Original Article
http://dx.doi.org/10.1590/1678-7757-2023-0118

JOURNAL OF APPLIED ORAL SCIENCE

Does radiation therapy affect adhesion of tricalcium silicate cements to root dentin?

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Abstract

Objective: This study aimed to analyze the effect of irradiation on the push-out bond strength of mineral trioxide aggregate (MTA) and Biodentine to radicular dentin. Methodology: A total of 60 extracted mature human teeth with single root canals were categorized into two groups (irradiated and non-irradiated) (n=30). Each group was further divided into two sub-groups based on cements used (Biodentine and MTA). Then, a cumulative radiation dose of 60 Gy was divided into 30 fractions (two Gy for every fraction) and administered for five successive days per week over six weeks. Obturation was then performed using MTA and Biodentine. Afterwards, 1.5 mm thick horizontal sections were procured from the middle one-third of all the specimens and then subjected to push-out bond test. Results were analyzed using one-way analysis of variance with post-hoc Tukey's test. Results: The bond strength of Biodentine and MTA to irradiated teeth was lower than non-irradiated teeth. Highest push-out bond strength was observed in non-irradiated specimens filled with Biodentine (p=0), followed by irradiated specimens filled with Biodentine (p=0); non-irradiated specimens filled with MTA (p=0); and irradiated specimens filled with MTA (p=0.9). Conclusion: The push-out bond strength of Biodentine and MTA to root canal dentin decreased significantly post irradiation.

Keywords: Adhesion. Biodentine. Bonding. Dental materials. Mineral trioxide aggregate. Root canal. Irradiation.

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Received: March 29, 2023
Revised: July 05, 2023
Accepted: August 03, 2023

Editor: Linda Wang

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Introduction

Tumors of the head and neck consists of a variety that affect the oral cavity and other surrounding structures, making them the seventh highest prevalent neoplasm worldwide with an incidence of about 640,000 cases annually.[1] From these, ninety percent of cases comprise of squamous cell carcinoma, the predominant histological type.[2] Nonetheless, such carcinomas are recognized at a later stage, and the survival rate was reported to be 57% in the first five years of diagnosis.[3] Treatment procedure consists of surgical, radio, and chemotherapy or an amalgamation of options.[4] Radiation therapy can be employed as prime modality, along with others.[5] Radiation fractionation is the conventionally used radiation therapy regimen since the exposure to normal tissues is restricted to a certain dose of radiation, reducing the adverse effects.[6] However, the surrounding non-carcinomic tissues are rarely preserved at the time of head and neck radiotherapy.[7] In three months post-radiation therapy of head and neck, the initial signs of damage to the teeth are evident.[8,9] Damage to teeth have been observed to significantly rise with irradiation dosage.[10] Changes in the inter, peri, and intratubular dentin are seen as the radiation doses are escalated. At 30 Gy, dentinal cracks become evident, and at the cumulative radiation dose of 60 Gy, the dentinal tubules become obliterated since fibers of collagen eventually fragment with the acceleration in radiation doses. Dentinal tubule obliteration happens due to the odontoblastic process degeneration,[11] chemical composition changes,[12,13] and decrease of dentin microhardness.[11,13] When the dental hard tissues are irradiated at 70 Gy, a significant disorganization of hydroxy apatite crystals can be observed.[13]

Previously, grossly decayed teeth were commonly considered for extraction pre-radiation therapy. However, nowadays, teeth undergo root canal treatment before radiation to avoid tooth removal[14] and enhance the 3-dimensional seal of the radicular filling material. Thus, it is essential to analyze various materials for the endodontic procedures of teeth post-radiation therapy.[15] A spectrum of dental products are evaluated in endodontics to test their capability to produce a seal (coronal or apical).

Being bioactive, tricalcium silicate cements (TSCs) form calcium phosphate and precipitate appetite on the interface of cement and dentin. Moreover, in dentin tubules, the TSCs form tags, as well as an interfacial hybrid layer, ultimately resulting in chemical and mechanical bonding.[16] Mineral trioxide aggregate (MTA) is a popular TSC due to its potential to withstand microleakage and excellent marginal adaptation to dentin.[17] It consists of tricalcium silicate, dicalcium silicate, bismuth oxide, tricalcium aluminate, and gypsum.[18] MTA is used in various clinical situations like direct pulp capping, perforation repairs, apexogenesis or apexification, retro-filling,[19] and as a coronal barrier after regenerative endodontic procedure.[20] Nevertheless, MTA presents cons, such as longer setting time, inferior handling properties, and teeth discoloration.[21]

Biodentine, which is also a TSC, is produced by Septodont (Saint Maur des Fosses, France), being a novel filling material with excellent mechanical properties. Furthermore, biodentine is also biocompatible and bioactive, and can be used as a substitute for dentin. It shows shorter time of setting (12 minutes) compared to MTA, which requires 3 to 4 hours.[22] Biodentine powder includes tricalcium silicate, calcium carbonate, and zirconium oxide (radiopacifier) and the liquid comprises of calcium chloride and water-soluble polymer.[23] Furthermore, it exhibits good sealing ability due to the creation of mineral tags in dentinal tubules, as well as high resistance to microleakage, assisted by minimal shrinkage due to being free of resin formula.[24] The marginal adaptation and bond strength of tricalcium cement to radicular dentin plays an essential role for the clinical usage of these cements.[25]

Previous studies have reported that radiotherapy before endodontic procedure decreases the bond strength (BS) of the dental materials (MTA and epoxy- based sealers) to root dentin since it negatively affects the inorganic and organic components of dentin.[11,26,27] However, effect of radiotherapy on bonding of these cements to radicular dentin is still unknown. No studies have been found to compare the BS of MTA and Biodentine to root dentin post- irradiation. Therefore, this study aimed to analyze the effect of gamma radiation on the push-out BS of MTA & Biodentine to radicular dentin. The null hypothesis tested was that no significant difference would occur in the push-out BS of MTA and Biodentine to radicular dentin before and after radiation therapy.

Methodology

Sample size estimation

The sample size was based on the influence of therapeutic cancer radiation on the bond strength of an epoxy or MTA-based sealer to root dentin.[26] The sample size was calculated at a confidence interval of 95% and 90% power, leading to 15 samples in each group.[24]

Sample selection

Ethical clearance was obtained from Kasturba Medical College and Kasturba Hospital institutional ethics committee review board for the use of human extracted teeth (IEC 701/2020). In total, 60 mandibular first premolar teeth with one root and one canal were chosen. Tissue attachments and debris on the samples were eliminated with the use of ultrasonic scalers. The teeth were stored in 0.2% sodium azide solution at 4°C until use. Radiographic evaluation of teeth was performed from the labial and mesial directions for a single round straight non-calcified root canal with mature apices.[28] Then, samples were categorized as two groups (irradiated and non-irradiated) (n=30).

Experimental design

Irradiation protocol

For the irradiated group, a glass container with distilled water was used to place the teeth while fully covering them to maintain a humid environment, simulating the oral cavity. The glass container was placed on a carbon fiber table at equal distance from the center of the beam to achieve a homogenous rate of dosage and total dose delivery/fraction. Radiation was estimated by a computer-assisted linear accelerator (Elekta Versa HD) with the help of six MV X- rays with 200 kVp and 25 mA energy with a standard copper filter of 0.3mm. A cumulative radiation dose of 60 Gy was divided into 30 fractions (2 Gy per fraction), which were administered for five successive days/week, over six weeks.[26] Between the irradiation cycles, the teeth were stored in daily renewed artificial saliva (pH 7.0, 37°C).

Root canal preparation and filling

Teeth in both groups were decoronated using a diamond disc. The working length (WL) was measured with a 10-K file (Mani Inc., Tochigi Ken, Japan) until it became visible at the apex (using magnifying loupes), followed by subtraction of one mm from the recorded length.[28,29] Canal preparation was kept uniform to 1.3 mm using #1- #4 Peeso reamer (Mani).

Irrigation was done with 5 mL of 2.5% NaOCl / 9% Dual Rinse HEDP (Medcem GmbH, Weinfelden, Switzerland) for one minute for every change of instrument followed by 5 mL 2.5% NaOCl / 9% Dual Rinse HEDP as a final rinse for one minute. Then, 5 mL distilled water was used for one minute. The entire irrigation procedure was done using a 30-G side-vented needle (Vista Dental Products, Racine, WI, USA), kept 1 mm short of WL. Following the final irrigation protocol, canals were dried using paper points (Dentsply Sirona Endodontics, Ballaigues, Switzerland).

Specimens in irradiated group and non- irradiated group were randomly categorized into two sub-groups each (n=15), based on obturation material used; irradiated and non-irradiated ProRoot MTA (Dentstply Sirona) groups and irradiated and non-irradiated Biodentine (Septodont) groups (Figure 1). ProRoot MTA and Biodentine were mixed following manufacturers' instructions.[30] In brief, a single dose container (0.20 mL) of Biodentine liquid was poured into a capsule that contained the powder (700 mg), being mixed for thirty seconds at 4000-4200 RPM to form a Biodentine paste. For MTA, one pouch of ProRoot® MTA was dispensed on to a mixing pad, and ProRoot MTA liquid was squeezed from the ampule. Both powder and liquid were gradually mixed for about a minute to ensure all the powder particles were hydrated. Later, using an MTA carrier, both cements were placed in the canals

MATERIALS	CHEMICAL COMPOSITION
MTA	Powder: Tricalcium silicate, Dicalcium silicate, Tricalcium aluminate, Calcium sulphate, Tetracalciumaluminoferrite, Bismuth oxide, Calcium oxide, Silicon oxide, Aluminum oxide; Liquid: water
BIODENTINE	Powder: Tricalcium silicate, Dicalcium silicate, Calcium carbonate, Zirconium Oxide (ZrO_2), Iron oxide; Liquid: Calcium Chloride

Figure 1- Composition of Calcium silicate-based cements, MTA, and Biodentine

of their respective groups and condensed with hand pluggers. The samples were then radiographed in bucco-lingual and mesio-distal aspects to confirm that obturated canals were filled densely with no voids. Every sample was stored at 37ºC, 100% humidity for a week (in a humidifier) to let the cements set completely.

Push-out bond strength measurement

Every sample was submerged in cold cure acrylic and sectioned in a horizontal manner from the middle one third using a hard tissue microtome under water cooling (continuous) to obtain a disc 1.5±0.1 mm thick. One disc/tooth was obtained. Diameter of the canal and height of each disc were noted using a digital caliper. The adhesion surface area was calculated by the equation: Adhesion surface area (mm sq.) = $2 \times \pi \times r \times h$, where π equals to 3.14, r is radius of the canal preparation, and h is thickness of the root disc. Push- out testing was performed using an universal testing machine. The force was delivered in the apico-coronal direction at a crosshead speed of one mm per minute with the help of stainless-steel plungers of 0.6 mm. The placement ensured that only the filling cement made contact with it. The highest force (F) that was applied at the time of bond failure (Newtons) was noted. The pushout BS was measured in mega Pascals:

Pushout BS (MPa) = Force (N)/Adhesion surface area (mm sq.). Values of push-out BS regarding ProRoot MTA and Biodentine to radicular dentin were presented as mean ± standard deviation.[28]

Fractographic analysis

Every sample from all groups was analyzed under stereomicroscopic at 40× magnification to evaluate the bond failure. The types of bond failures were classified as:

1. Adhesive failure: At canal walls and ProRoot MTA or Biodentine interface.

2. Cohesive failure: Within ProRoot MTA or Biodentine.

3. Mixed failure: Combination of adhesive and cohesive failures.

Statistical analysis

SPSS Statistics Version 25.0 software program (IBM Corp, Armonk, NY) was used to statistically analyze the data. Normality was evaluated using Kolmogorov-Smirnov test. Push-out BS data were analyzed using one-way ANOVA with the post hoc Tukey honest significant difference test. chi-square test was performed to analyze bond failures. $P<0.05$ was considered to be significant (95% confidence).

Results

On group analysis, the BS of Biodentine and MTA of irradiated teeth was lower than non-irradiated teeth. Regarding intergroup comparison, non-irradiated Biodentine group presented the highest push-out BS (7.2±2.2 MPa), followed by irradiated Biodentine group [3.3±1.2 MPa] (p=0), non-irradiated MTA group [3.1±1.6 MPa] (p=0), and irradiated MTA group (0.74±0.48 MPa) (p=0), respectively. Significant differences were not noted between Irradiated Biodentine group and non-irradiated MTA group (p=0.9), whereas irradiated MTA group presented significantly lower bond strength value than non-irradiated MTA group (p=.001) and irradiated Biodentine group (p=0). (Table 1, Figure 2)

Failure type analysis

The chi-square test demonstrated no significant differences between groups regarding disposition of failure rates. In irradiated MTA group, the type of bond failure was 13.3% (2) mixed, 73.3% (11) cohesive, and 13.3% (2) adhesive type. In irradiated Biodentine group, 33.3% (5) was mixed, 60% (9) cohesive, and 6.7% (1) adhesive type. In non-irradiated MTA group, 6.7% (1) was mixed, 86.7%

Table 1- Push-out bond strength (Mean) of tricalcium silicate cements before and after irradiation. Different superscripts represent significant difference

Groups	Mean± SD
Biodentine non-irradiated	7,2±2,2[a]
MTA non-irradiated	3,1±1,6[b]
Biodentine irradiated	3,3±1,2[b]
MTA irradiated	0,7±0,5[c]

Different superscripts represent significant difference.

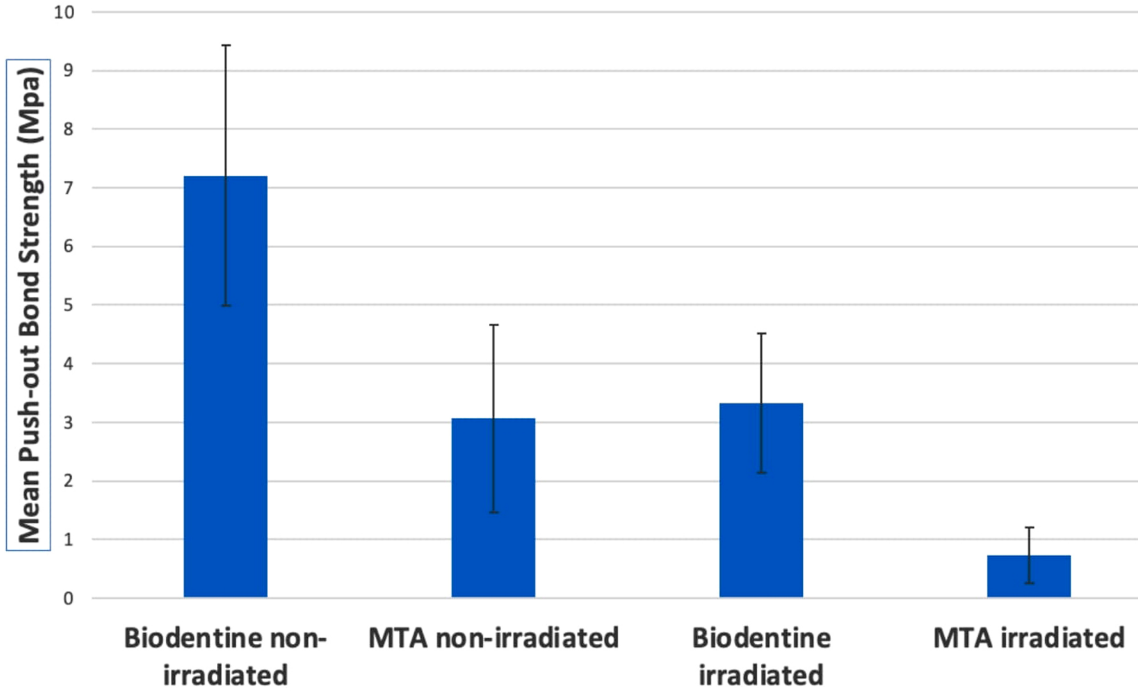

Figure 2- Push-out bond strength (Mean) of tricalcium silicate cements before and after irradiation

Table 2- Types of failures (Percentage) observed in different experimental groups

Groups Tested	Adhesive Failure	Cohesive Failure	Mixed Failure
Irradiated MTA (A1)	13.3%	73.3%	13.3%
Irradiated Biodentine (A2)	6.7%	60%	33.3%
Non- irradiated MTA (B1)	6.7%	86.7%	6.7%
Non- irradiated Biodentine (B2)	6.7%	53.3%	40%
Total Failures	8%	68%	23%

(13) cohesive, and 6.7% (1) adhesive type. In non-irradiated Biodentine group, 40% (6) was mixed, 53.3% (8) cohesive, and 6.7% (1) adhesive type. Overall, the experimental groups presented adhesive failure in 5 of 60 specimens (8%), mixed failure in 14 of 60 specimens (23%), and cohesive failure in 41 of 60 specimens (68%) (Table 2 and Figure 3).

Discussion

This *ex-vivo* study tested the push-out BS of tricalcium silicate cements to radicular dentin after irradiation protocol. The results suggest that irradiation significantly affects the push-out BS of tricalcium silicate cements tested in this study. Hence, the null hypothesis was rejected.

The highest push-out BS was observed for Biodentine in comparison to MTA in both irradiated and non-irradiated groups. This is in alignment with a previously conducted study, in which Biodentine demonstrated more BS in comparison to MTA when tested in non-irradiated teeth.[31] The push-out BS of MTA and Biodentine to root dentin was significantly higher in non-irradiated samples in comparison to irradiated samples. This can be due to the interplay of ionizing radiations with dentin causing excitement of the molecular particles, leading to a release of free radicals, such as oxygen (O^{-2}), hydroxyl (OH^-), and hydrogen (H^{+1}) ions, which get bound to other molecular entities and reorganize, leading to a variation in the ionic conformation of the chemical composition of dentin.[32] Previous studies using ATR-FTIR and Raman Spectroscopy have demonstrated that the rearrangement of dentin happens at the molecular level due to the energy released by ionization during radiation therapy,[13,33,34] which can, in turn, affect the bonding of tricalcium silicate cements with root dentin.

In this study, lower BS of the cements tested on irradiated samples could probably be related to deproteinization of collagen in root dentin and formation of fragments of the collagenous fiber

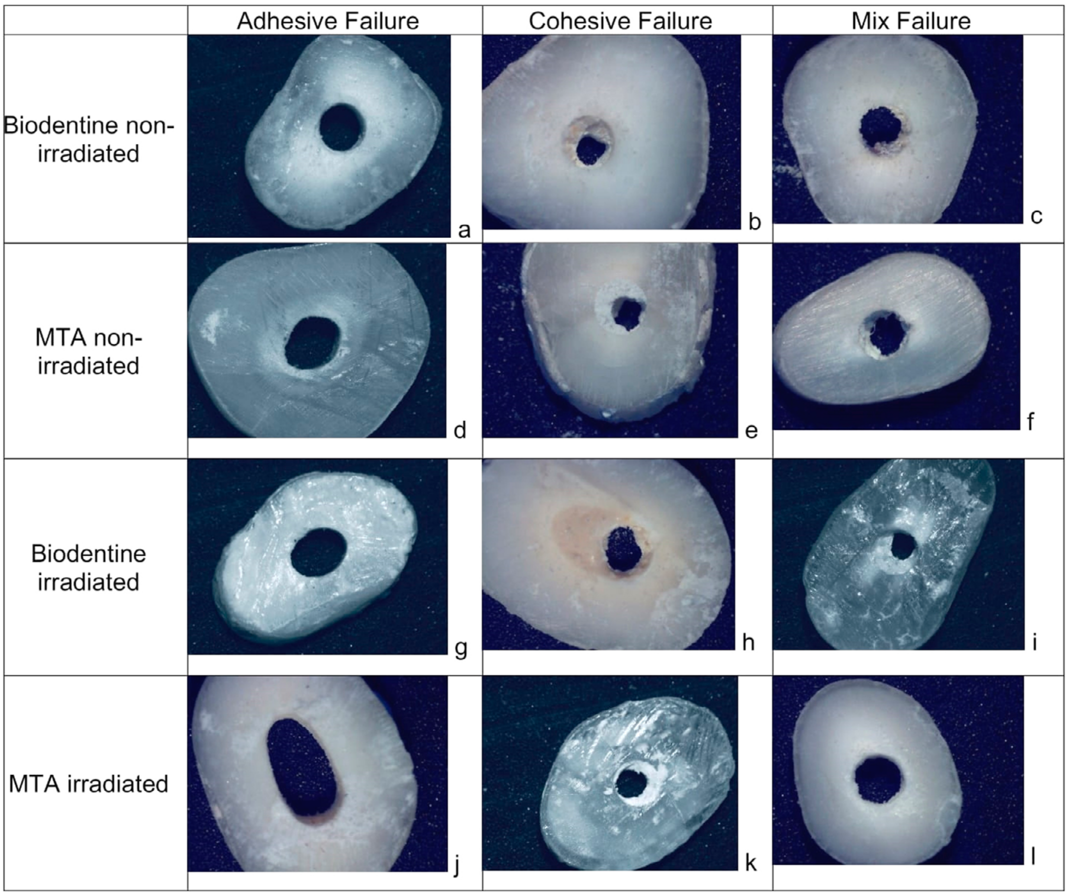

Figure 3- Representative stereomicroscopic images of the types of bond failures observed in experimental groups (A) Adhesive failure, (B) Cohesive failure, and (C) Mixed failure. In specimens with adhesive failure, clean root canal surface can be observed without any lining of the cements. In specimens with cohesive failure, cement lining can be observed throughout the diameter of the root canal

network.[11,35] Moreover, variations in the inter, peri, and intratubular dentin,[11,35,36] tubular obliteration of dentin,[11,37] and initiation and activation of matrix metalloproteinase (MMP) expression could occur due to radiation.[38] Furthermore, all of these could have resulted in a different bonding interface and less mineral tag formation at the cement/dentin interface.[39,40]

The protein to mineral ratio of dental hard tissues has been shown to decrease after radiation therapy.[41] Thus, it is assumed that variations in organic parts occur after radio therapy, presenting an indirect effect over the inorganic part of enamel and dentin, rather than direct.[11] Studies have concluded that radiotherapy was most detrimental to the organic part of the tooth structure, rather than to the inorganic content.[36,42]

The irrigant used in the current study during the endodontic treatment was 2.5% NaOCl / 9% Dual Rinse HEDP. A previous study has demonstrated that irrigation using 2.5% NaOCl / 9% Dual Rinse HEDP significantly increased the push-out BS of Biodentine on the radicular dentin when compared to 2.5% NaOCl followed by 17% EDTA.[25] Therefore, in this study, 2.5% NaOCl / 9% Dual Rinse HEDP combination irrigation was used.

Most managing options for patients suffering from head and neck cancer comprise of radiation dose ranging from 50 to 70 Gy, which depends on the stage and location of the tumor.[24,42,43] Thus, a total of 60 Gy was employed in the current study. The samples that underwent irradiation were disclosed to radiations once a day with a dose of two Gy per fraction delivered five days a week for six weeks. This follows the classic regimen employed for clinical management of cancer.[34,45]

The disc samples were kept in artificial saliva when not undergoing irradiation to maintain a humid environment, simulating the oral cavity. The specimens were stored in distilled water at the time of radiation delivery since viscosity and higher ion concentration of artificially manufactured saliva can affect the uniform distribution of radiations.[11,26] Additionally, since water is abundant in soft tissues, the usage of distilled water, both in physical and chemical terms, can simulate the neighbouring soft tissue by forming free radicals.[15] Push-out testing is widely used as a measure of the BS of filling materials in the root canal dentin.[46] This test leads to shear stress at the dentin-filling material interface, which can be compared to clinical settings. This study used dentin samples as discs of 1.5 mm thickness for push-out BS analysis. Various authors have suggested varying thickness for BS analysis of disc samples.[43] The usage of thicker discs seem to enhance the friction area, leading to an overestimation of the BS.[25]

Regarding the type of bond failures found, 68% were cohesive, 23% mixed, and 8% adhesive. The cohesive failures may be due to the better adhesion of tricalcium silicate cements to the canal walls. This can be due to their particle size, which is finer, enhancing the infiltration of the tricalcium silicate cement into the dentinal tubules.[44] Moreover, it can also be due to its bio-mineralization characteristic by forming tags.[47]

In the current study, the BS of Biodentine and MTA to root canal dentin was assessed immediately after irradiation of teeth. However, the long-term effect of radiation with different dosages on the BS of Biodentine and MTA on root canal dentin must be evaluated in further studies. Additionally, future studies should be conducted using radicular dentin surface treatment protocols such as laser and carbodiimide (EDC) application. These surface treatments can decrease the radiation effect to root canal dentin, as well as increase the adhesion of root filling materials.[48,49,50]

Conclusions

We conclude that the irradiation of root canal dentin reduced the push-out BS of Biodentine and MTA when compared to its control counterparts. The bond strength of Biodentine was superior when compared to MTA with and without irradiation.

Acknowledgements

The authors thank Medcem, GmbH, Weinfelden, Switzerland, for providing Dual Rinse HEDP capsules for this study.

Funding

This research received no external funding.

Conflicts of Interest

The authors declare no conflict of interest.

Data availability statement

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Authors´ contributions:

Khullar, Lochan: Data curation (Equal); Investigation (Equal); Resources (Equal). **Ballal, Vasudev**: Conceptualization (Equal; Data curation (Equal); Formal analysis (Equal); Investigation (Equal); Methodology (Equal); Project administration (Equal); Supervision (Equal); Validation (Equal); Writing – original draft (Equal); Writing – review & editing (Equal). **Eyuboglu, Tan Firat**: Formal analysis (Equal); Project administration (Equal); Supervision (Equal); Validation (Equal); Visualization (Equal); Writing – original draft (Equal); Writing – review & editing (Equal). **Ozcan, Mutlu**: Formal analysis (Equal); Project administration (Equal); Supervision (Equal); Validation (Equal); Visualization (Equal); Writing – original draft (Equal); Writing – review & editing (Equal).

References

1- World Health Organization. International Agency for research on Cancer. Global Cancer Observatory [internet]. Lyon: Global Cancer Observatory; 2023 [cited 2023 Aug 4]. Available from: http://globocan.iarc.fr

2- Casiglia J, Woo SB. A comprehensive review of oral cancer. Gen Dent. 2001;49(1):72-82.

3- Oral Cancer Foundation – OCF [internet]. Newport Beach, CA; 2023 [cited 2023 Aug 4]. Available from: http://oralcancerfoundation.org

4- Vishak S, Rangarajan B, Kekatpure VD. Neoadjuvant chemotherapy in oral cancers: selecting the right patients. Indian J Med Paediatr Oncol. 2015;36(3):148-53. doi: 10.4103/0971-5851.166716

5- Falk AT, Hébert C, Tran A, Chand ME, Leysalle A, Thariat J, et al. Radiotherapy for elderly patients and cetuximab, a monocentric study. Eur Arch Otorhinolaryngol. 2017;274(2):1061-65. doi: 10.1007/s00405-016-4336-3

6- Ferguson HW, Stevens MR. Advances in head and neck radiotherapy to the mandible. Oral Maxillofac Surg Clin North Am. 2007;19(4):553-63. doi: 10.1016/j.coms.2007.07.005

7- Galetti R, Santos-Silva AR, Antunes AN, Alves FA, Lopes MA, Goes MF. Radiotherapy does not impair dentin adhesive properties in head and neck cancer patients. Clin Oral Investig. 2014;18(7):1771-8. doi: 10.1007/s00784-013-1155-4

8- Vissink A, Jansma J, Spijkervet FK, Burlage FR, Coppes RP. Oral sequelae of head and neck radiotherapy. Crit Rev Oral Biol Med. 2003;14(3):199-212. doi: 10.1177/154411130301400305

9- Wöstmann B, Rasche KR.The influence of radiotherapy on survival time of teeth and restorations. A study on patients with maxillofacial defects. Zahnärztl Welt. 1995;104:627.

10- Lieshout HF, Bots CP. The effect of radiotherapy on dental hard tissue--a systematic review. Clin Oral Investig. 2014;18(1):17-24. doi: 10.1007/s00784-013-1034-z

11- Gonçalves LM, Palma-Dibb RG, Paula-Silva FW, Oliveira HF, Nelson-Filho P, Silva LA, et al. Radiation therapy alters microhardness and microstructure of enamel and dentin of permanent human teeth. J Dent. 2014;42(8):986-92. doi: 10.1016/j.jdent.2014.05.011

12- Campi LB, Lopes FC, Soares LE, Queiroz AM, Oliveira HF, Saquy PC, et al. Effect of radiotherapy on the chemical composition of root dentin. Head Neck. 2019;41(1):162-9. doi: 10.1002/hed.25493.

13- Martini GR, Bortoluzzi EA, Minamisako MC, Bordignon NCT, Rodrigues PM, Gondak R. Impact of radiotherapy on the morphological and compositional structure of intra-radicular dentin. Braz Dent J. 2023;34(1):45-51. doi: 10.1590/0103-6440202305101.

14- Lilly JP, Cox D, Arcuri M, Krell KV. An evaluation of root canal treatment in patients who have received irradiation to the mandible and maxilla. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1998;86(2):224-6. doi: 10.1016/s1079-2104(98)90129-9

15- Paiola FG, Lopes FC, Mazzi-Chaves JF, Pereira RD, Oliveira HF, Queiroz AM, et al. How to improve root canal filling in teeth subjected to radiation therapy for cancer. Braz Oral Res. 2018;32:e121. doi: 10.1590/1807-3107bor-2018.vol32.0121

16- Atmeh AR, Chong EZ, Richard G, Festy F, Watson TF. Dentin-cement interfacial interaction: calcium silicates and polyalkenoates. J Dent Res. 2012;91(5):454-9. doi: 10.1177/0022034512443068

17- Yavari H, Samiei M, Eskandarinezhad M, Shahi S, Aghazadeh M, Pasvey Y. An *in vitro* comparison of coronal microleakage of three orifice barriers filling materials. Iran Endod J. 2012;7(3):156-60.

18- Saghiri MA, Garcia-Godoy F, Gutmann JL, Lotfi M, Asatourian A, Ahmadi H. Push-out bond strength of a nano-modified mineral trioxide aggregate. Dent Traumatol. 2013;29(4):323-7. doi: 10.1111/j.1600-9657.2012.01176.x

19- Noetzel J, Ozer K, Reisshauer BH, Anil A, Rössler R, Neumann K, et al. Tissue responses to an experimental calcium phosphate cement and mineral trioxide aggregate as materials for furcation perforation repair: a histological study in dogs. Clin Oral Investig. 2006;10(1):77-83. doi: 10.1007/s00784-005-0032-1

20- Dawood AE, Parashos P, Wong RH, Reynolds EC, Manton DJ. Calcium silicate-based cements: composition, properties, and clinical applications. J Investig Clin Dent. 2017;8(2). doi: 10.1111/jicd.12195

21- Ber BS, Hatton JF, Stewart GP. Chemical modification of proroot mta to improve handling characteristics and decrease setting time. J Endod. 2007;33(10):1231-4. doi: 10.1016/j.joen.2007.06.012

22- Torabinejad M, Hong CU, McDonald F, Pitt Ford TR. Physical and chemical properties of a new root-end filling material. J Endod. 1995;21(7):349-53. doi: 10.1016/S0099-2399(06)80967-2

23- Stefaneli Marques JH, Silva-Sousa YT, Rached-Júnior FJ, Macedo LM, Mazzi-Chaves JF, Camilleri J, et al. Push-out bond strength of different tricalcium silicate-based filling materials to root dentin. Braz Oral Res. 2018;8;32:e18. doi: 10.1590/1807-3107bor-2018.vol32.0018

24- Arora V, Nikhil V, Sharma, Arora P. Bioactive dentin replacement. IOSR J. Dent. Sci. 2013;12(4):51-7.

25- Paulson L, Ballal NV, Bhagat A. Effect of root dentin conditioning on the pushout bond strength of Biodentine. J Endod. 2018;44(7):1186-90. doi: 10.1016/j.joen.2018.04.009

26- Martins CV, Leoni GB, Oliveira HF, Arid J, Queiroz AM, Silva LA, et al. Influence of therapeutic cancer radiation on the bond strength of an epoxy- or an MTA-based sealer to root dentine. Int Endod J. 2016;49(11):1065-72. doi: 10.1111/iej.12556

27- Kochueva MV, Ignatieva NY, Zakharkina OL, Snopova LB, Kulabukhova KS, Maslennikova A. Collagen structural changes in early radiation-induced damage. Biomed Investig. 2012;4:24-8.

28- Ballal NV, Roy A, Zehnder M. Effect of sodium hypochlorite concentration in continuous chelation on dislodgement resistance of an epoxy resin and hydraulic calcium silicate sealer. Polymers. 2021;13(20):3482. doi: 10.3390/polym13203482

29- Ballal NV, Kandian S, Mala K, Bhat KS, Acharya S. Comparison of the efficacy of maleic acid and ethylenediaminetetraacetic acid in smear layer removal from instrumented human root canal: a scanning electron microscopic study. J Endod. 2009;35(11):1573-6. doi: 10.1016/j.joen.2009.07.021

30- Dentsply Sirona. ProRoot MTA (Mineral Trioxide Aggregate) root canal repair material [internet]. Charlotte, USA; 2017 [cited 2023 Aug 4]. Available from: https://www.dentsplysirona.com/content/dam/Dentsply-Sirona-Flagship/australia/sds/ProRootMTA4620-52-Jun17.pdf

31- Badami V, Nadipineni A, Sooraparaju S, Kanumuru PK, Ahmed MK, Kommavarapu S, et al. Comparative evaluation of push out bond strength of two commercially available MTA and Biodentine - an *in vitro* study. Int J Health Sci Res. 2021;11:12-8.

32- Seredin P, Goloshchapov D, Prutskij T, Ippolitov Y. Phase transformations in a human tooth tissue at the initial stage of caries. PLoS One. 2015;22;10(4):e0124008. doi: 10.1371/journal.pone.0124008

33- Miranda RR, Silva AC, Dantas NO, Soares CJ, Novais VR. Chemical analysis of *in vivo*-irradiated dentine of head and neck cancer patients by ATR-FTIR and Raman spectroscopy. Clin Oral Investig. 2019;23(8):3351-8. doi: 10.1007/s00784-018-2758-6

34- Yamin PA, Pereira RD, Lopes FC, Queiroz AM, Oliveira HF, Saquy PC, et al. Longevity of bond strength of resin cements to root dentine after radiation therapy. Int Endod J. 2018;51(11):1301-12. doi: 10.1111/iej.12945

35- Siqueira Mellara T, Palma-Dibb RG, Oliveira HF, Garcia Paula-Silva FW, Nelson-Filho P, Silva RA, et al. The effect of radiation therapy on the mechanical and morphological properties of the enamel and dentin of deciduous teeth: an *in vitro* study. Radiat Oncol. 2014;22;9:30. doi: 10.1186/1748-717X-9-30.

36- Soares CJ, Castro CG, Neiva NA, Soares PV, Santos-Filho PC, Naves LZ, et al. Effect of gamma irradiation on ultimate tensile strength of enamel and dentin. J Dent Res. 2010;89(2):159-64. doi: 10.1177/0022034509351251

37- Grötz KA, Duschner H, Kutzner J, Thelen M, Wagner W. Neue Erkenntnisse zur Atiologie der sogenannten Strahlenkaries. Nachweis direkter radiogener Veränderungen an der Schmelz-Dentin-Grenze [New evidence for the etiology of so-called radiation caries. Proof for directed radiogenic damage od the enamel-dentin junction]. Strahlenther Onkol. 1997;173(12):668-76. German. doi: 10.1007/BF03038449

38- McGuire JD, Mousa AA, Zhang BJ, Todoki LS, Huffman NT, Chandrababu KB, et al. Extracts of irradiated mature human tooth crowns contain MMP-20 protein and activity. J Dent. 2014;42(5):626-35. doi: 10.1016/j.jdent.2014.02.013

39- Rodrigues RB, Soares CJ, Simamoto PC Junior, Lara VC, Arana-Chavez VE, Novais VR. Influence of radiotherapy on the dentin properties and bond strength. Clin Oral Investig. 2018;22(2):875-83. doi: 10.1007/s00784-017-2165-4

40- Lu H, Zhao Q, Guo J, Zeng B, Yu X, Yu D, et al. Direct radiation-induced effects on dental hard tissue. Radiat Oncol. 2019;14(1):5. doi: 10.1186/s13014-019-1208-1

41- Reed R, Xu C, Liu Y, Gorski JP, Wang Y, Walker MP. Radiotherapy effect on nano-mechanical properties and chemical composition of enamel and dentine. Arch Oral Biol. 2015;60(5):690-7. doi: 10.1016/j.archoralbio.2015.02.020

42- Yaduka P, Kataki R, Roy D, Das L, Goswami S. Effects of radiation therapy on the dislocation resistance of root canal sealers applied to dentin and the sealer-dentin interface: a pilot study. Restor Dent Endod. 2021;29;46(2):e22. doi: 10.5395/rde.2021.46.e22

43- Cheylan JM, Gonthier S, Degrange M. *In vitro* push-out strength of seven luting agents to dentin. Int J Prosthodont. 2002;15(4):365-70.

44- Guneser MB, Akbulut MB, Eldeniz AU. Effect of various endodontic irrigants on the push-out bond strength of biodentine and conventional root perforation repair materials. J Endod. 2013;39(3):380-4. doi: 10.1016/j.joen.2012.11.033

45- Pelloso AM, Miranda RR, Rossi ME, Bianchini AL, Marcelino FA, Silva EL, et al. Chemical analysis of irradiated root dentin and its interaction with resin cements. Clin Oral Investig. 2022;26(6):4315-25. doi: 10.1007/s00784-022-04395-z

46- Pane ES, Palamara JE, Messer HH. Critical evaluation of the push-out test for root canal filling materials. J Endod. 2013;39(5):669-73. doi: 10.1016/j.joen.2012.12.032

47- Singh S, Podar R, Dadu S, Kulkarni G, Vivrekar S, Babel S. An *in vitro* comparison of push out bond strength of Biodentine and Mineral Trioxide Aggregate in the presence of sodium hypochlorite and chlorhexidine gluconate. Endod. 2016;28(1):42-5. doi: 10.4103/0970-7212.184339

48- Lopes FC, Roperto R, Akkus A, Sliva Souza YT, Sousa- Neto MD. Evaluation of chemical and morphological changes in radicular dentin after different final surface treatments. Microsc Res Tech. 2018;81(9):973-9. doi: 10.1002/jemt.23060

49- Lopes FC, Roperto R, Akkus A, Queiroz AM, Francisco de Oliveira H, Sousa-Neto MD. Effect of carbodiimide and chlorhexidine on the bond strength longevity of resin cement to root dentine after radiation therapy. Int Endod J. 2020;53(4):539-52. doi: 10.1111/iej.13252

50- Zhou J, Yang X, Chen L, Liu X, Ma L, Tan J. Pre-treatment of radicular dentin by self-etch primer containing chlorhexidine can improve fiber post bond durability. Dent Mater J. 2013;32(2):248-55. doi: 10.4012/dmj.2012-134