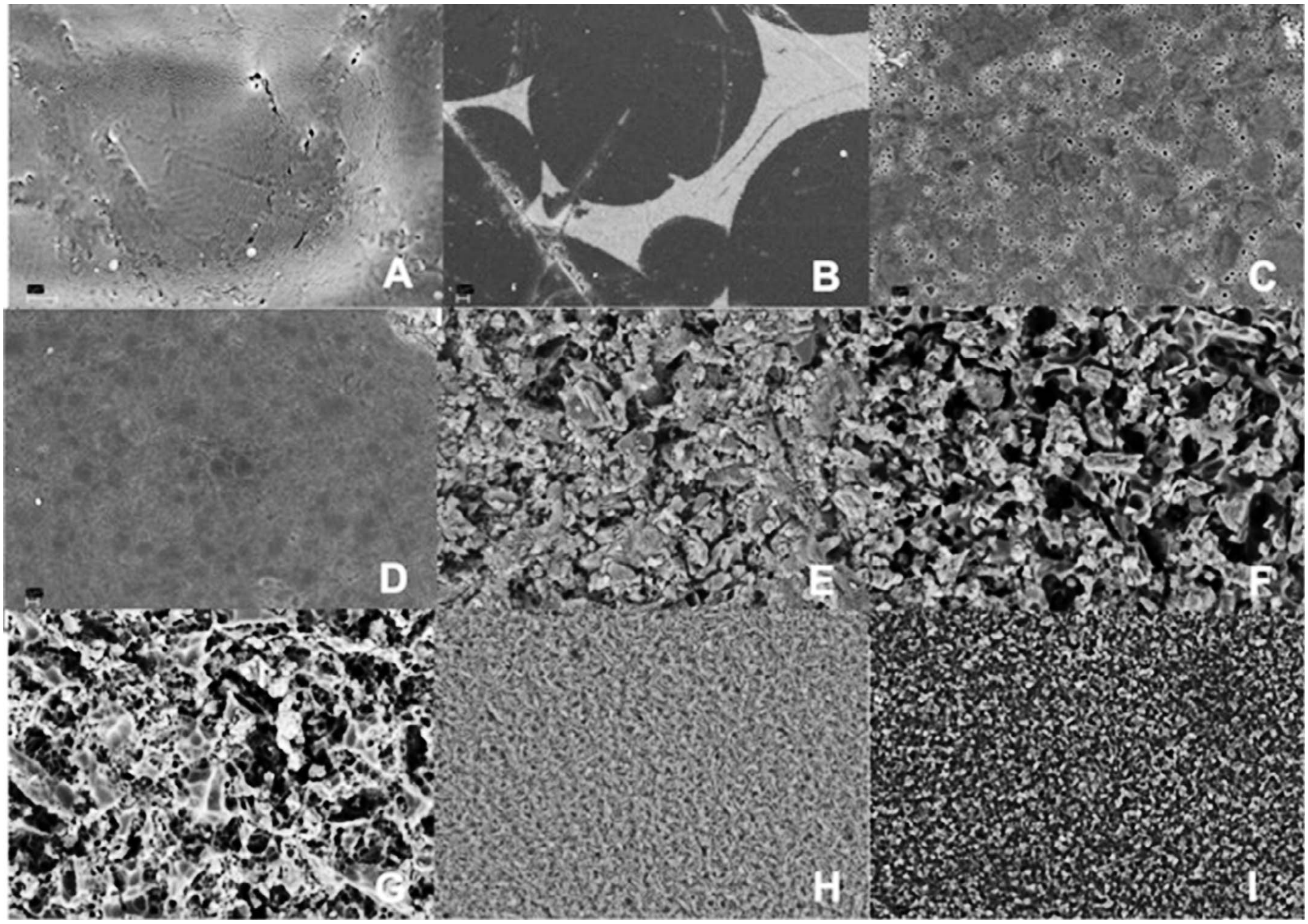

Figure 5. *Scanning electron microscope images of the microstructure of all tested materials: A: TC; B: VCT; C: TEC; D: LU; E: VE; F: VM; G: IEC; H: IEM; I: CD.*

microstructure of the leucite-reinforced ceramic is less dense and characterized by the single crystal formation of leucite ($KAlSi_2O_6$) without interlocking of the crystals.[44,47] Higher-strength ceramics also tend to be less translucent due to the necessary increased crystalline content.[48] Aluminosilicate glass in the lithium disilicate ceramic can result in lower transmitted irradiance values because aluminum compounds cause the ceramic to appear dull and opaque.[49] Feldspathic ceramic (VM) and composites based on tetraethyleneglycol dimethacrylate (TEGDMA) and urethane dimethacrylate (UDMA) (LU) showed the highest transmitted irradiance. In agreement with previous studies,[50,51] VE showed the lowest transmitted irradiance values. VE is a polymer-infiltrated feldspathic ceramic-network material with an 86 wt% ceramic part. The polymer part contains TEGDMA and UDMA monomers. It can thus be assumed that the low transmitted irradiance is related to the density and grain size of the ceramic matrix.

In accordance with previous studies[40,52,53] that investigated the translucency of ceramic materials, this investigation confirmed that material thickness significantly influences the transmitted irradiance. The second null hypothesis was therefore also rejected. In previous studies,[40,52] the glass-ceramic specimens showed a greater decrease in transmitted irradiance compared to zirconia, still in accordance with material thickness, when using standard-power and extra-power curing modes. A lower impact of material thickness on irradiance was observed in exposures to the high-power curing mode. Dental restorations involve various thicknesses, depending on the different conditions of the tooth, and therefore, for use of light-curing cementation, an accurate knowledge of the relationship between irradiance and thickness, depending on the shades, is fundamental to improving the long-term stability of ceramic restorations. The present study confirmed this.

Within one type of CAD/CAM material, thickness, or curing mode, no significant difference in transmitted irradiance was recorded until an exposure distance of 2 mm, and this decreased significantly for larger distances (4 mm). This was the result of the particular curing unit used in this study since the variation in irradiance with increasing exposure distance in all three modes showed a slight increase, up to an exposure distance of 2 mm, then decreased exponentially with the distance.[40] For this, the irradiance levels at 0 and 2 mm were comparable. This means that the third null hypothesis is rejected. The special concave glass lens at the tip of the curing unit can explain the impact of the distance between the curing light unit and specimens on the irradiance, where the emitted light is focused to a collimated beam with maximum irradiance at 2 mm. The highest significantly transmitted irradiance was recorded while using the extra-power mode, followed by the high- and standard-power modes. Thus, the fourth hypothesis is also rejected.

In general, it was found that the more translucent a CAD/CAM material, the greater the change in transmitted irradiance as a result of varying thickness. If the microstructure crystals are smaller than the wavelength of visible light (400-700 nm), the glass will look transparent.[49] The material will appear opaque in the case of light scattering and a diffuse reflection.[49] The monolithic CAD/CAM blocks are available in high-translucency (HT) and low-translucency (LT) versions. The LT CAD/CAM materials contain a high number of smaller lithium metasilicate crystals, whereas a small number of crystals are present in the precrystallized state of the HT materials.[46] To the best knowledge of the authors, all materials were ordered in similar A2 colors for the group comparisons; however, materials are offered in different tooth color systems, namely, VITA classic A1-D4 shade guide (classical method) and VITA 3D Master. For this study, the VITA 3D Master colors were translated into the classical colors using VCT and VE. In this study, VE was present in only one tooth color 3M2 (converted A3). Another limitation of this study was that TEC was analyzed in a HT shade, and no information was available for VCT, VE, and VM. It can be assumed that TEC in LT showed comparable transmitted irradiance values to those of the composite LU, but it must be emphasized here that the values obtained provide tendencies for the orientation of the irradiance values.

The transmitted irradiance was evaluated in this study using flat specimens of a standardized thickness. Future investigations should be performed directly on a dental restoration for greater clinical relevance. The influence of the fabrication process of CAD/CAM restorations, such as milling and finishing, could be integrated into these investigations.

Conclusions

Within the limitations of this laboratory investigation, the following conclusions can be drawn:

(1) VITA Mark II and Lava Ultimate showed the highest transmitted irradiance.
(2) The novel interpenetrating network ceramic, followed by the lithium (di)silicate ceramics, showed the lowest transmitted irradiance.
(3) The highest transmitted irradiance was recorded by exposing the material to the plasma mode, followed by the high- and standard-power modes.

Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects oversight committee guidelines and policies of the Department of Prosthodontics, Dental School, Ludwig-Maximilians University, Munich, Germany.

Conflict of Interest

The authors of this article certify that they have no proprietary, Financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

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