



Literature Review

THE ROLE OF CONTINUOUS MONITORING IN ONCOLOGY PATIENTS RECEIVING RADIOTHERAPY OR CHEMOTHERAPY. REVIEW

Davit Mathevosyan DDS, PhD¹¹Associate Professor, Department of Oral and Maxillofacial Surgery, Yerevan State Medical University after M. Heratsi, Yerevan, Armenia

Received: Dec 1, 2024; Accepted: Dec 22, 2024 Published: Jan 15, 2025

Abstract

Background: Oral cancer is a major public health problem worldwide and the prevention of oral cancer and its associated morbidity and mortality depends on early detection. Delayed diagnosis is a major contributor to the dismal oral cancer survival rate over five years. Currently, various monitoring methods have been actively used for the purpose of active early detection of asymptomatic oral cancer.

This study provides an overview of the main concepts and principles of organizing continuous monitoring in oncology patients receiving radiotherapy or chemotherapy.

Methods: This review was reported per the PRISMA guidelines and was conducted in publications covering scientific research on diagnostics, oral management protocols, prevention and monitoring in patients receiving radiotherapy, chemotherapy for malignant neoplasms in Medline, Scopus, Web of science, PubMed (search 162 which finally included 75 articles).

Two review authors screened the results of the searches against inclusion criteria, extracted data and assessed risk of bias independently and in duplicate.

Results: To prevent or minimize oral complications, an appropriate oncology protocol is needed which should include early oral assessment prior to treatment. Early recognition and diagnosis can improve patient survival and reduce morbidity.

Conclusion: Continuous monitoring of patients with in primary care settings receiving radiation therapy or chemotherapy may reduce oral complications and improve the effectiveness of combination therapy. To reduce the risk of complications in the oral cavity, it is very important to pre-treat existing oral diseases, and in this aspect, the cooperation of the dentist and oncologist as one team is very important. This review will help dental practitioners manage the risks and prevent potential complications in patients with oral complications requiring dental care.

Keywords: oral potentially malignant disorders, Oral cancer, chemotherapy, radiation therapy, prevent complications, monitoring oral cancer

INTRODUCTION

Treatment of cancer at early stages is one of the most urgent in medicine, since the results of standard generally accepted methods often do not give the desired results^{1,2}.

In the mid-1980s, when it was proven that adding chemotherapy to radiotherapy and/or surgery improves the survival of cancer patients, by means of multidisciplinary approach emerged in oncology³.

The treatment of cancers is ideally a multidisciplinary approach involving the efforts of

surgeons, radiation oncologists, chemotherapy oncologists, nutritionists, and rehabilitation as well as restorative specialists^{4,5}. The location, size of the tumor, lymph node involvement, and the presence or absence of distant metastases are important factors in choosing a specific treatment option. The most common cancer treatment is oncosurgery.

When treating a localized primary tumor with en bloc surgical procedures, this technique is the most effective method⁶.

Chemotherapy and radiation therapy are included in the complex methods of treatment of malignant diseases. Radiation therapy is the use of a special type of energy of electromagnetic radiation or beam

of elementary nuclear particles that can kill tumor cells or inhibit their growth and division⁷.

Radiation damages both normal cells and cancer cells. Normal cells can usually recover more quickly and maintain their normal functional status than cancer cells. Some healthy cells that fall into the irradiation zone are also damaged, but most of them are able to recover⁸.

Tumor cells divide faster than the healthy cells surrounding them. Therefore, radiation has a more destructive effect on them. These differences determine the effectiveness of radiation therapy for cancer. During radiotherapy, tumor cells experience a decrease in their proliferation rate due to DNA damage-induced cell cycle arrest⁹.

Radiation therapy before cancer surgery (neoadjuvant therapy) is aimed at shrinking the tumor. Radiation therapy after surgery (adjuvant therapy) will kill any microscopic tumor cells that remains¹⁰.

Often, to destroy tumor cells, radiation is carried out together with antitumor drugs (chemotherapy)¹¹⁻¹³.

To date, the agents found to be most effective for treating oral cancer include cisplatin, carboplatin, taxanes, 5-fluorouracil, methotrexate, and ifosfamide¹⁴.

Chemotherapeutic drugs act preferentially on cells that are divided at a higher rate, causing malignant cells to be destroyed faster than normal cells at the tumor site. However, chemotherapeutic drugs will also seriously affect normal cells, causing side effects including: myelosuppression (leukopenia, thrombocytopenia, and anemia), nausea, vomiting, diarrhea, mucosal ulceration, dermatitis, and alopecia¹⁵.

The choice of chemo-preventive drugs, dosage and duration of treatment is mainly based on the type and stage of cancer^{16,17}.

In most cases, a team of specialists including radiologists, dieticians, psychologists and a primary consultant jointly decide on treatment plans, dosage, duration of cycles and additional supplements.

Radiation therapy and chemotherapy like any other type of treatment, may be accompanied by general and local (in the area of tissue exposure to radiation) side effects^{18,19}.

These effects may be acute (short-term, occur during treatment) and chronic (develop several weeks or even years after the end of treatment). Long-term exposure to these drugs can have excessively adverse effects on the patient's physical and mental health, making it difficult to continue ongoing treatment. Side effects of radiotherapy most often manifest themselves in tissues and organs that have been

directly exposed to radiation. Most side effects that develop during treatment are relatively mild and are treated with medication or proper nutrition²⁰.

When using radiation therapy and chemotherapy, a number of complications arise in the oral cavity in the form of a number of oral diseases²¹⁻³¹.

Complications after radiotherapy and chemotherapy appear 7–14 days after the start of the course and have a significant impact on the quality of life of patients³²⁻³⁴.

This complication may lead to changes or interruptions in treatment, which affects cure rates. There are various factors in the etiopathogenesis of complications in the oral cavity associated with chemotherapy and radiation therapy for treatment of cancers³⁵⁻³⁷.

Chemotherapy and radiation therapy lead to the death of basal epithelial cells, slow or stop the growth of new cells, disrupt normal tissue healing, because of the replication of basal epithelial cells is disrupted^{38,39}.

Among the factors, pro-inflammatory cytokines and bacterial metabolic products may also play a role, also weaken the oral immune system due to the loss of tissue immune cells. Among complications in the oral cavity during radiotherapy and cancer chemotherapy, dental caries, periodontitis, mucositis, fibrosis, oropharyngeal candidiasis, oral infections (viral, fungal, bacterial), infection caused by the herpes simplex virus - herpetic gingivostomatitis, chronic recurrent aphthous stomatitis, hypofunction of the salivary glands and xerostomia, neurosensory disorders (pain in the mucous membrane and taste dysfunction)⁴⁰⁻⁴³.

Mucositis is the most common disease of the oral cavity, patients treated with chemotherapy/radiotherapy are effected up to 34%–43%.

Mucositis with clinical manifestations of varying severity, from ulceration to an inflammatory process, in which the patient has difficulty eating solid food can seriously affect the comfort and well-being of patients^{44,45}.

Mucositis patients are associated with an increased risk of infection, pain, decreased food intake and malnutrition, and can impact on the effectiveness of treatment⁴⁶. These complications significantly worsen the quality of life of patients. In some cases, oral mucositis is the reason for interrupting courses of antitumor therapy. Accordingly, the effectiveness of the planned and ongoing chemotherapeutic treatment is reduced. These same reasons can have a detrimental effect on the long-term results of the planned treatment as a whole.

This review provides an overview of the main concepts and principles of organizing continuous monitoring in oncology patients receiving radiotherapy or chemotherapy.

Methods

Comprehensive Search Strategy

This review was reported per the PRISMA guidelines and was conducted in publications covering scientific research on diagnostics, oral management protocols, prevention and monitoring in patients receiving radiotherapy, chemotherapy for malignant neoplasms in Medline, Scopus, Web of science, PubMed (search 162 which finally included 75 articles).

Review author screened the results of the searches against inclusion criteria, extracted data and assessed risk of bias independently and in duplicate. Potentially eligible studies underwent a full-text review, and discrepancies between reviewers were resolved through discussion. Reviewers identify and document the threats to validity of each study due to faulty execution or poor measurement.

Inclusion criteria: included clinical trials, considered randomized controlled trials, cross-sectional studies, case-control studies, and cohort studies in human subjects that evaluated the current literature on the oral cancer, oral squamous cell carcinoma, head and neck carcinoma, systematic screening, diagnostics, oral management protocols, prevention and monitoring in patients receiving radiotherapy, chemotherapy for malignant neoplasms written in English articles. There was no limitation on minimal quality, minimal sample size, or the number of patients.

Exclusion criteria were: original primary studies, due to language limitations, abstracts, letters to the editor, book chapters, case reports, conference abstracts, duplicate publications, and in vitro and in vivo animal experimental studies.

Data extraction

2 reviewers extracted data from the included studies using a standardized data extraction form. Reviewers identify and document the threats to validity of each study due to faulty execution or poor measurement. Discrepancies in data extraction were resolved by discussion.

Quality assessment

The effectiveness were evaluated by synthesising relevant outcome data extracted from selected studies. For prevention and monitoring in patients receiving radiotherapy, chemotherapy for malignant neoplasms, screening methods that reduce cancer incidence and detect precancerous lesions. The effectiveness' program in cancer screening, is usually

cancer mortality, defined as the number of deaths from the cancer.

Data synthesis

The results of this review were reported following the PRISMA guidelines. A narrative synthesis of the findings was provided.

Effect measures

Evaluating the effectiveness of a monitoring program for patients with malignant neoplasms receiving radiotherapy and chemotherapy is an important criterion.

Results of the search

Conducted a preliminary search and reviewed titles and abstracts in this review and 75 full-text articles were selected of high methodological quality. For a further description of our screening process, see the study flow diagram in figure 1.

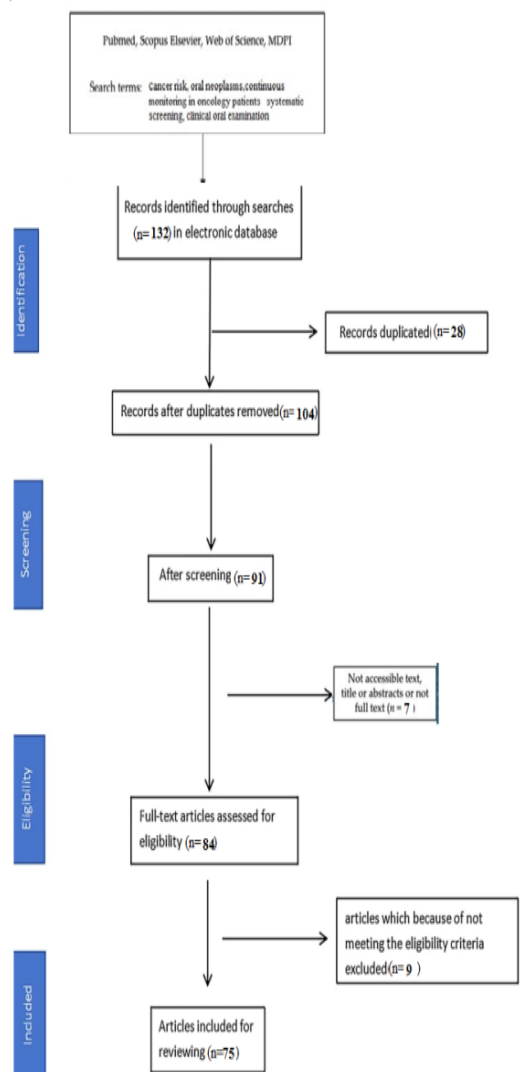


Figure 1. Diagram study flow method used the PRISMA

Risk of bias in included studies

In developing the data collection instrument, we considered. The form collects information needed to monitor the status of screening, reviewing and summarizing of each article by 2 reviewers.

Developing tables that summarize the body of evidence. The form captures detailed descriptive data about the intervention and evaluation.

Classifying other key characteristics of the intervention and assessing the quality of the study’s execution. Reviewers identify and document the threats to validity of each study due to faulty execution or poor measurement. This information is used as a criterion for continued inclusion of the study in the body of evidence for an intervention.

Following the study design, has identified domains rating the certainty of evidence: risk of bias, inconsistency, inconsistency, imprecision, and publication bias.

To reduce the side effects of chemotherapy and radiation therapy of the head and neck, it is necessary to develop a set of preventive measures and, when possible, use minimally invasive surgical methods such as (transoral robotic surgery, transoral laser microsurgery) ^{47,48}.

For oral care, complication chemotherapy and radiation therapy it is recommended to use standardized oral care protocol ⁴⁹⁻⁵¹ (figure 2).

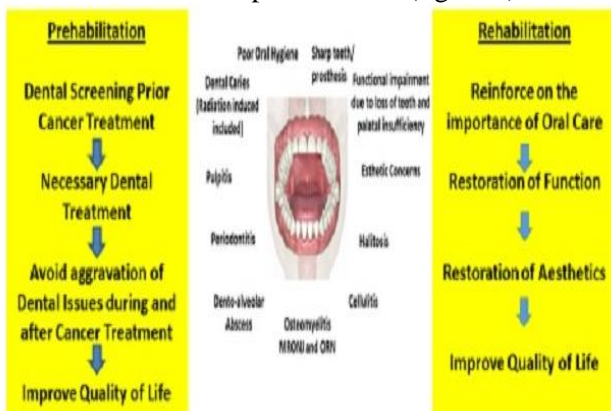


Figure.2 Oral care protocols complication chemotherapy and radiation therapy

Treatment is symptomatic, for pain relief, topical analgesics may be useful. Although protocols for the management of patients in this category are constantly updated, however, there are no universally effective protocols for the prevention of side effects of chemotherapy and radiation therapy for cancer. To prevent complications of chemotherapy and radiation therapy and achieve optimal comprehensive oral care, the key point is the organization of oral care rooms in cancer centers and constant dynamic

monitoring ⁵².

Many studies argue for a multidisciplinary approach to the management of these patients, cooperation of the dentist and oncologist as one team is very important ⁵³. The main role of the dentist during chemotherapy and radiation therapy is to minimize undesirable consequences and deliver timely treatments ⁵⁴⁻⁵⁶.

Cancer screening is indicated for all patients with cancer. The screening program for each disease is unique and includes a specific list of necessary examinations ⁵⁷⁻⁵⁹.

There are several types of tests and recommendations for cancer screening. The Cancer screening can be carried out using medical examinations, blood tests, radiological (visualizing) tests, such as computed tomography (CT) positron emission tomography and specific MRI parameters, and biomarker testing ⁶⁰⁻⁶³. Recommendations for cancer screening are different for people of different ages, as well as for each organ examined separately and depend on the risk factors that exist for a given type of cancer ⁶⁴.

Screening diagnostics contributes to effective treatment and maintaining the quality of life of this category of patients at a decent level. To establish a diagnosis, it is necessary to conduct a full-fledged comprehensive screening examination, which allows identifying pathological changes in the oral cavity at early stages ⁶⁵(figure3).

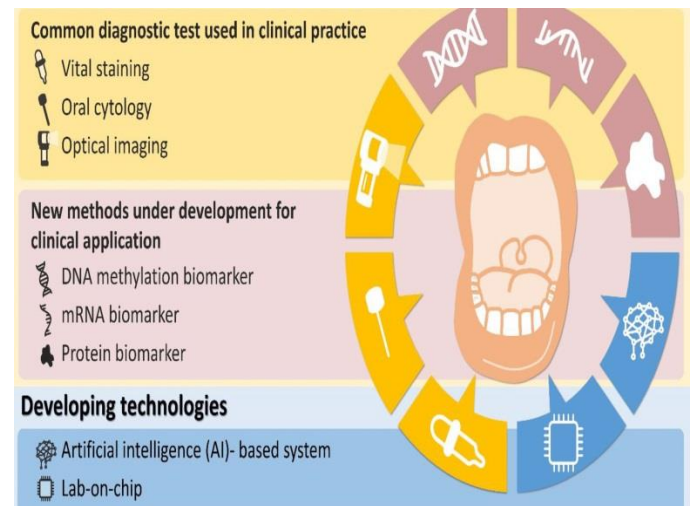


Figure 3. Examples of individual screening timing patterns

An oral/dental assessment including radiographs should be performed prior to initiating cancer therapy ^{66,67}.

- Identify existing oral diseases and potential risk for oral diseases.

- Eliminate oral/dental infectious foci prior to initiating cancer therapy.
- Prepare the patient for expected side effects of cancer therapy.
- Establish an adequate standard of oral hygiene to address increasing challenges during cancer therapy.
- Develop a plan for maintaining oral hygiene, providing preventive care, completing oral rehabilitation, and follow-up.
- Establish appropriate multidisciplinary collaboration within the cancer center to reduce/alleviate oral symptoms and consequences before, during, and after cancer therapy.

During external examination, it is necessary to pay attention to the configuration of the face, its symmetry, skin color, palpate the lymph nodes, study the condition of the temporomandibular joint, nasolabial folds, red border of the lips and skin around the lips.

During intraoral examination, the mucous membrane of the lips, cheeks, mucous membrane of the vestibular and oral surfaces of the alveolar process of the upper and lower jaws, hard and soft palate, pharynx, all surfaces of the tongue, the floor of the oral cavity should be studied (figure 4).

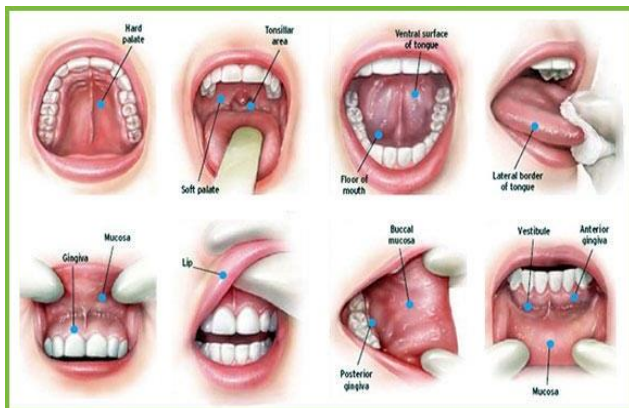


Figure.4 Oral Cancer Screening chart to check visual examination of the oral cavity (VOE)

A detailed assessment of the elements of the oral cavity lesion is carried out, which includes an assessment of the change in color, in which they could be white, red or combined, assess the change in relief, which can be smooth, convex, concave or elevated. Determine the violation of the integrity of the epithelium, localization, shape, size, depth of the lesion. Using palpation, it is possible to determine

pain in comparison with the surrounding tissues, determine the area of the lesion and its contours. Assess the condition of the periodontal tissues, determining the presence of supragingival and subgingival dental plaque, gum inflammation, the presence of periodontal pockets and gum recessions, tooth mobility, changes in the position of the teeth, the condition of the hard tissues of the teeth, dentures and dentition. Using dental radiographs, determine the foci of odontogenic infection, such as apical periodontitis.

Based on the clinical examination, according to the indications, conduct emergency care professional oral hygiene. Recommendations were given for oral care, hygiene products were selected. Monitoring should include not only clinical and instrumental examinations but also a survey^{68,69}.

The questionnaire should include questions regarding dental status and deterioration of quality of life due to pain, nutritional problems, communication difficulties. Patients (with the help of a dentist) should answer the proposed questions on a point scale.

1. Do you notice any tongue movement disorder/restriction?
 - none;
 - discomfort;
 - partially limited;
 - severely limited;
 - impossible.
2. Do you notice any taste disorder?
 - normal taste perception;
 - distorted taste perception in the presence of a stimulus;
 - distorted taste perception without a stimulus;
 - distorted taste perception with partial loss;
 - total absence of taste perception.
3. Do you notice any chewing disorder?
 - no difficulty;
 - discomfort;
 - partially limited;
 - severely limited;
 - impossible.
4. Do you notice any eating disorder?
 - no difficulty;
 - moderate discomfort;
 - severe discomfort;
 - limited, only liquid forms;
 - eating is impossible.
5. Do you notice any speech production disorder?

- none;
 - moderate discomfort during prolonged conversation;
 - severe discomfort during conversation;
 - limited;
 - impossible.
6. Do you/your loved ones notice halitosis (bad breath)?
- no smell;
 - weak, undetectable smell when speaking;
 - weak, but detectable smell when speaking;
 - moderately pronounced, unpleasant smell;
 - strongly pronounced, intolerable smell.
7. Burning sensation in the mouth:
- absent;
 - periodic, short-term;
 - periodic, prolonged;
 - constant, moderate intensity;
 - constant, intolerable (intensity)
 - significantly pronounced)
8. Painful sensations in the mouth:
- absent;
 - periodically occurring, short-term;
 - periodically occurring, prolonged (long-term);
 - constant, moderate intensity;
 - constant, intolerable.
9. Xerostomia (dry mouth):
- absent;
 - dry mouth appears after long conversations;
 - constant dry mouth, difficulty speaking and eating;
 - severe dry mouth, pain during talking and eating.

Evaluation of common side effects in patients receiving anticancer drugs should include myelosuppression, nausea, vomiting, oral complications, diarrhea, hypertension. Based on the clinical examination, according to the indications, conduct emergency care professional oral hygiene. Recommendations were given for oral care. Oral hygiene products were selected. Patients should be taught to record side effects of treatment when they occur. For safe complex antitumor treatment, patient monitoring is very important as it helps to identify toxicity and complications at an early stage, allows for quick action, prevents serious complications and possible hospitalization. To improve the quality of life for patients with malignant disease, who are

receiving cancer therapy that has implications for oral comfort and function, by promoting consistent, evidence-based high standards of oral care through a co-ordinated team approach⁷⁰.

The oncology patient will require a multidisciplinary approach to achieve the best oral outcomes⁷¹⁻⁷³.

This review provided useful information evaluating prophylactic interventions for oral complications in cancer patients.

Most patients who receive a course of radiotherapy and chemotherapy in the complex treatment of cancer experience various oral complications^{74,75}.

In patients receiving radiotherapy or chemotherapy the pathological changes appear on the mucous membranes of oral cavity, on the skin, in the subcutaneous tissue, salivary glands and in the bone marrow of the jaw bones. To reduce the risk of complications in the oral cavity, it is very important to pre-treat existing oral diseases, and in this aspect, the cooperation of the dentist and oncologist as one team is very important. There are different protocols for oral care, monitoring, cancer patients, in which the main focus is on prophylaxis and pain relief.

CONCLUSION

Continuous monitoring of patients with in primary care settings receiving radiation therapy or chemotherapy may reduce oral complications and improve the effectiveness of combination therapy. This review will help dental practitioners manage the risks and prevent potential complications in patients with oral complications requiring dental care.

DECLARATIONS

Conflicts of interest and financial disclosures

The author declares that he has no conflict percent and there was no external source of funding for the research in question.

Ethical approval

The study was approved by the Institutional Ethics Committee and was conducted in accordance with the Declaration of the World Medical Association.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Source of funding

The work was not funded.

REFERENCES

1. Debela DT, Muzazu SG, Heraro KD, Ndalama MT, Mesele BW, Haile DC, Kitui SK, Manyazewal T. New approaches and procedures for cancer treatment: Current perspectives. *SAGEOpenMed*.2021;12(9):20503121211034366. doi: 10.1177/20503121211034366.
2. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021; 71: 209–249.
3. Ruhstaller T, Roe H, Thürlimann B, Nicoll JJ. The multidisciplinary meeting: An indispensable aid to communication between different specialities. *Eur J Cancer*. 2006;42(15):2459-62. doi: 10.1016/j.ejca.2006.03.034
4. Taberna M, Gil Moncayo F, Jané-Salas E, Antonio M, Arribas L, Vilajosana E, Peralvez Torres E, Mesía R. The Multidisciplinary Team (MDT) Approach and Quality of Care. *Front Oncol*.2020;20;10:85. doi: 10.3389/fonc.2020.00085.
5. Bayat Mokhtari R, Homayouni TS, Baluch N, Morgatskaya E, Kumar S, Das B, Yeger H. Combination therapy in combating cancer. *Oncotarget*.2017;8(23):38022-38043. doi: 10.18632/oncotarget.16723.
6. Boriani S. En bloc resection in the spine: a procedure of surgical oncology. *J Spine Surg*. 2018;4(3):668-676. doi: 10.21037/jss.2018.09.02
7. Baskar R, Lee KA, Yeo R, Yeoh KW. Cancer and radiation therapy: current advances and future directions. *Int J Med Sci*. 2012;9(3):193-9. doi: 10.7150/ijms.3635.
8. Wang JS, Wang HJ, Qian HL. Biological effects of radiation on cancer cells. *Mil Med Res*. 2018;5(1):20. doi: 10.1186/s40779-018-0167-4.
9. Carlos-Reyes A, Muñiz-Lino MA, Romero-García S, López-Camarillo C, Hernández-de la Cruz ON. Biological Adaptations of Tumor Cells to Radiation Therapy. *Front Oncol*. 2021;11:718636. doi: 10.3389/fonc.2021.718636.
10. Huang, RX., Zhou, PK. DNA damage response signaling pathways and targets for radiotherapy sensitization in cancer. *Sig TransductTargetTher* .2020;5,60. <https://doi.org/10.1038/s41392-020-0150-x>
11. Anand U, Dey A, Chandel AKS, Sanyal R, Mishra A, Pandey DK, De Falco V, Upadhyay A, Kandimalla R, Chaudhary A, Dhanjal JK, Dewanjee S, Vallamkondu J, Pérez de la Lastra JM. Cancer chemotherapy and beyond: Current status, drug candidates, associated risks and progress in targeted therapeutics. *Genes Dis*. 2022;10(4):1367-1401. doi: 10.1016/j.gendis.2022.02.007.
12. Roxana Liana Lucaciu, Adriana Corina Hangan, Bogdan Sevastre, Luminița Simona Oprean. Metallo-Drugs in Cancer Therapy: Past, Present and Future. *Molecules* 2022, 27(19), 6485; <https://doi.org/10.3390/molecules27196485>
13. DeVita VT Jr, Chu E. A history of cancer chemotherapy. *Cancer Res*. 2008;68(21):8643-53. doi: 10.1158/0008-5472.CAN-07-6611.
14. Tsvetkova D, Ivanova S. Application of Approved Cisplatin Derivatives in Combination Therapy against Different Cancer Diseases. *Molecules*.2022;27(8):2466. doi: 10.3390/molecules27082466.
15. Yan H, Wang P, Yang F, Cheng W, Chen C, Zhai B, Zhou Y. Anticancer therapy-induced adverse drug reactions in children and preventive and control measures. *Front Pharmacol*. 2024;15:1329220. doi: 10.3389/fphar.2024.1329220.
16. Mattheolabakis G, Rigas B, Constantinides PP. Nanodelivery strategies in cancer chemotherapy: biological rationale and pharmaceutical perspectives. *Nanomedicine (Lond)*.2012;7(10):1577-90. doi: 10.2217/nmm.12.128.
17. El-Hussein A, Manoto SL, Ombinda-Lemboumba S, et al. A review of chemotherapy and photodynamic therapy for lung cancer treatment. *Anticancer Agents Med Chem* 2021; 21(2): 149–161
18. Liu YP, Zheng CC, Huang YN, He ML, Xu WW, Li B. Molecular mechanisms of chemo- and radiotherapy resistance and the potential implications for cancer treatment. *MedComm* 2021;2(3):315-340. doi: 10.1002/mco2.55.

19. Begg AC, Stewart FA, Vens C. Strategies to improve radiotherapy with targeted drugs. *Nat Rev Cancer*. 2011;11:239–253
20. Barazzuol L, Coppes RP, van Luijk P. Prevention and treatment of radiotherapy-induced side effects. *Mol Oncol*. 2020;14(7):1538-1554. doi:10.1002/1878-0261.12750.
21. Duncan, G. G. , Epstein J. B., Tu D., El Sayed S., Bezjak A., Ottaway J., et al.. Quality of life, mucositis, and xerostomia from radiotherapy for head and neck cancers: a report from the NCIC CTG HN2 randomized trial of an antimicrobial lozenge to prevent mucositis. *Head Neck* .2005.27:421–428.
22. Lalla RV, Brennan MT, Schubert MM: Oral complications of cancer therapy. In: Yagiela JA, Dowd FJ, Johnson BS, et al., eds.: *Pharmacology and Therapeutics for Dentistry*. 6th ed. Mosby Elsevier. 2011; 782-98.
23. Vidya Sankar, Yuanming Xu, Yuanming Xu. Oral Complications from Oropharyngeal Cancer Therapy. *Cancers*. 2023;15(18):4548; <https://doi.org/10.3390/cancers15184548>
24. 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.
25. Gupta N, Pal M, Rawat S, et al. Radiation-induced dental caries, prevention and treatment: a systematic review. *Natl J Maxillofac Surg*. 2015;6:160–6.
26. Elad, S.; Zadik, Y. Chronic oral mucositis after radiotherapy to the head and neck: A new insight. *Support. Care Cancer*. 2016;24:4825–4830.
27. Nishii, M.; Soutome, S.; Kawakita, A.; Yutori, H.; Iwata, E.; Akashi, M.; Hasegawa, T.; Kojima, Y.; Funahara, M.; Umeda, 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. *Support. Care Cancer*. 2020;28:1069–1075.
28. Hyer S, Kong A, Pratt B, et al.: Salivary gland toxicity after radioiodine therapy for thyroid cancer. *Clin Oncol*. 2007;19 (1): 83-6, 2007.
29. Ortigara GB, Schulz RE, Soldera EB, et al. Association between trismus and dysphagia-related quality of life in survivors of head and neck cancer in Brazil. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2019;128:235–42
30. Sroussi HY, Epstein JB, Bensadoun RJ, et al. Common oral complications of head and neck cancer radiation therapy: mucositis, infections, saliva change, fibrosis, sensory dysfunctions, dental caries, periodontal disease, and osteoradionecrosis. *Cancer Med*. 2017;6:2918–31.
31. Sroussi HY, Epstein JB, Bensadoun RJ, Saunders DP, Lalla RV, Migliorati CA, Heavilin N, Zumsteg ZS. Common oral complications of head and neck cancer radiation therapy: mucositis, infections, saliva change, fibrosis, sensory dysfunctions, dental caries, periodontal disease, and osteoradionecrosis. *Cancer Med*. 2017;6(12):2918-2931. doi: 10.1002/cam4.1221.
32. Al Barmawi M, Al Hadid LA, Alqudah HN, Al Hadid WA, Shamoun SA. Measuring the quality of life among head-and/or-neck cancer patients with oral mucositis using the functional assessment of cancer therapy-general in Jordan. *Asia Pac J Oncol Nurs*. 2018;5:320–6.
33. PDQ Supportive and Palliative Care Editorial Board. Oral Complications of Chemotherapy and Head/Neck Radiation (PDQ®): Patient Version. 2023 Dec 6. In: *PDQ Cancer Information Summaries* [Internet]. Bethesda (MD): National Cancer Institute (US); 2002. PMID: 26389169.
34. National Cancer Institute, Oral complications of chemotherapy and head/neck radiation (PDQ®), 2005, Accessed February 17, 2008
35. Volpato LE, Silva TC, Oliveira TM, Sakai VT, Machado MA. Radiation therapy and chemotherapy-induced oral mucositis. *Braz J Otorhinolaryngol*. 2007;73(4):562-8. doi: 10.1016/s1808-8
36. Popplewell L, Maghami E. Oral complications of cancer and cancer therapy: from cancer treatment to survivorship. *CA Cancer J Clin*. 2012;62(6):400-22. doi: 10.3322/caac.21157.694(15)30110
37. Prof James J Sciubba , David Goldenberg. Oral complications of radiotherapy. *The Lancet Oncology*. 2006; 7(2):175-183

38. Kim JH, Jenrow KA, Brown SL. Mechanisms of radiation-induced normal tissue toxicity and implications for future clinical trials. *Radiat Oncol*. 2014;32(3):103-15. doi: 10.3857/roj.2014.32.3.103
39. Otsuka S, Coderre JA, Micca PL, et al. Depletion of neural precursor cells after local brain irradiation is due to radiation dose to the parenchyma, not the vasculature. *Radiat Res*. 2006;165:582–591
40. Sankar V, Xu Y. Oral Complications from Oropharyngeal Cancer Therapy. *Cancers (Basel)*. 2023;15(18):4548. doi: 10.3390/cancers15184548.
41. Tarapan S., Matangkasombut O., Trachootham D., Sattabanasuk V., Talungchit S., Paemuang W., Phonyiam T., Chokchaitam O., Mungkung O.O., Lam-Ubol A. Oral Candida colonization in xerostomic postradiotherapy head and neck cancer patients. *Oral Dis*. 2019;25:1798–1808. doi: 10.1111/odi.13151.
42. Mathevossyan D, Hakobyan G. Oral Tissue Lesions Manifestation Cancer Patients Following Chemotherapy and Head and Neck Radiation Therapy. *J Oncology*. 2024; 4(1): 1127.
43. Kawashita Y., Funahara M., Yoshimatsu M., Nakao N., Soutome S., Saito T., Umeda M. A retrospective study of factors associated with the development of oral candidiasis in patients receiving radiotherapy for head and neck cancer: Is topical steroid therapy a risk factor for oral candidiasis? *Medicine*. 2018;97:e13073.. doi: 10.1097/MD.00000000000013073.
44. Elad S., Cheng K.K.F., Lalla R.V., Yarom N., Hong C., Logan R.M., Bowen J., Gibson R., Saunders D.P., Zadik Y., et al. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. *Cancer*. 2020;126:4423–4431. doi: 10.1002/cncr.33100
45. Lalla R.V., Bowen J., Barasch A., Elting L., Epstein J., Keefe D.M., McGuire D.B., Migliorati C., Nicolatou-Galitis O., Peterson D.E., et al. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. *Cancer*. 2014;120:1453–1461. doi: 10.1002/cncr.28592
46. Villa A., Sonis S.T. Radiotherapy-induced severe oral mucositis: Pharmacotherapies in recent and current clinical trials. *Expert Opin. Investig. Drugs*. 2023;32:301–310. doi: 10.1080/13543784.2023.2193324
47. Howard J, Dwivedi RC, Masterson L, Kothari P, Quon H, Holsinger FC. De-intensified adjuvant (chemo)radiotherapy versus standard adjuvant chemoradiotherapy post transoral minimally invasive surgery for resectable HPV-positive oropharyngeal carcinoma. *Cochrane Database Syst Rev*. 2018;3;2018(4):CD012939. doi: 10.1002/14651858.
48. Mella MH, Chabrilac E, Dupret-Bories A, Mirallie M, Vergez S. Transoral Robotic Surgery for Head and Neck Cancer: Advances and Residual Knowledge Gaps. *J Clin Med*. 2023 Mar 16;12(6):2303. doi: 10.3390/jcm12062303.
49. Pai RR, Ongole R, Banerjee S, Prasad K, George LS, George A, Nayak BS. Oral Care Protocol for Chemotherapy- and Radiation Therapy-Induced Oral Complications in Cancer Patients: Study Protocol. *Asia Pac J Oncol Nurs*. 2019;6(4):417-423. doi: 10.4103/apjon.apjon_30_19.
50. Southern H. Oral care in cancer nursing: Nurses' knowledge and education. *J Adv Nurs*. 2007;57:631–8.
51. Singh V, Malik S. Oral care of patients undergoing chemotherapy and radiotherapy: A review of clinical approach. *Int J Radiol*. 2007;6:1
52. Lee HJ, Han DH, Kim JH, Wu HG. The effect of comprehensive oral care program on oral health and quality of life in patients undergoing radiotherapy for head and neck cancer: A quasi-experimental case-control study. *Medicine (Baltimore)*. 2021 Apr 23;100(16):e25540. doi: 10.1097/MD.00000000000025540.
53. Mathevossyan et al. Prosthetic rehabilitation of patients with maxillary oncology defects using zygomatic implants *International Journal of Implant Dentistry*. 2024;10:31. <https://doi.org/10.1186/s40729-024-00545-y>
54. Elad S, Zadik Y, Hewson I. A systematic review of viral infections associated with oral involvement in cancer patients: a spotlight on Herpesviridae. *Support Care Cancer*. 2010;

18(8): 993-1006.

55.Hong CH, Napeñas JJ, Hodgson BD, et al.: A systematic review of dental disease in patients undergoing cancer therapy. *Support Care Cancer*. 2010; 18(8): 1007-21.

56.Epstein JB, Hong C, Logan RM, et al.: A systematic review of orofacial pain in patients receiving cancer therapy. *Support Care Cancer*. 2010; 18(8): 1023-31.

57.Loud JT, Murphy J. Cancer Screening and Early Detection in the 21st Century. *Semin Oncol Nurs*.2017;33(2):121-128.doi: 10.1016/j.soncn.2017.02.002.

58.Shieh Y, Eklund M, Sawaya GF, Black WC, Kramer BS, Esserman LJ. Population-based screening for cancer: hope and hype. *Nat Rev ClinOncol*.2016;13(9):550-65.doi: 10.1038/nrclinonc.2016.50.

59.Signs and Symptoms of OvarianCancer. 2016 <https://www.cancer.org/cancer/ovarian-cancer/detection-diagnosis-staging/signs-and-symptoms.html>.

60.Pulumati A, Pulumati A, Dwarakanath BS, Verma A, Papineni RVL. Technological advancements in cancer diagnostics: Improvements and limitations. *Cancer Rep (Hoboken)*.2023;6(2):e1764.doi: 10.1002/cnr2.1764.

61/Frangioni JV. New technologies for human cancer imaging. *J Clin Oncol*. 2008;26(24):4012-21.doi: 10.1200/JCO.2007.14.3065.

62.Loud JT, Murphy J. Cancer Screening and Early Detection in the 21st Century. *Semin Oncol Nurs*.2017;33(2):121-128.doi: 10.1016/j.soncn.2017.02.002

63.Shieh Y, Eklund M, Sawaya GF, Black WC, Kramer BS, Esserman LJ. Population-based screening for cancer: hope and hype. *Nat Rev Clin Oncol*. 2016;13(9):550–565.

64.Loud JT, Murphy J. Cancer Screening and Early Detection in the 21st Century. *Semin Oncol Nurs*.2017;33(2):121-128.doi: 10.1016/j.soncn.2017.02.002.

65.F.L. Vazquez. An oral cancer screening program in Brazil: Analysis of seven years of outcome after its implementation in the suburban

cities of São Paulo *Oral Oncology*154, 2024, 106826

66.Elad et al., Basic oral care for hematology–oncology patients and hematopoietic stem cell transplantation recipients: a position paper from the joint task force of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISSO) and the European Society for Bone Marrow Transplantation (EBMT). *Support Care Cancer*, 2015; 23, 223-36.

67.Pai RR, Ongole R, Banerjee S, Prasad K, George LS, George A, Nayak BS. Oral Care Protocol for Chemotherapy- and Radiation Therapy-Induced Oral Complications in Cancer Patients: Study Protocol. *Asia Pac J Oncol Nurs*. 2019;6(4):417-423.doi: 10.4103/apjon.apjon_30_19.

68.Basch E, Deal AM, Kris MG, Scher HI, Hudis CA, Sabbatini P, Rogak L, Bennett AV, Dueck AC, Atkinson TM, Chou JF, Dulko D, Sit L, Barz A, Novotny P, Fruscione M, Sloan JA, Schrag D. Symptom Monitoring With Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial. *J ClinOncol*.2016;20;34(6):557-65. doi: 10.1200/JCO.2015.63.0830.

69.Wahidi R, Mintz R, Agabalogun T, Mayer L, Badiyan S, Spraker MB. Remote Symptom Monitoring of Patients With Cancer Undergoing Radiation Therapy. *Cureus*. 2022;14(9):e29734. doi: 10.7759/cureus.29734.

70.Pai RR, Ongole R, Banerjee S, Prasad K, George LS, George A, Nayak BS. Oral Care Protocol for Chemotherapy- and Radiation Therapy-Induced Oral Complications in Cancer Patients: Study Protocol. *Asia Pac J Oncol Nurs*. 2019;6(4):417-423.doi: 10.4103/apjon.apjon_30_19.

71.National Confidential Enquiry into Patient Outcome and Death: For Better, For Worse? A Review of the Care of Patients Who Died Within 30 days of Receiving Systemic Anti-Cancer Therapy (London).2008;DOI:10.13140/RG.2.2.13698.61129

72.Molassiotis A, Brearley S, Saunders M, Craven O, Wardley A, Farrell C, Swindell R, Todd C and Luker K (2009) Effectiveness of a home care nursing program in the symptom

management of patients with colorectal and breast cancer receiving oral chemotherapy: a randomized, controlled trial *J Clin Oncol* 27 6191–8

73. Thanvi J, Bumb D. Impact of dental considerations on the quality of life of oral cancer patients. *Indian J Med Paediatr Oncol.* 2014;35(1):66-70. doi:10.4103/0971-5851.133724

74. Mathevosyan D, Hakobyan G. Prevention and Care of Oral Manifestations in Cancer Patients Receiving Chemotherapy and Head and Neck Radiation Therapy. Systematic Review. *JSM Head Neck Cancer Cases Rev.* 2024; 4(1): 1010.

75. Mathevosyan D, Hakobyan G. Dental Care for Cancer Patients in the Prevention of Complications of Chemotherapy and Head and Neck Radiation Therapy. *Journal of Tumor Science Research.* 2024. SRC/JTSR-138. DOI: doi.org/10.47363/JTSR/2024(3)127