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Irradiation therapy and chewing simulation: effect on zirconia and human enamel

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Abstract

Purpose: Ionizing radiation therapy (RT) is the main option for head and neck cancer treatment, but it is associated with multiple side effects. This study aimed to evaluate the effect of RT associated with chewing simulation on the surface of human enamel and Yttria-partially stabilized zirconia (Y-TZP).

Methods: Maxillary premolar cusps and Y-TZP slabs were divided in 7 experimental groups: CO: no RT (control); EZ groups had irradiation applied to both, enamel and zirconia samples (simulating restoration prior to RT); E groups had irradiation applied to enamel only (simulating restoration after RT). RT doses were either 30, 50 or 70 Gray (Gy). Enamel cusps were abraded against zirconia slabs in a chewing simulator (CS - one million cycles/ 80 N/ 60 mm/min, 2 mm horizontal path, artificial saliva, 37° C). Zirconia hardness was evaluated before CS; zirconia roughness and enamel volume (wear) were evaluated before and after CS. Hardness and wear data were analyzed by one-way Analysis of Variance and Tukey post hoc test. Roughness was analyzed by Repeated Measures test and Bonferroni test ($p=0.05$).

Results: There was no significant effect of enamel or zirconia irradiation on enamel cusp wear ($p=0.226$), regardless of the irradiation dose used - up to 70 Gy. Irradiation also did not affect Y-TZP surface roughness ($p=0.127$) and hardness ($p=0.964$).

Conclusions: RT does not promote significant changes to the surface characteristics of zirconia. Irradiated enamel abraded against zirconia does not show higher wear volume when compared to non-irradiated enamel.

Keywords: Polycrystalline ceramics, Ionizing irradiation, Hardness, Surface wear

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1. Introduction

Every year approximately half million new cases of head and neck cancer (HNC) are diagnosed worldwide [1]. Ionizing radiation therapy (RT) is one of the main options for the treatment of head and neck cancer [2], but it is associated with multiple side effects in the oral cavity [3]. RT is generally delivered in fractionated doses of 2 Gray (Gy)/day, 5 days/week [4]. The effect of RT is cumulative, so the fractionated radiation is based on a rule named "5Rs": repair, redistribution, reoxygenation, regeneration and radiosensitivity [5]. RT significantly increases the survival rate of patients diagnosed with HNC but clinical undesirable outcomes include loss of taste, hyposalivation, radiation-related caries and osteoradionecrosis [4, 6, 7]. Radiation-related caries is considered a chronic effect of RT and they affect both, cervical and occlusal surfaces of teeth. When those caries progress, the effects go from enamel cracks and cuspal wear to the destruction of the coronary structure [8, 9]. A retrospective study showed a dose-response

correlation between RT and tooth damage: minimal tooth structure damage happens below 30 Gy; the risk of tooth breakdown increases 2-3 times between 30 and 60 Gy due to the permanent damage of the salivary glands above 30 Gy; and the chance of tooth breakdown increases by 10 times above 60 Gy, suggesting radiation-induced damage to the tooth structure further to the reduced salivary flow [8, 10]. However, the *in vitro* exposure of tooth structure to standard head and neck RT protocol shows that the key dose for nanomechanical changes in enamel is between 30 and 50 Gy, and no further mechanical damage is observed above 50 Gy [8]. The maximum irradiation dose reported for the treatment of HNC is in the range of 70 Gy [4, 11], indicating long-term deleterious effects of RT to the teeth present in the field of irradiation.

Among the materials currently available for the indirect replacement of compromised tooth structure, Yttria-tetragonal zirconia polycrystalline (Y-TZP) is one of the most frequently used. Y-TZP was largely used in a bi-layer configuration, where a coping of zirconia was veneered with porcelain [12, 13]. Due to the frequent failure of the veneer porcelain and the development of more translucent zirconia-based materials, Y-TZP has been increasingly used as a monolithic restoration, without the application of veneer materials. Monolithic Y-TZP meets the demands of patients and dentists for a tooth-colored, strong and biocompatible restorative material, and it provides for proper intraoral function in both anterior and posterior regions [9, 14, 15]. Previous studies have demonstrated that polished zirconia causes

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less wear to the opposing enamel surface than enamel itself, glazed zirconia [16, 17] and other ceramics such as lithium disilicate glass, leucite-reinforced glass and feldspathic porcelain [18]. Occlusal adjustments of zirconia after insertion are considered of clinical concern due to changes in surface roughness and crystalline structure of zirconia [19–22], and also because it might affect the wear pattern of the opposing enamel [23]. Polishing the surface of zirconia with a fine diamond paste seems to be sufficient to generate a smooth surface [24–26]. The wear behavior of human enamel is also affected by enamel's hardness and resistance to friction, and irradiated enamel has lower hardness and higher friction coefficient than non-irradiated enamel [27]. Since the wear resistance of a substrate is inversely proportional to the friction coefficient of its surface [27], it is expected that irradiated enamel has lower wear resistance than non-irradiated enamel.

Some studies have already evaluated the effect of head and neck irradiation on tooth structure restored with direct restorative materials [27–29]. Metallic restorations, for example, can adversely affect the oral mucosa and the treatment planning of head and neck cancer patients [30]. To spare the oral mucosa from dose enhancement associated with backscattering, the use of intraoral mouthpieces [31] or the replacement of metal fillings with composite-based materials [32] is recommended before RT. A previous study evaluated the effect of different irradiation ions on Y-TZP [33] but noticeably, there is a lack of scientific studies evaluating the interaction between radiation, tooth structure and dental zirconia. It is not possible, therefore, to determine if zirconia casts any protection or damaging effect to the oral tissues and tooth structure. Thereafter, this study investigated the effect of different irradiation doses on the wear of human enamel abraded against irradiated and non-irradiated monolithic zirconia. Surface characteristics of zirconia before and after chewing simulation were also investigated. The study hypotheses were: ionizing irradiation will affect roughness and hardness of Y-TZP; ionizing irradiation will increase human enamel wear volume.

2. Materials and methods

2.1. Enamel specimens' preparation

Eighteen bicuspid teeth extracted for reasons not related to this study were collected after approval from the Research Oversight and Compliance Office (protocol preference #34680). The teeth were stored in 10% neutral buffered formalin solution [34] before having their roots removed 1 mm below the cementum-enamel junction (CEJ) with a diamond blade under water cooling (Buehler 15 LC; Isomet 1000; Buehler). Buccal and lingual cusps were separated by a mesial-distal cut in the central groove parallel to the tooth long axis, resulting in 36 cusps. The cusps were stored in distilled water at 37° C.

2.2. Zirconia specimens' preparation

Thirty-five zirconia samples were produced by cutting a pre-sintered block of 3 mol% Yttria-partially stabilized zirconia (3Y-TZP, IPS E.max Zircad, Ivoclar) with a diamond embedded blade (Buehler 15 LC) to obtain 8.5 mm x 8 mm x 2.5 mm slices.

After sintering the samples according to manufacturer's instructions, one surface was wet polished with 400 and 600- grit silicon carbide papers for 30–45 seconds and 6 µm followed by 3 µm diamond paste (4 min each) in a rotary grinding/polishing machine (Metaserv 250 Grinder/ Polisher, Buehler) at a speed of 300 rpm. The final dimension of the blocks was 6.5 mm x 6 mm x 2 mm. After being cleaned ultrasonically in acetone for 5 minutes and air-dried [35], the samples were annealed in a laboratory chamber furnace (CWF1300, Carbolite) with 5° C/min heating rate and 1200° C holding temperature for 2 hours [36], for relief of compressive stress. All samples were stored in distilled water at 37° C.

2.3. Experimental groups

Enamel and zirconia specimens were randomly allocated within 7 groups (n=5) according to the single dose irradiation protocol assigned [8], as follows (Table 1):

- CO: control, no irradiation on both, enamel and zirconia specimens;
- EZ 30: 30 Gy on both enamel and zirconia (Elekta Infinity Linac);
- E 30: 30 Gy on enamel only;
- EZ 50: 50 Gy on both enamel and zirconia;
- E 50: 50 Gy on enamel only;
- EZ 70: 70 Gy on both enamel and zirconia;
- E 70: 70 Gy on enamel only.

For the irradiation procedure, samples were fully submerged in a distilled water phantom and the irradiation (Elekta infinity linac, 6MV, filed size of 30x30 cm², Department of Radiation Oncology, Princess Margaret Cancer Center) was delivered using parallel opposed beams. Half of the irradiation dose was delivered from 0° angle and half of it from 180° angle for all experimental groups.

After irradiation, all samples were stored in distilled water (37° C) until further tests were applied.

2.4. Chewing simulation

Chewing simulation was used to simulate wear that happens as a consequence of *in vivo* mastication, as previously described by other studies [37, 38]. Enamel and zirconia specimens were embedded in polymethylmethacrylate (PMMA) and inserted into metallic holders. The metallic holders containing the zirconia specimens were fixed to the base and the enamel cusps in their respective holders were fixed to the upper arm of a chewing simulator (Mechatronik CS 4.4, SD Mechatronik GMBH). Four specimens of zirconia and four samples of enamel were cycled per time as follows: one million cycles/ 80 N/ 60 mm/min speed, 2 mm horizontal path, artificial saliva [39], 37° C.

2.5. Quantification of wear

Enamel samples were scanned before and after chewing simulation for individualized quantification of wear. The wear volume (in µm³) was calculated by subtracting the values obtained after CS from the initial volume values. The starting point was defined in a mesial incline of each cusp and dotted with a permanent marker before the measurements. Three guiding lines were drawn on the surface of the acrylic holder to use as a reference point to ensure that the same area was measured before and after aging. A stylus profilometer (Dektak Xt, Version 64 Operation and Analysis Software, Bruker Nano Surfaces Division, Bruker) was used to measure the volume of each cusp, by scanning 40 times, with 2.5 µm distance between each scan, with a 5 mg stylus force and a resolution of 0.666 µm of scan. Each scan was 2.5 mm in length and netted 3,765 data points.

For further characterization, one enamel sample from the non-irradiated (CO) and one enamel sample from EZ 70 groups, both abraded by CS, were cleaned in distilled water ultrasonic bath, coated with gold and analyzed under scanning electron microscopy (SEM; JSM 6610LV, JEOL) with high vacuum mode. Two images were taken from each sample, one overview of the abraded area and one at the interface between the abraded and non-abraded area.

2.6. Roughness analysis

The same profilometer used for wear (Dektak Xt, Bruker) was used for analysis of roughness, but with a 10 mg of stylus force. Samples were analyzed before and after CS. Ten scans were obtained for each sample with 200 µm distance between scans, 2 mm in length and 6,000 data point. Scan speed and resolution were set as previously mentioned for the

Table 1. Experimental groups according to the treatment applied.

Group	IR dose	Zirconia	Enamel
CO	None	Non-irradiated	Non-irradiated
EZ 30	30 Gy	Irradiated	Irradiated
E 30	30 Gy	Non-irradiated	Irradiated
EZ 50	50 Gy	Irradiated	Irradiated
E 50	50 Gy	Non-irradiated	Irradiated
EZ 70	70 Gy	Irradiated	Irradiated
E 70	70 Gy	Non-irradiated	Irradiated

analysis of wear.

2.7. Hardness test

Knoop hardness was measured on the surface of zirconia samples ($n=5$) for groups: CO, EZ30, EZ50 and EZ70. An indentation load of 500 grams (Tukon microhardness tester, Touchstone research laboratory) was applied for 15 s on three different areas of each sample. Indentation dimensions and load were considered for determination of hardness.

2.8. Analysis of data

One-way Analysis of Variance (ANOVA) and Tukey post-hoc (SPSS INC) were used to evaluate the effect of irradiation on percentage of wear for human enamel, zirconia roughness and zirconia hardness. Mixed repeated measures test associated with Bonferroni correction were performed to evaluate the effect of irradiation on zirconia roughness between before and after CS. All tests were performed at a confidence interval set at 95%.

3. Results

3.1. Wear

Analysis of data indicated that there was no significant effect of irradiation on the wear of enamel cusps ($p=0.226$). Mean and standard deviation are shown in Figure 1. Figure 2 shows SEM images of the enamel surface of control (a and b) and EZ 70 (c and d) groups, indicating the large variation in surface area due to the anatomical variations amongst cusps. There were no signs of enamel delamination or further discrepancies of wear pattern between control and irradiated enamel.

3.2. Roughness and hardness

One-way ANOVA showed that there was no significant effect of irradiation on roughness (RA) before CS ($p=0.057$). After checking the variance of covariance ($p=0.453$), repeated measures test demonstrated no significant effect of irradiation and CS on RA values ($p=0.127$) as well. Overall, there were no differences in RA among all experimental groups ($p=0.334$). Figure 3 provides means and standard deviation for RA after irradiation - before and after CS.

There was no effect of irradiation on zirconia hardness ($p=0.964$). Table 2 shows means and standard deviation for the evaluated groups.

4. Discussion

The most frequent treatment used for head and neck malignant tumors is fractionated irradiation in a total dose between 40 Gy and 70 Gy. The main purpose of using fractionated radiation is based on reparability and radio sensitivity of the soft tissues [5]. However, tooth structure and dental restorative materials do not present the same characteristics, and this is the reason why in the present study a single dose irradiation was used. This

not only saved significant experimental time but also kept the hospital equipment available for the treatment of patients.

Dentists have a vital role to play in supportive care before, during and after the radiotherapy treatment. The current protocol for patients who will undergo radiation therapy is to preserve asymptomatic teeth with no periapical lesions, and to either extract or restore teeth with carious lesions [40]. Mucositis is one of the negative outcomes of radiotherapy for head and neck cancer [30]. Mucositis frequently happens adjacent to metallic restorations, because dose scattering can lead to localized dose enhancement adjacent to soft tissues [30]. Fixed partial dentures (FPD) manufactured with ceramic veneer crowns cause a dose enhancement of 8% compared to 32% in gold crowns and 33% in all-metal restorations [30]. Although dose-scattering of zirconia-based materials has not been evaluated yet, it is a consensus that non-metallic restorations are highly recommended for the oral rehabilitation of patients who will undergo head and neck radiotherapy.

One of the challenges often encountered by clinicians is to find a suitable material to restore radiation-related caries and provide for long-lasting restorations. The chosen dental material should prevent secondary caries and provide proper adhesion to the tooth structure [29]. Y-TZP has mechanical properties that are far superior to other ceramics currently available for indirect restorations [25]. However, mechanical properties of Y-TZP are combined with very high surface hardness, which may end up being deleterious to the enamel structure already altered by irradiation. It is also known that polishing zirconia after occlusal adjustments does not decrease surface roughness significantly [19], making zirconia restorations even more challenging to human enamel. When considering zirconia for the treatment of patients with HNC, the outstanding mechanical properties of the material might be able to protect and support the tooth structure underneath, but it may offer a deleterious effect to the opposing dentition, which is already affected by irradiation and/or local salivary changes. Therefore, this study evaluated the effect of irradiation on the wear of human enamel using irradiated and non-irradiated zirconia as antagonist in order to simulate two scenarios: zirconia placed before or after ionizing irradiation therapy.

The irradiation doses applied in this *in vitro* study are correlated with the *in vivo* doses used for the treatment of HNC, and our findings indicate no significant cuspal enamel wear when treated (irradiated) cusps were compared with control (non-irradiated) cusps. A previous study demonstrated higher friction coefficient and deeper scratch of irradiated human enamel in comparison to non-irradiated enamel, and the authors observed that this could be an explanation for the delamination of dental enamel often observed after RT [27]. The similar wear values observed between irradiated and control cusps in the present study may be a consequence of the samples used: human premolar cusps were used rather than animal teeth or artificial enamel. Human teeth was the substrate of choice aiming at finding clinically meaningful results. But one has to agree that the shape and size of cusps vary significantly among patients and even within the same patient [41], which may have resulted in a large variability and, therefore, masked any possible effect of irradiation on enamel's surface's characteristics. Furthermore, it is also known that dentin plays a significant role in keeping the tooth structure strong. The clinical exposure of the DEJ to drastic salivary changes may have a "softening" effect on the dentin's mechanical properties, which leads clinically to the delamination of the overlying enamel. The absence of a more realistic *in vivo* component in the present study may have helped preserve the enamel and, therefore, mask the events taking place in the *in vivo* environment. Studies have shown that irradiation, depending on its total dose, may affect salivary flow [42], which changes the bacteria population, bone quality and structure [43, 44], and these factors could not be reproduced in the *in vitro* setting. But, as far as the authors are concerned, the experimental conditions used in the present study, combining human enamel cusps, artificial saliva and oral temperature, and a well documented process of chewing

Fig. 1. Mean and standard deviation for enamel wear as a function of irradiation and antagonist surface.

Fig. 2. Enamel cusps micrographs after CS: (A) overview of the abraded area of a CO (non-irradiated) enamel cusp; (B) higher magnification (x500) showing the interface between the abraded and non-abraded surface of a CO (non-irradiated) cusp; (C) overview of the abraded area of a 70 Gy irradiated cusp; (D) is a higher magnification (x500) showing the interface between the abraded and non-abraded surfaces of the 70 Gy irradiated enamel.

Fig. 3. Mean and standard deviation for RA values before and after CS.

Table 2. Mean and standard deviation of Knoop hardness (HK) for zirconia samples after irradiation.

Group	Knoop hardness	Standard deviation
CO	2612.06	±282.95
EZ30	2584.4	±347.95
EZ50	2646.8	±282.07
EZ70	2678.33	±299.41

simulation [37, 39], resulted in the simulation of an *in vivo* scenario in an *in vitro* environment, in spite of the limitations of the artificial conditions present in the laboratorial setting.

Data analysis also indicated that there was no effect of ionizing irradiation on both, surface hardness and roughness of Y-TZP. The surface roughness of Y-TZP plays a critical role in the relationship between plaque accumulation, periodontal inflammation and the wear of opposing tooth structure [15]. A rougher surface increases wear pattern of opposing enamel [23]. Previous studies found that polishing zirconia results in a surface smoother than glazing [15], but polished zirconia seems to be more deleterious to the wear of artificial enamel when compared to glazed zirconia and bi-layer (zirconia-porcelain) restorations [17]. All zirconia specimens were polished up to 1 µm in the present study. It is possible that the similar enamel wear results between control and irradiated were also a consequence of the high level of polishing of the opposing Y-TZP substrates. Therefore, it is not possible to infer that irradiated enamel would present wear volume similar to control enamel after occlusal adjustment of Y-TZP restorations, and this should be further investigated in future studies. Polishing the zirconia surface may also promote surface crystalline changes [20] that will lead to a rougher surface or generate a compressive stress layer [21] that will interact with the indenter during hardness measurement [21]. Nanoindentation of artificially aged Y-TZP has shown that the crystallographic planes may present a “noisy” behavior characteristic of the opening and closing of the martensitic plates as a function of successive loading-partial unloading functions [22]. In the present study, samples were annealed prior to application of the treatments to minimize compressive stresses [36] and, therefore, to reduce any deleterious effect of the sample preparation procedures on the crystalline stability of zirconia. No differences were observed in surface hardness of zirconia samples after irradiation and chewing simulation, which may be a strong indication that no changes occurred in the surface crystalline composition of zirconia. A previous study demonstrated that Y-TZP is one of the most resistant ceramics to irradiation. Samples exposed to 60 Kev Xenon (Xe) ions irradiation at several temperatures did not show signs of amorphization or crystalline changes [33].

The results of the present study demonstrated no effect of irradiation on both enamel and zirconia properties, but it does not mean that Y-TZP may be used inadvertently for the rehabilitation of patients (to be) treated with ionizing irradiation therapy. Among the limitations of the study, only one brand of zirconia was used, and it does not represent all the materials currently available. The specimens’ preparation for chewing simulation did not include the presence of a periodontal ligament, which may have affected forces’ distribution along the specimens or at the occlusal surface. Additionally, surface profilometry measured an area which was larger than the abraded area after CS, and this may have affected the overall reading of roughness. Lastly, because of the lack of effect of irradiation and chewing simulation on roughness and hardness, the researchers deemed not necessary to perform further crystalline analyses such as X-ray diffraction (XRD), atomic force microscopy (AFM) or Raman spectroscopy. However, further investigations of the interaction between mastication and ionizing irradiation using various materials are encouraged with a long-term aim of improving quality of life of head and neck cancer survivors.

5. Conclusion

Under the conditions of this study, it was not possible to detect any effect of irradiation on wear of human enamel and surface characteristics of zirconia. The wear pattern of irradiated enamel antagonist either irradiated or non-irradiated zirconia was similar. Also, there was no effect of

irradiation on zirconia’s microhardness and roughness. As a consequence, the type of zirconia used in the present study seems to be safe, in terms of wear potential, for the rehabilitation of patients treated with head and neck radiotherapy.

Conflict of interest

All authors declare that they have no conflict of interest.

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