DOI: 10.1111/ierd.13146

RESEARCH ARTICLE

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Masking capacity of minimally invasive lithium disilicate restorations on discolored teeth—The impact of ceramic thickness, the material's translucency, and the cement color

Thomas Attin Dr. med. dent.³ Ronald E. Jung Dr. med. dent.¹

Kevser Pala Dr. med. dent.¹ | Eva Maria Reinshagen Dr. med. dent.² | Jürg Hüsler Prof. em., Dr. phil. nat.⁴ |

Alexis Ioannidis Dr. med. dent.¹

¹Clinic of Reconstructive Dentistry, Center of Dental Medicine, University of Zurich, Zurich, Switzerland

²Doctoral Student at the Clinic of Reconstructive Dentistry, Center of Dental Medicine, University of Zurich, Zurich, Switzerland

³Clinic of Conservative and Preventive Dentistry, Center of Dental Medicine. University of Zurich, Zurich, Switzerland

⁴Department of Mathematical Statistics, University of Bern, Bern, Switzerland

Correspondence

Alexis Ioannidis, Clinic of Reconstructive Dentistry, Center of Dental Medicine, University of Zurich, Plattenstrasse 11, CH-8032 Zurich, Switzerland. Email: alexis.ioannidis@zzm.uzh.ch

Abstract

Objectives: To evaluate minimally invasive restorations' capacity to mask discolored teeth and explore the impact of ceramic thickness, translucency, and cement color. Materials and Methods: Twenty-four assessment pairs of naturally colored and dis-

colored bovine dentin samples were formed, using lithium disilicate specimens in six different thicknesses (0.3-0.8 mm), two different translucencies (high, low), and two cements (transparent, tooth-colored). Evaluators assessed the color differences in each assessment pair, and the threshold for detecting a color difference was determined using sequential testing and the Bonferroni-Holm method.

Results: A thickness of 0.6 mm effectively masked color differences using high translucent ceramic with transparent cement, detectable differences were still observed at 0.7/0.8 mm. A threshold thickness of 0.4 mm was seen using high translucent ceramic and tooth-colored cement, with color differences still discernible at 0.5 and 0.8 mm. A threshold thickness of 0.4 mm was detected using low translucent ceramic and transparent cement, while detectable differences persisted at 0.5, 0.7, and 0.8 mm. A 0.5 mm threshold thickness was observed when using low translucent ceramic and tooth-colored cement, and no detectable color differences were detected beyond this thickness.

Conclusions: Masking can be achieved with a thickness of 0.4-0.5 mm using a low translucent material and tooth-colored cement.

Clinical Significance: Understanding the impact of ceramic thickness, translucency, and cement color can aid clinicians in making informed decisions for achieving the best esthetic outcomes while preserving tooth structure. Effective masking can be accomplished with ceramic thicknesses starting at 0.4 mm, especially when employing a low translucent material and tooth-colored cement. However, clinicians should

Keyser Pala and Eva Maria Reinshagen equally contributing authors.

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be aware that discolorations may still be detectable in certain scenarios when using minimally invasive lithium disilicate restorations.

KEYWORDS

cement color, ceramic thickness, ceramic translucency, discoloration, lithium disilicate, masking capacity, minimally invasive

1 | INTRODUCTION

The selection of minimally invasive ceramic veneers as a treatment for discolored front teeth poses a challenge due to the lack of scientific evidence regarding the material's ability to correct underlying discoloration. Several factors, including material thickness, material translucency, and cement color, may influence the masking capacity of the restoration. However, the extent of impact of these factors on the masking capacity remains unclear.

The choice of veneer thickness can be tailored to the clinical situation, with varying thicknesses based on the desired treatment goal. In cases of discoloration, the restorative thickness is determined by the difference between the current tooth color and the desired outcome. Thinner veneers, start at a thickness of \geq 0.3 mm, while classic veneers typically measure \geq 0.5 mm and thicker veneers can reach \geq 0.6 mm.^{1.2} From a biological perspective, it is preferable to minimize the removal of sound tooth structure to reduce the risk of short- and long-term pulpal complications.^{2.3} However, selecting the appropriate thickness to effectively mask the color difference while preserving tooth structure can be challenging. In previous studies, there was a high variety in the needed ceramic thickness to mask discolored teeth with thicknesses ranging between 0.4 and 2.0 mm.^{4–7}

The degree of discoloration also influences material selection in the esthetic zone.⁸ For moderate to severe discolorations, materials such as zirconia and metal-ceramics are commonly recommended,⁸ but they require a more extensive tooth preparation, resulting in a medium to highly invasive treatment where significant amounts of tooth structure may be lost.⁹ In cases where minimally invasive restorative alternatives are desired, silica ceramics such as lithium disilicate are suitable due to their mechanical and optical characteristics.^{1,10,11} Lithium disilicate is available in different translucencies to match the optical characteristics of neighboring teeth and for achieving a restoration that blends with the adjacent natural teeth.¹² The translucency increases with decreasing material thickness, which in turn can affect the masking capacity.¹³ A previous study has shown that the translucency has an impact on the masking capacity, but has also stated that the ceramic thickness seems to have a greater impact on the masking capacity then the translucency.¹⁴ However, the precise impact of the translucency on the final color has not been sufficiently investigated.

Resin cements are commonly used for the adhesive cementation of silica ceramics.¹⁵ Selecting the appropriate cement color can be difficult, due to the wide range of available shades with different indications. The influence of the cement color has been questioned in general, considering its limited thickness underneath a restoration.¹⁶ A study revealed that the color of the cement had an influence on the final color

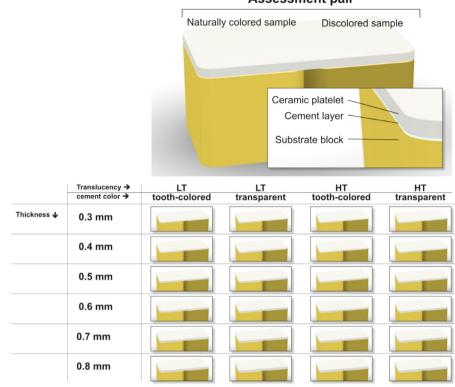
of lithium disilicate restorations,¹⁷ while other studies suggested that although different colors of cement may not strongly affect the final color, the impact becomes more pronounced with increasing translucency and decreasing thickness of the restoration.^{1,18,19} Consistently, another study indicated that the color of the cement had a higher impact on high translucent lithium disilicate compared to low translucent lithium disilicate.²⁰ Transparent cements have minimal impact on the final restoration color, and therefore, it can be assumed that they are more suitable when the restoration already matches well. Opaque cements have the greatest influence on the final shade with a high potential of masking capacity,^{19,21} as they contain a higher proportion of opaque components.¹³ Tooth-colored shades with varying lightness and chroma are also available. However, the exact impact of cement color on the masking capacity has not been sufficiently clarified.

In a systematic review, it was reported that metric methods are mostly used to calculate color differences, and there are many ways to do so.²² The results often cannot be converted to another method.²² The most commonly used method to determine the masking ability of restorative materials is the calculation of a color difference ΔE using CIELAB and CIEDE20000 formulas. However, it has been suggested that this method might not be clinically relevant.²² Therefore, visual thresholds are associated with ΔE values to express clinical evidence.²³ Visual thresholds are an important tool in dentistry and dental research.²⁴ These visual thresholds can be divided into perceptibility and acceptability thresholds. Perceptibility thresholds describe the smallest perceptible color difference that can be detected by observers, whereas acceptability thresholds refer to the smallest acceptable color difference.²⁴ These thresholds vary among studies, and there is no clear consensus on using one specific threshold.^{23,25-27} To assess the issue of masking capacities from a clinical point of view, human evaluators can be used to assess color differences instead of using spectrophotometrical devices. Moreover, distinct evaluator groups can be formed to investigate potential variations in visual thresholds.^{7,23,26}

For the above-mentioned reasons, it is crucial to gain knowledge about influencing parameters such as restorative thickness, material translucency, and cement color when restoring discolored front teeth using minimally invasive restorations. The aim of this in vitro study was to investigate the required thickness of lithium disilicate to effectively mask a discolored tooth and assess the impact of ceramic translucency and cement color on the perception of evaluators in three distinct groups: dentists, dental technicians and laypersons. Following research hypotheses were tested:

 The translucency of the ceramic has a significant impact on the masking capacity. **FIGURE 1** Set-up of the samples and assessment pairs with different transluciencies (LT, low translucency; HT, high translucency) different cement colors (tooth-colored; transparent) and different ceramic thicknesses (0.1–0.8 mm).

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The cement color has a significant impact on the masking capacity.
The evaluator group has a significant impact on the masking capacity.

2 | MATERIALS AND METHODS

2.1 | Groups

A total of 24 assessment pairs were created, consisting of two differently stained dentin blocks covered by monolithic lithium disilicate specimens (Figure 1). The lithium disilicate specimens were prepared in six different thicknesses and two different translucencies, and were adhesively bonded using two different cement colors. The assessment pairs were divided into four groups, with six pairs in each group. Each group included monolithic lithium disilicate specimens of varying thicknesses (0.3, 0.4, 0.5, 0.6, 0.7, and 0.8 mm). Two groups featured high translucency (HT) material, and the other two groups featured low translucency (LT) material. Furthermore, the HT and LT groups were further divided based on the cement color used, which was either transparent (tr) or tooth-colored (tc). The resulting four groups were HT-tr, HT-tc, LT-tr, and LT-tc.

2.2 | Fabrication of the substrate

As it was done in previous studies, stained bovine dentin blocks were used as substrate.^{22,28} A substrate consisted of a bovine dentin block with a planar test surface measuring 7×7 mm. The dentin blocks were created from extracted bovine incisors and canines. The root blocks were ground to obtain a planar surface (Planopol-2 and

waterproof silicon carbide grinding paper, SIC, US #600 grain size 15 μ m; Struers, Willich, Germany). All surfaces of the root blocks, except the test surface, were coated with transparent nail polish (Express Finish Base Brilliante transparent 01; Maybelline, New York City, NY, USA) and allowed to dry completely.

2.3 | Coloration of the substrate

Two types of black tea (Yellow Label Tea Quality No. 1; Lipton, Purchase, NY, USA / Extra strong teabags rich, bright & malty, Strong 3; Marks & Spencer, London, England) were used to stain the test surface of the dentin blocks. The staining solution was prepared by brewing the black tea with deionized water, adjusting the pH to 4 by adding citric acid (0.1 M), and monitoring the pH value continuously (827 pH lab; Metrohm, Zofingen, Switzerland). The dentin blocks were immersed in 20 mL of the staining solution for 20–60 min for the light substrates and 30–75 min for the dark substrates. The blocks were periodically removed to visually assess the color of the substrate. Once the desired color was achieved, the substrates were air-dried and stored in a dry plastic container.

2.4 | Spectrophotometric measurements and pairing of the substrates

After the substrates had dried for 2–3 days, the color of the test surface was measured using a spectrophotometer (CM-2600d; Konica Minolta, Chiyoda, Tokyo, Japan), and the Lab*-values were recorded 4 WILEY-

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(Spectra Magic NX; Konica Minolta, Chiyoda, Tokyo, Japan). The color difference (Δ E) between the differently colored substrates was calculated (Microsoft Excel; Redmond, WA, USA). The CIEDE2000 color difference formula was used. To form a pair, a dark substrate and a light substrate were selected, with a median Δ E value of 3.56. This process resulted in 24 pairs, each consisting of one light and one dark substrate, representing the assessment pairs.

2.5 | Fabrication of the ceramic specimens

Monolithic lithium disilicate specimens were prepared using lithium disilicate blocks (IPS e.max CAD LT and HT A2/C14; Ivoclar Vivadent, Schaan, Liechtenstein). Two different translucencies, high translucency (HT) and low translucency (LT), were used depending on the group allocation. A total of six different thicknesses (0.3, 0.4, 0.5, 0.6, 0.7, and 0.8 mm) were fabricated. Slices were cut from the blocks (Accutom-50 and Diamond Cut-off Wheel M0D10; Struers, Willich, Germany) and manually ground to achieve a uniform thickness (LaboPol-21, Struers, Willich, Germany; WS FLEX 18 C waterproof P80, Hermes Schleifmittel, Hamburg, Germany). The thickness was regularly verified using a digital micrometer (Mitutoyo, Kawasaki, Japan) until the desired thickness (±0.01 mm) was achieved. The ceramic specimens were then crystallized according to the manufacturer's instructions (Programat P510; Ivoclar Vivadent, Schaan, Liechtenstein).

2.6 | Adhesive cementation

The conditioning of the monolithic lithium disilicate specimens began by etching the innersurfaces of the specimens with 5% hydrofluoric acid (IPS ceramic etching gel; Ivoclar Vivadent, Schaan, Liechtenstein) for 30 s, followed by water rinsing and air-drying. A silane coupling agent (Monobond Plus; Ivoclar Vivadent, Schaan, Liechtenstein) was applied to the etched surfaces for 60 s, followed by an additional 60 s of air drying. Depending on the group allocation, two different flowable light-curing resin cements were used: transparent cement (tr: Variolink Esthetic LC neutral) and tooth-colored cement (tc: Variolink Esthetic LC warm; both Ivoclar Vivadent, Schaan, Liechtenstein). The cement was applied to the dentin surface, and the lithium disilicate specimens were positioned on the substrate. Excess cement was carefully removed, and the correct positioning of the specimens was verified. The cement was then light cured for 60 s at 1200 mW/cm² (Bluephase G2; Ivoclar Vivadent, Schaan, Liechtenstein).

2.7 | Sample pictures

The assessment pairs with the adhered ceramic specimens were embedded in 3D-printed insets using an epoxy resin (Loctite Stycast 1266 PTA and PTB; Henkel, Düsseldorf, Germany). Pictures of the assessment pairs were captured in a standardized setup using a digital camera (D7000; Nikon, Chiyoda, Tokyo, Japan) with settings of ISO 100, f/32 and 1.3 s of exposure, lateral flasthes set at 1/1. The camera

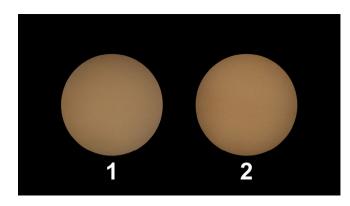


FIGURE 2 Example of an assessment pair as assessed by the evaluators.

was mounted on a tripod, and a polarization filter (CROSS-POLAR filter Nikon R1C1 flash system; IT logika, Vilnius, Lithuania), along with a gray card (GC – 1II 18% neutral gray; JJC Photography Equipment, Shenzhen, China), was used as a reference for white balance. After adjusting the gray value using photo editing software (Lightroom; Adobe, San José, CA, USA), illustrations (Figure 2) were created by cutting out two circular areas of different colors from an assessment pair and placing them in standardized sizes and positions on a black background (PowerPoint; Microsoft, Redmond, WA, USA). One-third of the samples were used to generate additional assessment pairs without a color difference by duplicating one circular area.

2.8 | Evaluation survey

An online survey (limesurvey, Hamburg, Germany) was created. The survey started with information slides to familiarize the evaluators with the survey's functionality and example/test slides displaying the assessment pairs in order to educate and train the evaluators for the survey. Furthermore, the evaluators were asked to set their screen lightness to 100% to ensure ideal color reproduction. Then, illustration and questioning slides where shown, where the evaluators had to select the correct answer. Each illustration slide was displayed for 3 s only (Figure 2). The evaluators could choose from 3 possible answer options: "Circle 1 is brighter," "Circle 2 is brighter," and "No difference." In the introduction, the evaluators were informed that there is not necessarily a difference between the samples. Evaluators, including dentists, dental technicians, and laypersons, were invited to participate in the survey. They were blinded to the study's design and objective.

2.9 | Statistical analysis

The statistical analysis involved two factorial generalized mixed linear models for the binary variables of a correct answer for translucency, cement color, and group, always with thickness including. Also, multifactorial models were applied with the factors translucency, cement color, group, and thickness, with also interactions terms. If these interaction terms are significant, we used sequential testing, using the order of the thickness, and the Bonferroni-Holm method using no order to understand the effects, in particular the thickness effect. Sequential testing was used to determine the threshold thickness where no color difference could be reliably detected for each group. The Bonferroni-Holm method was further applied to identify statistically significant differences among the evaluator groups at different thicknesses. No additional correction of the multiple testing of the different groups and different combinations of translucencies and cements is applied.

The sample size was based on the two independent group comparison with the binomial test with p = 0.8 versus p = 0.6, with alpha = 5% and power 80%, which needs a sample of 72 per evaluator group. The threshold for a group to differentiate the color difference correctly was set if at least 80% of the group gave the correct answer, tested one-sided with the exact binomial distribution.

3 | RESULTS

A total of 251 evaluators participated in the study, including 79 dentists, 72 dental technicians, and 100 laypersons. All the factors translucency, cement color, and group were significant (p < 0.001) including the thickness factor (p < 0.0001). The multifactorial model

revealed also significant two-factor and three-factor interaction terms. Therefore, we applied the sequential testing to describe in a better understandable way the results of the difference of the categories of translucency, cement color, and group.

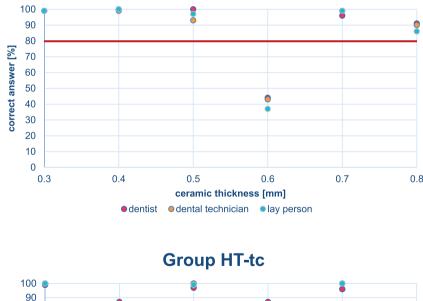
3.1 | High translucent ceramic (HT) with transparent cement (tr).

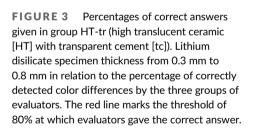
In the HT-tr group (Figure 3), sequential testing revealed that a thickness of 0.6 mm was the threshold where no color difference could be reliably detected for all groups. The Bonferroni-Holm method showed, however, that with a thickness of 0.7 mm in all groups and a thickness of 0.8 mm in the groups of dentist and dental technicians the color difference was still perceivable.

3.2 | High translucent ceramic (HT) with tooth-colored cement (tc).

Group HT-tr

In the HT-tc group (Figure 4), sequential testing identified 0.4 mm as the threshold thickness where no color difference was visibly detected.





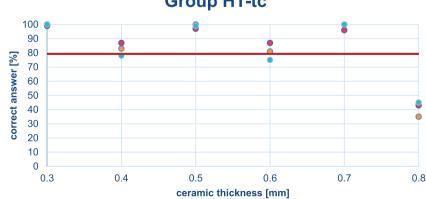


FIGURE 4 Percentages of correct answers given in group HT-tc (high translucent ceramic [HT] with tooth-colored cement [tc]). Lithium disilicate specimen thickness from 0.3 mm to 0.8 mm in relation to the percentage of correctly detected color differences by the three groups of evaluators. The red line marks the threshold of 80%.





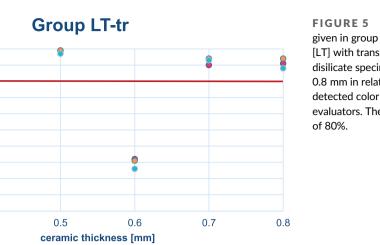


FIGURE 5 Percentages of correct answers given in group LT-tr (low translucent ceramic [LT] with transparent cement [tr]). Lithium disilicate specimen thickness from 0.3 mm to 0.8 mm in relation to the percentage of correctly detected color differences by the three groups of evaluators. The red line marks the threshold of 80%.



dental technician

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dentist

100

90

80

70

60

correct answer [%]

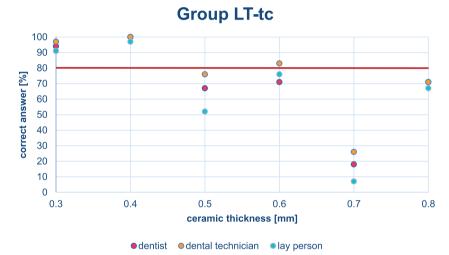


FIGURE 6 Percentages of correct answers given in group LT-tc (low translucent ceramic [LT] with tooth-colored cement [tc]). Lithium disilicate specimen thickness from 0.3 mm to 0.8 mm in relation to the percentage of correctly detected color differences by the three groups of evaluators. The red line marks the threshold of 80%.

The Bonferroni-Holm method revealed that all groups were still able to detect color differences with the thicknesses 0.5 mm and 0.7 mm.

3.3 | Low translucent ceramic (LT) with transparent cement (tr).

In the group LT-tr (Figure 5), sequential testing indicated that 0.4 mm was the threshold thickness where no color difference was perceivable by all the evaluator groups. The Bonferroni-Holm method showed, however, that with 0.5, 0.7, and 0.8-mm thicknesses, a perceivable color difference remained.

3.4 | Low translucent ceramic (LT) with a tooth-colored cement (tc).

In the group LT-tc (Figure 6), sequential testing found 0.5 mm to be the thickness, from which no color difference could be detected anymore for all the groups. The Bonferroni-Holm method showed consistent results. No color difference was detectable with thicknesses of 0.5–0.8 mm.

4 | DISCUSSION

The findings of this study provide valuable insights into the masking capacity of minimally invasive lithium disilicate restorations on discolored teeth. The results indicate that the choice of material thickness, material translucency, and cement color can significantly impact the ability to effectively mask color differences. All the three hypotheses were validated.

Regarding the material thickness, it was observed that a thickness of 0.4 mm in high translucent monolithic lithium disilicate restorations may be sufficient to cover a color difference when paired with a colored cement. The same applies when combining a low translucent material with a transparent cement. When using a low translucent material with a colored cement, a thickness of at least 0.5 mm is needed to achieve the same level of masking. By combining a high translucent material with a transparent cement, 0.6 mm thickness is needed to mask a discoloration. However, considering the other statistical method (Bonferroni-Holm method), the results were only consistent with sequential testing when looking at the results of low translucent material and tooth-colored cement. All other groups showed outliers in the results.

The results of this study indicate that material thickness plays a significant role in the masking capacity of minimally invasive lithium disilicate restorations. The threshold thickness at which no color difference was detectable varied between 0.4 and 0.6 mm. depending on the ceramic translucency and the color of cement used. Comparisons with other studies are necessary to gain a broader perspective on these findings. It was reported that with a low translucent restorative material and an abutment color C4, the color difference was below the perception threshold with a restoration thickness of 2.0 mm.⁴ Another study found that a 0.5 mm thickness of lithium disilicate can effectively cover an A4-colored block.⁵ This is consistent with a further study which investigated the masking capacity of A2-colored lithium disilicate in both high and low translucency variations with a thickness of 0.5 mm.⁶ Their findings demonstrated that this specific thickness was effective in successfully masking a B4-colored resin block.⁶ This is coherent with the thickness range showed in the present study. However, it is important to note that the same study as reported above, revealed limitations in masking color discrepancies, as a thickness of 0.5 mm was unable to fully cover A4-colored resin blocks.⁶ As mentioned before, it was assumed, that the lightness of the underlying substrate has an impact on the masking capacity.⁶ This was also shown in another study, investigating the masking capacity of feldspathic ceramic on discolored substrates.⁷

The translucency of the ceramic material and the use of colored or transparent cement were found to have an impact on the masking capacity. In the HT-tr group, where high translucent ceramic was used with transparent cement, the results demonstrated that a greater thickness of 0.6 mm was needed to achieve effective masking. Conversely, in the HT-tc group, where high translucent ceramic was used with tooth-colored cement, a lower threshold thickness of 0.4 mm was sufficient for effective masking. This may suggest that the use of a toothcolored cement can enhance the masking capacity of a translucent restoration. The LT-tr and LT-tc groups, which utilized low translucent ceramic, also exhibited different masking capacities. In the LT-tr group, a threshold thickness of 0.4 mm was identified, indicating that low translucent ceramic combined with transparent cement requires a similar thickness as high translucent ceramic with transparent cement for effective masking. On the other hand, in the LT-tc group, a threshold thickness of 0.5 mm was determined, indicating that a slightly greater thickness is necessary for effective masking when using low translucent ceramic with tooth-colored cement. Findings on the impact of the cement color on the masking ability also varies in the current literature. It was suggested that the cement color had an higher impact on the final color with increasing translucency and decreasing thickness of the restorative material.^{1,17,18,20} As expected, in the present study, the highest threshold thickness was shown with a high translucent material and a transparent cement. Logically, we would have expected the

lowest threshold thicknesses with a combination of a low translucent ceramic material with a tooth-colored cement.

Comparing the results in the existing literature is difficult. Perceptibility thresholds associated with ΔE values vary among studies, and there is no clear consensus on using one specific threshold.^{23,25-27} A strength of this study is the choice of a subjective assessment as a means of evaluation. In contrast to most of the existing literature, this study directly evaluated the perceptibility of the color difference by different groups of evaluators using a survey. This increases the clinical significance of the results and simplifies the comparison to results of other studies evaluating the subjective perceptibility of color differences by a binary system. Analyzing the results, it is difficult to simply interpret the influence of the evaluator group on the results due to the significant interaction terms. Often, the laypersons could not percept color differences as correctly as dentist or dental technicians could. Because of the significant interaction terms with the other factors, one cannot simply describe these differences. Therefore, we refer to the Figures 3-6, where one notice that often the laypersons showed lower percentages of correct answers. The percentages of correct answers of the dentists and the technicians do not differ significantly. Another strength of this study is the choice of dentin as a substrate. The underlying substrate is widely varying in the existing literature between materials such as composite, metals, and ceramics.²² In the above-mentioned systematic review, only one of the included studies used stained dentin as a substrate to test the masking capacity of restorative materials.²² There was another study that used stained dentin to assess the masking capacity of feldspar,²⁸ which was not included in the review. The use of dentin as a substrate is a further step in the concept of in-vitro studies to simulate the actual clinical situation as closely as possible, as artificially produced substrates show different material properties and therefore have a lower clinical validity. In addition, this study objectively defined the color difference that needs to be masked. Other studies mostly used color differences by selecting shades of the color scheme. This further complicates the comparison between different study results, since the color difference to be covered is not quantitatively defined.

Although the present study aimed to simulate the clinical situation as closely as possible by using stained dentin as a substrate, it was not feasible to follow all clinical steps of the adhesion process. Typically, dentin is prepared for cementation through etching, priming, and bonding. However, in this case, these adhesive steps could not be performed as the acid components of the materials dissolved the stain from the substrates. Future studies should explore more permanent methods of staining dentin to allow for the completion of all work steps. A further limitation is the presence of outliers in the results. One possible explanation for these outliers is the range of color differences ($\Delta E = 4-6$) within the assessment pairs. This could have an impact unrelated to the adhered lithium disilicate specimen. Furthermore, the method of evaluation could have caused these outliers, since it consisted of a subjective evaluation rather than an objective measurement. As discussed above, the chosen method of evaluation is closer to the clinical situation, but it could bring the disadvantage of not objectifying the results. Moreover, the color vision of the evaluators was not tested, nor were the

evaluators calibrated, which could also have impacted the results. Another point to discuss is the inhomogeneity between the samples in terms of lightness, chroma, and hue. Previous findings have shown that lightness, in particular, has a significant impact on the masking ability of overlaying materials.⁷ In our samples, the lightness values varied from 69.35 to 76.92, which could have influenced the visual color difference unrelated to the lithium disilicate. Additionally, the thickness of the cement layer in our samples was not precisely defined. The lithium disilicate specimens were applied to the substrate with finger pressure, probably resulting in varying cement thickness. As discussed above, studies have shown that the thickness of the adhesive layer may be a sensitive parameter when measuring colors and can influence the final color of the restoration.^{18,19} Inconsistencies in cement thickness, particularly in the groups with colored cement, could introduce bias in color difference. To address this limitation, future studies should regulate the thickness of the cement using standardized production methods.

5 | CONCLUSIONS

Within the limitations of this current study, it was concluded that:

- Minimally invasive lithium disilicate restorations were sufficient to mask discolorations to the extend tested in this study.
- The masking capacity was influenced by the translucency of the ceramic. Employing a low translucent restorative material, a restoration thickness of 0.4–0.5 mm was shown to be sufficient.
- A colored cement improved the masking effect.
- The perceptibility of color differences varied among different evaluator groups.

ACKNOWLEDGMENTS

The authors would like to thank Andrea Gubler, Claudia Cucuzza, and Marcus Zimmermann for their help in the fabrication of the samples. Furthermore, Marcel Arnold must be thanked for his support in the graphic design. Open access funding provided by Universitat Zurich.

CONFLICT OF INTEREST STATEMENT

The authors do not have any financial interest in the companies whose materials are included in this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Alexis Ioannidis 🕩 https://orcid.org/0000-0002-2110-3645

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How to cite this article: Pala K, Reinshagen EM, Attin T, Hüsler J, Jung RE, Ioannidis A. Masking capacity of minimally invasive lithium disilicate restorations on discolored teeth— The impact of ceramic thickness, the material's translucency, and the cement color. *J Esthet Restor Dent*. 2023;1-9. doi:10. 1111/jerd.13146