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Abstract: Orthodontic treatment with sequential aligners has seen a considerable surge in the last decades, and is currently used to treat malocclusions of varying severity. To enhance tooth movement and broaden the spectrum of malocclusions that can be treated with aligners, composite resin attachments are routinely bonded with the acid-etch technique on multiple teeth, a process known to impose irreversible alterations of the enamel structure, color, gloss, and roughness. Additionally, this clinical setting introduces a unique scenario of different materials applied in a manner that involves the development of friction and attrition between the attachment and the softer aligner material, all performing in the harsh conditions of the oral environment, which impact the aging of these materials. The latter may give rise to alterations of the aligners and the composite attachments and potential intraoral release of Bisphenol A, a known endocrine disrupting agent. Furthermore, at the final stages of contemporary aligner treatment, the removal of multiple, sometimes bulky, composite attachments with a volume and surface far greater than the remnant adhesive after debonding of brackets, through grinding that might be associated with pulmonary effects for the patient or staff. Because of the extensive enamel involvement in bonding, the release of factors from the attachment-aligner complex during service, the aging of these entities in the oral environment, and the laborious debonding/composite grinding process coupled with the hazardous nature of aerosol produced during the removal of these bulky specimens, appropriate risk management considerations should be applied and an effort to confine the application of multiple composite specimens bonded to enamel to the absolutely necessary should be pursued.

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The use of attachments in aligner treatment: analyzing the “innovation” of expanding the use of acid etching-mediated bonding of composites to enamel and its consequences

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Summary

Orthodontic treatment with sequential aligners has seen a considerable surge in the last decades and is currently used to treat malocclusions of varying severity. To enhance tooth movement and broaden the spectrum of treated malocclusions, composite resin attachments are routinely bonded with the acid-etch technique on multiple teeth of each patient, a process known to impose irreversible alterations of the enamel structure, color, gloss and roughness. Additionally, this clinical setting introduces a unique scenario of different materials applied in a manner which involves the development of friction and attrition between the attachment and the softer aligner material, all performing in the harsh conditions of the oral environment, which impact on the ageing of these materials. The latter may give rise to alterations of the aligners and the composite attachments and potential intraoral release of Bisphenol A, a known endocrine disrupting agent. Furthermore, at the final stages of contemporary aligner treatment, the removal of multiple sometimes bulky composite attachments with a volume and surface far greater than the remnant adhesive after debonding of brackets, through grinding that might be associated with pulmonary effects for the patient or staff. Because of the extensive enamel involvement in bonding, the release of factors from the attachment-aligner complex during service, the ageing of these entities in the oral environment, and the laborious debonding/composite grinding process coupled with the hazardous nature of aerosol produced during the removal of these bulky specimens, appropriate risk management considerations should be applied and an effort to confine the application of multiple composite specimens bonded to enamel to the absolutely necessary should be pursued.

Introduction

In the last decade, aligners have become an integral part of orthodontic armamentaria, and their use has been expanded to supposedly manage a wide range of malocclusions. At the same time, there is a populous list of companies offering aligner treatment either to professionals or directly to the public—sometimes even without the direct involvement of a dentist.

The establishment of aligners as a treatment modality for malocclusion was made possible with the introduction of bonded attachments, which enhanced the control of the crown's spatial orientation, offering far more possibilities for treatment compared to the initial introduction of aligners when the tooth movement was limited to tipping and a small derotations of anterior teeth. Whereas the multiplicity of attachment shape and size opened new possibilities in the treatment of rotations, bucco-lingual inclination variations and vertical repositioning of teeth, their use is not free of concerns.

The purpose of this narrative review is to discuss the concerns arising from the increasing use of composite resins bonded onto the labial surface of teeth, focusing primarily on the biological and environmental implications of their application.

Enamel involvement

One of the main advantages of the early phase of aligners was the absence of any involvement of enamel in the treatment of malocclusions. Although the application spectrum of aligner treatment was limited to class I crowding cases, the fact that orthodontic treatment of these cases involved no acid-etching mediated bonding offered an advantage owing to the maintenance of the structural integrity of enamel,¹⁻⁶ with favorable outcome on the potential for white spot lesions, decalcification,⁷ avoidance of the use of rotary instruments to grind the remnants of adhesives after debonding, and essentially lack of long-term change of the enamel's optical properties⁸⁻¹⁰ since the absence of resin tags warrants that the surface would be intact.

Expanding the spectrum of indications for aligners to tooth movement in all three planes of space necessitated the use of grips bonded onto the enamel to generate bucco-lingual, mesio-distal and incisal-cervical movement, which negated the advantage of an intact enamel surface (Figure 1). Such composite attachments used in conjunction with aligners have dimensions ranging from 2 to 5 mm,¹¹ thickness that

can exceed well 1 mm,¹¹ and are bonded most often on the labial surface of multiple teeth. Moreover, composite attachments used in aligner treatment possess a high surface-to-volume ratio, which affects their interaction with the environment.

In Orthodontics, specifically in bonding orthodontic brackets, the adhesive application mode effectively alters the exposure pattern of the material to the oral cavity with a potential effect on reducing its reactivity with liquids and other materials. The “sandwich” pattern of application involved, where the adhesive is bonded to both enamel and bracket base, allows only the margins of the material to be exposed to the oral cavity. The acid-etched enamel interface on the one side and the morphological irregularity of bracket base through the welded mesh wire or laser etching on the other side, provide a mechanism for the interlocking of the polymeric material in both structures (tooth and bracket).¹² The average thickness of the adhesive layer between the tooth and bracket has been estimated between 150 and 250 μm , depending on the morphological condition of the bracket base, with the smooth bases resulting in thinner adhesives owing to the homogeneous pressure and the lack of retentive sites for the entrapment of the adhesive whereas, the rougher bases lead to thicker adhesive layer. In Figure 2, the enamel bracket interface is depicted indicating the heavy filler loading of adhesives. Therefore, for a typical bracket with dimensions of 2.5 x 3.5 mm (height x width) bonded to enamel, the surface of the adhesive layer exposed in the oral cavity can be estimated to range somewhere in 12 mm perimeter range or $12\text{ mm} \times 200 \cdot 10^{-3}\text{ mm}$ or 2.4 mm^2 adhesive surface. This multiplied by 20 brackets -the average case- results in a sum of 48 mm^2 of material area exposed to the oral conditions. For wider brackets, which are introduced to provide better rotational and tipping control of teeth, these figures are expected to be increased.

Table 1 compares the surface area of adhesives or composites exposed to the oral environment in the routine case of orthodontic bonding and the corresponding values of aligner treatment with the use of attachments. The assumption for the aligner scenario was the use of 12 attachments per case with varying shape depending on their position (4 trapezoid, 4 rectangular and 4 elliptical attachments). However, the actual clinical use of composite for aligner attachments differs vastly from the provided crude theoretical comparison of exposed surfaces because of the following two reasons. First, the adhesive during bracket bonding is applied in a sandwich pattern, which decreases exposed surfaces and

its potential reactivity with the oral environment. Second, attachments in aligner treatment possess considerable thickness to assist in tooth positioning and as such, they are exposed to a daily snagging of the aligner during fitting, or mastication. Thus, apart from the larger surface exposed relative to the edges of the adhesive, aligner attachments are also subjected to masticatory stresses during eating and stresses arising from the fitting of the aligner on the teeth multiple times daily, which brings us to the next issue.

Treatment-induced alterations of aligners and attachments

Newly delivered aligners that have not been in clinical use have similarly rough surfaces on both sides, due to the reproducible industrial manufacturing process of stereolithography, milling, and polishing that doesn't include much human interference. Intraoral use of aligners during treatment has been reported to reduce the surface roughness of the aligner coming in contact with the composite attachments.¹⁴ This can be seen as soon as the first week of service and leads to a decreased coefficient of friction¹⁵ and subsequently reduced micromechanical retention of aligners with the tooth and its attachments. On the other hand, the lower roughness of as-retrieved aligners after one- or two-week exposure could be explained by the intraoral wear of both the aligner attachment and lingual area, with composite and enamel, respectively, indicating a "polishing" effect from the contact of the aligner with the much harder enamel or composite resin attachment surfaces.

Attachments used for aligner treatment are usually made from composite resins with a hardness of 400-700 N/mm² Marten's Hardness (HM) (Table II), while human enamel has a hardness of about 2866 N/mm².⁶ This translates to a 6-fold increase of hardness for composite resin and a 23-fold increase for human enamel compared to Invisalign® aligners. It can be therefore anticipated that aligners will be subject to severe wear by their contact with the attachments or the labial / lingual enamel, leading to smoother surfaces of as-retrieved aligners. Additionally, as there is a big difference in HM of composites and enamel, lingual surfaces might present more intense wear, but the surface morphology and roughness may in this case play a more decisive role. In particular, the composite resin attachment area is microscopically characterized by a striation pattern perpendicular to the tooth axis as a positive remnant of the thermoplastic transfer template.¹⁸ In contrast, the tooth enamel surface is lacking this

abrasive texture, and appears to be smoother than the non-polished composite resin.¹⁹ Relevant research from Barreda et al.¹⁸ identified attachment surface alteration depending on the hardness and filler loading of the composite used. Specifically, even if in the majority of patients the shape of the alignments was only slightly changed, noticeable changes were observed in the attachments' texture for most patients, which might include composite cracks or fractures.¹⁸ Additionally, significantly greater attachment wear was seen with a micro-filled composite with 76% filler content compared to a nano-filled composite with 72.5% filler content.

Intraoral aging likewise has a significant effect on the mechanical properties of orthodontic aligners, which can be seen even after one week.¹⁴ Invisalign® aligners received after periods of one or two weeks of intraoral use show reduced Marten's hardness and indentation modulus compared to new aligners, while the measured values fall into previously reported ranges.²⁰ The decrease in hardness indicates a material with reduced wear resistance that is more vulnerable to attrition under occlusal forces. On the other side, used Invisalign® aligners showed significantly increased relaxation index compared to as-received aligners, which to our knowledge, has not been studied extensively in vivo due to the requirement of bulky specimens for relaxation testing.²¹ This is associated with material softening or residual stress relaxation and is specifically important for aligners that like other orthodontic appliances are pre-activated (i.e. pre-strained) and then inserted into the mouth to release orthodontic forces. Under constant deformation the exerted force is lower, while under constant strain the material is relaxed.

Several explanations exist for this deterioration of the mechanical properties of aligners after intraoral use, with the first lying with the material itself. Fourier transform infrared spectroscopies have revealed that Invisalign® aligners are made of a polyurethane-based material,^{20,22-23} and thus under clinical conditions, might suffer from a polyurethane softening mechanism.²⁴ This is based on the fact that thermoplastic polyurethane consists of a two-phase microstructure with hard and soft segments, where the latter tend to be oriented perpendicular to the applied stresses, and then break into smaller pieces in order to receive further deformation. Other factors proposed to be explanatory of the intraoral deterioration of the aligners' mechanical properties include the possibility of residual stresses from by the manufacturing process and the leaching of matrix plasticizers.²⁰

According to the results of another study employing mechanical testing of various aligners (Table III),²³ Invisalign® aligners show significantly higher values compared with the other materials used in the laboratory (like A+®, Clear Aligner®, or Essix ACE Plastic®) in terms of Hardness, Modulus and Elastic Index but lower Creep Resistance. This finding can be ascribed to the different chemical structure between the materials. Significant differences are also seen among different PETG materials used for in-lab aligners, which might be attributed to two factors: one is a different molecular weight of the various PETGS polymers and the second is the thermoforming effect on the mechanical properties. Thermoforming may influence the molecular orientation, mean molecular weight and residual stresses due to rapid cooling of the thermoplastic materials on the stone models.²⁵ The HM of commonly used aligner materials varies considerably and lies within the range of 80 to 160 N/mm².²⁶⁻²⁷ Previous studies have reported that PETG materials have higher wear resistance compared with polypropylene materials,²⁸ but there is no similar comparison between PETG and polyurethane-based materials (like the one Invisalign® uses). Likewise, great variability exists in the indentation moduli of aligners, which range between 1500 and 2700 MPa.²⁷ Generally, a higher modulus of elasticity is preferred, as it increases the force delivery capacity of appliances under constant strain. Otherwise, aligners from materials with higher modulus of elasticity can be constructed with smaller thickness to provide similar forces.²⁷ The higher elastic index of one Invisalign® aligners have significantly higher elastic index than other materials (2467 MPa vs 2112-2374 MPa),²³ which indicates a slightly more brittle material. At the same time, the higher indentation creep of Invisalign® aligners implies that under constant occlusal forces exerted by the occlusion, they are more likely to deform and therefore attenuate the applied orthodontic forces. In summary however, data indicate that Invisalign® aligners show a preferred combination of higher hardness and higher modulus, but at the same time creep resistance than other aligner materials.

Release of compounds

Intraoral aging has been shown to affect the structural integrity and influence an important array of material properties, including mechanical performance,²⁹ hydrolytic stability,³⁰⁻³¹ corrosion, degradation resistance to the intraoral biochemical environment,^{29,32} and aggressive chemical stimuli (ie, fluorides,

bleaching agents, alcohol, and so on). As a result, component molecules from orthodontic materials might be released intraorally, with Bisphenol A (BPA) being mostly discussed.

BPA is a chemical produced in large quantities for use primarily in the production of polycarbonate plastics and epoxy resins and diet is the primary source of BPA exposure for most people. In dental materials, BPA is used as a raw material for formulation of Bis-GMA and polycarbonate products; as a general rule, the estrogenic action is confined to molecules with a double benzoic ring and its first implication with dental material was reportedly in the saliva of patients with dental sealants,³³ which however still remains disputed.³⁴⁻³⁵ Studies in the late 1990s reported increased prostate weights and other effects on the male reproductive system in mice exposed to levels of BPA below the safety standard (2 and 20 mg/kg).³⁶⁻³⁷ A wide array of other effects were subsequently reported, including increased mammary gland tumors,³⁸ precancerous lesions in prostates of neonatally exposed animals,³⁹ development of hyperglycemia and insulin tolerance,⁴⁰ elevation of reactive oxygen species,⁴¹ and oxidative stress. The resultant turmoil on the hormonal endocrinologic disruptors provoked the investigation of estrogenic action of the full spectrum of polymeric materials used in everyday activities including plastic utensils and biomaterials for medical and dental applications.

As an empirical rule, the potential of BPA release is restricted to materials that contain BPA as a precursor during the manufacturing process. Obviously, any polymer without an aromatic ring in its structure is free of this concern; therefore, acrylic retainers and other linear carbon chain polymers have no known risk for BPA release. Orthodontic materials used in aligner treatment and might be prone to BPA release include thermoformed aligners and composite resins used for attachment fabrication. Even though many manufacturers have reportedly abandoned processes that include Bis-GMA or BPA, essays have found traces of such. Also, it is important to note here that a BPA release assay may not constitute conclusive evidence in determining the potential of a material to give rise to BPA formation because of the threshold of chromatographic analyses used,⁴² which means that the release might be undetected.

For aligners, the evidence is contradictory, since BPA's implication in the use of these products has not been conclusive at the cell culture or analytical level. Assessment with immersion analysis of as-received or in vitro aged Invisalign® aligners failed to demonstrate measurable cytotoxic effects⁴³ or leaching.⁴⁴⁻⁴⁵ The lack of differences among the chemical composition between new and intraorally aged

Invisalign® aligners²⁰ comply with previous results that confirmed no residual monomers and/or byproducts release either in artificial saliva.²² This might be attributed to the stability of Invisalign® aligners, which are basically polyurethane-derived products. In contrast to the aromatic rings in the configuration of BisGMA, polyether urethanes used as raw materials for aligner manufacturing have short rigid portions (the aromatic rings and the ureas) joined by short flexible “hinges” (the diamine linker and the methylene group between the aromatic ring) and long flexible portions (the polyether).⁴⁶ On the other side, an in vivo study of patients who received after debonding in-lab vacuum formed retainers / aligners^{45,47} reported increased salivary BPA levels one week after insertion, which were reduced after one month.⁴⁷

The release potential from adhesives used for aligner attachments is even more unclear as no study up to date has directly assessed the release among patients with attachments bonded on the multiple teeth for aligner treatment. Several studies exist assessing qualitative and quantitative parameters of BPA release from adhesives used for bracket bonding, probably because of the varying methodologies that have been used.⁴⁸ Although discrepancies exist between studies, evidence indicates a rise in BPA release immediately after bonding of brackets or lingual retainers^{45,49-52} while an increase of the distance between the light-cure tip and the adhesive introduces a decrease in the degree of conversion of the polymer⁵³ that leads to greater BPA release. Furthermore, a clinical study found measurable amounts of BPA released in the saliva after bonding and also that thorough rinsing with water helps return salivary BPA to baseline levels.⁵⁴ It is important however to stress out that release phenomena from bulkier protruding aligner attachments that are under occlusal loads might considerably vary from those of the secluded adhesive layer between tooth and bracket.

Debonding and grinding

Aerosol hazards

At completion of orthodontic treatment with aligners it will be necessary to remove the bonded composite attachments. The point has already been made that compared with conventionally bonded fixed appliances, the use of clear aligners with around three attachments per quadrant has the potential to require considerably more composite to be removed at the completion of treatment. This is not only

theoretical as a direct result of the amount of composite used with clear aligner treatments, but also because at removal of conventional fixed appliances the locus of failure is rarely confined to adhesive/ bracket base interface, meaning that less composite will require removal from the enamel surface. The removal of this residual composite will, in most instances, require the use of rotary instruments, with the inevitable consequence that airborne particulates will be generated, along with the risk of some enamel surface damage directly as a result of contact between the rotary instrument and enamel surface.

Airborne particulates comprise either solid particles produced and emitted directly into the air, known as primary particles, or solid particles produced as a result of a chemical reaction between two or more gases, are known as secondary particles.⁵⁵ Such particulates are of concern if their mass mean aerodynamic diameter or MMAD (which is dependent on their geometric size, mass and shape) are such that they are likely to be inhaled. Of most concern with respect to health are aerosols where the MMAD of the particles is less than 10 μm , known as PM_{10} (PM = Particulate Matter). It is these which are most likely to be inhaled and deposited within the human respiratory system. The larger of the PM_{10} particles are only likely to reach the pharynx, whereas particles with smaller aerodynamic diameters may be deposited deeper and deeper within the respiratory system. Smaller particles, described as $\text{PM}_{2.5}$ where the MMAD is less than 2.5 μm , might reach the terminal bronchi of the lungs. Even smaller particles, known as Ultrafines (MMAD < 0.1 μm), might reach as deep as the bronchioles and alveoli of the lungs.⁵⁶ Small particulates, if not immediately inhaled, can also remain airborne almost indefinitely within modest air turbulence, and therefore continue to pose an inhalation risk some considerable time after their production.⁵⁷ Whereas PM_{10} particulates are usually quickly cleared by the respiratory mucociliary escalator in 1-2 days, very small particulates, $\text{PM}_{2.5}$ and specifically Ultrafines, may take days or months to be cleared from the lungs, as they must first be ingested by alveolar macrophages.⁵⁷ Not only might Ultrafines penetrate the deeper parts of the lungs, but animal studies have shown them to elicit a greater inflammatory response within the lungs per given mass, than larger particles.⁵⁸⁻⁶¹

Following the removal of metallic brackets, bands and residual adhesive, it is known that both PM_{10} and $\text{PM}_{2.5}$ particulates are produced in the air within the clinical environment.⁶² A laboratory study investigating particulates produced at removal orthodontic adhesive showed particles less than 0.75 μm in MMAD were produced, irrespective of whether a slow or a high-speed rotary instrument was used, run

either dry or under water cooling. However, the greatest quantity of these smaller particles was produced with the high-speed rotary instrument used in combination with water cooling.⁶³ The same will be true following the use of multiple composite attachments with clear aligners, but potentially to an even greater degree due to the volume of composite requiring removal.

The respirable particulates produced at composite removal have been shown to include: calcium and phosphorus, most probably from the tooth enamel; carbon and oxygen most probably from the bonding resin; tungsten from the tungsten carbide debonding bur⁶² and iron most probably from the head and bearings of the rotary handpiece. Iron is a highly toxic transition metal and in the PM_{2.5} fraction will be deposited in the deeper regions of the lung. The most frequently detected particles comprised silica from the composite bonding resin.⁶³ Although there are no reported cases of silicosis among orthodontists there are strict workplace exposure limits (WEL) for silica.

In combined a laboratory and clinical investigation into particulate production at enamel clean up following the use of both conventional metal and flash free ceramic brackets, silica was identified within the respirable fraction (<5µm MMAD) of the aerosols generated in all cases.⁶⁴ Although the WEL for dust was not exceeded, the WEL for silica (0.1mg/m³) was exceeded in every experiment, but this would only be the case if all the particulates produced were indeed composed of silica, which is unlikely. It was not possible to determine what fraction did in fact comprised silica alone. The WEL for silica is the time weighted average over 8 hours, and although it is unlikely any single operator would be removing composite continuously for 8 hours, the persistence of airborne particulates generated previously by the same or different operator, or where clinicians work in multi surgery clinical set-ups, could possibly contribute to such an exposure exceeding the WEL. Once again, the same would apply to the composite attachment removal at completion of clear aligner treatment, but possibly to a greater degree, dependent on the number and size of the composite attachments used.

In addition to the particulates so far described, the removal of residual bonding composite at completion of treatment will also lead to the generation of a bioaerosol. It is know that within as little as 5 minutes following fixed appliance removal and enamel clean up, there is a significant increase in the concentration of bioaerosol compared to pre-operative resting room levels, with micro-organisms derived from the patient's oral cavity.⁶⁵⁻⁶⁶ This concentration is likely to be influenced, all other things being equal,

on the time taken for composite removal and the surface area of composite previously exposed to the oral environment, and which might therefore be contaminated with oral micro-organisms. In both cases it is possible this may be greater in the case of multiple attachments used with clear aligners when compared with conventional fixed appliances.

As with conventional fixed appliance composite removal, when removing the composite attachments following clear aligner treatment the operator should make every attempt to minimize the inhalation risk by using a slow speed rotary handpiece and a spiral fluted tungsten carbide bur.⁶⁷ In this way the risk of enamel damage at composite removal will also be minimized.³ The operator should also wear a facemask, supplemented with the use of a high-volume evacuator held close to the patient's mouth. In addition, the composite removal should not be performed using a water coolant spray as this further increases the aerosol risk.⁶⁷

Xenoestrogenic action (bulk and ground particles) and other biological effects

As stated earlier, BPA molecules released intraorally might act as an endocrine disruptor, due to its similar chemical structure to natural estrogen (17-beta estradiol).⁶⁸ An immersion study with as-received Invisalign® aligners measured estrogenicity by the effect on the proliferation of the estrogen-responsive MCF-7 breast cancer cells that are known to express estrogen receptor- α , which is of primary importance for the proliferative effect of estrogens.⁴³ No significant xenoestrogenic effects were found, which was attributed to the structural stability of these polyurethane-based aligners.

As far as the xenoestrogenicity of orthodontic adhesives is concerned, limited evidence exists, where an in vitro assay employing the same MCF-7 breast cancer cells assessing orthodontic adhesives used for simulated bracket bonding found no considerable oestrogenic activity.⁴² On the other hand, another potential risk for endocrine disruption lies at the debonding stage where the particulate matter produced by grinding of the resin adhesive might have an estrogenic action.⁶⁹ This is of particular interest, since greater volumes of adhesive are bonded on the teeth for aligner attachments and must be subsequently ground. However, no such study has assessed this directly in order to quantify the underlying risk levels.

Apart from endocrine disruptions, one study with eluates obtained from soaking Invisalign® plastic in saline solution used on epithelial cells and found some changes in viability, membrane permeability, and adhesion of epithelial cells in a saline-solution environment. The secondary results of compromising epithelial integrity might be microleakage and hapten formation which, in consequence, could lead to isocyanate allergy, either systemic or localized to gingiva.⁷⁰ Finally, assessment of the cytotoxicity of various in-lab vacuum formed aligners found only slight levels of cytotoxicity for human primary gingival fibroblast, while the thermoforming process increased the cytotoxicity of Polyethylene terephthalate glycol materials.⁷¹

Concluding remarks

The application of aligners in the clinical setting introduces a unique scenario of different materials applied in a manner which involves the development of friction and attrition between the attachment and the softer aligner material, all performing in the harsh conditions of the oral environment, which impact on the ageing of these materials. The latter may give rise to alterations of the aligners and the composite attachments and potential intraoral release of Bisphenol A, a known endocrine disrupting agent.

Because of the extensive enamel involvement in bonding, the release of factors from the attachment-aligner complex during service, the ageing of these entities in the oral environment, and the laborious debonding/composite grinding process coupled with the hazardous nature of aerosol produced during the removal of these bulky specimens, appropriate risk management considerations should be applied and an effort to confine the application of multiple composite specimens bonded to enamel to the absolutely necessary should be pursued.

REFERENCES

1. Eliades T, Gioka C, Eliades G, Makou M. Enamel surface roughness following debonding using two resin grinding methods. *Eur J Orthod* 2004;26:333-8.
2. Brosh T, Kaufman A, Balabanovsky A, Vardimon AD. In vivo debonding strength and enamel damage in two orthodontic debonding methods. *J Biomech* 2005;38:1107-13.
3. Ireland AJ, Hosein I, Sherriff M. Enamel loss at bond-up, debond and clean-up following the use of a conventional light-cured composite and a resin-modified glass polyalkenoate cement. *Eur J Orthod* 2005;27:413-19.
4. Janiszewska-Olszowska J, Tomkowski R, Tandecka K, Stepien P, Szatkiewicz T, Sporniak-Tutak K, et al. Effect of orthodontic debonding and residual adhesive removal on 3D enamel microroughness. *PeerJ* 2016;4:e2558.
5. Mohebi S, Shafiee HA, Ameli N. Evaluation of enamel surface roughness after orthodontic bracket debonding with atomic force microscopy. *Am J Orthod Dentofacial Orthop* 2017;151:521-7.
6. Ioannidis A, Papageorgiou SN, Sifakakis I, Zinelis S, Eliades G, Eliades T. Orthodontic bonding and debonding induces structural changes but does not alter the mechanical properties of enamel. *Prog Orthod* 2018;19:12.
7. Ogaard B, Rølla G, Arends J. Orthodontic appliances and enamel demineralization. Part 1. Lesion development. *Am J Orthod Dentofacial Orthop* 1988;94:68-73.
8. Karamouzos A, Athanasiou AE, Papadopoulos MA, Kolokithas G. Tooth-color assessment after orthodontic treatment: a prospective clinical trial. *Am J Orthod Dentofacial Orthop* 2010;138:537.e1-8.
9. Joo HJ, Lee YK, Lee DY, Kim YJ, Lim YK. Influence of orthodontic adhesives and clean-up procedures on the stain susceptibility of enamel after debonding. *Angle Orthod* 2011;81:334-40.
10. Sifakakis I, Zinelis S, Eliades G, Koletsi D, Eliades T. Enamel gloss changes induced by orthodontic bonding. *J Orthod* 2018;45:269-74.
11. Dasy H, Dasy A, Asatrian G, Rózsa N, Lee HF, Kwak JH. Effects of variable attachment shapes and aligner material on aligner retention. *Angle Orthod* 2015;85:934-40.

12. Kechagia A, Zinelis S, Pandis N, Athanasiou AE, Eliades T. The effect of orthodontic adhesive and bracket-base design in adhesive remnant index on enamel. *J World Fed Orthod* 2015;4:18-22.
13. Eliades T, Viazis AD, Eliades G. Bonding of ceramic brackets to enamel: morphologic and structural considerations. *Am J Orthod Dentofacial Orthop* 1991;99:369-75.
14. Papadopoulou AK, Cantele A, Polychronis G, Zinelis S, Eliades T. Changes in Roughness and Mechanical Properties of Invisalign(®) Appliances after One- and Two-Weeks Use. *Materials (Basel)* 2019;12:E2406.
15. Kusy RP, Whitley JQ. Effects of surface roughness on the coefficients of friction in model orthodontic systems. *J Biomech* 1990;23:913-25.
16. Sifakakis I, Zinelis S, Patcas R, Eliades T. Mechanical properties of contemporary orthodontic adhesives used for lingual fixed retention. *Biomed Tech (Berl)* 2017;62:289-94.
17. Hassan MA, Zinelis S, Hersberger-Zurfluh M, Eliades T. Creep, Hardness, and Elastic Modulus of Lingual Fixed Retainers Adhesives. *Materials (Basel)* 2019;12:E646.
18. Barreda GJ, Dzierewianko EA, Muñoz KA, Piccoli GI. Surface wear of resin composites used for Invisalign® attachments. *Acta Odontol Latinoam* 2017;30:90-5.
19. Botta AC, Duarte S Jr, Paulin Filho PI, Gheno SM, Powers JM. Surface roughness of enamel and four resin composites. *Am J Dent* 2009;22:252-4.
20. Bradley T, Teske L, Eliades G, Zinelis S, Eliades T. Do the mechanical and chemical properties of invisalign™ appliances change after use? A retrieval analysis. *Eur J Orthod* 2016;38:27-31.
21. Fang D, Zhang N, Chen H, Bai Y. Dynamic stress relaxation of orthodontic thermoplastic materials in a simulated oral environment. *Dental Mater J* 2013;32:946-51.
22. Gracco A, Mazzoli A, Favoni O, Conti C, Ferraris P, Tosi G, et al. Short-term chemical and physical changes in invisalign appliances. *Aust Orthod J* 2009;25:34-40.
23. Alexandropoulos A, Al Jabbari YS, Zinelis S, Eliades T. Chemical and mechanical characteristics of contemporary thermoplastic orthodontic materials. *Aust Orthod J* 2015;31:165-70.
24. Qi H, Boyce M. Stress–strain behavior of thermoplastic polyurethanes. *Mech Mat* 2005;37:817-39.
25. Ryokawa H, Miyazaki Y, Fujishima A, Miyazaki T, Maki K. The mechanical properties of dental thermoplastic materials in a simulated intraoral environment. *Orthod Waves* 2006;65:64-72.

26. Kwon JS, Lee YK, Lim BS, Lim YK. Force delivery properties of thermoplastic orthodontic materials. *Am J Orthod Dentofacial Orthop* 2008;133:228-34.
27. Kohda N, Iijima M, Muguruma T, Brantley WA, Ahluwalia KS, Mizoguchi I. Effects of mechanical properties of thermoplastic materials on the initial force of thermoplastic appliances. *Angle Orthod* 2013;83:476-83.
28. Gardner GD, Dunn WJ, Taloumis L. Wear comparison of thermoplastic materials used for orthodontic retainers. *Am J Orthod Dentofacial Orthop* 2003;124:294-7.
29. Wu W, McKinney JE. Influence of chemicals on wear of dental composites. *J Dent Res* 1982;61:1180-3.
30. Ruyter IE, Svendsen SA. Remaining methacrylate groups in composite restorative materials. *Acta Odontol Scand* 1978;36:75-82.
31. Papagiannoulis L, Tzoutzas J, Eliades G. Effect of topical fluoride agents on the morphologic characteristics and composition of resin composite restorative materials. *J Prosthet Dent* 1997;77:405-13.
32. Munksgaard EC, Freund M. Enzymatic hydrolysis of (di)methacrylates and their polymers. *Scand J Dent Res* 1990;98:261-7.
33. Olea N, Pulgar R, Olea-Serrano F, Rivas A, Novillo-Fertrell A, Pedraza V, et al. Estrogenicity of resin-based composites and sealant used in dentistry. *Environ Health Perspect* 1996;104:298-305.
34. Nathanson D, Lertpitayakun P, Lamkin MS, Edalatpour M, Chou LL. In vitro elution of leachable components from dental sealants. *J Am Dent Assoc* 1997;128:1517-23.
35. Zampeli D, Papagiannoulis L, Eliades G, Pratsinis H, Kletsas D, Eliades T. In vitro estrogenicity of dental resin sealants. *Pediatr Dent* 2012;34:312-6.
36. Soto AM, Murai JT, Siiteri PK, Sonnenschein C. Control of cell proliferation: evidence for negative control on estrogen-sensitive T47D human breast cancer cells. *Cancer Res* 1996;46:2271-5.
37. Vom Saal FS, Timms BG, Montano MM, Palanza P, Thayer KA, Nagel SC, et al. Prostate enlargement in mice due to fetal exposure exposure to low doses of estradiol or diethylstilbestrol and opposite effects at high doses. *Proc Natl Acad Sci U S A* 1997;94:2056-61.

38. Munoz-de-Toro M, Markey CM, Wadia PR, Luque EH, Rubin BS, Sonnenschein C, et al. Perinatal exposure to bisphenol-A alters peripubertal mammary gland development in mice. *Endocrinology* 2005;146:4138-47.
39. Timms BG, Howdeshell KL, Barton L, Bradley S, Richter CA, vom Saal FS. Estrogenic chemicals in plastic and oral contraceptives disrupt development of the fetal mouse prostate and urethra. *Proc Natl Acad Sci U S A* 2005;102:7014-9.
40. Alonso-Magdalena P, Morimoto S, Ripoll C, Fuentes E, Nadal A. The estrogenic effect of bisphenol-A disrupts the pancreatic β -cell function in vivo and induces insulin resistance. *Environ Health Perspect* 2006;114:106-12.
41. Ooe H, Tkahiro T, Iguchi-Arigo SMM, Ariga H. Induction of reactive oxygen species by bisphenol A and abrogation of bisphenol A-induced cell injury by DJ-1. *Toxicol Sci* 2005;88:114-26.
42. Eliades T, Hiskia A, Eliades G, Athanasiou AE. Assessment of bisphenol-A release from orthodontic adhesives. *Am J Orthod Dentofacial Orthop* 2007;131:72-5.
43. Eliades T, Pratsinis H, Athanasiou AE, Eliades G, Kletsas D. Cytotoxicity and estrogenicity of Invisalign appliances. *Am J Orthod Dentofacial Orthop* 2009;136:100-3.
44. Schuster S, Eliades G, Zinelis S, Eliades T, Bradley TG. Structural conformation and leaching from in vitro aged and retrieved Invisalign appliances. *Am J Orthod Dentofacial Orthop* 2004;126:725-8.
45. Kotyk MW, Wiltshire WA. An investigation into bisphenol-A leaching from orthodontic materials. *Angle Orthod* 2014;84:516-20.
46. Eliades T, Eliades G, Silikas N, Watts DC. In vitro degradation of polyurethane orthodontic elastomeric chains. *J Oral Rehabil* 2005;32:72-7.
47. Raghavan AS, Pottipalli Sathyanarayana H, Kailasam V, Padmanabhan S. Comparative evaluation of salivary bisphenol A levels in patients wearing vacuum-formed and Hawley retainers: an in-vivo study. *Am J Orthod Dentofacial Orthop* 2017;151:471-6.
48. Kloukos D, Pandis N, Eliades T. Bisphenol-A and residual monomer leaching from orthodontic adhesive resins and polycarbonate brackets: a systematic review. *Am J Orthod Dentofacial Orthop* 2013;143:S104-12.e1-2.

49. Eliades T, Voutsas D, Sifakakis I, Makou M, Katsaros C. Release of bisphenol-A from a light-cured adhesive bonded to lingual fixed retainers. *Am J Orthod Dentofacial Orthop* 2011;139:192-5.
50. Kang YG, Kim JY, Kim J, Won PJ, Nam JH. Release of bisphenol A from resin composite used to bond orthodontic lingual retainers. *Am J Orthod Dentofacial Orthop* 2011;140:779-89.
51. Moreira MR, Matos LG, de Souza ID, Brigante TA, Queiroz ME, Romano FL, et al. Bisphenol A release from orthodontic adhesives measured in vitro and in vivo with gas chromatography. *Am J Orthod Dentofacial Orthop* 2017;151:477-83.
52. Halimi A, Benyahia H, Bahije L, Adli H, Azeroual MF, Zaoui F. A systematic study of the release of bisphenol A by orthodontic materials and its biological effects. *Int Orthod* 2016;14:399-417.
53. Sunitha C, Kailasam V, Padmanabhan S, Chitharanjan AB. Bisphenol A release from an orthodontic adhesive and its correlation with the degree of conversion on varying light-curing tip distances. *Am J Orthod Dentofacial Orthop* 2011;140:239-44.
54. Kloukos D, Sifakakis I, Voutsas D, Doulis I, Eliades G, Katsaros C, et al. BPA qualitative and quantitative assessment associated with orthodontic bonding in vivo. *Dent Mater* 2015;31:887-94.
55. CONCAWE. (2017) An Introduction to Air Quality. https://www.concawe.eu/wp-content/uploads/2017/09/DEF_AQ_AirQuality_digital.pdf
56. Möller W, Häussinger K, Winkler-Heil R, Stahlhofen W, Meyer T, Hofmann W, et al. Mucociliary and long-term particle clearance in the airways of healthy nonsmoker subjects. *J Appl Physiol* 2004;97:2200-6.
57. Hext PM, Rogers KO, Paddle GM. The health effects of PM2.5 (including ultrafine particles). Report no. 99/60, 1999, Brussels: CONCAWE.
58. Oberdörster G. Pulmonary effects of inhaled ultrafine particles. *Int Arch Occup Environ Health* 2001;74:1-8.
59. Oberdorster G, Oberdorster E, Oberdorster J. Nanotoxicology: an emerging discipline evolving from studies of ultrafine particles. *Environ Health Perspect* 2005;113:823-39.
60. Borm PJ, Robbins D, Haubold S, Kuhlbusch T, Fissan H, Donaldson K, et al. The potential risks of nanomaterials: a review carried out for ECETOC. *Part Fibre Toxicol* 2006;3:11.

61. Napierska D, Thomassen LC, Lison D, Martens JA, Hoet PH. The nanosilica hazard: another variable entity. *Part Fibre Toxicol* 2010;7:39.
62. Ireland AJ, Moreno T, Price R. Airborne particles produced during enamel cleanup after removal of orthodontic appliances. *Am J Orthod Dentofacial Orthop* 2003;124:683-6.
63. Day CJ, Price R, Sandy JR, Ireland AJ. Inhalation of aerosols produced during the removal of fixed orthodontic appliances: a comparison of 4 enamel cleanup methods. *Am J Orthod Dentofacial Orthop* 2008;133:11-7.
64. Vig P, Attack NE, Sandy JR, Sherriff M, Ireland AJ. Particulate production during debonding of fixed appliances: Laboratory investigation and randomized clinical trial to assess the effect of using flash-free ceramic brackets. *Am J Orthod Dentofacial Orthop* 2019;155:767-78.
65. Toroğlu MS, Haytaç MC, Köksal F. Evaluation of aerosol contamination during debonding procedures. *Angle Orthod* 2001;71:299-306.
66. Dawson M, Soro V, Dymock D, Price R, Griffiths H, Dudding T, et al. Microbiological assessment of aerosol generated during debond of fixed orthodontic appliances. *Am J Orthod Dentofacial Orthop* 2016;150:831-8.
67. Johnston NJ, Price R, Day CJ, Sandy JR, Ireland AJ. Quantitative and qualitative analysis of particulate production during simulated clinical orthodontic debonds. *Dent Mater* 2009;25:1 155-62.
68. Vom Saal FS, Hughes C. An extensive new literature concerning low-dose effects of bisphenol a shows the need for a new risk assessment. *Environ Health Perspect* 2005;113:926-33.
69. Gioka C, Eliades T, Zinelis S, Pratsinis H, Athanasiou AE, Eliades G, et al. Characterization and in vitro estrogenicity of orthodontic adhesive particulates produced by simulated debonding. *Dent Mater* 2009;25:376-382.
70. Premaraj T, Simet S, Beatty M, Premaraj S. Oral epithelial cell reaction after exposure to Invisalign plastic material. *Am J Orthod Dentofacial Orthop* 2014;145:64-71.
71. Martina S, Rongo R, Bucci R, Razionale AV, Valletta R, D'Antò V. In vitro cytotoxicity of different thermoplastic materials for clear aligners. *Angle Orthod* 2019;89:942-5.

FIGURE LEGENDS

Fig 1. Clinical example of a patient treated with aligners and composite resin attachments (creditDr. K. Papadopoulou).

Fig 2. Backscattered electron image of the enamel-adhesive interface. Note the presence of the highly-filled adhesive and the formation of resin tags which are depicted as a cloud of projection into the enamel (original magnification 1200x)

TABLE LEGENDS

Table I. Effective surface exposure area of adhesive in bracket bonding and lingual fixed retainer scenarios. Thickness values for adhesives were derived from Eliades et al.¹³

Table II. Mechanical properties of adhesives and composites used for the fabrication of attachments. Data adapted from Sifakakis et al.¹⁶ and Hassan et al.¹⁷

Table III. Mechanical properties (hardness, indentation modulus) of aligner materials. Adapted from Alexandropoulos et al.²³

Table I. Effective surface exposure area of adhesive in bracket bonding and aligner treatment with attachments

Procedure	Assumptions	Estimated exposure area
Bracket bonding	<ul style="list-style-type: none"> • 20 teeth • Brackets 2.5×3.0 mm • Adhesive thickness of $200 \mu\text{m}$ 	Margin exposure: (periphery 11.0 mm) \times (thickness 200×10^{-3} mm) $(2.2 \text{ mm}^2 \text{ per tooth}) \times (20 \text{ teeth})$ Total area = 44 mm^2
Attachments with aligners	<ul style="list-style-type: none"> • 12 teeth with attachments • 4 \times beveled attachments $3.0 \times 3.0 \times 1.5$ mm • 4 \times rectangular attachments $3.0 \times 2.0 \times 0.5$ mm • 4 \times ellipsoid attachments $3.0 \times 2.0 \times 1.0$ mm 	Beveled (Exposed surface 11 mm^2) \times (4 \times attachments) = 44 mm^2 + Rectangular (Exposed surface 11 mm^2) \times (4 \times attachments) = 44 mm^2 + Ellipsoid (Exposed surface 3.1 mm^2) \times (4 \times attachments) = 12 mm^2 Total area = 100 mm^2

Note. Thickness values for adhesives were derived from Eliades et al.¹³

Table II. Mechanical properties of adhesives and composites used for the fabrication of attachments

Material/manufacturer	Martens hardness (N/mm ²)
Transbond LR (3M, Espe)	785
Transbond XT (3M, Espe)	568
Accolate (Danville materials)	276
IPS Empress direct dentin (Ivoclar Vivadent)	487
ZNano (Danville materials)	375
Brace paste (American Orthodontics) ^a	456
Enlight LV (Ormco Corp) ^a	427
G-aenial (GC Corp) ^a	337
Flow Tain (Reliance Orthodontics)	268
Wave (SDL) ^a	260

Note. Values are indicative-source articles indicate non-statistically significant differences among materials possessing modulus in the range of 6.9 GPa to 7.4 GPa. Data adapted from Sifakakis et al.¹⁶ and Hassan et al.¹⁷

*

Does not contain 2,2-bis[4-(2-hydroxy-3-methacryloyloxypropyl)-phenyl]propane (Bis-GMA).

Table III. Mechanical properties (hardness, indentation modulus) of aligner materials

Aligner	Martens hardness (N/mm ²)
A+, Dentsply Raintree Essix Sarasota, Fla	100.0
Clear Aligner, Scheu-Dental GmbH, Iserlohn, Germany	91.8
Essix ACE plastic, Dentsply Raintree Essix, Sarasota, Fla	100.6
Invisalign, Align Technology, San Jose, Calif	117.8

Note. Adapted from Alexandropoulos et al.²³

