J Oral Med Oral Surg 2023;29:19
https://doi.org/10.1051/mbcb/2023020

https://www.jomos.org

JOMOS
Journal of Oral Medicine and Oral Surgery

## Original Research Article

# Correlation between number of dental amalgam restorations and severity of oral mucositis after head-neck radiotherapy

Maryam Baharvand[1], Marzie Kamali[2], Soheila Manifar[3], Ali Kazemian[4], Marzieh Alimohammadi[5,*]

[1] Department of Oral and Maxillofacial Medicine, School of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2] Department of Endodontics, School of Dentistry, Guilan University of Medical Sciences, Rasht, Iran
[3] Department of Oral and Maxillofacial Medicine, School of Dentistry, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran
[4] Department of Radiotherapy, School of Medicine, Radiation Oncology Research Center, Cancer Institute, Imam khomeini Hospital, Tehran University of medical Sciences, Tehran, Iran
[5] Department of Oral Medicine, Dental Faculty, Shahid Beheshti University of Medical Sciences, Tehran, Iran

(Received: 16 October 2022, accepted: 16 May 2023)

**Keywords:** Radiotherapy / mucositis / dental amalgam / cancer / oral mucosa

**Abstract – Background:** Head and neck radiotherapy causes side effects such as stomatitis. In vitro studies demonstrated local dose enhancement due to backscatter radiation near metal restorations. The aim of this study was to analyze correlation between number of amalgam restorations with severity of oral mucositis in patients with head and neck radiotherapy. **Method and materials:** This cross-sectional study was accomplished on 80 patients under head and neck radiotherapy referred to Cancer Institute (Tehran, Iran) in 2014–2015. Severity of mucositis and pain were measured by three examinations according to WHO criteria and visual analogue scale. Descriptive statistics and Spearman's correlation coefficient test used to analyze the data by IBM SPSS statistics V22.0. **Results:** There was no significant correlation between the number of amalgam restorations and severity of mucositis and pain on second and third examinations. However, severity of mucositis and pain were found to be significantly correlated with radiation dose per session ($p = 0.013$, $rs = 0.276$), ($p = 0.032$, $rs = 0.240$) and total radiation dose ($p < 0.001$ $rs = 0.393$), ($p < 0.001$, $rs = 0.445$) on second and third examinations respectively. **Conclusion:** This study showed that number of dental amalgam restorations have no impact on aggravation of oral mucositis caused by head and neck radiotherapy.

## Introduction

Oral mucositis is a side effect of head and neck radiotherapy [1], and is described as an inflammation, erythema, ulceration and finally pseudo membrane formation in the oral mucosa [2]. Due to severe oropharyngeal pain caused by mucositis it is necessary to take analgesic drugs [3,4]. Mucositis may also reduce quality of life arising from oral pain, bleeding, dysphagia, infections, anorexia, impairment of liquid and food intake, which eventually leads to severe weight loss, dehydration, and in severe cases, hospitalization [4].

Mucositis is very important due to its high prevalence [5]. The incidence of oral mucositis caused by head and neck radiation varies from 80% to 97% [6]. The severity of radiation-induced oral mucositis is dependent on age, gender, fraction size, radiation portals, fractionation, concurrent chemotherapy, type of cancer, type and location of radiotherapy, radiation dose per session and total radiation used [7,8]. One of the factors that may be related to the frequency and severity of oral mucositis is the number of metal restorations and other non-removable metal components in the mouth [9].

There is not enough information about the effect of metal restorations on the occurrence of oral mucositis after head and neck radiotherapy [8]. In addition, few clinical studies addressing this field accomplished so far. Prevention and management of mucositis are dependent to detection of predisposing factors; hence, we decided to conduct a clinical study to determine the correlation between the number of amalgam restorations and the number of quadrants containing amalgam restorations with the severity of oral mucositis induced by head and neck radiotherapy.

## Methods and materials

This cross-sectional study was accomplished on 80 consecutive patients under head and neck radiotherapy referred to Cancer Institute of Imam Khomeini Hospital (Tehran, Iran) in 2014–2015. Inclusion criterion was patients

* Correspondence: m.alimohamadi95@yahoo.com

**Table I.** Relative frequency of mucositis on three examinations.

| Grade of mucositis | First examination | | Second examination | | Third examination | |
|---|---|---|---|---|---|---|
| 0 | 22 | 27.5% | 2 | 2.5% | 1 | 1.3% |
| 1 | 50 | 62.5% | 24 | 30% | 27 | 33.8% |
| 2 | 8 | 10% | 30 | 37.5% | 22 | 27.5% |
| 3 | 0 | 0% | 24 | 30% | 30 | 37.5% |

undergoing head and neck radiotherapy. Edentulous patients, those having fixed or removable prosthesis, orthodontic brackets, metallic restorations except dental amalgam, mandibular plates and other metallic intra osseous components were excluded from the study. All patients were examined every week during their course of radiotherapy, but the severity of mucositis and pain were measured on three occasions. The first visit was performed on the first week of radiotherapy and data such as age, sex and number of amalgam restorations were recorded. The second visit accomplished on the middle of radiotherapy course, and the third visit was done on the last week of radiotherapy or the week after finishing radiotherapy. On each examination degree of mucositis was determined clinically according to WHO criteria (grade 0: no complaint. grade 1: mild soreness and erythema. grade 2: painful erythema, edema and ulcers, able to eat solid foods. grade 3: painful erythema, edema and ulcers, unable to eat solid but able to eat liquid foods. grade 4: unable to eat any food and need to intravenous feeding) [10].

In addition, the severity of pain was measured on each examination by means of a 100-cm visual analog scale (VAS). The patients were requested to describe their pain intensity by selecting a number between 0 and 100. The severity of pain was divided into three levels as: mild pain: $0 < \text{VAS} \leq 30$, moderate pain: $31 \leq \text{VAS} \leq 69$ and Sever pain: $70 \leq \text{VAS} \leq 100$ [11].

Information regarding total radiation dose and radiation dose per session were retrieved from patient's medical records. All patients were recommended to rinse their mouth by water regularly and use a soft, high protein, high calorie and non-irritating diet. Meanwhile, patients with stomatitis were prescribed mouthwash chlorhexidine 0.2% or nystatin suspension 100,000 u/mL in case of oral candidiasis according to already approved treatment protocols at Cancer Institute. Meanwhile, all potential sources of dental infection had to be removed or treated accordingly before starting radiotherapy [12].

To determine correlation between frequency and severity of mucositis and pain with number of amalgam restorations, radiation dose per session and total radiation dose, spearman correlation coefficient was used. Data were analyzed by IBM SPSS statistics V22.0.

### Ethical considerations

All participants of this study signed informed consent forms and their data kept confidential. This study was approved by research deputy of Shahid Beheshti Dental School with the code of ethics IR.SBMU.RIDS.REC.1394.3363.

## Results

In this study 80 consecutive patients under head and neck radiotherapy referred to Cancer Institute of Imam Khomeini Hospital (Tehran, Iran) including 39 women (48.75%) and 41 men (51.25%) with an average age of 38 years and ranging between 6 and 81 years were examined.

Fifteen patients (18.8%) were under chemotherapy simultaneously and 65 others (81.2%). Out of 80 patients, 76 (95%) were under compact radiotherapy and 4(5%) received various radiotherapy.

All patients had mucositis at least in one examination, and the frequency of mucositis was estimated 100% in the entire period of radiotherapy. Relative frequency for mucositis in 3 examinations is shown in Table I. According to Table I, on the first, second and third examination the relative frequency of mucositis was 72.5%, 97.5% and 98.8% respectively.

Thirty-six patients (45%) had no amalgam restorations, 11 patients (13.8%) had just one, 13 patients (16.3%) had amalgam restorations in one quadrant, 9 patients (11.3%) in two quadrants, 15 patients (18.8%) in three quadrants and 7 patients (8.8%) in four quadrants. The range of number of amalgam restorations were between 1 and 11 with the mean of 2.

Radiation dose per session was 200 cGy for 61 patients (76. 3%). Total radiation dose was 6000 cGy for 31 patients (38.8%) and 7000 cGy for 11 patients (13. 8%). The range of radiation dose was between 1800 and 7000 cGy with an average of 5498 cGy.

On first examination, 60 patients (75%) had pain, with the maximum pain severity of 60 (VAS).

On second examination, 78 patients (97.5%) had pain, with the maximum pain degree of 93. On third examination, all patients had pain, with maximum pain intensity of 95.

The relative frequency of pain severity in three examinations is presented in Table II.

The correlation between mucositis and pain with radiation dose and number of amalgam restorations is shown in Table III.

According to Spearman correlation coefficient, a significant and positive correlation was found between severity of mucositis and degree of pain on three examinations ($p < 0.0001$, $rs = 0.878$), ($p < 0.0001$, $rs = 0.953$) and ($p < 0.0001$, $rs = 0.940$).

Moreover, Spearman's correlation showed a significant and positive correlation between radiation dose per session and both degree of pain and mucositis on first examination; however, no significant correlation between total radiation dose and severity of pain and mucositis was found. On second

**Table II.** Relative frequency of pain intensity on three examinations.

| Degree of pain | First examination | | Second examination | | Third examination | |
|---|---|---|---|---|---|---|
| No pain | 20 | 25% | 2 | 2.5% | 0 | 0% |
| Mild | 53 | 66.3% | 26 | 32.5% | 31 | 38.8% |
| Moderate | 7 | 8.8% | 28 | 35% | 20 | 25% |
| Sever | 0 | 0% | 24 | 30% | 29 | 36.2% |

**Table III.** Correlation between degree of mucositis and pain and radiation dose per session and total radiation dose and the number of amalgam restoration.

| | | Radiation dose per session | Total radiation dose | Number of amalgam restoration |
|---|---|---|---|---|
| Degree of mucositis on second examination | *P*-value | 0.013 | <0.0001 | 0.589 |
| | Correlation coefficient | 0.276 | 0.393 | 0.061 |
| Degree of mucositis on third examination | *P*-value | 0.032 | <0.0001 | 0.808 |
| | Correlation coefficient | 0.240 | 0.445 | –0.028 |
| Degree of pain on second examination | *P*-value | 0.006 | <0.0001 | 0.329 |
| | Correlation coefficient | 0.303 | 0.387 | 0.110 |
| Degree of pain on third examination | *P*-value | 0.007 | <0.0001 | 0.921 |
| | Correlation coefficient | 0.300 | 0.438 | 0.011 |

and third examinations a significant and positive correlation between the degree of mucositis and severity of pain and with radiation dose per session and total radiation dose was found. However, Spearman's correlation showed no significant correlation between degree of mucositis and pain with number of amalgam restorations on both second and third examinations.

## Discussion

This study investigated the frequency and severity of oral mucositis and pain induced by head and neck radiotherapy as well as the correlation between severity of oral mucositis and pain with number of amalgam restorations. In addition, correlation between severity of mucositis and radiation dose per session and total radiation dose was evaluated. Contrary to other studies which were carried out in vitro, this study was performed in vivo and clinically in patients.

The results showed mucositis developed in all patients at least in one examination, and mucositis frequency was 100% in the whole period of radiotherapy. According to several previous studies, the prevalence of mucositis was reported over 80% which was similar to the present study [2–5,7,10,13–23]. The frequency of mucositis in all reviewed studies was consonant with the present study, but some disparities in results might be due to differences in population, diagnostic criteria for mucositis severity and the radiotherapy protocol.

Vera-Lionch studied variables such as age, sex, weight, alcohol and tobacco consumption, primary site, type and the stage of cancer, radiation dose, type of radiotherapy, concurrent chemotherapy and degree of mucositis in 450 patients undergoing head and neck radiotherapy and the overall incidence of mucositis was 83% [15].

Linda S Elting studied 2 groups of patients including 126 patients with oral or oropharyngeal cancer, and 65 patients with laryngeal or hypopharyngeal cancer. The results of this study were the most similar ones to ours in terms of frequency of mucositis (99% vs 100%). The intensity and frequency of mucositis and pain, the impact of mucositis on weight loss and quality of life, the use of analgesics and other treatments were investigated in this study. The risk of mucositis in this study was 99% in patients with oral or oropharyngeal cancers and 98% in patients with laryngeal or hypopharyngeal cancer [17].

A review study determined risk factors related to both patients and radiotherapy method. Risk factors related to patients included: location of tumor, age, oral health, nutritional status, functional status of kidneys and liver, and risk factors associated to radiotherapy were reported radiation patterns, portal radiations and radiation dose. The prevalence of mucositis was above 90% [7].

There was a significant and positive correlation between radiation dose per session and severity of mucositis and pain on first examination in the present study. Whereas no significant correlation was found between total radiation dose and severity

of mucositis and pain in the first examination. The reason was probably due to receiving lower total radiation dose on first examination, which was cumulated on second and third examinations, as one study showed that the first signs of mucositis in patients with head and neck radiotherapy would appear after 10 Gy and severe signs would occur after 30 Gy [10]. On the other hand, radiation causes destruction of cellular structures and vascular changes, therefore increasing radiation dose lead to more intensity of oral mucositis and pain [6,13]. That is why, on second and third examinations a significant and positive correlation was demonstrated between severity of mucositis and pain with both radiation dose per session and total radiation dose.

In a study on 326 patients, it was shown that severe oral mucositis was associated with different risk factors and 136 (41.7%) patients had grade 3 mucositis. Moreover, male sex, oropharyngeal cancer, low hemoglobin levels, low leukocytes or lymphocytes, concurrent chemotherapy, and oral feeding were shown to be significantly associated with a higher frequency of severe oral mucositis [23].

These studies investigated lots of variables but none of them investigated the effect of amalgam restorations on severity and frequency of mucositis. The present study, showed no correlation between the number of amalgam restorations with severity and frequency of oral mucositis after head and neck radiotherapy.

Obviously, oral cavity as a vital and physiological environment with vascular circulation is different from in-vitro conditions such as a phantom head. Hence, our results are not comparable with previously mentioned studies accordingly. In addition, in the present study patients were examined repeatedly and any erythema or infection in the oral cavity were detected and treated immediately.

Few experimental *in vitro* studies investigated dose distribution and enhancement near different dental materials such as:

- Chin revealed that additional radiation was absorbed by water which caused radiation attenuation. This study tested, dose distribution by radiotherapy near 23 dental materials and reported 2% dose enhancement adjacent to amalgam and also found that increased distance from metal restorations led to decreased radiation distribution [24].
- Kinhikar described the effect of mandibular titanium plates and screws on dose enhancement and showed 10% radiation dose enhancement. This study didn't evaluate radiation dose enhancement near amalgam [25].
- Serichetaphongse evaluated back- and forward-scattered doses from nine contemporary dental materials and revealed that atomic number and density of materials have a direct relationship with backscattered dose and an inverse relationship with forward-scattered dose [26].

One study showed that radiation dose distribution is dependent on both dental material and electron beam energy. Amalgam and higher energy showed the most dose distribution [27]. As present study indicated there was a significant and positive correlation between radiation dose per session and total radiation dose and severity of mucositis and pain, but there was not any correlation with amalgam restorations.

An *in vitro* study showed the highest back scattering radiation for Ni-Cr alloy and the lowest for ceramics [28]. Another *in vitro* study reported the effect of metal-containing topical agent on surface dose enhancement during radiotherapy. The results showed no significant difference in surface dose enhancement between metal containing topical agent and nonmetal_ containing topical agent in each thickness [29].

All of previous studies were done *in vitro*, which justifies the difference between our results and previous ones. Vital oral environment, vascular circulation and healing ability of oral tissue and also capability of saliva to absorb radiation lead to different results in our study [24].

## Conclusion

Although, the degree of mucositis and severity of pain were correlated with radiation dose; the number of amalgam restorations had no impact on frequency and severity of oral mucositis in patients under head-neck radiotherapy.

## Conflict of interest

There was no conflict of interest in this manuscript.

## Funding

The full cost of the study was paid by the authors.

## Ethical approval

This study was approved by research deputy of Shahid Beheshti Dental School with the code of ethics IR.SBMU.RIDS.REC.1394.3363.

## Informed consent

All participants of this study signed informed consent forms and their data kept confidential.

## Authors contribution

Maryam Baharvand designed the method and edited the manuscript. Marzieh Alimohammadi as a co responder performed an oral examination, searched for related articles, designed tables and now she is submitting the manuscript. Marzie Kamali performed the data analysis. Soheila Manifer and Ali Kazemian got the information, set up the database and drafted manuscript.

*Acknowledgments.* We are greatly thankful to staff members of Cancer Institute (Tehran University of Medical Science) for their utmost cooperation.

## References


1. Naidu MUR, Ramana GV, Rani PU, Suman A, Roy P. Chemotherapy-induced and/or radiation therapy-induced oral mucositis-complicating the treatment of cancer. Neoplasia 2004;6:423–31.
2. Taheri M, Najafi M, Salehi M. Clinical evaluation of the effects of radiotherapy on oral mucosa and gingival health in radiotherpy center of Ghaem Hospital. J Mashhad Dental School 2006;30: 87–98.
3. Raber-Durlacher JE, Elad S, Barasch A. Oral mucositis. Oral oncol 2010;46:452–456.
4. De Sanctis V, Bossi P, Sanguineti G, Trippa F, Ferrari D, Bacigalupo A, *et al.* Mucositis in head and neck cancer patients treated with radiotherapy and systemic therapies: Literature review and consensus statements. Crit Rev Oncol/Hematol 2016;100: 147–66.
5. Trotti A, Bellm LA, Epstein JB, Frame D, Fuchs HJ, Gwede CK, *et al.* Mucositis incidence, severity and associated outcomes in patients with head and neck cancer receiving radiotherapy with or without chemotherapy: a systematic literature review. Radiother Oncol 2003;66:253–262.
6. Laali E, Manifar S, Kazemian A, Jahangard-Rafsanjani Z, Gholami K. The effect of selenium serum levels on oral mucositis frequency and severity in patients with head and neck radiation. J Pharmaceut Care. 2018;39–43.
7. Moslemi D, Nokhandani AM, Otaghsaraei MT, Moghadamnia Y, Kazemi S, Moghadamnia AA. Management of chemo/radiation-induced oral mucositis in patients with head and neck cancer: a review of the current literature. Radiother Oncol 2016;120:13–20.
8. Jensen SB, Peterson DE, RCSE F. Oral complications of nonsurgical cancer therapies. Burket's Oral Med 2021;259.
9. Shimamoto H, Sumida I, Kakimoto N, Marutani K, Okahata R, Usami A, *et al.* Evaluation of the scatter doses in the direction of the buccal mucosa from dental metals. J Appl Clin Med Phys 2015;16:233–243.
10. Stokman M, Spijkervet F, Wymenga A, Burlage F, Timens W, Roodenburg J, *et al.* Quantification of oral mucositis due to radiotherapy by determining viability and maturation of epithelial cells. J Oral Pathol Med 2002;31:153–157.
11. Kelly A. The minimum clinically significant difference in visual analogue scale pain score does not differ with severity of pain. Emerg Med J. 2001;18:205–207.
12. McGuire DB, Fulton JS, Park J, Brown CG, Correa MEP, Eilers J, *et al.* Systematic review of basic oral care for the management of oral mucositis in cancer patients. Support Care Cancer 2013;21:3165–77.
13. Sonis ST, Fey EG. Oral complications of cancer therapy. Oncology (Williston Park, NY) 2002;16:680–686; discussion 6, 91.
14. Avritscher EB, Cooksley CD, Elting LS, editors. Scope and epidemiology of cancer therapy-induced oral and gastrointestinal mucositis. Seminars in oncology nursing 2004 Elsevier.
15. Vera-Llonch M, Oster G, Hagiwara M, Sonis S. Oral mucositis in patients undergoing radiation treatment for head and neck carcinoma: risk factors and clinical consequences. Cancer 2006;106:329–336.
16. Wong PC, Dodd MJ, Miaskowski C, Paul SM, Bank KA, Shiba GH, *et al.* Mucositis pain induced by radiation therapy: prevalence, severity, and use of self-care behaviors. J Pain Sympt Manag 2006;32:27–37.
17. Elting LS, Keefe DM, Sonis ST, Garden AS, Spijkervet F, Barasch A, *et al.* Patient-reported measurements of oral mucositis in head and neck cancer patients treated with radiotherapy with or without chemotherapy: demonstration of increased frequency, severity, resistance to palliation, and impact on quality of life. Cancer 2008;113:2704–2713.
18. Sonis ST. Oral mucositis in head and neck cancer: risk, biology, and management. Am Soc Clin Oncol Educ Book 2013;33:e236–e 240.
19. Maria O, Eliopoulos N, Muanza T. Radiation-induced oral mucositis. Front Oncol 2017;7:89.
20. Peng H, Chen B-B., Chen L, Chen Y-P., Liu X, Tang L-L, *et al.* A network meta-analysis in comparing prophylactic treatments of radiotherapy-induced oral mucositis for patients with head and neck cancers receiving radiotherapy. Oral Oncol 2017;75: 89–94.
21. Berger K, Schopohl D, Bollig A, Strobach D, Rieger C, Rublee D, *et al.* Burden of oral mucositis: a systematic review and implications for future research. Oncol Res Treatment 2018;41:399–405.
22. Bai X-H, Chen Z-M, Ma L-H, He Z, Li G. Prevention effect of low-temperature atomization inhalation for radiation induced oral mucositis in patients with head and neck cancer undergoing radiotherapy. Cancer Manag Res 2019;11:4327.
23. Nishii M, Soutome S, Kawakita A, Yutori H, Iwata E, Akashi M, *et al.* Factors associated with severe oral mucositis and candidiasis in patients undergoing radiotherapy for oral and oropharyngeal carcinomas: a retrospective multicenter study of 326 patients. Supportive Care Cancer. 2020;28:1069–75.
24. Chin DW, Treister N, Friedland B, Cormack RA, Tishler RB, Makrigiorgos GM, *et al.* Effect of dental restorations and prostheses on radiotherapy dose distribution: a Monte Carlo study. J Appl Clin Med Phys 2009;10:80–89.
25. Ashok Kinhikar R, Tambe CM, Patil K, Mandavkar M, Deshpande DD, Gujjalanavar R, *et al.* Estimation of dose enhancement to soft tissue due to backscatter radiation near metal interfaces during head and neck radiotherapy — a phantom dosimetric study with radiochromic film. J Med Phys. 2014;39(1).
26. Serichetaphongse P, Kunapinun T. Comparison of back-and forward-scattered radiation from different dental materials using therapeutic dose of radiation, in vitro. J Dent Assoc Thai. 2022;72:394.
27. Bahreyni Toossi MT, Ghorbani M, Akbari F, Mehrpouyan M, Sobhkhiz Sabet L. Evaluation of the effect of tooth and dental restoration material on electron dose distribution and production of photon contamination in electron beam radiotherapy. Austr Phys Eng Sci Med. 2016;39:113–22.
28. Azizi M, Mowlavi AA, Ghorbani M, Azadegan B, Akbari F. Dosimetric evaluation of scattered and attenuated radiation due to dental restorations in head and neck radiotherapy. J Radiat Res Appl Sci 2018;11:23–28.
29. Iyama A, Matsuyama T, Matsumoto E, Araki T, Inokuchi S, Yamashita M, *et al.* Effect of metal-containing topical agents on surface doses received during external irradiation. J Radiat Res 2018;59:794–799.