Journal of Dentistry 56 (2017) 84–98

Contents lists available at ScienceDirect

Journal of Dentistry

journal homepage: www.intl.elsevierhealth.com/journals/jden

Own brand label restorative materials—A false bargain?

Gaute Floer Johnsen[a], Minh Khai Le Thieu[a], Badra Hussain[a], Elzbieta Pamuła[b], Janne Elin Reseland[a], Ståle Petter Lyngstadaas[a], Håvard Haugen[a,*]

[a] University of Oslo, Department of Biomaterials, Institute of Clinical Dentistry, Faculty of Dentistry, Geitmyrsveien 71, Oslo, NO 0455, Norway
[b] AGH University of Science and Technology in Kraków, Kraków, Małopolska, Poland

ARTICLE INFO

Article history:
Received 22 June 2016
Received in revised form 25 October 2016
Accepted 7 November 2016

Keywords:
Own brand label
Composites
Flexural strength
Residual monomers
Degree of conversion
Cytotoxicity

ABSTRACT

Objectives: This study aims at evaluating and comparing mechanical, chemical, and cytotoxicological parameters of a commercial brand name composite material against two 'own brand label' (OBL) composites.
Methods: Parameters included depth of cure, flexural strength, degree of conversion, polymerization shrinkage, filler particle morphology and elemental analyzes, Vickers hardness, surface roughness parameters after abrasion, monomer elution, and cytotoxicity.
Results: The conventional composite outperformed the OBLS in terms of depth of cure ($p < 0.001$), degree of cure at the first and last time intervals ($p < 0.001$), hardness ($p < 0.001$), and post-abrasion roughness ($p < 0.05$). The polymerization volumetric shrinkage ranged from 2.86% to 4.13%, with the highest shrinkage seen among the OBLs. Both Monomer elution from the OBLs was statistically significantly higher ($p < 0.001$). Statistically significantly higher cytotoxicity combined with altered morphology and loss of confluence was detected in the cells exposed to extracts from the OBLs.
Conclusions: The OBLs were in general outdone by the conventional composite.
Clinical significance: OBLs restorative materials have become pervasive in the dental market. Manufacturers often promise equal or better characteristics than existing brand-name composites, but at a lower price. Dentists are highly recommended to reconsider utilization of OBLs lacking sound scientific scrutiny, and our findings underscore this recommendation.

1. Introduction

At present there are a myriad of manufacturers producing a plethora of resin-based restorative composites (RBCs). The chemical and mechanical variations in these materials will affect their quality in terms of wear resistance, strength, elution of monomers, degree of curing, and indication for use [1]. Materials with poorer and undesirable properties will increase the risk for secondary caries, mechanical failure, and deterioration [2].

From a socio-economical and public health perspective, dentist should use materials with independently tested longevity and safety. Recently, less expensive and largely unknown own brand label (OBL) composite materials are appearing in public tenders where price often matters the most. Furthermore, local public purchasing groups do not necessarily possess the expertise or resources to satisfactorily evaluate these tendered materials [3]. There is anecdotal evidence that sales of dental composites (OBL) are increasing, as dentists wish to become more cost-effective in times of economic recession. However, the purchase of less expensive composites could be a false economy if their performance falls below accepted standards [4,5].

RBCs are placed into a harsh and hostile environment where they are exposed to relatively large mechanical loads, major changes in both temperature and pH-values, enzymatic degradation of the polymer matrix and even individual changes in saliva flow and buffering capacity over time [6,7]. In addition to having the necessary mechanical requirements and physical properties, RBCs cannot be detrimental to the neither patients' nor clinicians' health nor safety. There are great demands on the physical and chemical properties of the materials in order to fulfill the clinical expectations of both performance, longevity, and safety [8]. In addition to the intrinsic and extrinsic oral challenges facing RBCs, there are inherent material characteristics that place limits on their overall performance. Some of these limitations include shrinkage and polymerization-induced shrinkage stresses,

* Corresponding author.
E-mail addresses: gautefj@odont.uio.no (G.F. Johnsen), mkthieu@student.odont.uio.no (M.K.L. Thieu), badrah@student.odont.uio.no (B. Hussain), epamula@agh.edu.pl (E. Pamuła), j.e.reseland@odont.uio.no (J.E. Reseland), s.p.lyngstadaas@odont.uio.no (S.P. Lyngstadaas), h.j.haugen@odont.uio.no (H. Haugen).

http://dx.doi.org/10.1016/j.jdent.2016.11.004
0300-5712/

restricted toughness and hardness, and residual monomers following polymerization [9].

Independent data on OBLs is scarce, and it has been altogether lacking from the scientific literature until a recent publication by Shaw et al. also highlighting the need for more research [5]. This fact was underpinned by Burke [4] who examined results from a total of 444 abstracts presented at the 2011 89th General Session & Exhibition of the International Association of Dental Research (IADR) and found no evidence of research on OBLs . . . There is a definite need for scientific scrutiny of OBLs in order to reveal if they meet, exceed or fail to meet prevailing standards.

Numerous and extensive composite fillings from an early age are more common among individuals from vulnerable socioeconomic groups [26]. The long-term adverse risks from exposure to RBCs are unknown. It is therefore imperative that the materials used in public dental care have undergone extensive independent scientific study.

The aim of this study was to determine if OBLs meet accepted standards. This study compared parameters (depth of cure, flexural strength, elemental analysis, polymerization shrinkage, degree of conversion, monomer elution, cytotoxicity, hardness, and surface roughness) of two OBL composite materials versus a name brand composite widely used in the public dental services in Norway. The examinations of the RBCs were either based on applicable ISO standards or validated and recognized tests from the scientific literature.

In order exclude batch variability and to increase the validity of the study, several batches of each material were tested. The null hypothesis was that name brand composite does not out-perform the two OBL composite materials.

2. Materials and methods

2.1. Selection of materials and curing light

The examined composite materials were the RBC and OBLs with the largest purchasing volume in the public dental services in the Akershus Region of Norway). Akershus Region has 11.06% of the entire population in Norway and thus seemed representative for the entire nation (Table 1). All of the composites were non-expired and of the same shade (A3).

All the composites were cured with the same LED curing light, LEDemetron II Light (1600 mW/cm2) (Kerr Corporation, Orange, CA, USA), selected on the basis of recommended light intensities for the different material manufacturers (Z250 > 400 mW/cm^2 and 4U < 1000 mW/cm^2). The OBL brand TD did not provide any recommendation on light intensity. The output of the curing unit was controlled by using the built-in radiometer.

2.2. Depth of cure

Depth of cure (DOC) was determined according to ISO 4049: 2009 (E) *Dentistry – Polymer-based restorative materials* (ISO 4049) [27]. A stainless steel mold was used to prepare cylindrical test bodies with the same diameters (4 mm) and heights (6 mm). Six test bodies were made for every material, three from each batch. The cylindrical wells were filled with the composite paste, and all the materials were cured from the top side for 20 s. Curing depth (mm) was then calculated by dividing the measurement by two.

2.3. Flexural strength

Determination of three-point bending strength (flexural strength) was based on the standards put forth in ISO 4049 [27] on a Zwicki (Zwick/Roell) with the testXpert (Zwick/Roell, Ulm, Germany) software. Five identical test bodies from each batch (n = 30) were prepared from stainless steel molds with the following dimensions and permissible deviations (25 ± 2)mm $\times (2.0 \pm 0.1)$mm $\times (2.0 \pm 0.1)$mm. The top and bottom surfaces were then polymerized with the use of six overlapping irradiations of 20 s on each side. The cured specimens, still embedded in the mold, were placed in a water bath (ISO 3696 grade 2 water [37 ± 1 °C)) for 15 min. The flexural strength (σ) of a material is defined as the maximum stress that a material can resist before failure when subjected to a bending load (Eq. (1)) [28]; F is the maximum load (Newtons), L is the distance between supports, B is

Table 1
Composite material documentation from wrapper/carton and as provided by IFUs, MSDSs, Promotional Material and Technical Product Files.

Material	Batch numbers		Manufacturer	Recommended light intensity (mW/cm^2)	Curing depth (mm) according to manufacturer	Classification[a]	Fillers, wt%, Size	Organic Matrix (wt%)
	Batch «1»	Batch «2»						
Filtek Z250	N495027	N548402/ N644277	3 M ESPE	≥ 400	2.5	Universal	Zirconia/silica 0.01–3.5 μm	TEGDMA < 1–5% Bis-GMA < 1–5% Bis-EMA 5–10% UDMA 5–10%
4U (OBL)	5303806	5310212	Nordenta, LIC Scadenta	≥ 1000	2.0	Nano-hybrid with fluoride/micro-hybrid, universal[a]	Barium glass and fumed silica 0.05 – 1.5 μm	Mixture of poly- and difuncitional methacrylates. Resin based on BisGMA[b]
Top Dent (OBL)	NXU13062101	NXC1403312	DAB Dental, LIC Scadenta	n.a.	2.0	Nano-hybrid/micro hybrid[a]	No information provided	TEGDMA 1–5% Bis-GMA 1–10% Bis-EMA 1–15% UDMA 1–10% TMPTMA <1%

n.a. – not analyzed.
[a] 4U and TD had inconsistencies in their classifications in the IFUs, MSDSs, and Promotional Material.
[b] No detailed information on exact types of monomers and their wt.% apart from containing BisGMA.

the width of the specimen, and H is the height of the specimen.

$$\sigma = \frac{3FL}{2BH^2} \quad (1)$$

2.4. Degree of conversion

Attenuated total reflection Fourier transform infrared spectroscopy, ATR-FTIR (Spectrum 100, PerkinElmer Instruments, Waltham, MA, USA) was used to analyze the degree of conversion of monomers (percentage of reacted methacrylate) in every material on the top and bottom of the cured test specimens at the following time intervals post-cure: immediately following curing (T_1); 0.5 h (T_2); 1 h (T_3); 4 h (T_4); and 24 h (T_5). A total of five specimens from each material batch (n = 30) were prepared in the previously described stainless steel metal molds. Samples were cured between two transparent polyester films to avoid oxygen inhibition of polymerization. The sampling was performed under following conditions: Mid-IR wavelength, 2 cm^{-1} resolution and 32 scans. The calculation of the degree of conversion (DC%) as previously described [29].

2.5. Polymerization shrinkage

Polymerization shrinkage was measured by utilizing a previously documented micro X-ray microcomputed tomography (μCT) methodology [30,31]. μCT-scans were performed in dark conditions using desktop SkyScan 1172 (Bruker, Aartselaar, Belgium). Uncured samples (n = 3 for each composite type) with a mean size of 40.21 mm^2 were mounted vertically in customized tubes. Scanning parameters were set to 17.77 μm pixel size, x-ray source with 100 kV and 100 mA and using 500 μm Al and 38 μm Cu filters. Samples were rotated 360° around their vertical axis with a rotational step of 0.7°. Next, the composites were cured for 60 s with the LEDemetron II Light to ensure optimal curing. This method allowed for scanning of 5 samples at a time. Shrinkage was calculated based on the differences in volume evaluated using calculation described by Sun & Lin-Gibson [30] where shrinkage is $S_{\mu CT}$, volume of uncured composite is V1, and volume of cured composite is V1 (Eq. (2)):.

$$S_{\mu CT} = \frac{(V1 - V2)}{V1} \quad (2)$$

2.6. SEM-EDS

Morphology of fillers and distribution in the matrix were determined by scanning electron microscopy (SEM) in a Hitachi Analytical Table Top Microscope/Benchtop SEM TM3030 (Hitachi High-Technologies Europe, Berkshire, UK) operating at an accelerating voltage of 15 kV. For determination of the morphology of the filler uncured material was dissolved in acetone and chloroform, centrifuged and the particles dissolved in ethanol according to a washing technique by Beun et al. [32]. The EtOH-filler suspension was smeared on a glass slide, desiccated at 37 °C for 6 h and gold sputtered before observation at ×3000 and ×5000 magnifications. Elemental analysis for the determination of elements in the filler particles was performed by the Bruker Quantax 70 energy dispersion X-ray spectrometer (EDS) attachment on the aforementioned apparatus on the inorganic fillers, but without any coating.

2.7. Hardness

Five square specimens of each material (n = 15) were cured in a steel mold (7 mm × 7 mm × 2 mm) between two strips of polyester to avoid oxygen inhibition of curing and to obtain a smooth surface. Ten indentations were made on both sides of the samples, at a load of 1.00 kg for 15 s using a Zwick/Roell ZVH30 (Zwick/Roell). The indentations were placed from one side to the other within the area directly under the curing tip.

2.8. Surface roughness parameters

Surface roughness parameters for the different materials were determined after three-body abrasion in a modified (Minimize, Buehler GmbH, Dusseldorf, Germany) toothbrush and slurry/reference toothpaste (ISO 11609: 2010 (E)) apparatus. Slurry/reference toothpaste was mixed from ISO Silica (SIDENT®, AT25747, EVONIK Industries, Hanau, Germany). Test bodies were polished with 4000 grit sandpaper surface parameters measured with 50× objective (Nikon, Japan) on a profilometer (Sensofar PLμ 2300, Terrassa, Spain) (n=9 per composite). The toothbrush bristle heads (Butler Gum 311, GUM, Chicago, IL, USA) were kept 24 h in ISO 3696 grade 2 water at 37 ± 1 °C prior to testing. After curing, the test bodies were stored at constant temperature (37 ± 1 °C) ISO 3696 grade 2 water before circular brushing (simulating Fone's brushing technique) [33] with 30,000 brush cycles commenced. After brushing, the test bodies dried at 37 °C for 24 h before surface parameters (surface roughness (Sa) and total peak height (St)) were measured and compared with measurements procured before abrasion.

2.9. Filler content

The total filler content (wt.%) of inorganic fillers was determined for each of the materials using the thermogravimetric analysis apparatus STA 449 F3 (Netzsch GmbH, Selb, Germany). The mass of a substance was monitored as a function of temperature or time as a sample specimen is subjected to a controlled temperature program [34]. The composite sample was placed in an aluminum crucible (DSC/TG pan Al) and heated at a flow rate of 20 °C/min to 610 °C under nitrogen atmosphere.

2.10. Monomer elution (HPLC)

Residual monomer analysis was based on the guidelines for analysis of ISO 20795-1: 2013 (E) [35]. The amount of residual monomer is presented as weight percentage of the organic matrix (resin). Cured material was stored in acetone for seven days prior to liquid chromatographic analysis with UV detection (UV wavelength 205 nm) in an Agilent 1100 HPLC (Agilent Technologies, Santa Clara, CA, USA). Chromatography was performed at ambient temperature using a Symmetry C18 column (150 mm × 150 mm,

Table 2
Selected Monomers for Detection by HPLC.

Monomers	Abbreviation	CAS number	Molecular Weight	Supplier	Purity
Bisphenol A glycerolate dimethacrylate	BisGMA	1565–94–2	512	Sigma-Aldrich	≥90%
Triethylene glycol dimethacrylate	TEGDMA	109–16–0	286	Sigma-Aldrich	95%
Diurethane dimethacrylate	UDMA	72869–86–4	471	Sigma-Aldrich	≥97%
Trimethylolpropane trimethacrylate	TMPTMA	3290–92–4	338	Sigma-Aldrich	90%

5 μm particle size, 100 Å pore size) with an injection volume of 50 μl; flow rate: 1 ml/min; eluent A: acetonitrile in H_2O (50:50 v/v %); eluent B: acetonitrile. The following gradient was used: 0–5 min 100% eluent A, 5–10 min 20% eluent A, 10–20 min 20% eluent A, 20–22 min 100% eluent A. The external standards (Table 2) were used for ten different concentrations from 0.1 μg/ml to 100 μg/ml with logarithmic increments. The standard curves were fitted with $r^2 > 0.99$. The materials were tested for a selection of monomers based on composite composition given by the respective manufacturers (Table 2).

2.11. Biocompatibilty and cytotoxicological analyzes

The biocompatibility and cytotoxicological analyzes were based on ISO 10993-5: 2009 (E) and ISO 7405: 2008 (E) [36,37]. The cytotoxicity and metabolic activity were assessed in cell cultures of A549 cells (a human epithelial, lung carcinoma cell line), human gingival fibroblasts (HGF), and on primary human osteoblasts after 24 h and 48 h incubation in conditioned medium. Twelve identical struts for each composite type were prepared according to the method described for flexural testing. Two struts made up one sample and six replicates were prepared for each composite type (n = 18). After curing the samples were rinsed with deionized water. The composite struts (200 mm^2) was incubated in 6.25 ml of cell culture medium, corresponding to a ratio of 6.25 ml/day per tooth (following a major work's recommendation [40]).

The culture growth medium for the A549 cells contained low glucose DMEM GlutaMAX cell culture medium (Life Technologies, Carlsbad, CA, USA) supplemented with 10% fetal bovine serum (Biosera, Boussens, France), 100 U/ml penicillin and 100 μg/ml streptomycin (Biowest, Nuaille, France). The A549 cell line was obtained from the American Type Culture Collection (ATCC, Manassas, VA). The cells were grown in RPMI 1640 medium supplemented with 10% (v/v) fetal bovine serum (FBS, PAA Laboratories), 100 U/ml penicillin and 100 μg/ml streptomycin (Biowest, Nuaille, France). Cells were subcultured 1:4 before reaching confluence using PBS and trypsin/EDTA [41].

HGF were obtained from Provitro GmbH (Berlin, Germany). Cells were cultured at standard conditions of 37 °C and 5% CO_2, and maintained in low glucose DMEM GlutaMAX cell culture medium (Life Technologies,) supplemented with 10% foetal bovine serum (Biosera, Boussens, France), 100 U/ml penicillin and 100 μg/ml streptomycin (Biowest, Nuaille, France). Cells were subcultured1:4 before reaching confluence using PBS and trypsin/EDTA [41].

Primary human osteoblast (NHO) (Lonza, Walkersville, MD, USA) were cultured in osteoblast basal media (OBM; Lonza) supplemented with 10% fetal bovine serum, 0.1% GA-1000 and 0.1% ascorbic acid.

The composite samples were stored for 24 h at 37 °C and 5% CO_2. The resulting extracts were subsequently transferred to sterile microcentrifuge tubes: "24 h extracts"; and stored at 4 °C. Immediately after taking the first "24 h extracts", the composites were transferred to fresh 6.25 ml of cell culture media to see if any additional monomer eluted from the composites after another 24 h would still have a cytotoxic potential. All groups were placed for 24 h at 37 °C and 5% CO_2. The resulting extract was subsequently transferred to sterile microcentrifuge tubes: "48 h extracts"; and stored at 4 °C. All extracts were pre-warmed at 37 °C for 12 h prior to cytotoxicity testing. To test the effect of the liquid extracts of the different dental composites on cell toxicity, 2×10^4 cells were seeded in each well (48-well plate) and cultured with growth medium for 72 h. After this period, growth media was changed and replaced with the liquid extracts of dental composites (n = 6) for 24 h. In addition, untreated cells with culture media (low control, n = 6) and cells cultured with culture media supplemented with Triton X-100 1% (high control, n = 6) were used as assay controls according to manufacturer's instruction (Roche Diagnostics, Mannheim, Germany).

Lactate dehydrogenase (LDH) activity in the culture media after 24 h incubation with the exudates was used as an index of cell death. LDH activity was determined spectrophotometrically after 30 min incubation at 25 °C of 100 μl of culture and 100 μl of the reaction mixture by measuring the oxidation of NADH at 490 nm in the presence of pyruvate, according to the manufacturer's kit instructions (Roche Diagnostics). Results are presented relative to the LDH activity in low control and high control (set to be 100% cell death) [42]:

For cell morphology visualization of the HGF and A549 cells, cells cultured for 24 h with the different extracts were fixed for 15 min with 4% formaldehyde in PBS at room temperature. Representative phase-contrast images of cells were taken at 10× of magnification, and compared to untreated cells at the same time point.

2.12. Statistics

Statistical analyzes were performed using the statistical software SigmaPlot 13.0 (Systat Software, San Jose, USA). All tests were performed at a confidence level of 95% and *post hoc* retrospective power analyzes were performed to find the statistical power of the tests (alpha = 0.050). Normality (Shapiro-Wilk [p-value to reject 0.050]) and equal variance tests (Brown-Forsythe [p-value to reject 0.050]) were performed prior to further

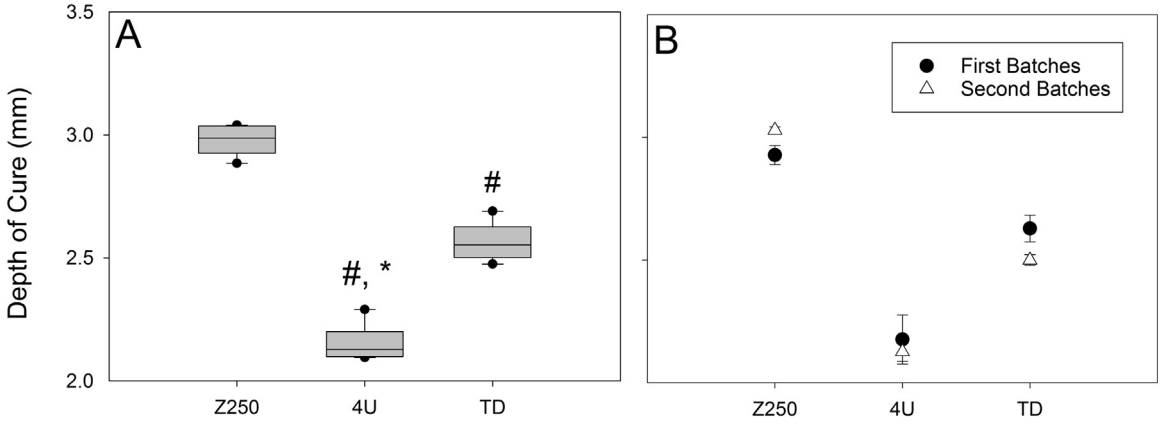

Fig. 1. Depth of cure (mm) for combined batches (A) and batch comparisons (B). Box plots are shown with median in solid line, whiskers represent maximum/minimum values, and solid dots represent 5th/95th percentiles. Statistically significant difference compared to Z250, #$p < 0.01$; compared to TD, * $p < 0.01$.

statistical testing of the combined batch values. When the datasets were found normally distributed, statistical comparison of the different groups was performed using one-way analysis of variance (ANOVA) test followed by *post hoc* tests for pairwise comparisons performed using Student–Newman–Keuls test. The datasets that failed normality or equal variance test were analyzed using non-parametric Kruskal–Wallis one-way ANOVA with multiple comparisons performed using Tukey test, or Dunn's method in case of differences in the group sizes. Statistical significance was considered at a probability $p < 0.05$. Comparison of the means was performed using Student *t*-test after testing for normality. Mann-Whitney Rank Sum Test was used for failed normality for Student's *t*-test. Statistical significance was considered at $p < 0.050$.

A correlation study was performed on all tested parameters with a bivariate regression analysis, Spearman two-tailed, using the computer software Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) version 22.0 for Windows. The results were interpreted as follows: no correlation if $|r| < 0.3$, correlation if $0.3 < |r| < 0.5$, and strong correlation if $0.5 < |r| < 1$. A negative r indicated a negative correlation while a positive r indicated a positive correlation. [43].

3. Results

The mean and standard deviation (mean [SD]) of the combined batches in ranked order from deepest to most shallow cure (mm) was Z250 2.98 (0.06) > TD 2.56 (0.08) > 4U 2.15 (0.07). Overall, Z250 outperformed the rest of the materials ($p < 0.001$) and TD showed statistically significantly deeper cure than 4U ($p < 0.001$) (Fig. 1). There were no statistically significant differences between the batches for any of the materials in terms of depth of cure (Fig. 1).

Fig. 2 depicts the data from the flexural strength testing. The combined mean (SD) of the flexural strength (MPa) in descending order was Z250 138.4 (23.5) > 4U 91.3 (10.6) > TD 88.6 (24.3). There was a statistically significant difference in the mean flexural strength between the two batches TD 77.0 (11.6) vs. 97.7 (7.14) ($p = 0.005$, power: 0.88). Several of the samples for both 4U and TD fell below the MPa minimum value of 80 MPa according to the ISO-4049:2009(E).

The ranked DC% measured on the top, bottom, and their combined values for the four materials at the five time intervals for all of the materials showed changes over time (Fig. 3). The DC% on top of the samples increased for all of the materials from T_1–T_5, except for TD. The increase was only statistically significant for 4U, 63.3 (0.18)–69.8 (0.38) ($p = 0.004$, power: 0.99) and this was the same for the decrease of TD, 70.0 (0.21)–63.3 (0.37) ($p = 0.013$, power: 0.88). The difference in the cross-over of means between 4U and TD from T_4–T_5 was statistically significant ($p = 0.024$, power: 0.68). The DC% of Z250 was significantly greater than both 4U and TD at T_1 and T_5 ($p < 0.001$). The intra-material DC% differences between 4U and TD were statistically significant at both T_1 and T_5 ($p < 0.001$ and $p = 0.026$, respectively). The apparent dips for Z250 and 4U from T_1–T_2 only demonstrated a statistically significant decrease for 4U (paired *t*-test, $p = 0.035$, power: 0.66). The differences in means when comparing all the time intervals on the top of the samples were significantly different ($p < 0.05$) for Z250 between T_2 and T_5; between T_2 and T_5 for 4U (; between T_1 and T_5, T_2 and T_5, T_3 and T_5, and T_4 and T_5 for TD (Fig. 3).

The DC% on the bottom of the samples increased for all the materials from T_1-T_5, except for TD. The increase in DC% for 4U was statistically significant from T_1 53.3 (10.70) to T_5 65.1 (0.67) ($p = 0.023$, power: 0.76).At T_1 Z250 was significantly greater than 4U ($p = 0.003$). At T_5 the DC% of Z250 was significantly greater than TD ($p = 0.034$).

Combined DC% for Z250 demonstrated statistically significant differences ($p < 0.05$) between T_2 and T_5 and T_3 versus T_5. The same was noted in 4U between the two intervals T_2 and T_5 and T_3 and T_5 (both $p < 0.05$). There were no statistically significant trends calculated for TD.

The differences between the top to bottom for the different materials are presented in Table 3. Whenever a difference presented itself, the higher DC% was observed on the top of the material versus the bottom. There were no statistical differences between the top and bottom at the final time interval (T_5) for any of the composites.

The polymerization volumetric shrinkage for all the materials ranged from 2.86% to 4.13%, with the lowest observed value seen in Z250 and the highest in 4U (Fig. 4). The mean (SD) of the composites from least to most volumetric shrinkage was Z250 (3.15 (0.46)) < TD (3.40 (0.29)) < 4U (3.40 (0.29)). There were no observed statistically significant differences ($p = 0.096$) among the composites.

Fig. 5 depicts the data from the top, bottom and top versus bottom hardness testing. There was a statistically significant difference between the top and bottom in both TD and 4U ($p < 0.05$, power: 0.91 and 0.64, respectively). The hardness of both the top, bottom and combined of the Z250 samples were statistically significantly higher than both 4U and TD ($p < 0.001$). Vickers Hardness (HV) of Z250 was around 100 HV, while both TD and 4U were significantly lower ($p < 0.001$) at about 60 HV. Table 5 shows the Top/bottom ratios (bottom mean value/top mean value) of the Vickers Hardness data for the three composites.

The surface roughness (S_a) ranged from 0.096 μm to 1.036 μm for all the three composites after toothbrush abrasion, with the maximum S_a seen in TD and the lowest in Z250 (Fig. 6). The composites were ranked from roughest to smoothest according to their S_a-value (mean [SD]): TD 0.33 (0.282) > 4U 0.192 (0.060) > Z250 0.125 (0.024).

Both 4U and TD were significantly rougher post-abrasion than Z250 ($p < 0.05$). The S_a for TD and 4U showed a statistically significant increase from pre- to post-abrasive wear while Z250 showed a decrease ($p < 0.05$, power: 1.00).

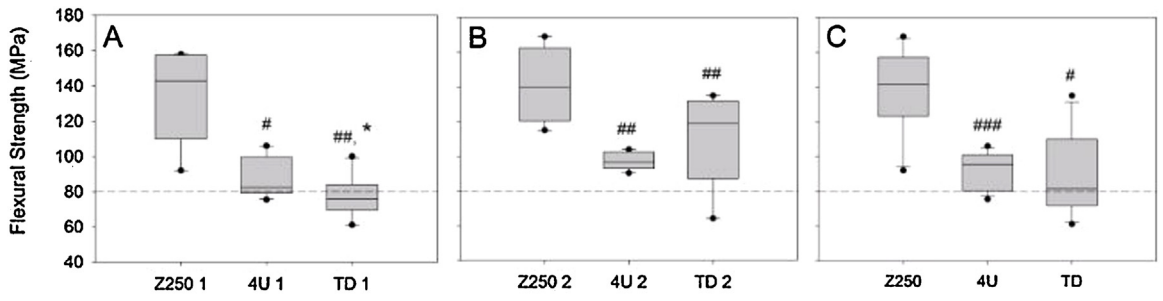

Fig. 2. Flexural strength testing results from different (A,B) and combined batches (C). Box plots are shown with median in solid line, whiskers represent maximum/minimum values, and solid dots represent 5th/95th percentiles. Statistically significant difference compared to Z250: # $p < 0.001$, ## $p < 0.01$, ### $p < 0.05$; compared to TD: * $p < 0.05$.

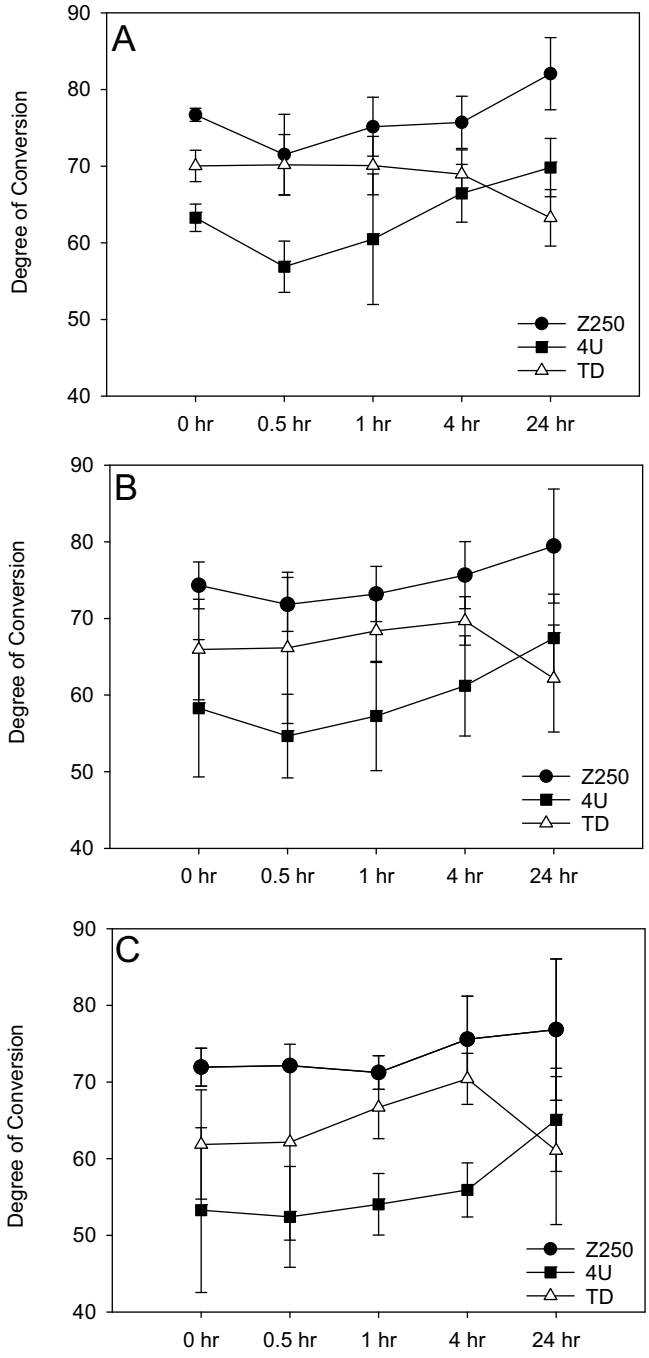

Fig. 3. Change in the degree of conversion (DC%) over time (mean [SD]) on the top of samples (A), combined samples (B), and bottom of samples (C).

Table 3
Degree of Conversion (DC%) Comparison of Top versus Bottom.

Material/Time	0 h	0.5 h	1 h	4 h
Z250	0.048 (0.028)*	–	–	–
4U	–	–	–	0.11 (0.03)**
TD	–	–	0.034 (0.026)*	–

* $p < 0.05$.
** $p < 0.01$.

The St for all composites ranged from 2.430 μm to 17.551 μm after wear, with the maximum value seen in TD and the lowest in 4U. The mean (SD) for the composites after toothbrush abrasion ranked from the highest St-value to lowest was TD 11.52 (4.44) > 4U 6.02 (2.06) > Z250 3.87 (0.83). The S_t for 4U and Z250 showed a statistically significant decrease from pre- to post-tooth brushing ($p < 0.05$, power: 0.71 and 1.00 respectively). The post-abrasive S_t of Z250 was significantly lower than that of TD ($p < 0.05$).

The type and wt.% of eluted monomers from the different composite materials is visualized in Table 2. All the monomers, Bis-GMA, UDMA, TEGDMA, and TMPTMA, were detected in the HPLC analysis (Fig. 7). The mean (SD) elution of Bis-GMA from 4U and TD was 2.54 (0.14) and 2.27(0.30), respectively. Bis-GMA was also detected in Z250. Elution of UDMA was only detected in the OBL composites. There was a significantly larger amount of UDMA residual monomers eluted from 4U compared to TD (t-test, $p < 0.001$, power: 1.00). Detection of the monomer TEGDMA was only found in the analyzes of TD at a mean (SD) of 2.64 wt.% (0.03). The monomer TMPTMA was detected from 4U at 2.78 wt.%and from TD. The amount of monomer elution was ranked according from the highest to the lowest amount (mean [SD]): 4U 2.71 (0.19) > TD 1.05 (0.92) > Z250 0.0 (0.0). Significantly higher amounts of monomers eluted from 4U compared to TD ($p < 0.001$).

The total inorganic filler (wt.%) was determined by thermogravimetric analysis, and the ranked mean (SD) from highest to lowest filler content of composites was as follows: Z250 80.68 (0.03) > 4U 74.51 (0.40) > TD 74.29 (0.55). The filler content for Z250 was similar to producer claims, no information was provided for TD, and there was incongruity between the data provided for 4U (81 wt.%) and our findings.

The SEM study uncovered mainly spherical particles interspersed with a few irregularly shaped (smooth edged) filler particles in Z250. The filler particles in 4U and TD were irregularly (angular) shaped with sharp edges and interspersed with splintered particles (Fig. 8). The results from the EDS analysis are shown in Table 4.

Fig. 9 shows the results of cytotoxicity tests at the two separate time intervals for the HGF, the A549 cells, and the human primary osteoblasts. The extracts obtained after 48 h provoked significantly higher percentage of cell death for the HGFs exposed to eluent from OBL 4U. The cell death of osteoblasts were above the maximum accepted threshold of 30% of cytotoxicity of medical devices according to the ISO-10993:5 for all materials after 24 h, but only the OBLs had a sustained effect on cell viability above this level after 48 h. In the case of the A549 cell-line there was a statistically significant increase in release of LDH after 48 h for the cells exposed to eluent from the OBL 4U.

No discernible differences were detected in the cell morphologies for the cells exposed to any of the composites compared to the low control for either of the time intervals (Figs. 9). However, a reduced cell number and loss of confluence along with morphological features of cell death was observed in A549 cells incubated with the 48 h extracts for the OBL 4U.

The correlation results from the correlation study can be seen in Table 6. Those parameters that did not show any statistically significant correlations were omitted from Table 6. Notable is strong correlation between curing depth, flexural strength and degree of conversion and osteoblastic response for all tested materials. The OBLs were also the only material to show correlation between monomer release and cytotoxicity.

4. Discussion

The present study raises concern surrounding OBL dental materials lacking sound scientific documentation. The results of the present investigation suggest that both 4U and TD are inferior and inadequate when compared to Z250 in terms of physical characteristics, monomer elution, surface parameters after being subjected to wear, and even cytotoxicological effects.

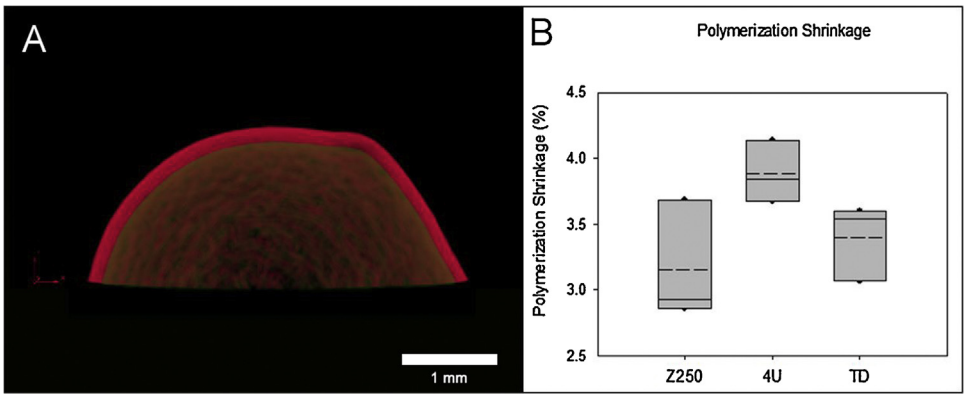

Fig. 4. (A) Superimposed 3D-rendering of 4U composite uncured (red) and cured (green). Comparison of polymerization shrinkage (B) (dashed line: mean; solid line: median; whiskers: standard deviation; dots: 5th/95th percentiles).

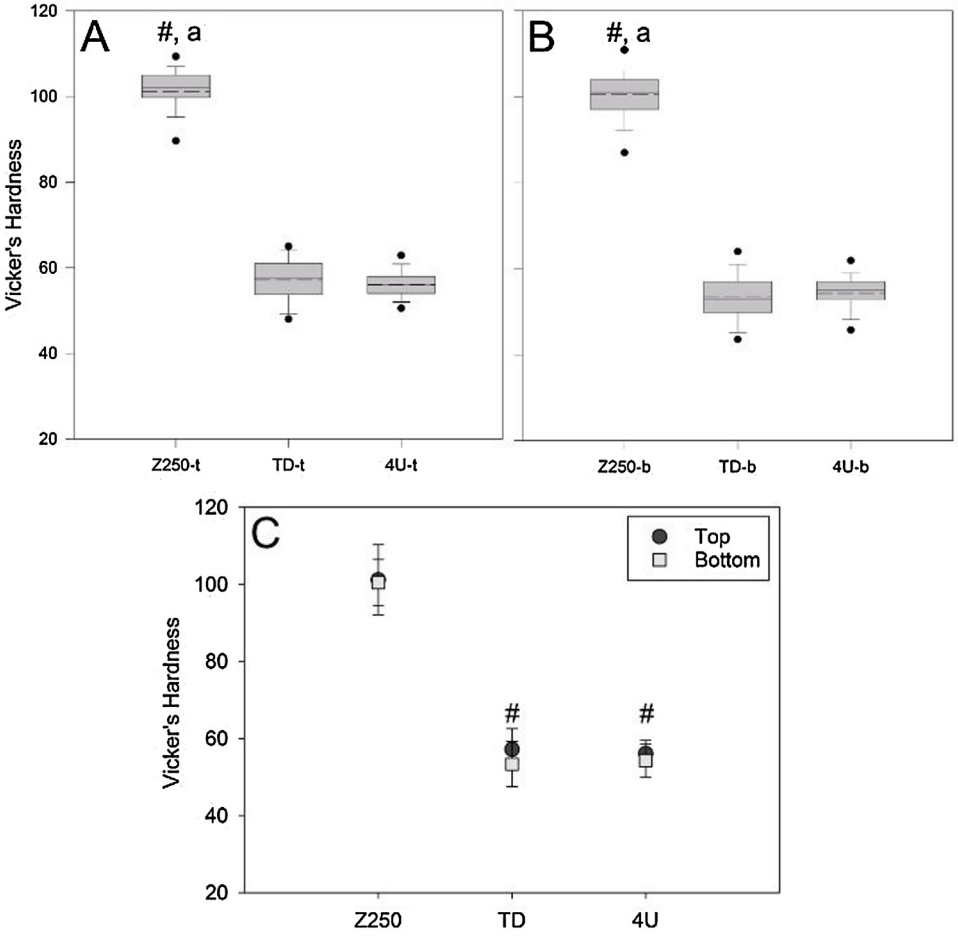

Fig. 5. Vickers hardness measured on the top of the samples (A), bottom (B), and the combined values (C). Statistically significant difference compared to Z250 (A, B): # $p < 0.001$, ## $p < 0.01$, ### $p < 0.05$. Statistically significant difference between the top and bottom (C): # $p < 0.05$. Box plots are shown with median in solid line, mean in dashed line, whiskers represent maximum/minimum values, and solid dots represent 5th/95th percentiles.

Table 5
Hardness Top/Bottom Surface Ratio.

Material	Top of Samples Mean (SD)	Bottom of Samples Mean (SD)	Hardness Ratio (Bottom mean: Top mean)
Z250	101.18 (9.10)	100.50 (5.93)	0.99
4U	56.10 (3.38)	54.28 (4.35)	0.97
TD	57.16 (5.43)	53.34 (5.93)	0.93

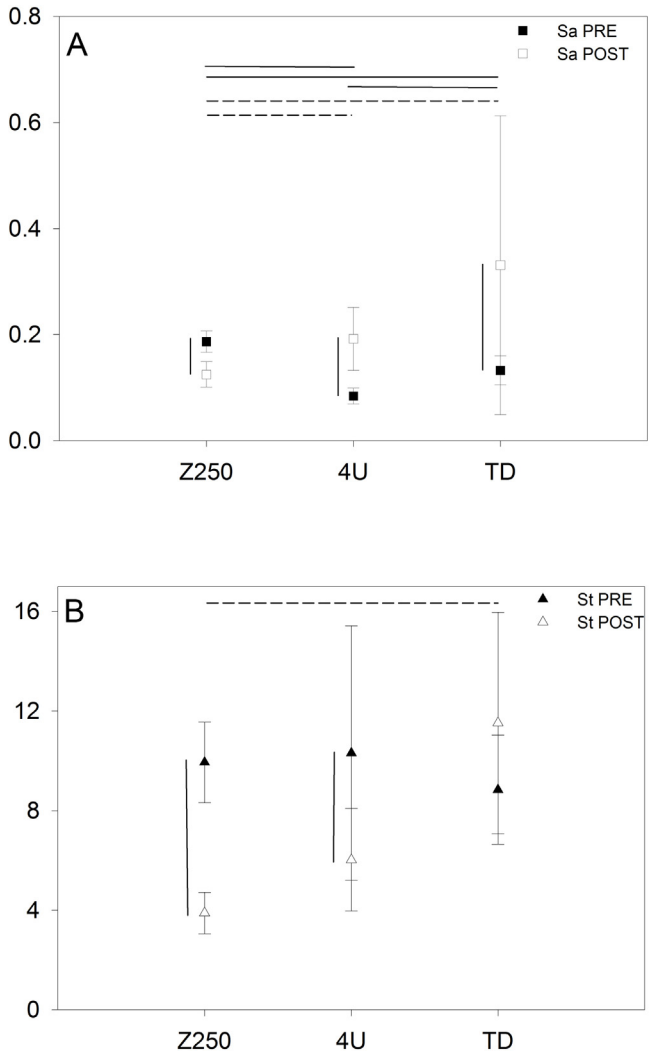

Fig. 6. Selected Surface Topography Parameters of composites before and after wear. Surface roughness (Sa [A]) and top-to-bottom (St [B]) of the three composites pre-and post-wear. Solid vertical lines signify intra-material statistically significant differences between pre- and post-abrasion ($p < 0.05$). Solid horizontal lines signify inter-material statically significant differences pre-abrasion, while dashed horizontal lines are for post-abrasion ($p < 0.05$).

Positive laboratory testing results of RBCs does not guarantee clinical success. Nevertheless, rigorous testing of dental materials under controlled laboratory conditions will reveal important information regarding positive or negative material characteristics[4]. This information can certainly be used to compare one material with another for ranking purposes. Both the tested OBLs, and in particular 4U, showed several shortcomings in comparison to the commonly used RBC Filtek Z250.

The same shade (A3) was used for all the tests in the present study as some studies have found that this characteristic can have an effect on the DOC [44]. It is unclear if opalescence/translucency is more critical than shade or pigmentation [45]. Whatever the case may be, the DOC is dependent on the nearly linear inverse relationship between translucency and filler content [46]. This was confirmed in a study by Frauscher and Ilie [47] on five resin based composites. In the present study, the highest mean DOC and highest particle loading was recorded in Z250. Contrariwise, the lowest mean DOC was measured in the 4U samples with comparable filler content to TD. This dissimilarity can only be explained by differences in resin monomer content of the composites. The OBL 4U is marketed as a nanohybrid with a particle size range of 0.05–1.5 μm [48], while Z250 in comparison has a range of 0.01–3.5 μm [48]. Light scattering from nano-particles in a nanohybrid has been shown to be minimal and is a possible explanation for higher DOCs in these types of materials [47]. It could thus be reasoned that the low DOC in 4U is a result of the nano-particle fraction being too low to mitigate the detrimental effects of refraction [49] as well as differences in resin chemistry (*i.e.* photoinitiator type and concentration [50,51]).

Dental composite fillings are often placed in regions subjected to large chewing loads with complex chewing patterns, and must therefore have physical/mechanical properties that can withstand high flexural stresses [28]. The flexural strength results cannot be directly extrapolated to the clinical situation, but the test is very useful for ranking RBCs [56].

The technical profile brochure for the OBL 4U [48] states that it has a flexural strength of 140 MPa (Product Specifications, 4U, LIC Scadenta). Our tests found a much lower flexural strength for both batches tested than claimed by the manufacturer. It is not possible to discern what type of flexural strength test was used to produce their results. We cannot preclude the possibility that the manufacturers' higher flexural strengths may be due to the entire sample being cured at once compared to using an overlapping technique, which will lead to inhomogeneously cured samples [28]. The value asserted by the manufacturer for Z250 [57] was within our tested standard deviation (estimated SD from Technical Product File: 34.78). We find it highly disconcerting that, aside from our test results, no information or documentation for TD in regards to flexural strength is available.

The clinical performance of resin-based dental materials depends on adequate polymerization. Since polymerization never yields a complete conversion of double to single bonds (DC% generally in the range of 52–75%), many of the mechanical properties as well as the clinical performance of resin-based dental materials are thought to depend on the highest possible DC% [58]. The degree of conversion has been analyzed in several other studies. Lin et al. found that a higher content of Bis-GMA increased the elastic modulus, while a higher TEGDMA content increased conversion. In a separate study of Lin et al. the superior chemical, mechanical and biological properties were found at the highest degree of conversion [59,60]. Ergun et al. analyzed various commercial composite materials, and found a clear correlation between DC% and cytotoxicity [61]. Furthermore, DC% has also been directly related to strength, Young's modulus, hardness, and solubility [62–64], which are all important mechanical parameters for clinical success. The top-to-bottom distance of each sample was 2.0 mm, which is the recommended maximum thickness for incremental placement of conventional dental composites [65].

Alshali et al. [58] evaluated changes in DC% in bulk-fill flowable resin composite materials, conventional flowable, and regular resin composite materials immediately post-cure and after a storage time of 24 h. Their general finding was a uniform and statistically significant time-dependent increase in DC% of all the composites included in their study. The same increase in DC% was reported in a study done by Tonetto et al. examining two different resin cements [66]. The two aforementioned studies stored their composites in dry conditions at 37 °C, while our samples were stored wet at the same physiological temperature. Our methodology may be more relevant from a clinical point of view to see what happens to the DC% over time in an *in vitro* setup that resembles *in vivo* physiological conditions. In any case, our findings underscore the well-known fact that polymerization kinetics is complex and warrants further study. In our study Z250 and 4U demonstrated this previously observed increase, while TD actually decreased on both the top and bottom of the samples. The increase in DC% of composites is determined by several factors such as the type of photo-initiator, initial available number of radicals, and viscosity

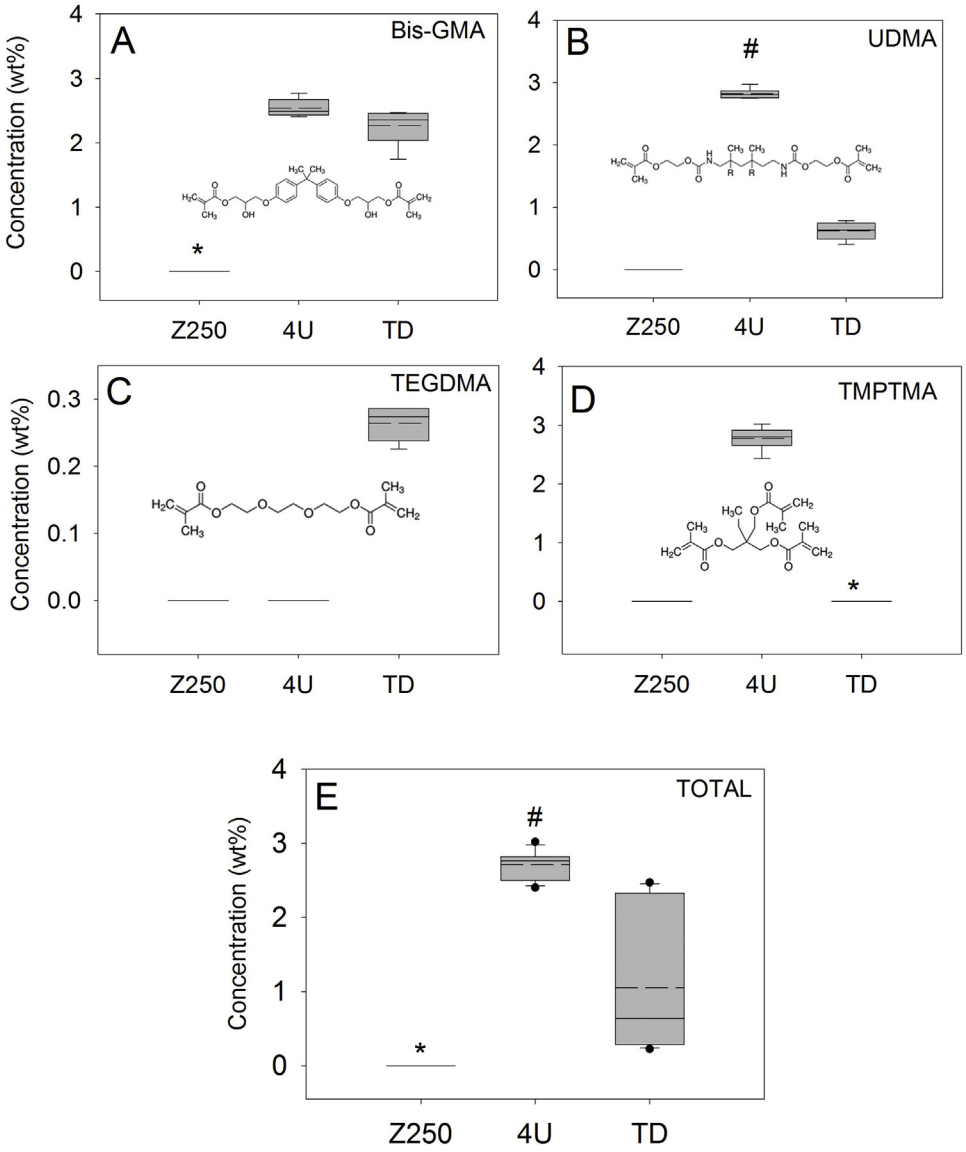

Fig. 7. Elution of the four different monomers (A–D) and total monomer elution (E). Statistically significant difference compared to TD: # $p < 0.001$. * signifies detection of monomer by HPLC, but under 0.0001 wt.%.

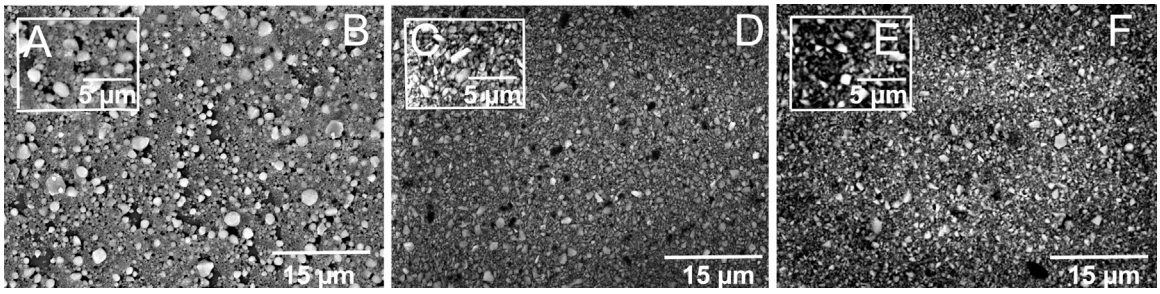

Fig. 8. SEM images of the filler particles of the three composites (A/B: Z250; B/C: 4U; D/E: TD) observed at 3000 x (upper case) and 5000× (lower case).

and flexibility of the chemical structure [58]. The dip statistically significant dip in DC% measured on top of the 4U samples may be from disproportionation in the termination of the polymerization of methacrylates, which creates new C=C double bonds. These double bonds are not from unreacted monomers, but will result in false lower DC% [10].

The overall decrease of DC% observed in TD has not been previously been reported in other RBCs, and may be a result of polymer degradation from storage in water. A strong inverse

Table 4
Elemental composition by EDS/EDX of filler particles (normalized wt.% (errors in%)). Hyphen signifies element was not detected.

Material/Element	O	Si	C	Al	Ba	Zr
Z250	41.07 (4.56)	32.05 (1.29)	8.12 (1.30)	0.63 (0.05)	–	18.12 (0.66)
4U	39.94 (4.25)	28.85 (1.13)	8.39 (1.25)	5.06 (0.24)	17.60 (0.49)	0.16 (0.03)
TD	41.06 (4.22)	26.48 (1.01)	6.96 (1.04)	4.28 (0.20)	21.17 (0.57)	0.05 (0.0015)

correlation between elution of monomers and DC% [10], and the same relationship was found for 4U but not TD. Nevertheless, the exact composition of TD is unknown and there is a possibility that certain monomers with more than one C=C double bond (*e.g.* TMPTMA) converted resulting in an initially higher DC%, which may decrease as the monomer eluted over time from the matrix to due perhaps degradation of the matrix [10].

The exact DC%-threshold for clinical success has yet to be determined, but values below 55% have been found to correlate with poor clinical performance [58].

Degree of conversion is intimately related to shrinkage-strain [69], which is an undesirable property in RBCs. Satterthwaite et al. [70] found a definite trend of lower shrinkage–strain values in experimental composites containing spherical filler particles compared to those with irregular shaped particles. Our study found higher DC% in Z250 (spherical particles) compared with 4U and TD (both with irregular particles). Nevertheless, even though Z250 demonstrated the lowest mean shrinkage values (Z250 < TD < 4U) there were no statistically significant differences in polymerization shrinkage among the resins. Comparing the different materials is challenging because the filler load is different and will influence shrinkage values. One of the greatest challenges to the success of composites is the shrinkage that occurs during polymerization [30]. This unwanted effect can result in marginal gap formation, which again predisposes the restoration/tooth interface to discoloration, as well as degradation of hybrid layer, and formation of secondary caries. The typical degree of volumetric shrinkage has been reported to vary between 2 and 3% in conventional dental composites [71]. Our findings were generally in agreement with this range. Aside from extrinsic parameters such as irradiation source and/or time and *in situ* temperature, the difference in shrinkage between composites also depends on intrinsic factors like matrix composition, filler loading, filler morphology and degree of silanization [72]. There was no available information from literature or manufacturers on volumetric shrinkage for the 4U or TD. The technical product file for Z250 [57] reports volumetric shrinkage measured after 60 s irradiation, but the exact method of measuring was elusive. Nevertheless, the recorded shrinkage was a little more than 2.00% with a very narrow standard deviation. The same report also gives results from mercury dilatometer testing after irradiating for 40 s with a 400 mW/cm^2 curing light. Here, the shrinkage was approximately 2.00% after 5 min and 2.10% after 30 min, without any standard deviations presented in the figure. Several studies have evaluated the degree of volumetric shrinkage in Z250 using varying methodologies and have found values ranging from 1.99% (SD 0.032) to 4.45% (0.36) [73,74]. Our findings were in partial concordance with the aforementioned findings for Z250. Our results demonstrate that shrinkage values depend on the applied methodology, but the ability to correctly rank materials according to shrinkage is not impaired [74].

Previous studies have unveiled a direct relationship between (micro)hardness and wear resistance [75]. Wear of indirect composite restorations is a multifactorial and complex process with many proposed parameters affecting wear resistance. Among all the different parameters, hardness has been identified as a predictor of a material's resistance to wear [76]. However, Sagsoz et al. [77] did not find a correlation between a material's hardness and wear resistance.

Furthermore, there is a positive correlation between hardness and DC% [63], and the bottom/top hardness ratio can be used as a reliable indicator for degree of conversion [78]. This ratio is used as a measure of how well the bottom surface is cured, and the minimally acceptable values have been set to either 0.80 or 0.85 [79]. The ratios' of all the three composites in this study well exceeded these limits, but Z250 yielded almost twice as large Vickers hardness numbers as the OBLs. In other words, the OBLs were softer than Z250 by almost a factor of two.

The chosen surface parameters to measure surface roughness were surface roughness (S_a), and surface-to-top (S_t). The S_a describes the surface roughness of the composite while S_t is a measure of the total height of summits; height between the highest peak and deepest valley. The statistically significant reduction in total height of summits from pre- to post-wear for Z250 and 4U indicates a smoothening process for these two materials, but the high values for standard deviation in the case of 4U gives a less certain picture for this material. High values for S_a are intimately related to wear as they increase friction coefficients, which will predispose a material to loss in mass (wear) [80]. It might be expected that 4U and TD being smoother materials in terms of S_a pre-abrasion would result in less roughness than the Z250 post-abrasion with its rougher pre-abrasion surface. However, it seems like this is not the case and that inter-particle spacing, filler particle size and density has a greater influence on post-abrasion roughness [80]. Our results support this assumption, which also highlights the multifactorial complexity of tribological wear of composites.

A RBC's resistance to fracture has a direct relationship to its filler fraction, *i.e.* a higher filler content results in higher fracture resistance [52]. The highest filler content was found in Z250, which also performed significantly better than both 4U and TD (Fig. 2). Furthermore, 4U and TD had comparable filler loads and there was no statistical difference in their fracture strength. The mean filler content values of Z250 were found to be in accordance with the documented values from the material safety data sheet [54]. Expected filler content of TD was unknown as this information is not made publically available by the manufacturer. The OBL composite 4U had a discrepancy of >5 wt% between the content documented from manufacturer (81 wt.%) and our findings [48]. Leprince et al. [55] explain that filler content inconsistencies can be due to the different methods manufacturers use to evaluate this parameter. Measuring filler content prior to or after adding coupling agent (silane) as well as the TGA method used for assessment can yield discrepancies. It is unknown how the manufacturer evaluated the mass fraction of particle loading in 4U, but it is clear from our findings that independent research on OBL composites is warranted.

Highly filled (70 wt.% loading of 0.7 μm irregular particulate barium (Ba) glass) experimental composites do not allow for optimal light transmission, degree of conversion or curing depth [49]. Our SEM-EDS analysis found that 4U and TD filler particles are mainly made up of barium aluminum silicate glass and the filler concentration for both was >74%. Shortall et al. [14] demonstrated a greater resin/filler refractive index mismatch between

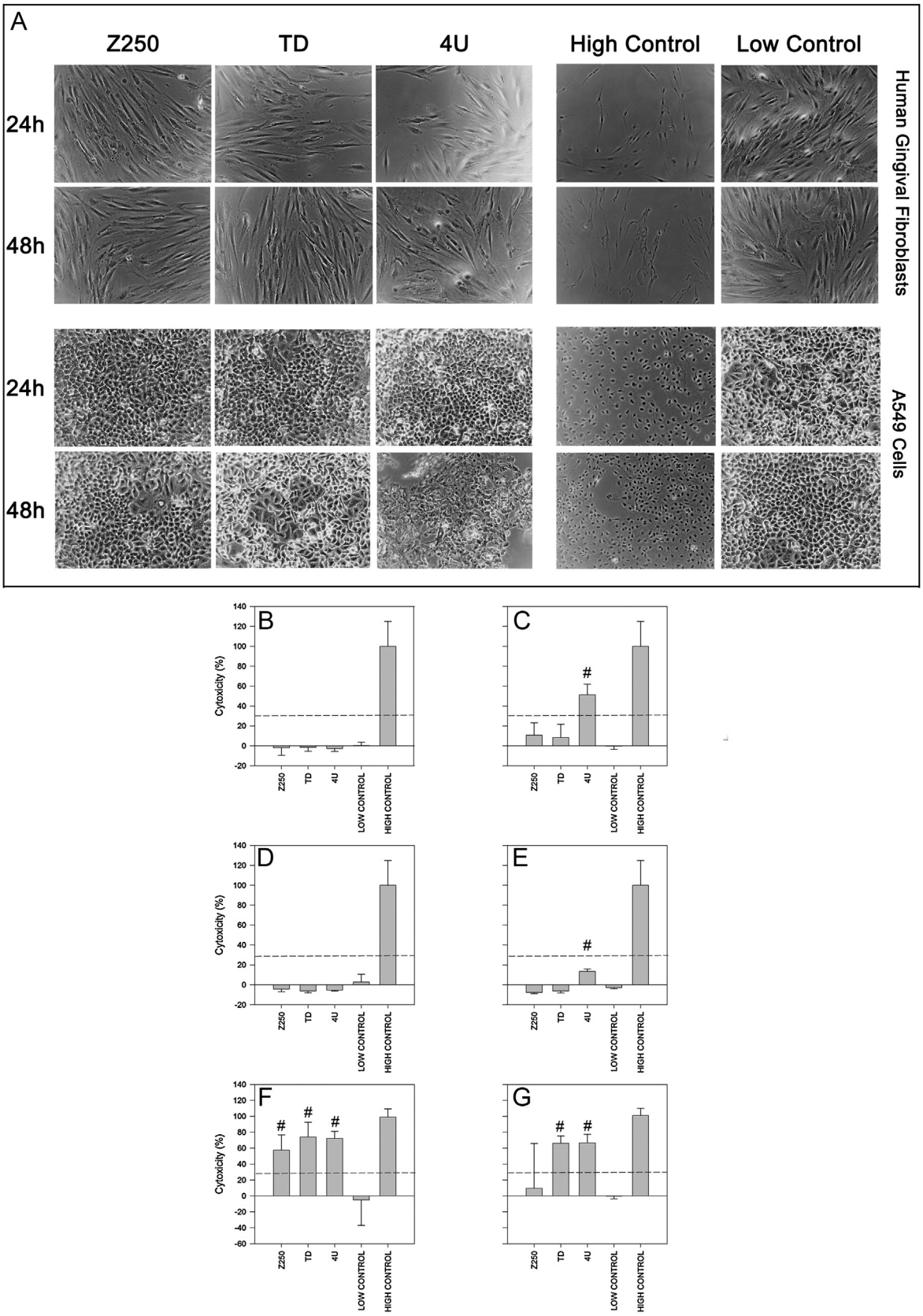

Fig. 9. Cell morphology (A) from representative phase-contrast photographs at 10× magnification. LDH activity measured from culture media of Human Gingival Fibroblasts (B,C), A549 cells (D,E), and human primary osteoblasts (F, G) at 24 h and 48 h. High control (100%) was growth medium supplemented with Triton X-100 1%. Low control (0%) was growth medium. Differences between groups were assessed by Student *t*-test or Mann-Whitney test depending on their normal distribution: # $p < 0.001$ versus low control.

Table 6
Spearmen rank coefficient, |r |, showing correlation between the investigated parameters. No correlation if $0 < |r| < 0.3$; correlation if $0.3 < |r| < 0.5$; and strong correlation if $0.5 < |r| < 1$ [19]. A negative r indicated a negative correlation while a positive r indicated a positive correlation. The table only display parameters were a correlation was found.

		DC%	Cure_Depth	Flex	hardness_t	hardness_b	Osteo_24	Osteo_48	A549_48
Z250	DC%	–	0.926**	−0.982**	–	–	−0.833*	−0.926**	
	Cure_Depth	0.926**		1.000**	–	–	–	−0.943**	–
	Flex	−0.982**	−1.000**	–	–	–	–	0.943**	–
TD	DC	–	0.986**	0.997**	–	–	−0.975**	0.975**	–
	Cure_Depth	0.986**	–	1.000**	–	–	−0.900*	1.000**	–
	UEDMA	–	–	–	–	–	–	−0.900*	–
	BisGMA	–	–	–	–	–	–	–	0.900*
	Total Monomer	–	–	–	–	0.331*	–	−0.900*	–
	Flex	0.997**	1.000**	–	–	0.598*	−0.900*	−1.000**	–
4U	DC	–	0.971**	0.994**	–	–	–	−0.883*	−0.883*
	Cure_Depth	0.971**	–	1.000**	0.899*	–	–	−0.829*	−0.886*
	Total Monomer	−0.994**	−1.000**	−1.000**	–	–	–	0.829*	0.886*
	Flex	0.994**	1.000**	–	–	–	–	−0.829*	−0.886*

– = no correlation.
Note: All parameters in this study were tested for correlations. Those parameters that did not show any statistically significant correlations were omitted from the table.

experimental composites with a high content of TEGDMA containing Ba-glass versus Strontium-(Sr)-glass. The same analysis also showed that Z250's fillers are mainly made up of silica and zirconium. Zirconium filler is harder than heavy-metal glasses such as barium. Other disadvantages of barium fillers are that they are more soluble, softer, and do not couple as easy to the matrix as other fillers [82].

It is interesting to note that the differences in filler concentration in 4U and TD were not statistically significant. The differences in mechanical properties between 4U and TD in this study must therefore depend more on differences in matrix composition (monomers), filler morphology, degree of silanization, *etc.* than the filler concentration.

The *in vitro* testing of RBCs' cytotoxicity does not replicate the clinical situation, but the results serve as a means to compare and rank the various materials. Resin monomer release is most pronounced shortly after placement in the mouth [16], and that most of the leaching is complete with the first 24 h [85]. The cytotoxicological effect on the osteoblasts from exposure to extract from Z250 was on par with the OBLs after the first 24 h, but tapered off during the following 24 h. The OBLs, and in particular 4U, had prolonged cytotoxicological effects on the A549 cells and primary osteoblasts. In fact, 4U and TD was above the 30% on the osteoblasts at both time intervals, which is the maximum value accepted for cytotoxicity for medical devices according to ISO-10993:5. This sustained toxicological effect from the OBLs was unexpected and undesirable.

Dental resin monomers are shown to be cytotoxic to pulp cells and gingival cells *in vitro* [87,88].

The change from DNA-damage to a mutation is difficult to identify as it does not always follow an easy-to-track sequential progression. Further studies investigating the potential methacrylates have to create mutations are needed [90]. *In vivo* studies indicate that it will require tremendously large amounts of eluted monomers in order for them to be harmful to humans [92,93]. Monomers can be harmful to fetal development in mammals [94], and studies of mice show reduced fertility and non-viable offspring with exposure to monomers [95,96]. This is of course a question of dose-response and whether this can be directly related to humans is uncertain. From a public health perspective one is still left questioning if eluted products from resin-based dental materials could be harmful in the long term. The current literature is, however, clear on the fact that RBCscan induce serious and debilitating allergies in both dental personnel and patients [97].

The OBL 4U had by far the gravest cytotoxicological effect on the three cell types tested in our study. Interestingly, the only time-dependent and statistically significant increase in cytotoxicity was seen in 4U on both HGFs and A549 cells. Reichl et al. [99] found detrimental cytotoxicological effects from resin monomers (TEGDMA, HEMA, UDMA, and BisGMA) on HGFs in their LDH assay, but there was only a time-dependent increase (1.68-fold) with UDMA from 24 h to 48 h. The notably higher elution of UDMA from 4U compared to TD (almost three-fold) and Z250 (no UDMA detected) together with the detection of residual TEGDMA from TD may partly explain the observed increase. Walther et al. [22]. found a time-dependent effect on cytotoxicity on A549 from HEMA and TEGDMA, but they also noted that the A549 cells were the least sensitive out of their two test alveolar epithelial cell-lines. The A549 cells showed the most resilience in our study, as well. Malignant cells are known to have higher levels of cellular glutathione and this has also been found to be the case for A549 cells [22]. Reduced levels of intracellular glutathione have been found to correspond with increased toxicity to dental monomers [100,101], but the depletion of glutathione does not offer the whole explanation for mechanisms behind cytotoxic reactions to dental monomers in every cell type [102].

There are no studies in the dental literature on the di-functional monomer TMPTMA present in both 4U and TD with regards to its cytotoxicity. Molecular weight (MW) has been found to have a positive correlation with cytotoxicity (Bis-GMA = 512, UDMA = 471, TEGDMA = 286) [103] and TMPTMA has a MW of 338. It is also worth mentioning that smaller molecules such as TEGDMA and TMPTMA are better quantified with systems such as LC/MS (Liquid Chromatography/Mass Spectroscopy) or even GC/MS (Gas Chromatography/Mass Spectroscopy) [40,104,105].

It is not only the monomers and co-monomers that pose a cytotoxic threat, but also reaction and degradation by-products, additives, and contaminants such as TPP and TPSb [106]. Previous studies have also demonstrated that filler particles can induce cytotoxicological and inflammatory responses [107,108]. The presence of impurities in the composites under study was not analyzed, but we find it imperative that future studies test for these and other cytotoxic components in both brand name and OBL composites alike.

Polymerization kinetics in dental composite resins is extremely complicated and multifactorial [9]. The exact content in a dental composite is often proprietary with regards to exact the monomer type, their ratios, type of stabilizers, photoinitiators, *etc.* [109]. One

must therefore be cautious to extrapolate results from well-controlled experimental composites to commercially available resins, but in the very least the aforementioned findings serve as further explanation for the general poorer performance seen in the OBLs (TD and 4U) compared with that of Z250.

A recent study by Shaw et al. [5] compared three branded materials against five OBLs in terms of filler percentages, DC%, and flexural strength and modulus. Their results on Z250 are in concordance with the comparable parameters. Their main finding was that their chosen OBLs performed adequately compared with the branded, but batch-to-batch differences among the OBLS leave their use questionable.

The correlation study revealed a strong inverse relationship between DOC and total elution of monomers in 4U, which coincides with findings by Kopperud et al. [29]. As expected, there was also strong negative correlation between total elution of monomers and DC% in 4U, which was also demonstrated by Durner et al. [10]. The same inverse relationship for 4U included flexural strength versus total monomer elution coinciding with previous findings [110].

The OBLs both demonstrated strong positive correlations for DC % vs. flexural strength and DOC vs flexural strength. Contrariwise, a strong negative correlation was found for the same parameters for Z250. The literature reports that a higher DC% coincides with increased flexural strength as seen in the OBLs [111], but the opposite findings in Z250 were unexpected as this material showed both significantly higher DC% and flexural strength. The mechanical characteristics are not governed by a single factor, and experiments with altering the monomer composition have shown that a high DC% does not necessarily yield higher mechanical properties [112] Cytotoxicity was negatively, positively and not correlated with DC% for the different RBCs. Monomer elution was negatively correlated to DC% in 4U, which indicates that more polymerization leads to less leaching. However, DC% had a significant inverse correlation to cytotoxicity in osteoblasts (48 h) and the A549 cells (48 h). Jagdish et al. also found both negative and positive correlations between DC% cell death commercially available orthodontic adhesives, and conclude other factors also affect cytotoxicity [113].

5. Conclusion

Our null hypothesis that the name brand composite would not out-perform the OBL composite materials was falsified and rejected. The OBL composites performed in general inferior to the name brand composite. These findings cannot be explained by a batch problem as similar results were found between the batches. The authors question the use of these particular OBL and raises concern for their clinical performance and safety for both patients as well as dental personnel.

Our findings warrant a legitimate concern regarding OBLs on the whole, and we caution the general use of OBLs lacking independent scientific experimental scrutiny along with clinical success from long-term randomized clinical trials. The long-term biological effect of resin monomers elution remains uncertain, and as such we consider our findings worrisome. Close monitoring and vigorous testing of new and untested/undocumented materials should be prioritized and remain ever vigilant. At the present, the OBLs studied herein, must be considered at the very least a false bargain.

Conflict of interest

The authors declare that they have no conflict of interest.

Statement of authorship

Per the criteria defined by the International Committee for Medical Journal Editors (ICJME), please note the contribution made by each author listed in the manuscript.

The submitting author affirms that all individuals listed as authors agree that they have met the criteria of authorship and agree to the conclusions of the study.

Contributed to conception and design: Contributed to acquisition, analysis, and interpretation: Drafted manuscript: Critically revised manuscript: Gave final approval:

Johnsen, G.F.: Contributed to conception and design; Contributed to acquisition, analysis, and interpretation; Drafted manuscript; Critically revised manuscript; Gave final approval; Agrees to be accountable for all aspects of work ensuring intergrity and accuracy.

Le Thieu, M.K.: Contributed to design; Contributed to analysis, and interpretation; Drafted manuscript; Critically revised manuscript; Gave final approval; Agrees to be accountable for all aspects of work ensuring intergrity and accuracy.

Hussain, B.: Contributed to design; Contributed to acquisition, analysis, and interpretation; Drafted manuscript; Critically revised manuscript; Gave final approval; Agrees to be accountable for all aspects of work ensuring intergrity and accuracy.

Pamuła, E.c: Contributed to design; Contributed to acquisition, analysis, and interpretation; Critically revised manuscript; Gave final approval; Agrees to be accountable for all aspects of work ensuring intergrity and accuracy.

Reseland, J.E.: Contributed to design; Contributed to acquisition, analysis, and interpretation; Drafted manuscript; Critically revised manuscript; Gave final approval; Agrees to be accountable for all aspects of work ensuring intergrity and accuracy.

Lyngstadaas, S.P.: Critically revised manuscript; Gave final approval; Agrees to be accountable for all aspects of work ensuring intergrity and accuracy.

Haugen, H.J.: Contributed to conception and design; Contributed to analysis, and interpretation; Drafted manuscript; Critically revised manuscript; Gave final approval; Agrees to be accountable for all aspects of work ensuring intergrity and accuracy.

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