

# Effect of ionizing radiation on the taste function of patients submitted to head and neck radiotherapy\*

*Efeito da radiação ionizante sobre o paladar em pacientes submetidos a radioterapia para a região da cabeça e pescoço*

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**Abstract Objective:** To evaluate the effects of ionizing radiation on the taste function in patients submitted to radiotherapy in the head and neck region. **Materials and Methods:** Twenty patients diagnosed with head and neck tumors and undergoing treatment in the Division of Radiotherapy at Santa Casa de Misericórdia de Belo Horizonte, MG, Brazil, were selected. For their taste function testing, four solutions were manipulated with salt (NaCl), sugar (sucrose), citric acid (for acidity), and urea (for bitterness), at three different (low, medium and high) concentrations. Weekly tests were performed during the first three weeks of radiotherapy, with random administration of the solutions (three drops each) respecting the order of their concentration levels (low, medium and high). After the application of each solution, the patient reported which flavor he/she tasted. **Results:** A statistically significant difference was observed in the loss of taste function as the results in the 1st and 4th weeks of treatment were compared, with salty solution at the three concentration levels, with the sweet solution at low and medium concentrations, and with the sour and bitter solutions, only at low concentration. **Conclusion:** Ionizing radiation alters the taste function of patients submitted to head and neck radiotherapy. **Keywords:** Ionizing radiation; Radiobiology; Ageusia.

**Resumo Objetivo:** Avaliar os efeitos da radiação ionizante sobre o paladar, em pacientes que foram submetidos a radioterapia na região de cabeça e pescoço. **Materiais e Métodos:** Foram selecionados 20 pacientes que possuíam diagnóstico de tumor na região de cabeça e pescoço, que iniciaram tratamento no Setor de Radioterapia da Santa Casa de Misericórdia de Belo Horizonte, MG, Brasil. Para testes do paladar, foram manipuladas quatro soluções (salgada – NaCl; doce – sacarose; azeda – ácido cítrico; amarga – ureia) em três concentrações diferentes (fraca, média e forte), administradas por meio de conta-gotas, três gotas de cada solução de maneira aleatória, respeitando a ordem das concentrações fracas, médias e fortes. Após a aplicação de cada solução, o paciente relatava o sabor que sentia. O procedimento foi realizado semanalmente durante as três primeiras semanas de radioterapia. **Resultados:** Foi observada diferença estatisticamente significativa na perda do paladar dos pacientes em tratamento radioterápico, quando se compararam a 1<sup>a</sup> e 4<sup>a</sup> semanas de tratamento na solução salgada, nas três concentrações, na solução doce nas concentrações fracas e médias e nas soluções azedas e amargas, apenas quando se testaram as concentrações fracas. **Conclusão:** A radiação ionizante altera o paladar de pacientes submetidos a radioterapia de cabeça e pescoço. **Unitermos:** Radiação ionizante; Radiobiologia; Ageusia.

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## INTRODUCTION

Like in other structures, the biological effects of ionizing radiations on structures of the oral cavity vary according to the size of the irradiated area, the dose, the type and rhythm of irradiation, as well as the devel-

opmental stage of the irradiated tissue. In the development of the taste buds, such effects range from mild growth retardation to total destruction<sup>(1)</sup>.

Radiotherapy is the therapeutic modality that utilizes ionizing radiation in the fight against neoplasias, with the purpose of reaching malignant cells, impairing their multiplication by mitosis and/or determining cell death. The treatment may be uti-

lized with curative or palliative intent and the radiotherapy scheme will depend on the total dose required and the radiotherapist's evaluation<sup>(2)</sup>.

Ionizing radiation is capable of producing deleterious effects on the oral mucosa, salivary glands, taste, dentition, periodontium, bone, muscles and joints. Such effects are classified into immediate effects, which occur up to three months after the application; intermediate effects, which occur between three and six months after the application; and late effects, which occur after six months from the application of radiotherapy<sup>(1)</sup>.

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Treatment options are divided into two modalities: teletherapy (radiotherapy with a remote radiation source) and brachytherapy (proximity of the lesion with the radioactive material, by means of implants, intraluminal or intracavitary applicators)<sup>(3)</sup>. Teletherapy may be performed with cobalt therapy equipment or linear accelerators, utilizing conventional, three-dimensional or conformational planning techniques. Although teletherapy is widely utilized, its side effects affect particularly the oral cavity, causing significant alterations in the stomatognathic system. Xerostomia, trismus, radiation caries, candidiasis, mucositis and osteoradionecrosis are the main acute or late side effects of radiotherapy on the oral cavity<sup>(2,4-6)</sup>.

An important alteration caused by ionizing radiation in patients submitted to radiotherapy is the change in taste. It occurs rapidly and many times precedes the occurrence of mucositis. Head and neck radiotherapy directly affects taste thresholds, chewing, deglutition and food intake, which may result in weight loss and malnutrition. Most of patients submitted to this kind of treatment are affected by total or partial loss of taste function and distinction among flavors<sup>(7)</sup>. In a study by Conger, it was observed that the loss of taste function is exponentially enhanced with doses above 30 Gy (three-week treatment), 2 Gy per fraction<sup>(8)</sup>.

The loss of taste function is generally transitory, with a gradual recovery to normal levels one year after radiotherapy, although such recovery period may take up to five years after radiotherapy. The level of taste function and flavor sensation recovery will depend on the radiation dose received by the patient and the patient's subjective taste sensation<sup>(9,10)</sup>.

Considering the scarcity of literature reporting comparison of deleterious effects of ionizing radiation on the region of the taste buds as well as on the taste function, the present study has the general objective of evaluating the effects of ionizing radiation on the taste function in patients submitted to head and neck radiotherapy.

## MATERIALS AND METHODS

After approval by the Committee for Ethics in Research of Faculdade de Odon-

tologia, PUC Minas, 20 patients with head and neck neoplasms, undergoing treatment at Santa Casa de Misericórdia de Belo Horizonte, were selected. Initially, an initial anamnesis was carried out in order to collect personal information and data on the type of neoplasm, radiation dose to be used in the treatment, period in which the radiation would be administered and the fields that would receive treatment. During the first evaluation, an intraoral examination was performed in all patients to evaluate the taste buds condition. Such an examination was aimed at detecting the presence of possible pre-existing alterations.

For the taste function tests of the taste buds, with basis on the study developed by Gomez et al.<sup>(10)</sup>, four different solutions were manipulated (salty, sweet, sour and bitter) at three different concentrations (low, median and high): NaCl (1%, 5% and 10%), sucrose (5%, 20%, and 40%), citric acid (0.5%, 1.5% and 5%) and urea (5%, 20% and 40%). The patients were asked to brush their teeth and their tongues and then rinse the mouth with 50 ml of water for three times, during 30 seconds in order to remove any impurities from the oral cavity and standardize the study. With a dropper, three drops of each solution were randomly administered, but always following the concentration order from low to high. After administration of each solution, the patient reported whether the flavor was felt. When the flavor was not felt the attributed value was 0 (zero). When it was felt the attributed value was 1 (one). At every change of solution the patients were asked to rinse their mouth with 50 ml of water to clear the flavor from the previous solution.

Such procedure was performed on a weekly basis during the first three weeks of radiotherapy, starting on the first session which was considered the control week. Thus, it was possible to observe whether changes in taste function occurred at the moment of radiotherapy. For data analysis the Cochran's Q statistical test was utilized along with descriptive analyses with a significance level of 5%.

## RESULTS

The authors observed that the 20 patients with ages between 13 and 79 years,

received total radiation doses that ranged between 35 and 60 Gy, distributed in daily doses ranging between 0.8 and 3 Gy/day (Table 1).

With the NaCl solution at low concentration (1%) the patients presented a significant loss of taste function early on the first week of radiotherapy. At the medium concentration (5%), the patients could feel the salty flavor after the first week of radiotherapy; however such flavor was not felt on the remaining weeks. With the high concentration (10%), the loss of taste function was significant only in the last week of evaluation ( $p < 0.05$ ) (Table 2).

With the sucrose solution at low concentration (5%), the patients presented a significant loss of taste function on the first week of radiotherapy, being such loss enhanced by the third week ( $p < 0.05$ ). At medium concentration (20%), the patients could feel the sweet flavor on the first two weeks of radiotherapy; however such flavor could not be felt on the last week of evaluation ( $p < 0.05$ ). As the high concentration (40%) was utilized, no taste function loss was observed ( $p > 0.05$ ) (Table 2).

With the citric acid solution (sour flavor) at low concentration (0.5%), the patients presented a significant loss of taste function on the first week of radiotherapy. Such loss was enhanced on the second and third weeks ( $p < 0.05$ ). Both at medium (1.5%) and at high (5%) concentrations, no loss of taste function was observed ( $p > 0.05$ ) (Table 2).

With the urea solution at low concentration (5%), the patients presented a significant loss of taste function (bitter flavor) only on the last week of radiotherapy ( $p < 0.05$ ). Both with the medium (20%) and high (40%) concentrations, no loss of taste function was observed ( $p > 0.05$ ) (Table 2).

As the solutions at low concentration are compared, the loss of taste for the salty flavor was greater on the first week of radiotherapy. On the second week, only the bitter flavor was significantly perceived. However, on the last week, the loss of taste was generalized with all the solutions at low concentration ( $p < 0.05$ ) (Table 3).

At medium concentration, even with the medians remaining at the 1 value, loss of taste functions was observed for all the fla-

**Table 1** General characteristics of the studied population.

Patient	Age	Tumor	Site	Irradiated fields	Applications	Dose/day	Total dose
1	17	Undifferentiated tumor of the nasal cavity	Right nasal cavity	Two fields on the face	30	1 Gy	50 Gy
2	33	Ductal adenocarcinoma	Right parotid	Two fields on the face	27	2 Gy	54 Gy
3	63	Ductal adenocarcinoma	Left parotid	Two fields on the face	27	2 Gy	54 Gy
4	13	Embryonal rhabdomyosarcoma	Left parotid	Two fields on the face	20	1.9 Gy	36 Gy
5	64	Ocult carcinoma in the face	Left/right face	Three fields on the face	22	2 Gy	44 Gy
6	45	Ductal adenocarcinoma	Right parotid	Two fields	20	3 Gy	60 Gy
7	51	Squamous cell carcinoma	Larynx	Three fields	25	0.8 Gy	45 Gy
8	46	Lymphoma	Larynx	Two fields	20	1.8 Gy	35 Gy
9	60	Cervical metastasis	Neck	Two fields	20	1 Gy	40 Gy
10	16	Cervical lymphoepithelioma	Left neck	Six fields	22	2 Gy	44 Gy
11	52	Squamous cell carcinoma	Tongue and larynx	Three fields	25	1.8 Gy	45 Gy
12	78	Cervical metastasis from primary tumor	Neck	Two fields	20	2 Gy	40 Gy
13	63	Squamous cell carcinoma	Oropharynx	Three fields	30	2.2 Gy	54 Gy
14	46	Squamous cell carcinoma	Oral cavity and base of the tongue	Three fields	25	1.8 Gy	45 Gy
15	48	Anaplastic carcinoma	Thyroid	Three fields	25	1.8 Gy	45 Gy
16	29	Squamous cell carcinoma	Base of the tongue	Three fields	25	1.8 Gy	45 Gy
17	47	Squamous cell carcinoma	Oropharynx	Three fields	25	1.8 Gy	45 Gy
18	59	Squamous cell carcinoma	Tongue – base and back	Three fields	22	2 Gy	44 Gy
19	56	Squamous cell carcinoma	Larynx	Three fields	25	1.8 Gy	45 Gy
20	49	Parotid adenocarcinoma	Right parotid	Two fields	27	2 Gy	54 Gy

**Table 2** Comparison of degrees of taste loss with the three different concentrations for each flavor.

	NaCl			Sucrose			Citric acid			Urea		
	1%	5%	10%	5%	20%	40%	0,5%	1,5%	5%	5%	20%	40%
Control week	A	A	A	A	A	A	A	A	A	A	A	A
First week	B	B	A/B	B	A	A	A/B	A	A	A	A	A
Second week	B	C	A/B	B/C	A	A	B/C	A	A	A	A	A
Third week	B	C	B	C	B	A	C	A	A	B	A	A

Note: Equal letters do not statistically differ among themselves in columns in the Cochran's Q test ( $p < 0.05$ ).

**Table 3** Comparative evaluation of taste loss with four flavors at three different concentrations (low, medium and high).

	Low concentration				Medium concentration				High concentration			
	NaCl 1%	Sucrose 5%	Citric acid 0,5%	Urea 5%	NaCl 5%	Sucrose 20%	Citric acid 1,5%	Urea 20%	NaCl 10%	Sucrose 40%	Citric acid 5%	Urea 40%
First week	A	B	B	B	A	A/B	A/B	B	A	A	A	A
Second week	B	B	A/B	A	B	A	A	A	A	A	A	A
Third week	A	A	B	B	C	B	A	A	B	A	A	A

Note: Equal letters do not statistically differ among themselves in columns in the Cochran's Q test ( $p < 0.05$ ).

vors, except for bitter on the first week ( $p < 0.05$ ). On the second week, the salty flavor presented the most significant loss ( $p < 0.05$ ). On the third week, most significant loss was observed in the salty and sweet flavors as compared with the others ( $p < 0.05$ ) (Table 3).

At high concentration no statistically significant difference was observed as the four solutions were compared on the first and second weeks ( $p > 0.05$ ). At the fourth evaluation, a significant loss of taste function was observed for the salty flavor ( $p < 0.05$ ) (Table 3).

**DISCUSSION**

The deleterious effects of ionizing radiation on the head and neck region are described as more noticeable effects, since this area is composed of structures with different radiosensitivities, such as the epi-

thelial, connective, muscular and nervous tissues<sup>(1,11)</sup>. Because of the presence of deleterious effects, the inclusion of new clinical practices is required to minimize such effects, providing improvement in the quality of life of patients submitted to radiotherapy<sup>(1-12)</sup>.

The radiation dose required for the treatment of tumors is based on their malignancy and also on whether such treatment will be concomitantly associated with some other treatment modality, either surgery or chemotherapy<sup>(1,13)</sup>. Most patients undergoing treatment for head and neck tumors receive radiation doses ranging from 50 to 70 Gy, such total dose being usually delivered over a period of five to seven weeks, once a day in fractionated doses of 2 Gy<sup>(13,14)</sup>.

The taste function in patients with head and neck tumors may be altered both by chemotherapy drugs and by radiotherapy. Because of the decreased taste function, many patients end up developing food aversion, becoming intolerant to some food textures, high temperatures and excessive acidity of some foods<sup>(15)</sup>.

Hypogeusia, or reduced taste function, is a complication that may be reported on the second week right after the beginning of radiotherapy, differently from data found in the research, since the loss of taste function in patients was observed on the second evaluation, a period compatible with the first week of radiotherapy<sup>(7)</sup>.

The hypogeusia severity and duration depend upon the radiation dose and the irradiated fields; higher doses and irradiation fields closer to areas of taste receptors cause stronger deleterious effects<sup>(7,15,16)</sup>. In the present study, it was expected that patients receiving higher doses of ionizing radiation on fields closer to taste receptors would present stronger deleterious effects, a fact that was confirmed during the data analysis.

In a study developed by Kamprad et al.<sup>(16)</sup> decreased taste function was observed in patients receiving radiotherapy doses  $\geq$  40 Gy. In the present study, loss of taste function was reported by patients receiving doses  $\geq$  35 Gy, demonstrating that lower doses can cause deleterious effects on tissues, depending on the irradiation field.

In the study developed by Almeida et al.<sup>(4)</sup>, the severity and duration of the taste function loss depended on the radiation dose reaching areas of taste receptors and generally compromised the whole flavor spectrum (sweet, salty, sour and bitter). In the present study, in spite of the daily doses ranging between 0.8 and 3 Gy, all the patients presented some degree of taste function loss.

The loss of taste function may become permanent, although some patients may partially recover the sensation of taste about 20 to 60 days after concluding radiotherapy, or present complete recovery 2 to 4 months after conclusion of the treatment. Patients try to compensate for such loss by eating sucrose-rich foods, which would contribute to the development of radiation caries, or by using larger amounts of spices, increasing the discomfort caused by mucositis<sup>(1)</sup>.

Among other factors, the age of the patients plays a significant role in the loss of taste function. Patients under the age of 20 are more prone to more severe loss of taste function because of the presence of a higher number of taste buds. Other factors that may influence the loss or change of taste function are the following: systemic disorders, diabetes, use of alcohol or tobacco, and dental materials<sup>(16)</sup>.

The change in taste function was reported by a high number of the patients submitted to head and neck radiotherapy in a study, and it was explained by the gradual taste buds atrophy and increased salivary viscosity<sup>(4)</sup>. In the present study comprising an original method, 100% of patients presented some type of change in taste function, from minor loss of some flavors to total loss of taste function, with the salty flavor presenting the highest losses, while the bitter flavor presented the smallest losses.

## CONCLUSION

The ionizing radiation utilized in radiotherapy for head and neck tumors caused deleterious effects on the taste function of patients in all flavors. The salty flavor was most affected, with losses on the first week of treatment, while the bitter flavor was the least affected during the evaluations.

## REFERENCES

1. Vissink A, Burlage FR, Spijkervet FKL, et al. Prevention and treatment of the consequences of head and neck radiotherapy. Oral sequelae of head and neck radiotherapy. *Crit Rev Oral Med.* 2003; 14:213-25.
2. Sawada NO, Dias AM, Zago MMF. O efeito da radioterapia sobre a qualidade de vida dos pacientes com câncer de cabeça e pescoço. *Rev Bras Cancerol.* 2006;52:323-9.
3. Bonan PRF, Lopes MA, Alves FA, et al. Aspectos clínicos, biológicos, histopatológicos e tratamentos propostos para a mucosite oral induzida por radioterapia: revisão da literatura. *Rev Bras Cancerol.* 2005;51:235-42.
4. Silva DP, Ferraz AR, Durazzo MD, et al. Radioterapia em cabeça e pescoço: efeitos colaterais agudos e crônicos bucais. *Rev Bras Patol Oral.* 2004;3:62-9.
5. Jham BC, Freire ARS. Complicações bucais da radioterapia em cabeça e pescoço. *Rev Bras Otorrinolaringol.* 2006;72:704-8.
6. Lima AAS, Figueiredo MAZ, Krapf SMR, et al. Velocidade do fluxo e pH salivar após radioterapia da região de cabeça e pescoço. *Rev Bras Cancerol.* 2004;50:287-93.
7. Erkurt E, Erkiş M, Tunali C. Supportive treatment in weight-losing cancer patients due to the additive adverse effects of radiation treatment and/or chemotherapy. *J Exp Clin Cancer Res.* 2000;19:431-9.
8. Conger AD. Loss and recovery of taste acuity in patients irradiated to the oral cavity. *Radiat Res.* 1973;53:338-47.
9. Tomita Y, Osaki T. Gustatory impairment and salivary gland pathophysiology in relation to oral cancer treatment. *Int J Oral Maxillofac Surg.* 1990;19:299-304.
10. Gomez FE, Cassis-Nosthas L, Morales-de-León JC, et al. Detection and recognition thresholds to the 4 basic tastes in Mexican patients with primary Sjögren's syndrome. *Eur J Clin Nutr.* 2004; 58:629-36.
11. Scully C, Epstein JB. Oral health care for the cancer patient. *Eur J Cancer B Oral Oncol.* 1996;32B: 281-92.
12. Schiodt M, Hermund NU. Management of oral disease prior to radiation therapy. *Support Care Cancer.* 2002;10:40-3.
13. Dobbs J, Barrett A, Ash D. Practical radiotherapy planning. London, UK: Hodder Arnold Publication; 1999.
14. Hall EJ. Radiobiology for the radiobiologist. Philadelphia, PA: Lippincott Williams & Wilkins; 2000.
15. Chasen MR, Bhargava R. A descriptive review of the factors contributing to nutritional compromise in patients with head and neck cancer. *Support Care Cancer.* 2009;17:1345-51.
16. Kamprad F, Ranft D, Weber A, et al. Functional changes of the gustatory organ caused by local radiation exposure during radiotherapy of the head-and-neck region. *Strahlenther Onkol.* 2008; 184:157-62.