



Functional-structural reorganisation of salivary glands in oncological pathology: A mini-review

Larysa Posolenyk*

PhD in Medical Sciences, Associate Professor

I. Horbachevsky Ternopil National Medical University of the Ministry of Health of Ukraine

46001, 1 Maidan Voli, Ternopil, Ukraine

<https://orcid.org/0000-0002-1656-4420>

Abstract. Dysfunctions of salivary glands during the treatment of benign and malignant tumours are a widely diagnosed problem among oncology patients. This study aimed to investigate the disruption of the structure of salivary glands as a result of the treatment of oncological diseases and methods for their correction and elimination. 39 scientific papers were analysed. Methods of search, comparison, systematisation, and combination of the results of the conducted studies were used. The destructive effect of chemo- and radiotherapy and the treatment of malignant tumours by increasing the body's overall temperature on the structure of salivary glands in the experiment was proven. The influence of low-intensity ultrasound on the submandibular gland demonstrates its tissues' high adaptive and regenerative properties. Data from clinical studies on the correction and elimination of salivary gland dysfunctions in oncological patients showed an ambiguous result. The simultaneous application of photobiomodulation and radiotherapy in patients with head and neck tumours significantly improves organ function: it stimulates salivation, regulates saliva composition, controls the redox mechanism of salivary glands, and locally eliminates inflammation. A slight compensation of the mineralising function of saliva was found with substitution therapy using biologically active components and a remineralising agent in children with malignant tumours undergoing chemotherapy. A positive effect of betanechol and vitamin E in protecting salivary glands during the treatment of head and neck cancer with radiotherapy has been noted, which consists of improving the structure and function of the glands in the long term and is the same in women and men. Studies of vitamin C intake after radioiodine therapy in patients with head and neck cancer have shown its insufficient restorative effect on the quantitative and qualitative composition of saliva. The results of this review can serve as a basis for an accurate assessment by oncologists of salivary gland damage and the pathogenesis of their dysfunctions as a result of cancer therapy, provide an opportunity to reconsider existing views on the problem, develop new methods for preventing and treating these complications, and improve the quality of life and recovery process for patients

Keywords: oncology; dysfunction; chemotherapy; morphometry; radiation

INTRODUCTION

At the present stage of human evolution, cancer incidence worldwide continues to rise steadily year by year, with GLOBOCAN 2020 projecting a 47% increase in diagnosed cancer cases over the next 20 years [1]. In treating cancer patients, clinicians employ advanced surgical techniques, precise and safe radiotherapy, polychemotherapy, and hormone therapy, as well as innovative methods such as interventional radiology, immunotherapy, and targeted therapy. However, these treatments often lead to the development of so-called drug-induced iatrogenic conditions,

disrupting the functioning of the patient's organs and systems, as described by S.M. Schleicher *et al.* [2]. The onset of concurrent dental pathology is no exception among oncology patients. J.Y.A. Kyaw *et al.* [3] highlight the link between systemic cancer treatment and salivary gland damage, leading to dysfunctions such as hyposalivation and xerostomia, which are the most common. Saliva plays a crucial role in maintaining homeostasis, preserving the integrity of oral tissues, and supporting the natural digestive processes. Therefore, ensuring the proper functioning

Suggested Citation:

Posolenyk L. Functional-structural reorganisation of salivary glands in oncological pathology: A mini-review. *Bull Med Biol Res.* 2024;6(3):60–65. DOI: 10.61751/bmbr/3.2024.60

*Corresponding author



of saliva is particularly important in conditions that impair salivary gland activity, as pointed out in the study by N. Gevkaliuk *et al.* [4].

The onset of xerostomia, commonly known as “dry mouth”, is a frequent complication of cancer treatment. Patients often experience thirst, difficulties in eating, altered taste perception, speech impairments, roughness of the oral mucosa, as well as periodic pain and burning sensations in the mouth, all of which significantly reduce their quality of life. T.S. Deshpande *et al.* [5] found a strong positive correlation between xerostomia and dysgeusia in both the short- and long-term among patients with oropharyngeal cancer who underwent proton therapy. The examinations were conducted at 2 weeks, 8 weeks, 6 months, and 2 years post-treatment, with xerostomia and dysgeusia being present at all time points. In a literature review, L.T. Galaniha & A.A. Nolden [6] identified taste dysfunction in 17.6-93% of cancer patients and xerostomia in 40.4-93% as two of the most common symptoms during cancer and its treatment. Y. Iijima *et al.* [7] observed grade 1 dysgeusia (altered taste sensation) and hyposalivation caused by chemotherapy in patients with colorectal, breast, and gynaecological cancers. I.M.V. Silva *et al.* [8] demonstrated in a clinical study of breast cancer patients that quality of life deteriorated after just the second cycle of antitumour therapy. They attributed the altered taste and xerostomia to the cytotoxic effects of chemotherapy, leading to loss of appetite, early satiety, nausea, and reduced overall food intake, which in turn has psychological and social consequences for the patient. I. Brook [9] identified long-term side effects in patients undergoing radiotherapy for head and neck cancer, highlighting hyposalivation and xerostomia as prominent issues. To treat salivary gland dysfunction, the author suggests the use of saliva substitutes, non-pharmacological saliva stimulation, salivary stimulants, laser treatment, and increased fluid intake. R.R. Riantinigtayas *et al.* [10] conducted a cross-sectional study in head and neck cancer patients using psychophysical tests to assess tactile sensitivity, the ability to discern food texture and temperature, as well as salivary function, consistency, pH, volume, and buffering capacity. They found a low somatosensory response in these patients, which was linked to reduced salivary secretion. Z. Huang *et al.* [11] investigated the prevalence of salivary gland damage caused by radioactive iodine, assessing progressive changes in the glands through ultrasound imaging. In patients who underwent total or near-total thyroidectomy followed by postoperative radioiodine therapy, ultrasound-detected salivary gland alterations increased from 2.0% to 33.0% after 20 months, with most of these changes persisting at 36 months, indicating irreversible gland damage. A literature review by B.A. Klein *et al.* [12] demonstrated that immune system-related side effects are common and can affect any organ system, including exerting toxic effects on the salivary glands.

Despite significant advancements in cancer treatment, chemotherapy, radiotherapy, and radiation therapy remain the primary methods for cancer treatment, yet they cause a range of side effects. The most common among these are xerostomia and altered taste, which contribute to loss of appetite, cachexia, and reduced resistance in patients already weakened by their primary disease – the tumour. Physicians and scientists worldwide are investigating these

issues to alleviate the suffering of cancer patients and improve their quality of life and recovery process. This study aimed to analyse the structural changes in salivary glands during cancer treatment and explore methods for preventing and mitigating these effects.

To achieve the stated objective, a comprehensive literature search was conducted on the PubMed, Medline, and Scopus platforms. Over 50 publications, including clinical data, experimental studies, and literature reviews, were analysed. The search strategy was developed following the PICOS framework. A systematic search was performed using relevant keywords and search terms aligned with the PICO criteria. The study investigated the impact of the most common cancer therapies across different tumour locations, their side effects – particularly the damage to the structure and function of the salivary glands – and measures aimed at improving or restoring the function of these organs. The inclusion criteria for publications were the originality of data, clinical and experimental results published in Ukrainian, English, and Russian (as a significant number of professional publications in Ukraine were published in Russian before 2014). Studies that lacked control group data in clinical trials, as well as those only available as conference abstracts or in collections of scientific papers, as well as research abstracts, were excluded from this review. During the search for verification methods of salivary gland damage, prevention, and treatment in cancer therapy, a shortage of literature from 2018 onwards was identified, prompting an extension of the review period to cover 2006 to 2023. As a result, 39 sources were included in this study.

✦ MORPHOMETRY OF SALIVARY GLANDS UNDER VARIOUS CANCER TREATMENTS IN EXPERIMENTAL STUDIES

Chemotherapy is widely used in oncology treatment. S. Herashchenko *et al.* [13] analysed and described changes in the submandibular salivary gland under the influence of cisplatin, demonstrating that intraperitoneal administration of cisplatin to rats over 9 weeks resulted in both degenerative and compensatory changes in the parenchyma and stroma of the gland, including fibrosis of the interductal connective tissue. Throughout the experiment, the acini appeared collapsed, with a reduction in their external diameter and area compared to controls, along with a decrease in the height and number of serous cells. The intercalated ducts exhibited varying changes in external diameter and lumen size, showing both decreases and increases (the highest values observed on day 28). In striated ducts, the external diameter progressively increased, while the lumen decreased. The interlobular ducts consistently showed an increase in both external diameter and lumen size. From day 3 to day 28, the epithelial cells of the intercalated, striated, and interlobular ducts showed signs of sloughing, with their number and height decreasing up until day 14, after which regeneration began. In the periductal stroma, fibrosis increased up to day 28, with activated fibroblasts (showing large connective tissue bundles) being observed, as reported by R.A.L. Willems *et al.* [14], C.C. Kirwan & E.L. Blower [15]. A. Farokh *et al.* [16], and S.R. Bomeli Farokh *et al.* [17] investigated the effects of radiation on the submandibular glands of rats 180 days post-irradiation. They found that during this period, diffuse fibrosis

developed in both the inter- and intralobular stroma, indicating long-term structural changes and damage resulting from radiation exposure.

L. Radfar & D.A. Sirois [18] developed a model of radiation-induced salivary gland injury in Hanford minipigs using the same irradiation protocol employed in contemporary clinical practice, which involved a daily radiation dose of 70 Gy. The irradiated glands exhibited significant loss of parenchyma, pronounced atrophy, and interstitial fibrosis of the acinar cells, along with an increase in the nuclei of these cells, as well as dilation and proliferation of the excretory ducts. This was accompanied by a loss of secretory granules and infiltration of lymphocytes and plasma cells. Notably, these structural changes were more pronounced in the submandibular glands compared to the parotid glands, as noted by F. Huisman *et al.* [19] and V. Mercadante *et al.* [20]. E. Bidram *et al.* [21] discovered that the lumens of the excretory ducts of the submandibular glands contained sloughed epithelial cell layers.

Ultrasound is frequently employed to stimulate and accelerate physiological reactions or to selectively disrupt tissues in the jaw through heating methods or by enhancing the plasticity of bone tissue, as indicated by B de Lucas *et al.* [22]. L. Tarasenko & M. Bilets [23], along with V.N. Patel & M.P. Hoffman [24], investigated the stress factor associated with the effects of low-intensity ultrasound on the submandibular gland. The following results were interpreted: dilation of the excretory ducts with flattened, vacuolated epithelial cells, a significant predominance of mucous secretion over protein secretion, accumulation of lymphocytic cells and macrophages around microvessels while preserving structural components, and an increase in the number of mast cells in the interlobular connective tissue and the stroma of the interlobular vessels at the beginning of the experiment, with subsequent subsidence of these processes in the later stages. Chemotherapy, radiation exposure, and hyperthermia in experimental animals lead to the destruction of salivary gland structures. Ultrasonic correction of bone tissue has an impact on the structure of the submandibular salivary gland, suggesting high adaptive and regenerative properties of its tissues.

★ METHODS OF CORRECTION AND ELIMINATION OF SALIVARY GLAND DYSFUNCTIONS

In a clinical study by G.C. Louzeiro *et al.* [25], the impact of photobiomodulation on salivary secretion, saliva composition, xerostomia, and the quality of life of patients undergoing radiotherapy for head and neck cancers was evaluated over a short-term observation period. A diode laser was employed for intraoral and extraoral applications to the salivary glands, administered three times a week throughout the radiotherapy course. Xerostomia and salivary pH were assessed, and both unstimulated and stimulated salivary secretion were measured before the onset of radiotherapy, after the 15th session, upon completion of radiotherapy, and 60 days post-treatment. The concentrations of calcium, total proteins, chloride, sodium, potassium, and the activity of amylase and catalase were evaluated in stimulated saliva samples. Researchers T.D. Debela *et al.* [26] and P. Roth *et al.* [27] demonstrate that photobiomodulation can stimulate salivary secretion, regulate the composition

of saliva, and control the redox mechanisms of salivary glands, thereby reducing local inflammation when applied concurrently with radiotherapy. However, the question remains as to whether the increase in salivary secretion can be sustained, whether it has a radioprotective effect and whether it can be widely applied in clinical settings.

P. Tkachenko *et al.* [28] conducted a study on the salivation rate and mineralising potential of oral fluid, along with their correction in children with malignant soft tissue tumours of various anatomical locations. The study involved a group of children aged 7 to 15 with morphologically verified soft tissue malignancies that were responsive to chemotherapy (such as nephroblastoma, hepatoblastoma, rhabdomyosarcoma, retinoblastoma, reticulosarcoma, and central nervous system tumours). The patients underwent courses of combined chemotherapy lasting 3-4 weeks. The first group of children was treated according to the standard medical care protocol for this category of patients, with the addition of a conventional oral care regimen. In the second group of study participants, in addition to the standard treatment, gel-based preparations were administered as part of a replacement therapy. These gels contain biologically active components (centaury, echinacea, sage), which stimulate the functional activity of the salivary glands, possess anti-inflammatory properties, and a remineralising gel with calcium, fluoride, and phosphorus. The research was conducted before the commencement of treatment and following the completion of the first course of polychemotherapy. In the first group of children, there was a progressive decrease in the mineralising potential of the oral fluid during the polychemotherapy, accompanied by a reduction in salivation rate. In the second group, only partial compensation of this mineralising imbalance was observed, as reported by A. Nolden *et al.* [29] and A.K. Larsen *et al.* [30].

A significant portion of the research by S. Manoharan *et al.* [31] and S. Campagna *et al.* [32] is focused on finding methods to protect and prevent damage to the salivary glands during radiotherapy for head and neck cancers. D. Campanhã *et al.* [33] proposed the use of bethanechol to prevent salivary gland dysfunction in patients undergoing radioactive iodine therapy. Patients received bethanechol (25 mg twice daily) or a placebo (control group) two hours after therapy and for up to one month. Saliva flow was monitored, and quality of life was assessed using the University of Washington Quality of Life Questionnaire at 10-, 30-, and 90-day post-therapy. Pain and swelling of the salivary glands were more common among patients taking the placebo at both 10 and 30 days. Those in the bethanechol group demonstrated improved saliva production and a more positive outlook. Bethanechol proved effective in reducing acute salivary gland damage.

A. Upadhyaya *et al.* [34] studied the radioprotective effect of vitamin E on the parotid and submandibular salivary glands following radioiodine therapy for differentiated thyroid cancer. Patients in the three study groups received vitamin E orally at doses of 100, 200, and 300 mg/day for 1-4 weeks after therapy. Salivary gland function was assessed using salivary gland scintigraphy immediately before and six months after treatment. The findings of T. Buttiron Webber *et al.* [35] and L.T. Tchelebi *et al.* [36] demonstrated improved functional parameters of the salivary glands,

indicating a high compensatory capacity of the major salivary glands, with vitamin E showing significant protective effects on both parotid and submandibular glands in both men and women.

Y. Liu *et al.* [37] conducted a study on the protective effects of vitamin C on salivary glands following iodine-131 therapy in patients with differentiated thyroid cancer. To determine the optimal timing of vitamin C administration, patients were divided into two groups: a 2-hour group and a 24-hour group based on the time of vitamin intake post-radiation therapy. They received 100 mg of vitamin C every hour (excluding sleep from 23:00 to 6:00) for five consecutive days. Clinical symptoms such as swelling, pain, dry or bitter mouth, dysphagia, reduced taste, and the function of major salivary glands were evaluated, including secretion index and saliva concentration index. The study found that I¹³¹ treatment caused some salivary gland damage: the incidence of gland injury (17.39%) in the 2-hour group was lower compared to the 24-hour group (26.96%). The frequency of acute gland injury (15.22%) and chronic gland injury (26.09%) in the 24-hour group was higher than in the 2-hour group (4.78% and 18.26%, respectively). Differences in the concentration indices of the left and right submandibular glands were observed after treatment in both groups, indicating a limited protective effect of vitamin C administration post-I¹³¹ therapy, as noted by G. Hayek & B. Kastler [38] and M. Faruque *et al.* [39].

Photobiomodulation can stimulate saliva production, regulate its composition, and control the redox mechanism of the salivary glands, reducing local inflammatory processes when used alongside radiation therapy. However, its long-term application requires further investigation. Replacement therapy with biologically active components that stimulate the functional activity of the salivary glands, combined with anti-inflammatory agents and remineralising treatments during polychemotherapy, provides only partial compensation for the remineralising function of saliva and does not affect its secretion rate. Oral administration of the parasympathomimetic bethanechol and vitamin E protects the salivary glands from damage during radiotherapy and enhances salivation. Vitamin C, used as a protector of the salivary glands during iodine-131 therapy, did not achieve the desired effect.

◆ CONCLUSIONS

The salivary glands are highly sensitive organs in various approaches to cancer treatment and often respond with partial or complete loss of function, leading to a significant decline in dental health, well-being, and overall quality of life for patients during therapy.

Studies on the effects of various cancer treatments on the submandibular salivary gland in experimental animals have revealed several morphological changes. Chemotherapy induces both degenerative and compensatory changes

◆ REFERENCES

- [1] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021;71(3):209–49. DOI: [10.3322/caac.21660](https://doi.org/10.3322/caac.21660)
- [2] Schleicher SM, Bach PB, Matsoukas K, Korenstein D. Medication overuse in oncology: Current trends and future implications for patients and society. *Lancet Oncol.* 2018;19(4). DOI: [10.1016/S1470-2045\(18\)30099-8](https://doi.org/10.1016/S1470-2045(18)30099-8)

es in the gland's parenchyma and stroma, accompanied by fibrosis of the interductal connective tissue. Radiation exposure leads to the destruction of epithelial cells in the granular excretory ducts and terminal sections, followed by short-term regenerative responses. However, after prolonged periods post-irradiation (180 days), there are disruptions in the nuclear-cytoplasmic ratios of exocrine cells, a reduction in interstitial space, and the accumulation of secretions in serous cells. High-frequency heating causes venous hyperaemia, stasis, hypertrophy, an increase in capillary numbers, and excessive detachment of epithelial cells in the excretory ducts. The use of ultrasound for selective tissue destruction of jaw tissues, activation of degenerative changes in glandular cellular structures at the beginning of the experiment and restoration of their structure and function in the long term are observed.

The use of photobiomodulation alongside radiotherapy has demonstrated positive outcomes in stimulating salivation, regulating saliva composition, and maintaining the redox mechanism in salivary glands, while also reducing inflammation. Topical applications of gel-based treatments containing functional salivary gland stimulants, anti-inflammatory agents, and remineralising properties, when administered during chemotherapy, proved insufficiently effective and resulted in only partial compensation of mineral imbalance. Bethanechol, used as a radioprotective agent, effectively reduced acute salivary gland damage, improving both physiological and subjective health indicators in patients. A six-month follow-up of patients who received vitamin E after iodine-131 therapy for thyroid cancer showed an improvement in the functional performance of major salivary glands, confirming the substantial restorative effect of this vitamin on the glands in both men and women. Short-term vitamin C intake following radioiodine therapy produced only a minor positive effect.

The onset and progression of structural and functional reorganisation of the salivary glands in oncological pathology necessitate exploring unconventional perspectives on the issue, as well as the development of innovative methods and approaches for its prevention, the restoration of glandular structure and function, and subsequent rehabilitation measures for clinical application. Greater emphasis should be placed on the use of supplementary diagnostic techniques for assessing salivary gland damage, including morphometric analysis, which enables the identification of specific structural changes and supports a more individualised approach to selecting corrective treatment methods.

◆ ACKNOWLEDGEMENTS

Professor Fedonyuk L. for their valuable advice on this manuscript.

◆ CONFLICT OF INTEREST

None.

- [3] Kyaw JYA, Rendall A, Gillespie EF, Roques T, Court L, Lievens Y, et al. Systematic review and meta-analysis of the association between radiation therapy treatment volume and patient outcomes. *Int J Radiat Oncol Biol Phys.* 2023;117(5):1063–86. DOI: [10.1016/j.ijrobp.2023.02.048](https://doi.org/10.1016/j.ijrobp.2023.02.048)
- [4] Gevkaliuk N, Sydljaruk N, Posolenyk L, Vydoinyk O, Kuchyrka L. [The state of oxidative homeostasis in children with influenza stomatitis](#). *Wiad Lek.* 2019;72(3):405–8.
- [5] Deshpande T, Gunn GB, Fuller CD, Ye R, Rosenthal DI, Garden AS, et al. Xerostomia impacts dysgeusia in oropharyngeal cancer patients treated with proton therapy. *Int J Radiat Oncol Biol Phys.* 2019;105(1). DOI: [10.1016/j.ijrobp.2019.06.1517](https://doi.org/10.1016/j.ijrobp.2019.06.1517)
- [6] Galaniha LT, Nolden AA. The role of saliva in taste dysfunction among cancer patients: Mechanisms and potential treatment. *Oral Oncol.* 2022;133:106030. DOI: [10.1016/j.oraloncology.2022.106030](https://doi.org/10.1016/j.oraloncology.2022.106030)
- [7] Iijima Y, Yamada M, Endo M, Sano M, Hino S, Kaneko T, Horie N. Dysgeusia in patients with cancer undergoing chemotherapy. *J Oral Maxillofac Surg Med Pathol.* 2019;31(3):214–17. DOI: [10.1016/j.ajoms.2019.01.006](https://doi.org/10.1016/j.ajoms.2019.01.006)
- [8] Silva IMV, Donaduzzi LC, Perini CC, Couto SAB, Werneck RI, de Araújo MR, et al. Association of xerostomia and taste alterations of patients receiving antineoplastic chemotherapy: A cause for nutritional concern. *Clin Nutr ESPEN.* 2021;43:532–35. DOI: [10.1016/j.clnesp.2021.03.006](https://doi.org/10.1016/j.clnesp.2021.03.006)
- [9] Brook I. Late side effects of radiation treatment for head and neck cancer. *Radiat Oncol J.* 2020;38(2):84–92. DOI: [10.3857/ROJ.2020.00213](https://doi.org/10.3857/ROJ.2020.00213)
- [10] Riantiningtyas RR, Valenti A, Dougkas A, Bredie WLP, Kwiecien C, Bruyas A, Giboreau A, Carrouel F. Oral somatosensory alterations and salivary dysfunction in head and neck cancer patients. *Support Care Cancer.* 2023;31(12):627. DOI: [10.1007/s00520-023-08086-7](https://doi.org/10.1007/s00520-023-08086-7)
- [11] Huang Z, Chen Y, Pan L, Feng H, Wu J, Chen P, Wang J, Ouyang W. Progressive changes in the major salivary gland after radioiodine therapy for differentiated thyroid cancer: A single-center retrospective ultrasound cohort study. *Ultrasound Med Biol.* 2021;47(9):2514–22. DOI: [10.1016/j.ultrasmedbio.2021.05.013](https://doi.org/10.1016/j.ultrasmedbio.2021.05.013)
- [12] Klein BA, Alves FA, de Santana Rodrigues Velho J, Vacharotayangul P, Hanna GJ, et al. Oral manifestations of immune-related adverse events in cancer patients treated with immune checkpoint inhibitors. *Oral Dis.* 2022;28(1):9–22. DOI: [10.1111/odi.13964](https://doi.org/10.1111/odi.13964)
- [13] Herashchenko S, Hvozdyk I, Dyel'tsova O. [Morpho-functional changes of the submandibular gland under the influence of cisplatin and their correction with enterosgel in the experiment](#). *Sci Bull Uzhhorod Univ.* 2010;(38):7–11.
- [14] Willems RAL, Winckers K, Biesmans C, de Vos-Geelen J, ten Cate H. Evolving data on cardiovascular complications in cancer. *Thromb Res.* 2022;213(Suppl 1). DOI: [10.1016/j.thromres.2022.01.003](https://doi.org/10.1016/j.thromres.2022.01.003)
- [15] Kirwan CC, Blower EL. Contemporary breast cancer treatment-associated thrombosis. *Thromb Res.* 2022;213(Suppl 1):8–15. DOI: [10.1016/j.thromres.2021.12.025](https://doi.org/10.1016/j.thromres.2021.12.025)
- [16] Farokh A, Pourmadadi M, Rashedi H, Yazdian F, Navaei-Nigjeh M. Assessment of synthesized chitosan/halloysite nanocarrier modified by carbon nanotube for pH-sensitive delivery of curcumin to cancerous media. *Int J Biol Macromol.* 2023;237:123937. DOI: [10.1016/j.ijbiomac.2023.123937](https://doi.org/10.1016/j.ijbiomac.2023.123937)
- [17] Bomeli SR, Desai SC, Johnson JT, Walvekar RR. Management of salivary flow in head and neck cancer patients – a systematic review. *Oral Oncol.* 2008;44(11):1000–8. DOI: [10.1016/j.oraloncology.2008.02.007](https://doi.org/10.1016/j.oraloncology.2008.02.007)
- [18] Radfar L, Sirois DA. Structural and functional injury in minipig salivary glands following fractionated exposure to 70 Gy of ionizing radiation: An animal model for human radiation-induced salivary gland injury. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2003;96(3):267–74. DOI: [10.1016/S1079-2104\(03\)00369-X](https://doi.org/10.1016/S1079-2104(03)00369-X)
- [19] Huisman F, Van Elst JM, Reyners AKL, De Haan JJ, Oei M, Visser O, Kramer EPA. [Taste and smell changes resulting from cancer therapies](#). *Ned Tijdschr Geneesk.* 2021;165:D5696.
- [20] Mercadante V, Jensen SB, Smith DK, Bohlke K, Bauman J, Brennan MT, et al. Salivary gland hypofunction and/or xerostomia induced by nonsurgical cancer therapies: ISOO/MASCC/ASCO guideline. *J Clin Oncol.* 2021;39(25):2825–43. DOI: [10.1200/JCO.21.01208](https://doi.org/10.1200/JCO.21.01208)
- [21] Bidram E, Esmaeili Y, Ranji-Burachaloo H, Al-Zaubai N, Zarrabi A, Stewart A, Dunstan DE. A concise review on cancer treatment methods and delivery systems. *J Drug Deliv Sci Technol.* 2019;54:101350. DOI: [10.1016/j.jddst.2019.101350](https://doi.org/10.1016/j.jddst.2019.101350)
- [22] de Lucas B, Pérez LM, Bernal A, Gálvez BG. Ultrasound therapy: Experiences and perspectives for regenerative medicine. *Genes.* 2020;11(9):1086. DOI: [10.3390/genes11091086](https://doi.org/10.3390/genes11091086)
- [23] Tarasenko L, Bilets M. [Mechanisms of oral cavity tissues stress damages \(a brief review of the literature and our own research\)](#). *Ukr Dent Almanac.* 2016;2(1):23–25.
- [24] Patel VN, Hoffman MP. Salivary gland development: A template for regeneration. *Semin Cell Dev Biol.* 2014;25-26:52–60. DOI: [10.1016/j.semcdb.2013.12.001](https://doi.org/10.1016/j.semcdb.2013.12.001)
- [25] Louzeiro GC, Cherubini K, de Figueiredo MA, Salum FG. Effect of photobiomodulation on salivary flow and composition, xerostomia and quality of life of patients during head and neck radiotherapy in short term follow-up: A randomized controlled clinical trial. *J Photochem Photobiol B.* 2020;209:111933. DOI: [10.1016/j.jphotobiol.2020.111933](https://doi.org/10.1016/j.jphotobiol.2020.111933)
- [26] Debela DT, Muzazu SG, Heraro KD, Ndalama MT, Mesele BW, Haile DC, et al. New approaches and procedures for cancer treatment: Current perspectives. *SAGE Open Med.* 2021;9. DOI: [10.1177/20503121211034366](https://doi.org/10.1177/20503121211034366)
- [27] Roth P, Winklhofer S, Müller AMS, Dummer R, Mair MJ, Gramatzki D, et al. Neurological complications of cancer immunotherapy. *Cancer Treat Rev.* 2021;97:102189. DOI: [10.1016/j.ctrv.2021.102189](https://doi.org/10.1016/j.ctrv.2021.102189)
- [28] Tkachenko P, Kaskova L, Popelo Y. [Correction of speed of salivation and mineralizing potential of the oral fluid in children with malignant tumors of soft tissues, who receive chemotherapy](#). *Ukr Dent Almanac.* 2015;5:65–70.

- [29] Nolden AA, Hwang L-D, Boltong A, Reed DR. Chemosensory changes from cancer treatment and their effects on patients' food behavior: A scoping review. *Nutrients*. 2019;11(10):2285. DOI: [10.3390/nu11102285](https://doi.org/10.3390/nu11102285)
- [30] Larsen AK, Thomsen C, Sanden M, Skadhauge LB, Anker CB, Mortensen MN, Bredie WLP. Taste alterations and oral discomfort in patients receiving chemotherapy. *Support Care Cancer*. 2021;29(12):7431–39. DOI: [10.1007/s00520-021-06316-4](https://doi.org/10.1007/s00520-021-06316-4)
- [31] Manoharan S, Thangavelu L, Dua K, Chellappan DK. Advanced drug delivery systems in oral cancer. In: *Advanced drug delivery systems in the management of cancer*. New York: Academic Press 2021; p. 235–42. DOI: [10.1016/B978-0-323-85503-7.00022-5](https://doi.org/10.1016/B978-0-323-85503-7.00022-5)
- [32] Campagna S, Gonella S, Sperlinga R, Giuliano PL, Marchese R, Pedersini R, et al. Prevalence, severity, and self-reported characteristics of taste alterations in patients receiving chemotherapy. *Oncol Nurs Forum*. 2018;45(3):342–53. DOI: [10.1188/18.ONF.342-353](https://doi.org/10.1188/18.ONF.342-353)
- [33] Campanhã D, Pereira Lima EN, Alves FA, Jaguar GC. Bethanechol used to prevent salivary gland dysfunction in patients submitted to radioactive iodine therapy: A double-blind, placebo-controlled, randomized study. *J Stomatol Oral Maxillofac Surg*. 2022;123(5): 626–30. DOI: [10.1016/j.jormas.2021.12.014](https://doi.org/10.1016/j.jormas.2021.12.014)
- [34] Upadhyaya A, Meng Z, Wang P, Zhang G, Jia Q, Tan J, et al. Effects of first radioiodine ablation on functions of salivary glands in patients with differentiated thyroid cancer. *Medicine (Baltimore)*. 2017;96(25). DOI: [10.1097/MD.00000000000007164](https://doi.org/10.1097/MD.00000000000007164)
- [35] Buttiron Webber T, Briata IM, DeCensi A, Cevasco I, Paleari L. Taste and smell disorders in cancer treatment: Results from an integrative rapid systematic review. *Int J Mol Sci*. 2023;24(3):2538. DOI: [10.3390/ijms24032538](https://doi.org/10.3390/ijms24032538)
- [36] Tchelebi LT, Shen B, Wang M, Gusani NJ, Walter V, Abrams R, et al. Impact of radiation therapy facility volume on survival in patients with cancer. *Cancer*. 2021;127(21):4081–90. DOI: [10.1002/cncr.33777](https://doi.org/10.1002/cncr.33777)
- [37] Liu Y, Wang Y, Zhang W. Optimal administration time of vitamin C after 131I therapy in differentiated thyroid cancer based on propensity score matching. *Front Surg*. 2022;9:993712. DOI: [10.3389/fsurg.2022.993712](https://doi.org/10.3389/fsurg.2022.993712)
- [38] Hayek G, Kastler B. Interventional radiology for treatment of bone metastases. *Cancer*. 2020;24(5):374–78. DOI: [10.1016/j.canrad.2020.04.006](https://doi.org/10.1016/j.canrad.2020.04.006)
- [39] Faruque M, Wanschers M, Ligtenberg AJ, Laine ML, Bikker FJ. A review on the role of salivary MUC5B in oral health. *J Oral Biosci*. 2022;64(4):392–99. DOI: [10.1016/j.job.2022.09.005](https://doi.org/10.1016/j.job.2022.09.005)

Структурно-функціональна реорганізація слинних залоз при онкопатології: міні огляд

Лариса Посоленик

Кандидат медичних наук, доцент
Тернопільський національний медичний університет імені І. Я. Горбачевського
Міністерства охорони здоров'я України
46001, майдан Волі, 1, м. Тернопіль, Україна
<https://orcid.org/0000-0002-1656-4420>

Анотація. Дисфункції слинних залоз при терапії доброякісних та злоякісних пухлинних захворювань є широко діагностованою проблемою серед онкопацієнтів. Метою даної роботи стало вивчення порушення структури слинних залоз внаслідок лікування онкологічних хвороб та методів їх корекції й усунення. Було проаналізовано 39 наукових робіт. Використано методи пошуку, порівняння, систематичії та об'єднання результатів проведених досліджень. Доведено деструктивний вплив хіміо- та радіотерапії, лікування злоякісних пухлин шляхом підвищення температури всього тіла на структуру слинних залоз в експерименті. Вплив ультразвуку низької інтенсивності на піднижньощелепну залозу демонструє високі адаптивні та регенеративні властивості її тканин. Дані клінічних досліджень щодо корекції та усунення дисфункцій слинних залоз у онкохворих показали неоднозначний результат. Застосування фотобіомодуляції одночасно із променевою терапією у пацієнтів із пухлинами голови чи шиї значно покращує функціонування органа: стимулює слиновиділення, регулює склад слини, контролює окислювально-відновний механізм слинних залоз та місцево усуває запалення. Виявлено незначну компенсацію мінералізуючої функції слини при замісній терапії біологічно активними компонентами та ремінералізуючим препаратом у дітей зі злоякісними пухлинами при хіміотерапії. Відмічається позитивний ефект застосування бетанехолу та вітаміну Е у протекції слинних залоз при лікуванні раку в ділянках голови та шиї методом радіотерапії, який полягає у покращенні структури та функції залоз у довготривалому періоді та є однаковим у жінок і чоловіків. Дослідження вживання вітміну С після радіоїодтерапії у пацієнтів з раком голови чи шиї показало його недостатній відновлюваний ефект кількісного і якісного складу слини. Результати проведеного огляду можуть стати підґрунтям для точної оцінки онкологами уражень слинних залоз та патогенезу їх дисфункцій внаслідок онкотерапії, надати можливість переглянути вже існуючі погляди на проблему, розробити нові методи запобігання і лікування вказаних ускладнень, покращити якість життя і процес виживання пацієнта

Ключові слова: онкологія; дисфункція; хіміотерапія; морфометрія; радіація