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Delayed photo-activation and addition of thio-urethane: impact on polymerization kinetics and stress of dual-cured resin cements

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Abstract

Objective—1) to determine the moment during the redox polymerization reaction of dual cure cements at which to photo-activate the material in order to reduce the polymerization stress, and 2) to evaluate possible synergistic effects between adding chain transfer agents and delayed photo-activation.

Methods—The two pastes of an experimental dual-cure material were mixed, and the polymerization kinetics of the redox phase was followed. The moment when the material reached its maximum rate of redox polymerization (MRRP) of cement was determined. The degree of conversion (DC) and maximum rates of polymerization ($R_{p_{max}}$) were assessed for materials where: the photoactivation immediately followed material mixing, at MRRP, 1 min before and 1 min after MRRP. Thio-urethane (TU) additives were synthesized and added to the cement (20% wt), which was then cured under the same conditions. The polymerization kinetics was evaluated for both cements photo-activated immediately or at MRRP, followed by measurements of polymerization stress, flexural strength (FS) and elastic modulus (EM). Knoop hardness was measured before and after ethanol storage.

Results—Photo-activating the cement at or after MRRP reduced the $R_{p_{max}}$ and the polymerization stress. Addition of TU promoted additional and more significant reduction, while not affecting the $R_{p_{max}}$. Greater hardness loss was observed for cements with TU, but the final hardness was similar for all experimental conditions. Addition of TU slightly reduced the EM and did not affect the FS.

Conclusion—Delayed photo-activation and addition of TU significantly reduce the polymerization stress of dual-cured cements.

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Keywords

Pre-polymerized additives; Polymerization stress; Resin cement

Introduction

Dual-cured resin cements are largely used for cementation of indirect restorations due to a combination of the favorable characteristics of self- and light-cured agents. For example, those cements still offer some control of working time, and ensure that the margins of the restoration can be polymerized to relatively high degrees of conversion right after cementation, to avoid premature dissolution – those all being features one can harness from the photo-activated components [1–4]. However, photo-activation cannot guarantee high conversion values in areas that are inaccessible to light, either due to reflection, absorption or scattering phenomena through thick and opaque indirect restorative materials [5,6]. In those areas, the chemical [or redox] components ensure that the conversion progresses to the extent necessary to provide acceptable mechanical properties. One drawback that is still present with dual cure cements is the polymerization stress that may results in cracks on the cement line or the restorative material itself, gaps on margins and post-operative sensitivity, compromising the longevity of restorative procedures [7,8]. Polymerization stress is closely related to the C-factor, defined as the ratio between bonded and non-bonded surface. In general, the higher C-factor, the greater the polymerization stress [9]. Resin cements are used in the worst scenario in terms of C-factor, since only the margins of the cement layer are able to deform and accommodate part of the polymerization stress [10]. Thus, clinical approaches or materials able to reduce the polymerization stress can be envisioned to improve the longevity of restorations.

Usually, dual-cured cements are photo-activated by clinicians immediately after restoration placement and removal of excess cement. However, some studies evaluating three commercially available dual-cured resin cements suggest that delaying the photo-activation might be able to reduce the polymerization stress caused by the resin cement [11,12]. It was speculated that differences on crosslinking density affecting the elastic modulus would explain the results [11]. In those prior studies, compositional differences among the cements might have affected the speed of the chemically activated reaction to some extent. With that being said, using the same delay period (3 or 5 minutes) for all materials, Faria-e-Silva et al. [11] observed differences on maximum rate of polymerization ($R_{p_{max}}$) and degree of conversion after 30 minutes (maximum period of evaluation) among the cements evaluated when photo-activation was delayed. Others have attempted to tackle the stress issue by using compositions with different polymerization mechanisms, including the use of thiol-ene polymerizations and/or the incorporation chain transfers agents (thiols) into methacrylate polymerizations [13]. When photo-activation is used, thiol-ene polymerizations progress through a radically assisted step-growth mechanism, in which diffusion limitations occur at higher DC or, in other words, gelation and vitrification are delayed to higher values of conversion [14]. The same effect is observed in thiol-methacrylate polymerizations, even at off-stoichiometry ratios [14]. Therefore, the stiffness of the network does not build up until later in conversion, which in turn allows dimensional changes (and stress) to be

accommodated with significantly lower stress generation [14–16]. A recent study demonstrated that adding thiol-terminated thio-urethane oligomers to dual-cured resin cement was able to significantly reduce the polymerization stress when compared to a control [17]. However, in that study, both experimental (containing thio-urethane) and control cements were photo-activated immediately after mixing.

There might be advantages to combining delayed gelation/vitrification strategies with delayed photoactivation protocols in dual-cure cements to ultimately reduce polymerization stress. These two strategies are more useful to relieve/avoid part of the stress that is developed in regions of the cement/restoration that are effectively reached by light. In the regions where polymerization progresses “in the dark”, the redox mechanism prevails, and there is limited stress generation [2,5,11]. However, except for the free margin where the material can comply to the deformation imposed by polymerization, stresses develop rapidly under confinement in the regions where the photoactivation is efficient. Thus, the aims of the present study were 1) to determine the moment during the redox polymerization reaction of dual cure cements at which to photo-activate the material in order to reduce the polymerization stress, and 2) to evaluate possible synergistic effects between adding chain transfer agents and delayed photo-activation of dual-cured cements in terms of on polymerization stress, reaction kinetics, mechanical properties and degradation after storage in ethanol. The hypothesis was that delaying the photo-activation of dual-cured cements containing thio-urethane results in additional reduction of polymerization stress.

Material and Methods

This study was divided in two aims: 1) to determine if delaying the photo-activation of a dual cure cement can lead to reduction in polymerization stress; 2) to determine whether the addition of a stress-reducing thio-urethane oligomer would act synergistically with the delayed photo-activation of dual-cured cements. Both types of materials, in the several delayed activation protocols tested, were evaluated for polymerization stress, reaction kinetics, mechanical properties and degradation after storage in ethanol. The statistical analysis was conducted separately for each aim, and the presentation of the results aligns with that design.

Cement formulation

An experimental dual-cured resin cement was formulated using the monomers BisGMA (Bis-phenol A diglycidyl dimethacrylate) and TEGDMA (tri-ethylene glycol dimethacrylate) at a 2:1 mass ratio, all from Esstech (Essington, PA, USA). Fillers of 0.7- μ m silane-treated Barium glass (Esstech) were added at 60% wt%. To the base paste, 0.2 wt% of dl-camphoroquinone, 3.5 wt% of a tertiary amine (EDMAB [ethyl 4-dimethylaminobenzoate]), and 0.1 wt% of inhibitor (BHT [2,6-di-tert-butyl-4-methylphenol]) were added. To the catalyst paste, 3.5 wt% of benzoyl-peroxide was added. Those concentrations were determined to produce polymerization levels of 30% or more in 20 min, according to the results of a pilot study. We acknowledge the poor performance of EDMAB as a redox pair for BPO, as previously demonstrated [18]. However, we opted for keeping due to its good performance as a co-initiator for CQ, as the photoinitiated reaction was the

one to more likely benefit from the inclusion of the TU additive. Previously published results show that the high concentration of amine is not detrimental to the polymerization initiated by the CQ/EDMAB pair, as long as the concentration of CQ was kept above 0.2 wt % [19]. All initiators were obtained from SigmaAldrich (St. Louis, MO, USA).

For the materials containing thio-urethane, thiol-functionalized oligomers were synthesized by combining 1,6-hexanediol-diisocyanate (aliphatic) with pentaerythritol tetra-3-mercaptopropionate (PETMP), according to previously reported methods (13). The same cement composition describe above was used in aim 1 was used here, except that thio-urethane oligomers were added to the base paste at the concentration of 40 wt%. This resulted in a 20 wt% thio-urethane concentration after mixing base and catalyst pastes.

Pilot study on the purely redox activation of cements with and without thio-urethane oligomer

To define the delay period between the end of the spatulation of the dual-cured cement and the start of light exposure, a pilot study was conducted. A portion of the experimental cements, with and without thio-urethane, was mixed and placed in the specimen holder of the infra-red spectrometer (Nicolet 6700, Thermo Scientific, Pittsburgh, PA, USA) equipped with an InGaAs detector, 3 minutes after spatulation. Spectra were collected in real-time for 20 min, at 4 cm^{-1} resolution, 2Hz acquisition rate, following the same protocol described in detail in a subsequent section (DC and polymerization kinetics). This had the objective of obtaining the polymerization kinetics profile of the redox-activated reaction only. From those curves ($n=3$) shown in Figure 1, the maximum rate of polymerization ($R_{p_{\max}}$) and the degree of conversion (DC) at $R_{p_{\max}}$ and after 10 min or 24 hours were determined. Then, the times required to reach those points were determined. Those times were then chosen to delay the photoactivation after mixing the dual-cure cement, in four levels: immediately after spatulation, during autoacceleration of the redox reaction, at the maximum rate or during deceleration of redox activated polymerization reaction. For the cement without thio-urethane, $R_{p_{\max}}$ (0.13 %/s) was observed at around 420 s, and this time was used as a reference for selection of the different times to start the photo-activation: immediately (5 s); 1 min before the maximum rate of redox polymerization (MRRP) (360 s); at MRRP (420 s) and 1 minute after MRRP (480 s). For the cement containing thio-urethane, the polymerization was fast from the beginning of spatulation, and by the time the material was placed in the spectrometer's sample compartment, the reaction kinetics was already in the acceleration region. Therefore, the $R_{p_{\max}}$ value for the redox reaction for this material is likely underestimated at 0.24 %/s, recorded at approximately 70 s (Figure 1). However, since the mixing and sample preparation procedures were standardized, we adopted the 70 s time as the MRRP.

DC and polymerization Kinetics

Equal amounts of each paste were mixed for 15 s and inserted in cylindrical silicone rubber molds ($n=3$; diameter=6 mm; thickness=0.8 mm), sandwiched between two glass slides. Polymerization kinetics was monitored in near-infrared using a spectrometer (Nicolet 6700). The standard delay between the end of sample preparation and the start of FTIR spectra collection was 3 minutes, as determined in the pilot study, which allowed sufficient time for

specimen preparation and placement on the IR holder. The monitoring of polymerization kinetics, therefore, started 3 minutes after the beginning of cement mixing, and was followed for 10 minutes. Cements were then photoactivated according to the delay times described above (5, 360, 420 or 480 s) using a LED-based light-curing unit Demi (Kerr, Orange, CA, USA) for 20 s. DC (2 scans/spectrum, 4 cm⁻¹ resolution, >2 Hz data acquisition rate) was calculated based on the area of the methacrylate vinyl overtone at 6165 cm⁻¹. The polymerization rate (Rp) was calculated as the first derivative of the conversion vs. time curve. The DC at the start of photo-activation, at Rp_{max} and after 10 min were recorded. Polymerized specimens were stored dry for 24h and the DC was measured again.

Polymerization stress

Polymerization stress development (in MPa) was followed in real-time for 20 min using the Bioman [20]. Standardized mass of mixed resin cement (around 0.8 g) was placed over a silane-treated (Ceramic Primer, 3M-ESPE) glass plate held to the device with a cylindrical bolt, where the tip of light-curing unit (Demi) was positioned. A metallic rod (5.6 mm of diameter) was then placed over the cement to produce disc specimens with 0.75 mm thickness (configuration factor = 3.73). The light-curing was performed according to light-curing protocols defined above (n = 4).

Knoop hardness (following experimental design for aim 2 only)

After DC measurement, Knoop micro-hardness (KHN) was tested on the same specimens using a hardness tester (Duramin, Struers, Cleveland, OH, USA) under a load of 490 N (50 gf) for 5 s. In each sample, five measurements were obtained and the Knoop micro-hardness values (KHN: kg/mm²) were recorded as the average of the five indentations per specimen. The specimens were then immersed in absolute ethanol for 24 h to evaluate KHN loss after solvation.

3-point bending test (following experimental design for aim 2 only)

The dimensions of bars required by the International Organization for Standardization (ISO) specification 4049, which establishes the standards for performing the 3-point bending test for polymer-based dental materials was modified in this study to allow for a single exposure per sample. This was done to keep the same exposure protocols used for the other tests in the mechanical properties evaluation. Resins cements were inserted in rubber molds measuring 14×2×1 mm, and then photo-activated immediately or at the moment when the redox activated reaction reached its maximum rate. The dimensions of the bars were checked with a digital caliper accurate to 0.01 mm (Mitutoyo Corporation, Tokyo, Japan). The specimens were positioned in a 3-point bending device coupled to a mechanical testing system (Q-test, MTS Inc., Orono, ME, USA). The distance between supports was 10 mm and the load was applied to the center of specimen. The diameter of both supports and of the loading rod was 2 mm. The tests were performed at a crosshead speed of 1.0 mm/min until failure, and the load was monitored by the testing machine software (TestWorks v.3.08, MTS Inc., Orono, ME, USA.). To calculate flexural strength (σ_f), in MPa, the following equation was used:

$$\sigma f = \frac{3FI}{2bh^2}$$

where F is the maximum load (N) exerted on the specimen, l is the distance (mm) between the supports, and b is the width (mm) and h the height (mm) at the center of the specimen.

The Elastic modulus (E) was calculated using the following equation:

$$E = \frac{F_1 I^3}{4bdh^3}$$

where F1 is the load (N) exerted on the specimen and d is the deflection corresponding to the load F1.

Statistical analysis – Aim 1

Data from DC at each time (immediately after spatulation, during autoacceleration of the redox reaction, at the maximum rate of reaction or during deceleration of redox activated polymerization reaction, as well as after 10 min or 24h), Rp_{max} and polymerization stress were individually analyzed with one-way ANOVA. For DC at the moment when the photo-activation started, data from immediate photo-activation were excluded from statistical analysis once no DC was observed at that time. Multiple comparisons were performed by Student-Newman-Keuls (SNK) method and the significance level was set at $\alpha = 0.05$ for all analyses. Data analysis was performed using the SigmaStat v.3.5 statistical software package (Systat Software Inc., Chicago, IL, USA).

Statistical analysis – Aim 2

Except for DC at moment when photo-activation started, data of DC, Rp_{max} , flexural strength, elastic modulus and polymerization stress were individually analyzed by 2-way ANOVA. Data from DC at the moment when photo-activation started were analyzed with Student's t-test, as values of DC at immediate photo-activation were not included in the analysis (value of 0). Data of KHN and hardness loss were grouped by experimental condition (moment when photo-activation started x addition of thio-urethane) to increase the test power of the statistical analysis. Two-way Repeated Measure ANOVA was used to analyze the data from KHN, and the percentage of hardness loss was analyzed by one-way ANOVA. Pearson's correlation test was used to assess a possible correlation between Rp_{max} and hardness loss. Multiple comparisons were performed by Student-Newman-Keuls (SNK) method and the significance level was set at $\alpha = 0.05$ for all analyses.

Results

Aim 1

ANOVA showed that the factor “protocol of photo-activation” significantly affected the DC observed at Rp_{max} ($p < 0.001$), at the moment when photo-activation started ($p < 0.001$), and after 10 min ($p = 0.015$), but not the DC measured after 24 h ($p = 0.248$). The Rp_{max} also

was significantly affected by the moment when the photo-activation started ($p < 0.001$). The results are displayed in Table 1. Starting the photo-activation immediately and 1 min before MRRP resulted in similar values of Rp_{max} , while these values were higher than those observed for the other protocols. No difference on Rp_{max} was observed between the photo-activation started at or 1 min after MRRP. The opposite was observed for DC measured at Rp_{max} , and starting the photo-activation at or 1 min after MRRP resulted in highest values. After 10 minutes, starting the photo-activation immediately after spatulation resulted in higher DC than when the photo-activation was started 1 min after MRRP. The moment when the photo-activation was started did not affect the DC measured after 24 hours. Figure 2 illustrates the Rp development as a function of DC.

ANOVA showed that the moment when the photo-activation started significantly affected the polymerization stress ($p = 0.002$). The results are presented in Figure 3. Starting the photo-activation at or 1 min after MRRP resulted in similar values of polymerization stress, which were lower than those observed for the photo-activations started prior to MRRP.

Aim 2

The results for DC and Rp_{max} are presented in Table 2. 2-way ANOVA showed that only the “protocol of photo-activation” significantly affected the DC observed at Rp_{max} , ($p < 0.001$), whereas the “addition of thio-urethane” ($p = 0.100$) and the interaction ($p = 0.057$) were not significant. Irrespective of the addition of thio-urethane, starting the photo-activation at MRRP resulted in highest values of DC at Rp_{max} . Similarly, the Rp_{max} was affected only by “protocol of photo-activation” ($p < 0.001$), while the “addition of thio-urethane” ($p = 0.390$; for interaction $p = 0.638$) did not affect the Rp_{max} . Delaying the photo-activation reduced the Rp_{max} . The factor “addition of thio-urethane” ($p = 0.005$) and the interaction ($p = 0.045$) affected the DC measured after 24 h, while the “protocol of photo-activation” ($p = 0.219$) was not significant. Adding thio-urethane to the dual-cured cement increased the DC only for the photo-activation started at MRRP. For cements with photo-activation started at MRRP, the addition of thio-urethane did not affect the DC measured at moment when the photo-activation was started ($p = 0.074$). Figure 4 illustrates the Rp development as a function of DC, and the average polymerization stress curves are showed at Figure 5. Maximum polymerization stress was affected by “protocol of photo-activation” ($p < 0.001$) and the “addition of thio-urethane” ($p < 0.001$), while the interaction $p = 0.129$) was not significant. Delayed photo-activation and addition of thio-urethane were able to reduce the polymerization stress.

The results for KHN and hardness loss are displayed in Table 3. Repeated-measured two-way ANOVA showed that “experimental condition” (protocol of photo-activation x addition of thio-urethane; $p = 0.013$), “storage” ($p < 0.001$) and the interaction were significant. Before the ethanol storage, cements containing thio-urethane demonstrated highest KHN values irrespective of the photo-activation protocol. However, no difference on KHN among the experimental conditions was observed after storage. For both photo-activation protocols, the two cements presented significant reduction on KHN values within ethanol storage. One-way ANOVA showed that the “experimental condition” significantly affected the hardness loss ($p = 0.006$). Cements containing thio-urethane showed the highest hardness loss, while

the photo-activation protocol did not affect the hardness loss for either cement. Pearson's correlation test showed an indirect weak and non-significant correlation between hardness loss and $Rp_{\max}$ ($r = -0.268$; $p = 0.400$).

The results for 3-point bending test are presented in Table 4. For flexural strength, 2-way ANOVA did not show significant effect for the factors "protocol of photo-activation" ($p = 0.396$) and "addition of thio-urethane" ($p = 0.520$); and for interaction ($p = 0.916$). All experimental conditions resulted in similar flexural strength. For elastic modulus, 2-way ANOVA showed significant effect only for the factor "addition of thio-urethane" ($p = 0.047$); whereas the factor "protocol of photo-activation" ($p = 0.237$; interaction – $p = 0.136$) did not affect the values of elastic modulus.

Discussion

Based on the kinetics of redox activated polymerization, the first aim of this study was to determine whether there would be a benefit to delaying the photo-activation of a dual-cure resin cement, and if so, what would be the optimal waiting time after the spatulation to expose the material to light, with the main goal of reducing polymerization stress. The research question we wanted to answer was whether waiting until the redox portion of the polymerization had undergone its acceleration/deceleration to only then expose the material to light to start the faster, light-cured portion would have any effect on network formation and polymerization stress. Using experimental dual-cured cements, it was observed that waiting until the redox polymerization reaches its maximum rate of polymerization before starting the photo-activation of cement led to reduced polymerization stress. Polymerization stress is mainly related to volumetric shrinkage, conversion and modulus development [9,21], but the effect of polymerization speed has been demonstrated to be limited within the range of irradiances normally used in clinical practice [22]. Even considering that volumetric shrinkage directly correlates with degree of conversion, it is expected that the moment when the photo-activation was started would not significantly affect the volumetric shrinkage of the cement [23,24]. Even though shrinkage was not measured in this study, it is reasonable to infer that differences observed on polymerization stress were mainly related to alterations on network formation caused by the moment when the photo-activation was started. It can be speculated that delaying the gelation/vitrification stages allowed higher accommodation of strain caused by shrinkage [21, 25–27].

Delayed photo-activation of dual-cured cements results in a two-staged kinetic profile for polymerization, caused by the delayed activation of photo-initiators. This photo-activated reaction resulted in $RP_{\max}$ that was, as expected, up to 57-fold higher than observed for the redox-activated reaction alone. However, the actual $Rp_{\max}$ of the photo-initiated portion of the polymerization was much lower for the groups where light exposure was started at MRRP or 1 min after MRRP (deceleration of redox activated reaction), compared to the groups where light exposure was performed immediately after the material was placed in the IR chamber. It is acknowledged that this was still 3 min after the initial mixing of the material, so the rate of reaction and conversions reported here are relative to the measurements at that time. This, in one hand, is a recognized limitation of this study, but on the other hand mimics the clinical situation, since crown seating is also delayed by a certain

period of time after cement manipulation. Still, it is possible to infer that the reduction in the $R_{p_{max}}$ for the photoactivated portion of the curve is explained by fact that this portion of the reaction starts when diffusional limitations are already imposed by the relatively high conversion at that time [28]. Further to diffusion limitations, the reduced concentration of non-reacted monomers in increased DC values also limits the $R_{p_{max}}$. Again, it is important to note that the DC values measured then (24.7 to 31.8 %) are also underestimated, because the start of the mixing of the two pastes starts 3 min prior to the measurement. In contrast, photo-activating the cement at lower DC, such as is the case for those groups where light exposure started only 1 min prior to MRRP, means that the photo-activated portion of the reaction starts when a lot more diffusional mobility is still likely in the medium, leading to the increased $R_{p_{max}}$ observed for those groups.

The photo-activation initiated at and 1 min after MRRP also showed increased DC at the moment when the photo-activated reaction reached its $R_{p_{max}}$. The $R_{p_{max}}$ indicates that the radicals responsible for polymerization become trapped within the network as it vitrifies, resulting in reduction of reaction speed [29]. Thus, delaying the photo-activation until the MRRP can be speculated to also delay the vitrification of polymer, explaining the reduction on the polymerization stress. Based on this fact, it was also expected that the final DC for the cements photo-activated with these protocols would be higher. Interestingly, waiting for the redox-activated reaction to reach its peak before the photo-activation did not affect the DC measured after 24 hours. A possible explanation for the similar final DC between the protocols of photo-activation can be related to later conversion of carbon double bonds participating in formation of crosslinks rather than chain growth per se [30]. Thus, despite differences observed at values of $R_{p_{max}}$ and at DC when the $R_{p_{max}}$ was reached, the polymerization reaction continues until the medium does not allow for additional diffusion of non-reacted monomers. The DC when this reactional limitation occurs is probably similar for materials with same monomeric composition, irrespective of differences in polymerization kinetics.

In the second aim of this study, only two protocols of photo-activation were used: light exposure immediately after mixing/placement, which is more commonly used by clinicians; and starting light exposure at MRRP, which was the delayed photo-activation protocol best able to reduce the polymerization stress as per the results shown in aim 1. In this case, the research question was whether adding thio-urethane oligomers, which have been demonstrated to effectively delay gelation and vitrification in polymer networks [31], could further the stress reduction observed with the delayed light exposure, as shown in aim 1. In fact, the addition of thio-urethane oligomers to light-cured composites has been demonstrated to increase the final DC at the same time it reduces polymerization stress [17]. These advantageous effects are attributed to the ability of thiol pendant groups present on thio-urethane structures to delay gelation/vitrification stages, as already mentioned, via chain-transfer reactions [14,32]. Up to this point, in all studies involving thio-urethane addition to cements, dual-cured or not, the cements were photo-activated immediately after its mixing [13,17], so the possible effects of thio-urethane addition on delayed light exposure in dual-cure cements has not been evaluated to date. An important observation was that the addition of thio-urethane increased the $R_{p_{max}}$ of only redox activated polymerization reaction (0.15 and 0.26 for cements without and with thio-urethane,

respectively) by almost 2-fold. Furthermore, the polymerization kinetics curve (Figure 1) showed higher rate of polymerization in the first seconds of reaction, while the peak rate is reached earlier than when the thio-urethane was not used (70 and 420 s, respectively). One important observation is that redox initiators (BPO and EDMAB) were used in concentrations higher than that commonly used for dual-cured cement [17, 33]. Although EDMAB is an efficient co-initiator of photoactivated reaction when used with camphoroquinone, the low nucleophilicity of this amine hinders its reaction with BPO at ambient temperature [34]. Thus, higher concentrations of both redox initiators was used to accelerate the redox reaction and allow them to reach the RP_{max} at a clinically acceptable time to start the photoactivation. Previous studies have demonstrated that the excess of amine does not interfere with CQ initiated polymerizations, as long as the CQ concentration is kept above 0.1 wt% [19].

In the present study, we used the most common redox activation system, by adding a tertiary amine to the “base” paste and benzoyl peroxide to the “catalyst” paste of the cement. In this system, the mechanism for radical generation occurs by formation of amine radical cation and benzoylate anion, resulting in benzaloxo radical [35]. Interestingly, the thiol terminations can also function as reducing agent and react with benzoyl peroxide to initiate the polymerization of cement [36]. This reaction would not be expected to be particularly efficient, but for the concentration of thiols tethered to the oligomer and the concentration of benzoyl peroxide used in this study, it resulted in the stability of the cement being very poor when the TU was added to the paste containing the benzoyl peroxide (“catalyst”). In addition, it could be expected that Michael addition reactions of the vinyl to the thiol, which are accelerated in the presence of a base, such as a tertiary amine would have decreased the stability of the “base” paste, but for the conditions used in this study, the use of BHT as the inhibitor proved very successful at stabilizing the material. Based on these facts, the thio-urethane was added only to the “base” paste at concentration of 40%, which resulted in a final concentration in the mixed cement of 20 wt% thio-urethane. Indeed, in the curve of R_p x time (Figure 1) it can be observed that the values of R_p for the cement containing thio-urethane starts at around 0.17 %/s, which is a greater initial R_p value than what is observed for the material without thio-urethane. It is also observed that the RP_{max} for that material is reached only a few seconds after the kinetics measurement is started. This happens because as soon as the two pastes are mixed, the base (tertiary amine) comes in contact with the thio-urethane, and the efficient Michael addition reaction described above commences immediately. Thus, specifically for these groups, the lag time between insertion of the material in the mold and the start of the FTIR spectra collection was likely too long, and the measurement essentially “missed” the beginning of the redox activated polymerization reaction of cement containing thio-urethane. Moreover, considering that the DC is calculated based on the first spectrum collected, the final DC values for cement with thio-urethane were underestimated. In fact, previous studies have demonstrated that the addition of thio-urethane increases the final DC of methacrylate-based composites and that the RP_{max} is reached at higher values of DC, which is broadly justified by the delayed gelation and vitrification afforded by the chain-transfer reactions of the thiols to the vinyls [13,17]. However, in the present study, no difference on DC at RP_{max} was observed between cement with or without thio-urethane, irrespective of the protocol of photo-activation. This can be

partially explained by the limitation of the method described above. Therefore, it is not unexpected that the final DC values were only slightly higher (significant only for photo-activation at MRRP) than the ones observed for the cement without thio-urethane. Thus, considering the underestimated values of DC, cements containing thio-urethane probably presented higher DC than those without this additive after 24 h and at $R_{p_{max}}$, while the higher DC at this last moment of evaluation would indicate delayed vitrification, partially explaining the reduced values of polymerization stress.

The addition of thio-urethane to the cement reduced the maximum values of polymerization stress for both protocols of photo-activation. An important observation was that, while delaying the photo-activation resulted in around 14% less polymerization stress, the addition of thio-urethane reduced approximately stress by approximately 29% when the specimen was exposed to light immediately after mixing. Furthermore, adding thio-urethane and delaying the photo-activation led to 53% reduction on polymerization stress. Thus, the hypothesis of the study was accepted. It is important to reiterate that the combination of these two approaches is likely more relevant in areas where the light penetration is sufficient for the photoactivated reaction to dominate the polymerization. In regions where the redox mechanism is predominant (i.e., in regions where light penetration is poor), the stress generation is limited due to the great potential for strain accommodation under viscous flow [11,21]. It is in the regions beyond the free margin and prior to the “dark regions” of the restoration that avoiding the rapid stress development under confinement become more relevant.

It is important to emphasize that this stress reduction did not come at the expense of mechanical properties, as was evidenced by the hardness test results. The difference in hardness before and after storage in 100% ethanol was used in this study as a proxy to crosslinking density [36]. The loss of hardness after ethanol storage was only slightly greater for the cements containing thio-urethane. It is important to highlight, however, that no difference was observed on hardness after ethanol storage among cements with and without thio-urethane, whereas the use of this additive increased the initial hardness (probably due to higher DC).

Conclusions

Photo-activating dual-cured resin cements after the redox activated polymerization reaches its maximum rate of polymerization leads to reduced polymerization stress. The addition of thio-urethane to the same dual-cured resin cements results in more substantial reduction on polymerization stress, mainly when both strategies (thio-urethane and delayed photo-activation) are used.

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Clinical implications

The addition of thio-urethanes to dual-cured resin cements significantly reduced the polymerization stress without compromise to the conversion and mechanical properties of the material. The use of this additive combined with delayed photo-activation further improved these parameters. Clinically, this has the potential to minimize the effects of the extreme confinement imposed to the cement layer, at least in the regions of the restoration where light penetration is effective, and where stress develops rapidly after photoactivation.

Figure 1.
Development of R_p in function of time for only redox activated reactions.

Figure 2.
Development of R_p in function of DC for each start of photo-activation.

Figure 3. Development of polymerization stress in function of time for each level of photo-activation. For maximum values of polymerization stress, distinct letters indicate statistical difference ($p < 0.05$).

Figure 4. Development of R_p in function of DC for each experimental condition (start of photo-activation x addition of thio-urethane).

Figure 5.

Development of polymerization stress in function of time for each experimental condition (start of photo-activation x addition of thio-urethane). For maximum values of polymerization stress, distinct letters (uppercase for cements with TU; lowercase for cements without TU) indicate statistical difference between the moments for start of photo-activation ($p < 0.05$). * Indicate statistical difference between the cements of the start of photo-activation ($p < 0.05$).

Table 1

Results (means; 95% CI) for polymerization kinetics measured in aim 1.

Start of photo-activation	Rp _{max} (%/s)	Degree of conversion (%)			
		At light-curing	At Rp max	After 10 min	After 24 hours
Immediately	6.7 ^A (6.1–7.3)	-	30.4 ^B (29.2–31.6)	75.9 ^A (74.8–77.1)	84.8 ^A (83.7–85.9)
1 min before MRRP	7.4 ^A (6.2–8.6)	11.3 ^B (4.9–17.7)	33.8 ^B (30.8–36.9)	73.8 ^{AB} (72.5–75.2)	84.4 ^A (82.8–86.0)
At MRRP	4.9 ^B (3.7–6.0)	24.7 ^A (18.1–33.3)	42.5 ^A (38.3–46.8)	73.8 ^{AB} (72.7–74.8)	84.3 ^A (84.2–84.5)
1 min after MRRP	4.2 ^B (3.1–5.3)	31.8 ^A (24.6–38.9)	43.4 ^A (37.8–49.0)	72.4 ^B (71.6–73.2)	83.8 ^A (83.8–83.9)

Distinct letters indicate statistical difference ($P < 0.05$) among the times when the photo-activation was started for each outcome (comparison within each column). MRRP – Maximum rate of redox polymerization.

CI – Confidence interval.

Table 2

Results (means; 95% CI) for polymerization kinetics measured in aim 2.

Resin cement	DC (%)						Rp _{max} (%/s)		
	At moment of photo-activation *	At Rp _{max}		After 24 h		Start of photo-activation			
		Start of photo-activation		Start of photo-activation					
		Immediate	At MRRP	Immediate	At MRRP				
Without TU	24.7 (18.1–33.3) ^A	30.4 (29.2–31.6) ^{Ba}	42.5 (38.3–46.8) ^{Aa}	84.8 (83.7–85.9) ^{Aa}	84.3 (84.2–84.5) ^{Ab}	6.7 (6.1–7.3) ^{Aa}	4.9 (3.7–6.0) ^{Ba}	0.15 (0.13–0.16) ^b	
With TU	19.8 (17.6–22.0) ^A	30.8 (23.7–38.0) ^{Ba}	37.4 (36.1–38.8) ^{Aa}	85.8 (84.6–87.0) ^{Aa}	87.9 (86.3–89.6) ^{Aa}	6.4 (6.1–6.8) ^{Aa}	4.8 (4.5–5.1) ^{Ba}	0.26 (0.26–0.27) ^a	

* It was not evaluated for immediate photoactivation considering that non-significant DC was observed at this moment. Superscript letters (uppercase for line, lowercase for row) indicate statistical difference ($p < 0.05$). TU – thio-urethane; MRRP – Maximum rate of redox activated polymerization. CI – Confidence interval.

Table 3

Results (Means, 95% CI) for hardness test.

Resin cement	Start of photoactivation	Hardness (KHN)		Hardness loss (%)
		Before *	After *	
Without TU	Immediate	42.7 (40.3–45.2) ^{Ab}	19.6 (18.9–20.4) ^{Ba}	54.0 (52.9–55.2) ^B
	At MRRP	43.0 (41.7–44.3) ^{Ab}	19.1 (18.4–19.9) ^{Ba}	55.5 (52.6–58.6) ^B
With TU	Immediate	48.0 (47.0–49.1) ^{Aa}	19.0 (18.2–19.9) ^{Ba}	60.4 (58.1–62.7) ^A
	At MRRP	47.3 (45.9–48.7) ^{Aa}	18.7 (18.1–19.3) ^{Ba}	60.5 (58.7–62.2) ^A

* Ethanol storage. Superscript letters (uppercase for line, lowercase for row) indicate statistical difference ($p < 0.05$). TU – thio-urethane. CI – Confidence interval.

Table 4

Results (Means, 95% CI) for 3-point bending test.

Resin cement	Flexural Strength (MPa)		Elastic modulus (GPa)		
	Start of photoactivation		Start of photoactivation		Pooled average
	Immediate	At MRRP	Immediate	At MRRP	
Whitout TU	89.6 (70.4 – 108.8)	83.2 (63.3 – 103.1)	5.1 (4.2 – 6.0)	4.0 (3.5 – 4.5)	4.6 (4.0 – 5.2) ^A
Whith TU	81.4 (68.4 – 94.4)	76.8 (64.8 – 88.8)	3.6 (2.8 – 4.4)	3.8 (2.8 – 4.7)	3.7 (3.1 – 4.3) ^B

For pooled average, superscript letters indicate statistical difference ($p < 0.05$). TU – thio-urethane; MRRP – Maximum rate of redox polymerization. CI – Confidence interval.