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Laboratory Research

The Effect of Radiotherapy on the Marginal Adaptation of Class II Direct Resin Composite Restorations: A Micro-computed Tomography Analysis

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Clinical Relevance

When restorations are placed below the cemento-enamel junction after radiotherapy, a universal adhesive system with the application of the etch-and-rinse mode might be preferred.

SUMMARY

This laboratory study was designed to evaluate the marginal adaptation of Class II mesio-occluso-distal (MOD) restorations at the cervical region with micro-computed tomography (micro-CT). Two groups of restorations were compared: 1) those that had been exposed to radiotherapy before restoration was performed using a universal adhesive in etch-and-rinse and self-etch modes; and 2) those that had previously been restored using a universal adhesive in etch-and-rinse and self-etch modes and had subsequently undergone radiotherapy.

Sixty intact human molars were randomly divided into groups according to irradiation status: no radiotherapy (control group); radiotherapy followed by restoration (radiotherapy-first group); and restoration followed by radiotherapy (restoration-first group). These three groups were then subdivided into two groups each on the basis of

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adhesive application type (etch-and-rinse and self-etch modes), for a total of six groups (n=10/group). Standardized Class II MOD cavities were prepared. A universal adhesive (Clearfil Universal Bond Quick, Kuraray, Okayama, Japan) was applied. The teeth were restored with resin composite (Estelite Posterior Quick, Tokuyama, Tokyo, Japan). The radiotherapy protocol was conducted with 60 gray (Gy) at 2 Gy/day, five days a week for six weeks. Adhesive defects were analyzed in distal and mesial views and evaluated with micro-CT (SkyScan 1174v2, Kontich, Antwerp, Belgium) on the basis of the volume of black spaces between the cavity walls and the restorative materials (mm^3). The data were analyzed using the Kruskal-Wallis, Mann Whitney U and Wilcoxon tests ($p<0.05$).

The radiotherapy protocol did not affect the marginal adaptation of the universal adhesive at the cervical regions. Regarding the application modes, for the radiotherapy-first group, the self-etch mode caused significantly higher adhesive defects than the etch-and-rinse mode at the dentin margin. For the no-radiotherapy group, the adhesive defects at the dentin margin were significantly higher than at the enamel margin with the application of the etch-and-rinse mode.

INTRODUCTION

Head and neck cancer (HNC) represents 4% of cancer incidence worldwide and causes 360,000 deaths annually.[1] Malignancies in the head and neck region comprise salivary gland tumors, squamous cell carcinoma, thyroid cancer, and also hematological malignancies such as lymphoma or myeloma.[2] Radiotherapy is a mandatory component of modern cancer therapy, in combination with chemotherapy and surgical management. This treatment includes irradiation of the tumor mass with ionizing radiation. Modern radiation therapy approaches aim to preserve neighboring vital tissue function while giving the tumor a tumoricidal dose. The majority of radiation-induced biological damage originates from the reaction of the target tissue with free radicals, including hydroxyl radicals (OH) and hydrated electrons generated by the action of radiation on water. This irradiation mechanism supports the consensus of dental literature that radiotherapy of the head and neck region affects the dental tissues.[3]

Previous studies have indicated that alterations in the nature of enamel, dentin, and the dentino–enamel junction are mostly dose and mineral/organic content dependent; high doses of radiotherapy can jeopardize the stability of these structures.[4,5] The adverse effects of radiotherapy comprise the lack of the enamel prism, obliterated dentinal tubules, collagen fiber degeneration, gap formation at the enamel-dentin junction and decrease in microhardness.[6] In addition, random changes to the aromatic and aliphatic bonds of the organic matrix have been detected in irradiated composite resins.[7]

From a mechanical perspective, the aforementioned changes in dental structures have directed the attention of researchers to the potential adhesion impairment effects of irradiation. The studies have mostly concentrated on micro/macro bond strength tests with different surface conditioning protocols.[8,9,10] However, the conclusions have been contradictory, and no consensus has been reached about guidelines for the restoration of irradiated teeth with direct resin technology. The controversies about bond strength values have mostly been based on the adhesive systems used.[8,10,11,12]

The latest generation of adhesives are referred to as "universal adhesives" and have been extensively implemented due to their versatility.[13] Universal adhesives offer advantages to clinicians because of their user-friendly, simplified application protocols and multi-mode applicability to various substrates with etch-and-rinse and self-etch modes.[14] Dental literature about universal adhesive systems applied to irradiated tooth structures is scarce[8,9] and limited to bond strength testing and the examination of fracture patterns.

The cavity adaptation of a resin composite restoration predominantly determines the overall quality and longevity of the restoration, which is affected by several factors, such as substrate type (for example irradiated, eroded, or affected dental substrates), polymerization shrinkage, the type of adhesive system, and the skill of the operator. These factors impact adhesion, and microgaps may occur at the resin-dental substrate interface. Bacterial leakage and secondary caries formation basically originate at the cervical margins of Class II restorations.[15] Today, modern technologies are used to analyze marginal adaptation without destroying the samples. These include optical coherence tomography and micro-computed tomography.[16,17]

There are limited data in the literature about the marginal adaptation of universal adhesive systems at irradiated enamel and dentin substrates. Therefore, the aims of this laboratory study were to use micro-CT to evaluate the marginal adaptation of Class II MOD restorations at the cervical regions located in enamel and root dentin: 1) that have undergone radiotherapy; and 2) that have already been restored using a universal

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adhesive in etch-and-rinse and self-etch modes and have subsequently undergone radiotherapy.

The research study's null hypothesis was as follows: Irradiation would not affect the marginal adaptation of Class II MOD restorations made using a universal adhesive applied in self-etch and etch-and-rinse modes at the cervical regions located in enamel and root dentin.

METHODS AND MATERIALS

The local ethics committee approved this laboratory study (Process no. 11/265).

Sample Size Calculation

The sample size was determined on the basis of the estimated effect size between groups, in accordance with the literature.[18] In the present study, 10 samples were required for each group to obtain a medium effect size (d=0.50), using 95% power and a 5% type 1 error rate.

Sample Preparation and Restorative Procedures

A total of 60 intact human molars, free of caries, were obtained, cleaned, and stored in saline solution until testing. Figure 1 provides a schematic illustration of the experimental protocol. The restorative materials, lot numbers and composition used in this study are summarized in Table 1.

The teeth were randomly divided into three main groups by one author (DB) according to exposure to and timing of irradiation (n=20), and each main group was divided into two groups according to the adhesive application type (n=10).

Standardized Class II mesio-occluso-distal (MOD) cavities (2.5 mm occlusal depth, 4 mm width, 4 mm depth at mesial box and distal box, depth 1 mm beyond the cemento-enamel junction) were prepared in each tooth with a coarse diamond fissure bur (FC Diamond, G&Z Instrumente, Lustenau, Austria). In the mesial proximal box, 4-mm depth preparations were performed in all teeth to achieve a cervical margin on the enamel surface, while in the distal proximal box, cemento-enamel junctions were visually determined and preparations performed 1 mm beyond them to obtain a cementum margin.[19] A digital caliper was used to validate the dimensions of the cavity preparation. The floor of the mesial and distal boxes was controlled for presence of enamel and cementum with a stereomicroscope (SMZ 1000, Nikon, Japan), respectively.

Group 1) Control (no-radiotherapy) group with etch-and-rinse mode—This group did not receive radiotherapy. Standardized Class II MOD cavities were prepared.

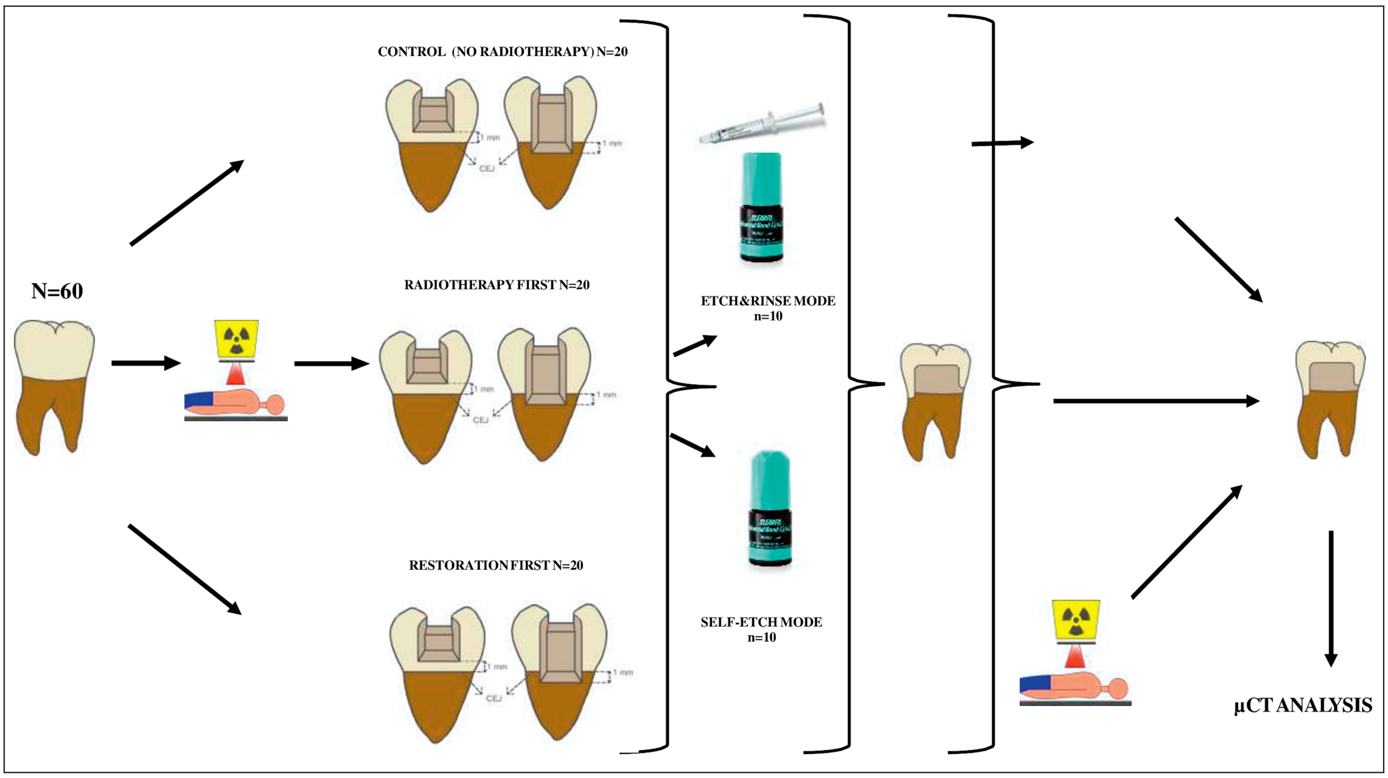

Figure 1. *A schematic illustration of the experimental protocol.*

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Table 1: *The Brand Names, Lot Numbers and Composition of Restorative Materials Used in this Study*

Brand Names	Lot Number	Composition
Scotchbond Universal Etchant 3M Oral Care (St Paul, MN, USA)	6870788	32 wt% phosphoric acid, 60% water, 5% synthetic amorphous silica
Clearfil Universal Bond Quick (Kuraray, Okayama, Japan)	000036	10-MDP, Bis-GMA, HEMA, hydrophilic amide monomers, Colloidal silica, Silane coupling agent, Sodium fluoride, Camphorquinone, Ethanol, Water (pH=2.3)
Estelite Posterior Quick (A2 Shade) (Tokuyama Dental Corp, Tokyo, Japan)	W143	Organic Matrix Composition: Bis-GMA, TEGDMA, Bis-MPEPP, Radical-Amplified Photopolymerization initiator technology (RAP) Inorganic Filler Particulate: (83% wt, 70% vol) Silica-zirconia filler: 0.1-10 μm (2 μm)

Abbreviations: 10-MDP, 10-methacryloyloxydecyl dihydrogen phosphate; BIS-GMA, bisphenol A glycidyl methacrylate; HEMA, 2-hydroxyethyl methacrylate; TEGDMA, triethylene glycol dimethacrylate; Bis-MPEPP, bis-methacryloxyethoxy phenyl propane; mm, micrometer; wt%, weight percentage; vol%, volume percentage.

The enamel and dentin surfaces were etched with 37% phosphoric acid (Scotchbond Universal Etchant, 3M Oral Care, Monrovia, CA, USA) for 15 seconds, rinsed with water for 5 seconds, and blot-dried with a cotton pellet. Clearfil Universal Bond Quick (Kuraray) was applied with a rubbing motion with a microbrush for 20 seconds, air-dried until the bond did not move, and light-cured for 10 seconds (irradiance of 1000 mW/cm^2) with a light-emitting diode (LED) light-curing unit (Valo, Ultradent, South Jordan, UT, USA). The light intensity was checked with a radiometer (Demetron LED Radiometer, Kerr Corp, Orange, CA, USA). A metal auto matrix (SuperMat assorted kit, Kerr) was placed around the tooth. The resin composites were applied in 2-mm increments. For each increment, the resin composites were light-cured for 10 seconds. After removal of the auto matrix, the composite resin was light-cured again from the distal and mesial surfaces for 10 seconds on each side.

Group 2) Control (no-radiotherapy) group with self-etch mode—This group did not receive radiotherapy. Standardized Class II MOD cavities were prepared. Clearfil Universal Bond Quick was applied without acid etching. The rest of the restoration procedures were applied as described for the etch-and-rinse group.

Group 3) Radiotherapy-first group with etch-and-rinse mode—The samples first received radiotherapy in accordance with the experimental protocol for six weeks. After radiotherapy, standardized Class II MOD cavities were prepared. The adhesive system with etch-and-rinse application and restorative procedures was applied as described above.

Group 4) Radiotherapy-first group with self-etch mode—The samples first received radiotherapy in accordance with the experimental protocol for six weeks. After radiotherapy, standardized Class II MOD cavities were prepared. The adhesive system with self-etch application protocol and restorative procedures was applied.

Group 5) Restoration-first group with etch-and-rinse mode—Standardized Class II MOD cavities were prepared. The adhesive system with etch-and-rinse application protocol and restorative procedures was applied as mentioned before. Then the samples received radiotherapy in accordance with the experimental protocol for six weeks.

Group 6) Restoration-first group with self-etch mode—Standardized Class II MOD cavities were prepared. The adhesive system with self-etch application and restorative procedures was applied as mentioned before. Then the samples received radiotherapy in accordance with the experimental protocol for six weeks.

All restorations were finished and polished with an extra-fine diamond bur (FC Diamond, G&Z) and a one-step polisher (Opti1step Polisher, Kerr) according to the manufacturer's instructions. The samples were kept in distilled water at 37°C until analysis. All cavity preparations and restorative procedures were performed by a single operator who was blinded to the presence of irradiation (BO).

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Radiotherapy Protocol

Irradiation of the teeth was performed at the radiotherapy center of the oncology clinic. Prior to the irradiation, the output dose of the device and deep-dose tables were used. Manual planning was performed to mimic the clinical scenario of an adult patient with HNC. During the planning process, the analytical anisotropic algorithm dose calculation was employed to provide the same radiation dose to the samples. The roots of the teeth were embedded in modeling wax contained in a plastic box. The wax surface was set at a distance of 2 mm from the cemento-enamel junction and the teeth positioned 0.5 cm apart from each other to prevent scattering and to allow for direct irradiation. Then the box was filled with distilled water in order to imitate the oral cavity.[5]

A Cobalt60 CisBio International CIRUS model teletherapy device (312TBq, Healvita GmBH, Vienna, Austria) was used. Collimators made of tungsten, steel, and natural uranium mixtures allowed the rays to fall on the treatment surface more evenly and form a homogeneous dose. The distance of the material surface from the source was detected as 80 cm, and the surface area to be irradiated was 12 x 12 cm^2. The irradiation dose rate was determined as 29.83 centigray (cGy)/min, the irradiation room temperature was 24°C, the pressure (P) was 1019 hectopascals (hPa), and the humidity was kept at 60%. Fixed irradiation was performed with a 98% deep dose. Teeth were kept 2 cm deep from the surface and 1.25 mega electron-volt (MeV) gamma rays were applied to the samples. The radiotherapy protocol was performed as 30 fractions daily, 2 Gy per fraction, five days a week for six weeks, and the total given dose was calculated as 60 Gy.[20] A dosimeter was used to control the quality of irradiation. An experienced physician performed the whole radiotherapy protocol (AHE).

Micro-CT Analysis

The analysis of marginal adaptation was done using a micro-CT device (SkyScan 1174v2, Bruker). The samples were fixed in the scanning chamber and scanned at 24.21 μm pixel size and 512 x 652 resolution for an exposure time of 2500 milliseconds. The micro-focus X-ray source was set at 50-kVp (peak kilovoltage) accelerating voltage, 800 μA (microampere) beam current and 40 W power, using a 0.25 mm Al filter. Each sample was scanned over 360 degrees with a rotation step of 0.90 degrees and with an approximately average scanning time of 40 minutes. For each sample, 400 raw data points were recorded in tagged image file format (TIFF) and reconstructed with NRecon (Ver. 1.6.10.2, Micro Photonics Inc, Allentown, PA) software; approximately 339 transverse tomographic sections were obtained in bitmap file format (BMP).

Image analyses of adhesive defects, based on the volume of black spaces, were carried out with three-dimensional analysis from CTAn software (CT-Analyser software, Version 1.16.4.1; SkyScan), and were used to create quantitative parameters and visual models and enabled densitometric and morphometric measurements. Black spaces were detected from the volumes of interest (VOI), which were created from all two-dimensional images in the region of interest (ROI) (Figure 2). A threshold value was determined in the histogram to differentiate the voxels of the sample to be examined and the voxels of the surrounding air. The threshold value was detected on the histogram where the black voxel is denoted with 0 and represents the minimum intensity, and the white voxel is denoted with 255 and indicates the maximum intensity. The volumetric rates were calculated separately with the determined ROIs and threshold value data. The data of the samples were transferred to CTVol (Ver. 2.3.2.0, SkyScan) software and three-dimensional modeling images of the samples were obtained (Figure 3). The images were recorded from the buccal to the lingual surfaces and from the outer surface to the axial wall for each proximal area per sample. In the mesial and distal views, the adhesive defects were quantified through analysis between the cavity walls, and the restorative materials were determined in mm^3.

Statistical Analysis

Statistical analysis was conducted using SPSS 22.0 for Windows (SPSS Inc., Chicago, IL, USA). The Shapiro-Wilk test was first used to indicate the normality of variables, and the data were then analyzed using the Levene test for homogeneity of variances. The data were analyzed with nonparametric tests since they did not satisfy parametric test assumptions. The Kruskal–Wallis test was performed to compare between-group differences according to the radiotherapy protocol. The Mann–Whitney-U test was used to compare between-group differences according to the application type. The Wilcoxon test was used to compare within-group differences according to the tooth substrate. Statistical significance was considered at a confidence level of 0.05 for all analyses.

RESULTS

The mean adhesive defects with standard deviations and median values (mm^3) obtained with micro-CT for all tested groups are presented in Table 2. When comparing the radiotherapy protocols, there were no significant differences in marginal adaptation

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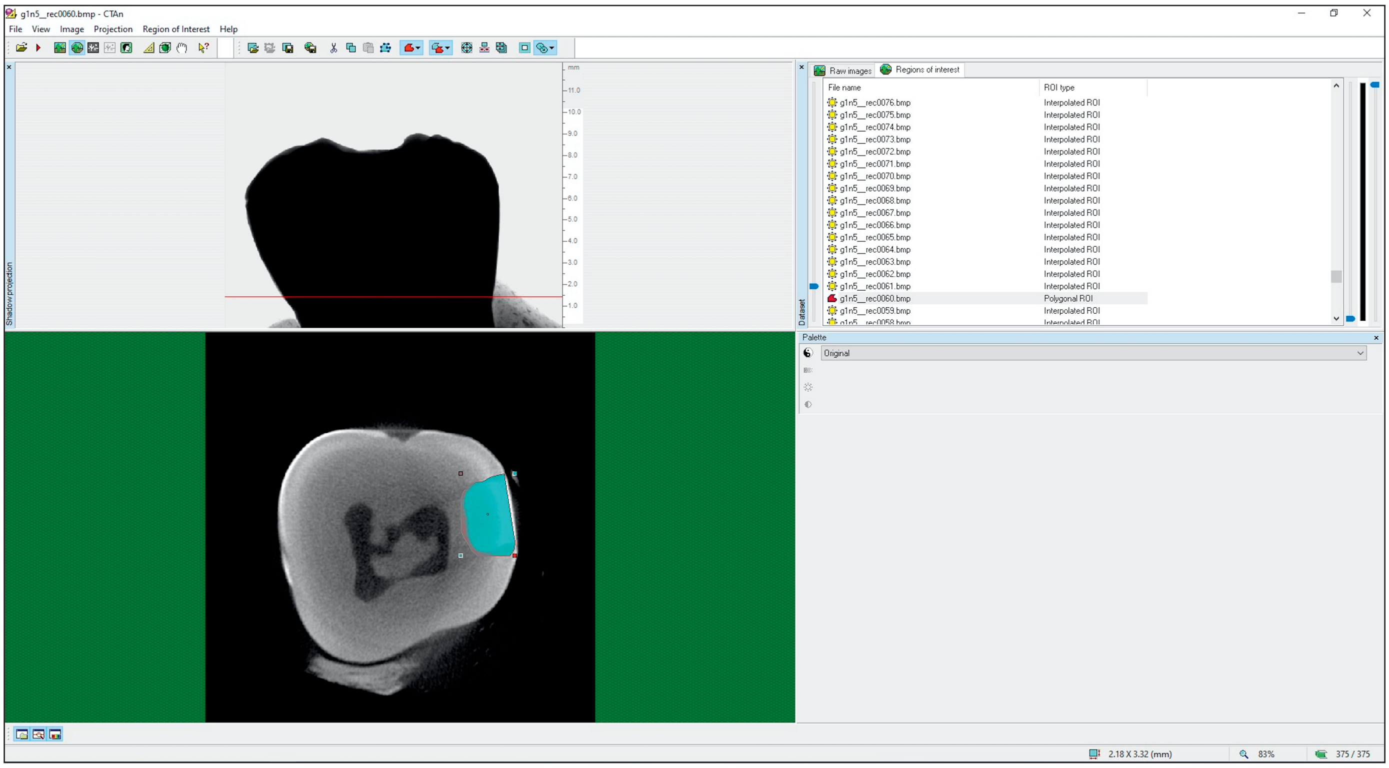

Figure 2. *Representative images of the sample analysis using micro-CT. A software version 1.16.4.1, of the volume of black spaces (adhesive defects). Two-dimensional (2D) axial sections of the restoration, showing the region of interest (ROI; blue square).*

with either the etch-and-rinse or self-etch mode applications for enamel and dentin margins (p>0.05). Regarding the application modes, the self-etch mode caused significantly higher adhesive defects than the etch-and-rinse mode for dentin for the radiotherapy-first group (p<0.05). No significant differences in marginal adaptation were detected among application modes on enamel for all tested groups with respect to the radiotherapy application types (p>0.05). When comparing the enamel and dentin substrates, adhesive defects for dentin were significantly higher than for enamel with the application of the etch-and-rinse mode for the no-radiotherapy group (p<0.05). No significant differences in marginal adaptation were observed between enamel and dentin, irrespective of the adhesive application mode and irradiation type, for the other tested groups (p>0.05) (Figure 4).

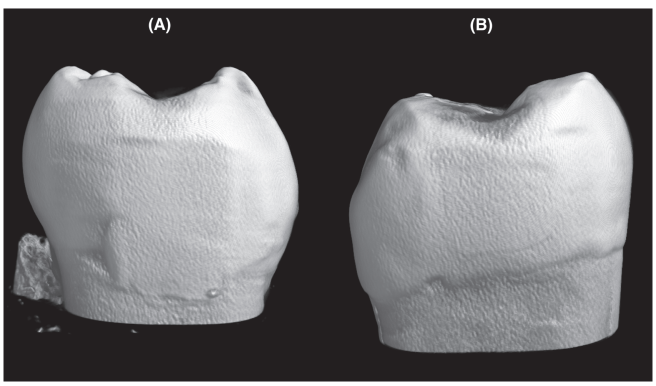

Figure 3. *Representative three-dimensional volume modeling images of the samples: distal (A) and mesial (B) views.*

DISCUSSION

In this study, the marginal adaptation of Class II MOD restorations at the cervical regions located in enamel and root dentin: 1) that had undergone radiotherapy; and 2) that were already restored using a universal adhesive in etch-and-rinse and self-etch modes and had subsequently undergone radiotherapy, were evaluated with micro-CT. Based on the results, the null hypothesis, that irradiation would not affect the marginal adaptation of Class II MOD restorations at the cervical regions located in enamel and root dentin using a universal adhesive applied with self-etch and etch-and-rinse modes, was partially rejected.

In the context of increasing dental awareness and an aging population, more dental patients are diagnosed with head and neck cancer that requires radiotherapy. Thus, clinicians should be aware of the effects of radiotherapy on dental tissues.[21] Reduced microhardness and lower stability of the dentinoenamel junction in dental hard

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Table 2: *Mean Adhesive Defects with Standard Deviations (SD) and Median Values (mm³) Obtained with Micro-CT for all Tested Groups* (p=0.05)

		Below the Cemento-Enamel Junction (Dentin)			Above the Cemento-Enamel Junction (Enamel)			*p*-values Between Enamel and Dentin	
		Etch&rinse (ER)	Self-etch (SE)	*p*	Etch&rinse (ER)	Self-etch (SE)	*p*	ER	SE
No radiotherapy	Mean values ± SD	0.254 ± 0.242	0.172 ± 0.100	0.481	0.095 ± 0.053	0.087 ± 0,053	0.481	0.017	0.074
	Median values	0.175 [0.107-0.310]	0.167 [0.070-0.279]		0.084 [0.062-0.121]	0.064 [0.049-0.130]			
Radiotherapy first	Mean values ± SD	0.106 ± 0.092	0.259 ± 0.159	0.023	0.080 ± 0.055	0164 ± 0.146	0.123	0.646	0.074
	Median values	0 101 [0.015-0.186]	0.193 [0.122-0.425]		0.060 [0.042-0.110]	0.100 [0.055-0.243]			
Restoration first	Mean values ± SD	0.122 ± 0.068	0.138 ± 0.135	0.853	0.090 ± 0.071	0.131 ± 0.150	0.739	0.333	0.959
	Median values	0.131 [0.049-0.177]	0.070 [0.052-0.238]		0.072 [0.031-0.142]	0.096 [0.031-0.149]			
p		0.123	0.078		0.802	0.598			

tissues after irradiation have been reported as adverse results of radiotherapy.[22,23] It is noted that the properties of restorative materials, such as surface roughness, flexural strength, and water sorption, could be affected by radiotherapy.[24] In addition, it has been indicated that the tooth-restoration interface could be negatively influenced by degenerated collagen network, obliterated dentin tubules, and loss of enamel prism in the hybrid layer.[25] The disarrangement of the crystalline portion of the enamel and a denaturation of the organic matrix, which induces changes in the crystalline organization and protein interprismatic links, have been observed.[26] Furthermore, Cheung and others[27] have reported that irradiation might destroy the chemical bonds of restorative materials and consequently weaken their adhesion at the tooth-restoration interface. Therefore, adhesive systems have to be selected according to the substrate, and the selection of the most appropriate restorative material may be important in cases in which irradiation is involved.

The radiotherapy protocol used in this study was based on a previous study and actual clinical scenarios

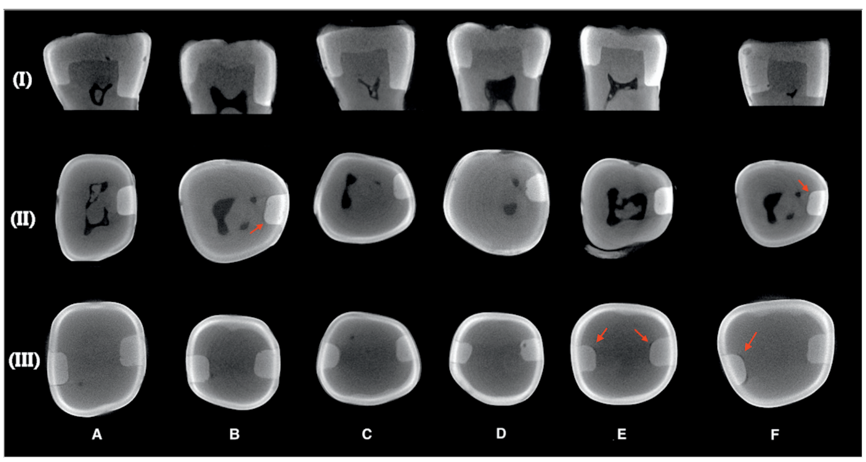

Figure 4. *Representative two-dimensional (2D) micro-CT images of all tested groups. The adhesive defects are detected between teeth and restorations (red arrows). Illustrative 2D images of the specimens are visualized: sagittal section (I), axial section for cementum margin (II) and axial section for enamel margin (III). (A): control (no-radiotherapy) group with etch-and-rinse mode. (B): control (no-radiotherapy) group with self-etch mode. (C): radiotherapy-first with etch-and-rinse mode. (D): radiotherapy-first with self-etch mode. (E): restoration-first group with etch-and-rinse mode. (F): restoration-first group with self-etch mode. Red arrows: adhesive defects.*

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which contained cumulative fractioned doses of 2 Gy daily on weekdays, up to the final dose of 60 Gy.[28] Doses are generally fractioned between radiation sessions to allow time for the tumor cells to be oxygenated, making them more sensitive to irradiation; this also considers the difference in sub-lethal repair responses between tumor tissue and normal tissue.[29] The study design used molar teeth, since molar teeth have been found to receive the highest dose of irradiation during radiotherapy.[20] During radiotherapy the samples were kept in distilled water, since submersion in artificial saliva could hinder proper delivery of the irradiation because of its viscosity and high concentration of ions.[30]

Micro-CT is an imaging tool which acquires images of the three-dimensional structures of small objects with a high level of spatial resolution. Due to the penetrating capacity of X-rays, this method has been widely used to analyze the cavity adaptation of restorations without sectioning the samples and ensure the acquisition of precise information.[18,31,32] Thus, in this study, micro-CT was used to quantify the adhesive defects between the cavity walls and the restorative materials as the volume in mm^3.

Effective adhesion between the cavity walls and the restorative materials is one of the main goals in operative dentistry.[33] Previous studies have indicated that adhesive defects were mostly detected in the marginal walls and internal areas, especially on the mesiodistal and buccolingual walls of restorations.[34,35] Adhesive defects can originate from insufficient bonding at the tooth-restoration interface as a result of these factors: degradation of the adhesive layer, polymerization shrinkage, different thermal expansion coefficients between the dental substrates and the resin composite, poor application technique, and poor finishing and polishing procedures.[36] Thus, the evaluation of both internal and marginal adhesive defects was needed to evaluate in detail the properties of the restorative materials.[37]

The polymerization of composite resins creates stresses because of their contraction. These stresses could be carried to the restoration margins, possibly influencing the marginal quality.[38] When the marginal quality is inadequate, it can lead to plaque accumulation, discoloration, hypersensitivity, gap formation, bacterial leakage, recurrent caries, pulpal irritation, and consequent loss of restoration.[37,39] Thus, marginal adaptation is considered a main factor affecting the longevity of composite resin restorations.[40]

Recurrent caries is a multifactorial disease, involving marginal sealing and the characteristics of the material, the type of dental substrate on which the composite will be placed and bonded, the cavity size, the position of the tooth in the mouth, and the caries risk of the patient.[41,42] The gingival margin of Class II restorations is the most susceptible configuration for recurrent caries and also the place where maladjustments, misfits, and gaps occur, usually located gingivally (at cervical margins).[40,42] Moreover, when restorations are placed below the cemento-enamel junction, the quality of marginal integrity is doubtful.[17] In this study, cervical margins in mesial and distal views of Class II restorations were evaluated because they are the type of restorations with the highest incidence of recurrent caries formation.

It is well known that the cavity configuration (C-factor), the ratio between bonded and unbonded surfaces of the composite restoration, plays an important role in polymerization shrinkage.[36] Cavities with a high C-factor and those with large dimensions exhibit increased polymerization shrinkage and decreased bond strength. In particular, though manifesting a lower C-factor compared to Class I cavities, large Class II cavities with dentin and cementum margins[43] are susceptible to damage to marginal integrity due to polymerization shrinkage. This shrinkage stress is still a relevant trigger for the failure of restorations because of the impairment of the adhesion,[44] in particular, as the pulpal floor interface seems to be a weak spot for the effects of shrinkage stress on the adhesion of the tooth-restoration interface.[43]

A new universal adhesive system, Clearfil Universal Quick (Kuraray Noritake Co., Tokyo, Japan), containing 10-methacryloyloxydecyl dihydrogen phosphate (10-MDP) and a multifunctional hydrophilic amide monomer, has been introduced.[45] This adhesive system is used after a short time, following a "no-wait" concept: it is light-cured without waiting and features a mildly acidic pH.[46] Previous studies have reported that this monomer exhibits resistance to hydrolysis and a high bond strength.[45,47] In addition, it has good wettability to dental substrates because of the fact that amide monomer is more hydrophilic than 2-hydroxyethyl methacrylate (HEMA).[47] In particular, it can provide good adhesion in the cervical region because, due to a shorter manipulation time, the bonding procedure is not exposed to adhesion-impairing factors such as moisture in the oral cavity, gingival crevicular fluids, or bleeding from the gingiva.[48]

Ionizing radiation induces the action of reactive oxygen species (ROS) such as hydroxyl radicals, superoxide anion, and hydrogen peroxide.[30] Reactive oxygen species can be generated in dental tissues with higher water content levels, such as dentin, but also in the storage media of teeth subjected to *in vitro* radiotherapy. In addition, although water constitutes

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a very small portion of enamel, its presence affects the mechanical properties of the enamel structure when it is dehydrated.[49] Irradiation significantly decreases the intrinsic resistance of enamel and dentin, with a deleterious effect on their proteic components, decreasing the stability of dentinal tissues.[50] In addition, ROS can act as a polymerization inhibitor of the adhesive system, affecting its immediate bond strength to enamel or dentin.

To the authors' knowledge, this is the first laboratory micro-CT analysis examining the quality of the marginal adaptation of direct resin restorations of irradiated teeth. Most of the literature on this issue consists of bond strength evaluations or the analysis of microleakage with visual imaging by SEM. In this study focusing on the radiotherapy protocol, no significant differences in marginal adaptations were observed with either the etch-and-rinse or the self-etch mode applications for enamel and dentin margins. Bulucu and others[12] have evaluated the effect of radiotherapy on the microleakage of enamel and dentin margins with Class V restorations using the self-etch and etch-and-rinse adhesive systems and have reported no statistically significant differences between the restoration-first and the no-radiotherapy groups, for both enamel and dentin substrates, in terms of microleakage. However, chemical alterations of dental microstructures were highlighted and the effect of the composition of the adhesive system on the achievement of successful adhesion was emphasized.[12] By comparison, Jornet and others,[26] evaluating the effect of daily applications of artificial saliva, fluoride mouth rinses, and chlorhexidine on microleakage in Class V irradiated bovine teeth, reported that a significant increase in microleakage was detected for composite resin restorations after radiotherapy. Furthermore, in the present study, the self-etch application mode caused significantly higher adhesive defects than the etch-and-rinse mode on dentin for the radiotherapy-first group. However, the application modes did not significantly affect the marginal adaptation for other tested groups. This finding could be explained by the fact that the shorter application time of this adhesive system in the self-etch mode might have resulted in insufficient removal of the smear layer and infiltration of the resin monomers to obliterated dentinal tubules. Bulucu and others[12] have indicated that etch-and-rinse adhesive systems caused significantly higher microleakage than self-etch adhesive systems on dentin for the restoration-first and no-radiotherapy groups.

Enamel contains organic components and some water, although significantly less than dentin. Therefore, it is not exclusively an inorganic tissue.[12] It has been reported that adhesion to enamel resulted in less adhesive defects and greater stability than bonding to dentin due to dentin's tubular structure and intrinsic wetness.[51] Thus, effective and durable adhesive systems are needed to obtain better cavity adaptation. In particular, the absence of enamel at the cervical margin could lead to weak adhesion of restorations. Cheung and others[27] have indicated that irradiation damage of collagen fibers could lead to decreased bond strength between dentin and composites. In this study, adhesive defects with dentin were significantly higher than with enamel with the application of the etch-and-rinse mode for the no-radiotherapy group. Previous studies[14,52] have reported that bond strength to dentin decreased with the phosphoric acid etching of dentin before the application of the adhesive system. The main reason for this decrease in bond strength has been reported to be the incomplete resin monomer infiltration of the deeply demineralized collagen network because phosphoric acid can decalcify dentin more deeply than an adhesive is designed to infiltrate.[51] In addition, in this study, no significant differences in marginal adaptation were detected between enamel and dentin for the restoration-first and the radiotherapy-first groups. This finding is in contrast with Bulucu and others,[12] who indicated that dentin had higher microleakage than enamel for the restoration-first groups. The divergence in outcomes could be attributed to the differences in adhesive systems used (etch-and-rinse and self-etch adhesives) or the aging procedure.

Regarding the limitations of the current study, the paper evaluated only the short-term effects of radiotherapy on the marginal adaptation of universal adhesive systems at cervical regions with etch-and-rinse and self-etch modes. The aging procedures of resin composite restorations are known to negatively influence cavity adaptation.[53] Furthermore, it is well known that residual reactive oxygen radicals can be responsible for unfavorable effects on the dental substrates, even when irradiation has been completed. Therefore, further studies should focus on the effect of high doses of radiotherapy on the long-term structural changes of restorations with selective etch, self-etch, and etch-and-rinse application modes.

CONCLUSIONS

The results of this study suggest that the etch-and-rinse mode of application might be preferred when the universal adhesive system is used for restorations placed below the cemento-enamel junction after radiotherapy. Within the limitations of this study, it can be concluded that:

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1. The radiotherapy protocol did not affect the marginal adaptation of the universal adhesive at the cervical regions.
2. When comparing the application modes, for the radiotherapy-first group, the self-etch mode caused significantly higher adhesive defects than the etch-and-rinse mode at the dentin margin.
3. When comparing the dental substrates, for the no-radiotherapy group, adhesive defects at the dentin margin were significantly higher than at the enamel margin with the etch-and-rinse application mode.

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Regulatory Statement

The local ethics committee approved this laboratory study (Process no. 11/265).

Conflict of Interest

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

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