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SYSTEMATIC REVIEW

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Materials and effects of intraoral device technologies for complication protection in head and neck cancer radiotherapy: a scoping review

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Abstract

Background This review aims to analyze the effectiveness of intraoral devices, emphasizing predominant materials, key manufacturing technologies, and their prophylactic role in mitigating complications during radiotherapy for head and neck cancer patients.

Methods The searches were conducted in the PubMed, ScienceDirect, Medline, VHL, Cochrane Library, SciELO, INCA, and MedRxiv databases using the MeSH descriptors "radiation therapy," "intraoral devices," and "protection." These descriptors were connected by the Boolean operator "AND," with a focus on articles published up to 2024. The study, carried out by two independent reviewers following the PRISMA checklist, focused on analyzing intraoral radiation protection devices. It explores the materials used in their fabrication, beam type, dose, and irradiation techniques employed during radiotherapy sessions. Additionally, the study investigates the side effects associated with and without the use of these devices in patients.

Results Evidence emphasizes the specific dental needs of head and neck cancer patients. Furthermore, the hypothesis regarding the benefits of these devices in reducing setup errors and minimizing toxic doses to healthy tissues during radiotherapy is supported. These devices are composed of different materials, with varying densities and designs tailored to their intended function. 3D printing proves to be an effective tendency in the manufacturing of these instruments.

Conclusion These findings indicate a positive impact of using these devices for functional preservation, improvement in quality of life, and a reduction in the demand for oral treatments and rehabilitation. The analysis underscores the importance of determining the applicability for each clinical case of the specific radiotherapeutic treatment.

Keywords Radiation therapy, Head and neck cancer, Intraoral devices, Oral radiation protection

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Background

Radiotherapy (RT) is a widely employed treatment modality in the management of head and neck cancer (HNC), whether as a primary therapeutic approach or in conjunction with surgical and/or chemotherapeutic interventions. While effective against tumour cells, RT also affects healthy tissues in the vicinity of the tumor due to its non-selective action, thereby posing a significant challenge in light of the presence of critical structures in the region (Wang 2021; Verrone 2014).

The primary oral and dental impacts of RT include mucositis (present in up to 80% of cases), xerostomia, osteoradionecrosis, radiation-induced caries, trismus, infections, dysgeusia, tissue necrosis, and mucosal pain, among others. These effects may be either temporary or permanent, and their worsening may lead to the interruption of cancer treatment, which in turn may adversely impact prognosis and quality of life (Colloc 2020; Brandão 2021). This highlights the crucial role of dentists as members of the multidisciplinary team, responsible for managing RT-induced conditions, preventing these impacts, providing treatment, rehabilitating patients, and ensuring the necessary dental care (Colloc 2020).

Advancements such as Intensity-Modulated Radiation Therapy (IMRT) have enhanced dose precision; however, they have not yet achieved the goal of eliminating damage to healthy tissues. In this context, intraoral protection devices (IPDs) have demonstrated the potential to reduce the radiation dose to soft tissues, mitigate side effects, and facilitate greater treatment tolerance without compromising effectiveness (Rocha 2017; Appendino 2019).

These devices, typically composed of polymethyl methacrylate or combined with metallic alloys such as lead or Cerrobend, facilitate the physical displacement of normal tissues beyond the radiation field. However, materials such as lead raise concerns regarding toxicity, and three-dimensional printing emerges as a viable technology for their production, enabling customization (Singh 2022, Hawari 2022, Souza 2023). In addition, few or no studies provide technical justification for the use of these materials (Nejaim 2015, Brandão 2021, Hoff 2021). Establishing clinical standards is essential to promote the wider adoption and consistent use of these devices in radiotherapy, ensuring their safety, efficacy, and integration into routine clinical practice.

The objective of this study is to conduct a scoping review with the aim of investigating the impact of IPDs on the side effects of radiotherapy for head and neck cancer. In order to achieve this, the review will consider current treatment standards, as well as the materials and technologies employed in the manufacturing of these devices. The review will place particular emphasis on the predominant materials, key manufacturing technologies and the prophylactic role of these devices in reducing complications during radiotherapy.

The study underscores the need for further research to evaluate the efficacy of these devices and optimize their use in clinical settings. The findings indicate a positive impact on functional preservation, improved quality of life, and a reduced demand for oral treatments and rehabilitation. Furthermore, the analysis highlights the importance of tailoring their application to each clinical case and specific radiotherapeutic treatment. It is also worth noting that in studies involving various materials, authors often provide little to no technical justification for their selection, which further underscores the need for comprehensive evaluations and well-documented methodologies.

Methods

Protocol

The protocol for the review, as well as its final presentation, will be developed in accordance with the guidelines established by PRISMA/ScR (Preferred Reporting Items for Systematic Reviews and Meta-analyses / Scoping Reviews) (Page 2021).

Review question

This scoping review will be based on the following review question:

What are the side effects of head and neck radiotherapy on intraoral tissues, and how can an effective, non-toxic, adaptable intraoral radiation protection device be designed to minimize or prevent radiation-induced damage by utilizing materials with superior shielding and radiation-absorbing properties?

Inclusion criteria

To be eligible for this review, articles must meet the requirements determined by the PICO strategy used to guide the construction of review questions and literature searches [37], where:

P (Population): Patients undergoing radiotherapy in the head and neck region.

I (Intervention): Use of intraoral devices for protection during radiotherapy.

C (Comparison): Patients undergoing radiotherapy in the intraoral region without the use of these devices.

O (Outcome): Dosimetric reduction of radiation and side effects in healthy oral tissues, such as mucositis, xerostomia, pain, dysphagia, etc.

Concordance Criteria: 1) Adult patients undergoing radiotherapy in the head and neck region. 2) Studies that qualify and quantify the side effects caused by head and neck radiotherapy. 3) Use of intraoral devices during radiotherapy to protect healthy oral tissues. 4) Studies evaluating the effectiveness of intraoral devices in reducing radiotherapy side effects in the intraoral region. 5) Studies presenting results on mucositis, xerostomia, pain, dysphagia, or other side effects in the intraoral region.

Exclusion criteria

1) Studies where patients were not subjected to radiotherapy in the head and neck region.
2) Studies focusing on qualifying and quantifying effects on oral tissues by therapies other than radiotherapy.
3) Studies evaluating other therapies or interventions for preventing side effects besides intraoral devices.
4) Studies not presenting results on the side effects of radiotherapy in the intraoral region.
5) Research on the treatment of radiotherapy sequelae with drugs, laser, and other measures.
6) Studies evaluating devices applied to specialties other than head and neck oncology.

Data source

This review will include articles with randomized and non-randomized clinical trial designs, analytical observational studies (prospective and retrospective cohorts; case–control studies; prospective and retrospective cross-sectional studies), as well as individual case reports and case series conducted with humans. The review will consider articles published in the last 10 years (2013–2023) in Portuguese, English, and Spanish languages, focusing on topics related to head and neck radiotherapy, dentistry, and the use of IPDs.

Search strategy

A search strategy containing the following MeSH terms/descriptors will be employed: "radiation therapy," "intraoral devices," and "protection." The search strings defined in this initial search will be adapted using the boolean operator "AND" for consecutive electronic bibliographic databases: US National Library of Medicine National Institutes of Health (PubMed), Scientific Electronic Library Online (SciELO), MedLine/Virtual Health Library (VHL), Cochrane Library, Science Direct, MedRxiv. This search will be conducted individually by two appropriately trained researchers, who will later cross-verify the number of articles found in each database.

Study selection

The list of identified studies will be organized into spreadsheets containing the author's name, publication year, and abstract. After removing duplicates, a single file with all identified studies will be generated for subsequent selection. The selection process will be conducted individually by the same two researchers who performed the search. It will start with the reading of titles and abstracts and then progress to the full-text reading. At each stage of the process, the lists will be cross-verified, and in cases of discrepancies, a third researcher will be involved.

Data extraction

The data extraction spreadsheet is based on the Cochrane Consumers and Communication model, and the Review Group's template was adapted for this research. Two reviewers' authors (EGS, LSPSG) tabulated the scientific data of interest, and another reviewer (RGL) reviewed all the data.

Results

The searches were completed in June 2023 using the same search strategy described and applied to the selected databases (PubMed, SciELO, VHL, Cochrane, ScienceDirect and MedRxiv).

Description and characteristics of studies

A total of 321 studies related to the impact of IPDs were identified. Among these, 298 were located in the Science Direct database, 14 in Pubmed, 6 in BVS (Biblioteca Virtual em Saúde), and 3 in Cochrane; no articles were found in the other databases. Applying the filters: "Review Article," "Research Article," and "Case Report," the number of articles from Science Direct reduced to 108, and the number of articles from other databases remained unchanged. Additionally, four duplicates were removed.

Subsequently, the selection of 126 articles was carried out based on the reading of titles and the relevance of the topics, which were grouped into spreadsheets for abstract reading. After reviewing the abstracts, 24 articles were initially included for a review, considering the content's relevance to the research. Of the 24 articles read in full, after applying the six exclusion criteria used in the study (the reasons listed in the flowchart follow the same numbering as the applied criteria), 13 were deemed eligible for the present study (Khan 2014; Verrone 2014; Butson 2015; Rosen 2015; Doi 2017; Rocha 2017; Appendino 2019; Bruno 2020; Brandão 2021; Herpel 2021; Hawari 2022; Singh 2022; Srivastava 2022). Details of the screening and selection process are depicted in the PRISMA-ScR flowchart in Fig. 1.

From the included studies, the following data were tabulated: (1) author, (2) year, (3) country, (4) study design, (5) objective, (6) main types of HNC where radiation affects oral health, (7) effectives of RT toxicity in the oral cavity, (8) radiation dose quantity (grays) causing toxicity, (9) impacts on dentistry and resultant treatments, (10) main methods and devices used for protecting healthy

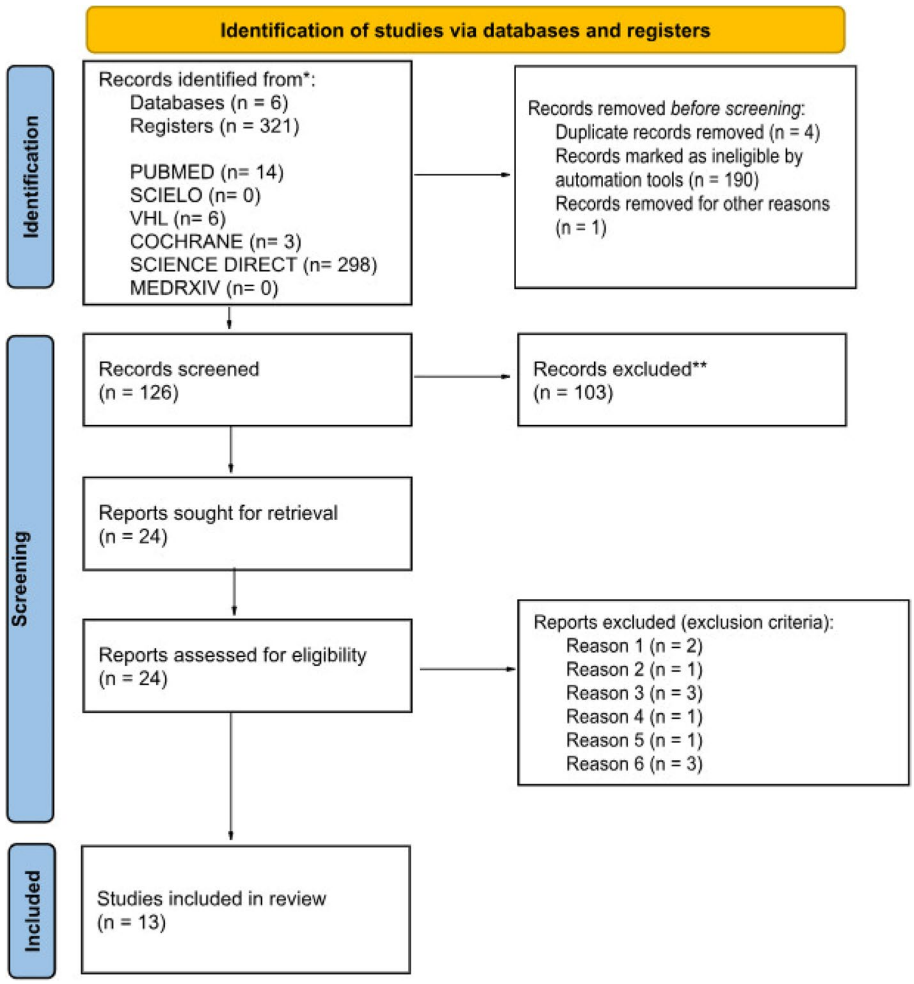

Fig. 1 Flow diagram summarizing the study selection process

tissues (intervention), (11) base material of the protector, (12) key results of protector use (control), (13) study limitations, (14) main conclusions: a) recommendations on the use of intraoral protection mechanisms and devices, b) contributions of the study to tissue protection against radiation and side effects control, c) innovations or technological advances presented in the study compared to previous works. These main characteristics of the IPDs are illustrated in Table 1.

Key themes explored in included studies

The main themes explored in the included studies encompassed the following aspects: assessment of the primary side effects associated with radiation emitted during head and neck radiotherapy, recommendations for the prevention and preservation of oral health during radiation treatment, the description of divergent techniques for the fabrication of IPDs, the compilation of different types of devices and corresponding recommendations, with a predominant focus observed in the included studies on the analysis of the effectiveness of IPD usage during radiotherapy in reducing toxic doses and side effects in healthy tissues adjacent to the tumor. This analysis included comparisons, when available, with patients who did not use devices during head and neck radiation exposure.

The studies discussed side effects and the use of IPDs for tumors with various tumor site regions. Not surprisingly, tumors located in the oral cavity and external oral region (lip, cheeks, and skin) are mentioned in all studies 13 of the included studies (Khan 2014; Verrone 2014; Butson 2015; Rosen 2015; Doi 2017; Rocha 2017; Appendino 2019; Bruno 2020; Brandão 2021; Herpel 2021; Hawari 2022; Singh 2022; Srivastava 2022).

Tumors in the pharyngeal region, including oropharynx, nasopharynx, and hypopharynx, appeared in two studies (Doi 2017; Appendino 2019; Herpel 2021; Singh 2022;), paranasal sinuses in three studies (Doi 2017;

Table 1 Classification of IPDs based on their materials and associated side effects reported in the literature

Study	Study Type	Device Type	Material	Beam Type	Average Dose (Gy)	Irradiation Technique	Cancer Type Indication	Pos-irradiation Side Effects using the Device	Main Outcomes
[2]	Review Study and Case Report	Customizable stents	Acrylic resin	Photons	60 to 70	IGRT and VMAT	Squamous cell carcinoma of soft palate Adenocarcinoma of minor salivary gland, hard palate, and nasal fossa	Grade 1 and 2 radiation toxicity (no grade 3) (3 cases were studied)	Experimental oral simulators revealed promising dosimetric data, showing protection against oral mucositis when combined with IMRT and VMAT
[3]	Systematic Review	Intraoral stents	Non specified	Non specified	Non specified	Majority IMRT	Tumors in the oral cavity	Mucositis, salivary changes and trismus moderate	Intraoral devices demonstrated potential in reducing radiation doses to non-target oral tissues, although conclusive evidence is still lacking. The study highlighted the effectiveness of intraoral stents in mitigating acute and late adverse effects of radiation therapy, with no risk of bias reported. A meta-analysis found significant reductions in oral mucositis, salivary changes, and trismus, although only two studies provided statistical testing across different devices
[5]	Case Report	Oral positioning stent	Occlusal splint material	Photons	50	IMRT	Squamous cell carcinoma of the right lateral border of the tongue	Non specified	The use of the device improved the preservation of healthy tissues and salivary glands, reducing radiation doses to the hard palate by 42%, the right parotid by 21%, and the left parotid by 8.5%. All teeth received lower radiation doses with device usage

Table 1 (continued)

Study	Study Type	Device Type	Material	Beam Type	Average Dose (Gy)	Irradiation Technique	Cancer Type Indication	Pos-irradiation Side Effects using the Device	Main Outcomes
[6]	Original Study	Electron shields	Combination of lead, copper, aluminum, and wax	Electrons (6, 8 e 10 MeV)	Ranging from 0 to 3 Gy in increments of 0.25 Gy (sample measurements)	Electron radiation therapy	Superficial and Subcutaneous Tumors of the Head and Neck Region	Non specified	A protective coating made of 0.6 mm copper (Cu), 1.0 mm aluminum (Al), and 1.5 mm of a filtering material minimized tissue/shielding interface doses to no more than 110% of the prescribed dose (Single dose—5 Gy)
[11]	Original Study	Intraoral stents	Polyethylene terephthalate (PET)	Photons	66 to 70	IMRT	Tumors in the maxillary and ethmoid sinuses, oropharynx, larynx, nasal and oral cavity	Non specified	CT image analysis, combined with dose planning, revealed reduced IMRT configuration errors in patients using stents (N = 6) compared to those who did not (N = 12), with reduced dose fractions in all three directions due to improved tissue immobilization
[15]	Review Study	Maxillofacial stents: a-) Radiation carriers b-) Leaded protective devices; c-) Tongue depressor d-) Positioning devices e-) Tissue remodeling devices f-) Intra-device positioning for stereotactic radiotherapy	a-) Polymethyl methacrylate (PMMA) resin b-) Lead or Cerrobend with PMMA Resin c-) PMMA Resin d-) PMMA Resin e-) PMMA Resin f-) Tungsten with PMMA Resin	Electrons, photon (flux of 6 and 15 mV)	Non specified	a-) Brachytherapy b-) Brachytherapy and external beam therapy c-) Brachytherapy or external beam therapy d-) Brachytherapy or external beam therapy e-) External beam therapy f-) Stereotaxic body radiation therapy	a-) Buccal mucosa, tonsillar pillars, pharynx, maxillary sinus and alveolus b-) Skin and oral lesions c-) Lesions of tongue and floor of mouth d-) Lesions of the floor of mouth, mandible, palate, tongue, or oral mucosa e-) superficial lesions of the floor of the mouth, the hard and soft palate, sinus, tonsils and nasopharynx	Non specified	The study highlights the use of intraoral devices for protection, positioning, and removal as efficient tools, representing invaluable assistance in head and neck radiotherapy

Table 1 (continued)

Study	Study Type	Device Type	Material	Beam Type	Average Dose (Gy)	Irradiation Technique	Cancer Type Indication	Pos-irradiation Side Effects using the Device	Main Outcomes
[17]	Case Report	Individualized 3D-Printed Tissue Retraction Devices	Combination of a 3D-printer (Pro2, Asiga) with dental splint resin (Freeprint splint 2.0, Detax). Customization of pre-fabricated TRDs with silicone material	Photons	70	IMRT	Tumors of the nasal or paranasal sinuses, oropharynx, lip, and oral cavity	Grade 1 or 2 mucositis occurred in 70% of cases (7 case in 10 cases studied)	Devices were welltolerated, had no technical complications, and contributed to proper positioning, spacing the tongue, lips, and cheeks. The devices allowed bilateral, caudal, and ventral displacement of the tongue (37.5 cm^3—23.6 cm^3), spacing between the lips and cheeks. Three sizes (S, M, and L) were sufficient for all patients. Positive effects regarding side effects were observed
[21]	Case Report	Intraoral radiation shield	Combination of self-polymerizing acrylic resin, lead sheet, and wax	Electrons	Non specified	Electron radiation therapy	Well-lateralized tumors of the oral cavity, parotid glands, lip, and cheek		Protective devices, made with dental materials available in the office, promote savings in clinical laboratory time, providing better comfort and prevention of side effects from radiotherapy
[37]	Original Study	Intraoral stents	Combination of Cerrobend alloy, lead (5 mm), wax and polyvinyl chloride film	Electrons	60 to 66	Electron radiation therapy	Early-stage head and neck	Grade 3 mucositis in unprotected areas (2 cases) and grade 1 xerostomia in 16.6% of cases (1 case in 6 cases studied)	Intraoral stents reduced adverse effects such as mucositis and xerostomia, resulting from radiation therapy in early-stage lip cancer patients and minimized radiation exposure

Table 1 (continued)

Study	Study Type	Device Type	Material	Beam Type	Average Dose (Gy)	Irradiation Technique	Cancer Type Indication	Pos-irradiation Side Effects using the Device	Main Outcomes
[39]	Case Report	Brachytherapy prosthesis	Combination of lead and thermopolymerized PMMA	Megavoltage photons	30	Brachytherapy	Intraoral angiosarcoma	Grade 1 mucositis one week after (only 1 case was studied)	Brachytherapy prostheses maximize the distance between the target site of brachytherapy and surrounding structures minimizing the radiation exposure
[42]	Review Study	a-) Shielding prostheses b-) Radiation Carriers c-) Positioning stents d-) Radiation Mouthguards	a-) Lead, Lipowitz alloys, or Cerrobend with acrylic resin b-) Radium needles, cobalt, radon, iridium, or cesium with acrylic resin c-) Acrylic resin, disposable wood blade, thermoplastic components, and vinyl polysiloxane d-) Non specified (suggest a material with relatively low atomic number and physical density)	a-) Electron beam and orthovoltage b-) Non specified c-) Proton beam d-) Non specified	Non specified	a-) Electron radiation therapy an orthovoltage b-) Brachytherapy c-d-) External beam radiotherapy for head and neck cancers	a-) Superficial tumors b-) Treat palatal, nasal, pharyngeal, and buccal lesions c-) Nasal cavity and paranasal sinuses lesions	Late-onset palatal mucositis and moderate xerostomia	The study demonstrated that the use of IPDs can be adjuncts in head and neck radiotherapy to limit post-radiation morbidities, even in modern treatment techniques

Table 1 (continued)

Study	Study Type	Device Type	Material	Beam Type	Average Dose (Gy)	Irradiation Technique	Cancer Type Indication	Pos-irradiation Side Effects using the Device	Main Outcomes
[45]	Case Report	Intraoral stent (Bilabial-protruding, mouth-opening and tongue-depressing stent for proton radiation therapy)	Transparent thermopolymerized acrylic resin	Protons	60	IMPT (Intensity-Modulated Proton Therapy)	Polymorphous Salivary Adenocarcinoma (T2N0M0) of the minor salivary glands of the upper left lip and adjacent oral mucosa	Moderate mucositis and dysgeusia (1 case)	The use of the device demonstrated in the study allowed for the displacement of the upper lip in the IMPT field and away from the underlying maxillary bone, mandible, and tongue. According to the radiation dose volume histogram, she received an average dose of 61.233 Gy (range 60.727 to 65.492 Gy) for the clinical target volume with only 0.058 Gy to the mandible, 0.005 Gy to the tongue, and 0.003 Gy to the parotid glands. It was estimated that without the stent, she would have received doses exceeding 50 Gy in a larger portion of the maxilla and lower lip, and over 30 Gy in parts of the anterior tongue and mandible. Additionally, a larger extent of radiation-induced oral mucositis and dysgeusia, along with a higher risk of osteoradionecrosis, would have been encountered

Table 1 (continued)

Study	Study Type	Device Type	Material	Beam Type	Average Dose (Gy)	Irradiation Technique	Cancer Type Indication	Pos-irradiation Side Effects using the Device	Main Outcomes
[50]	Original Study	Intraoral stents	Acrylic resin	Photons	67.4 ± 3.9	IMRT	Squamous cell carcinoma of the tongue and floor of the mouth	Grade 3 mucositis one week after the control group (33 cases divided in control (14) and test group (19))	The intraoral stent contributed to delaying the onset of severe mucositis by reducing the number of days of oral pain and the use of opioid analgesics Dose reduction of 6.8 Gy in the ipsilateral parotid and 14.9 Gy in the maxilla

* Additional information can be found in the supplementary material

Herpel 2021; Singh 2022), nasal cavity in three studies (Doi 2017; Appendino 2019; Singh 2022), and larynx in two studies (Doi 2017; Helmers 2018). For studies like Rocha et al. [37], participant selection was based on tumor location and stage. In this specific case, early-stage lip cancers were chosen to facilitate the creation and evaluation of the potential mitigating effects of IPDs regarding side effects.

Current techniques in radiotherapy for minimizing side effects in head and neck cancer

An analysis of the ionizing radiation delivery methodologies employed in the studies revealed, in accordance with Appendino et al. [2], that technology has evolved considerably with optimizations in the delivery modality, focusing on minimizing toxic doses to healthy tissues. This is reflected in currently adopted technologies such as Intensity-Modulated Radiation Therapy (IMRT) or Volumetric Modulated Arc Therapy (VMAT). These technologies enable individualized planning based on images and advanced software, providing greater precision in delivery through the emission of multidimensional beams with control over depth, intensity, and target (tumor) range (Appendino 2019).

Considering these technologies, the majority of studies included in this survey that specified the radiation delivery mode mentioned the IMRT technique (Verrone 2014; Doi 2017; Appendino 2019; Brandão 2021; Herpel 2021; Singh 2022; Srivastava 2022), and two of them mentioned VMAT (Appendino 2019; Singh 2022). In the series by Appendino et al. [2], three patients undergoing VMAT for tumors located at or above the hard palate in the anterior third of the mouth were investigated. Brachytherapy was the radiation treatment cited in two studies (Rosen 2015,Singh 2022), and it was identified as the treatment of choice in the experiment conducted by Rosen et al. [39] for an intraoral angiosarcoma. Another treatment modality present is unidimensional or bidimensional delivery technologies, referred to as orthovoltage or superficial therapy, mentioned in two studies (Butson 2015; Rocha 2017).

Among the studies that discussed delivery using IMRT technology, three opted for the use of photon beams, specifically in the treatment of cancers in deeper regions surrounded by vital structures at higher risk due to greater dosimetric control (Doi 2017; Singh 2022; Srivastava 2022;. Meanwhile, the specification of electron beams used for so-called superficial therapies was described in two out of the two studies that observed this therapeutic approach (Butson 2015; Rocha 2017;). Among the studies reviewed, Khan et al. (2014) instructed on the practical manufacturing of a IPD in the office; however, they do not report either the radiation delivery methodology or the beam specification to which the patient was exposed. In this perspective, this research demonstrates that, despite the use of advanced planning and state-of-the-art RT techniques such as IMRT, significant challenges persist in the treatment of cancer in this region, as recurrent local–regional toxicities and side effects are common (Appendino 2019). As a result, there are direct impacts on the quality of life of patients due to dose-dependent damage to healthy tissues near the tumor area (Rocha 2017; Bruno 2020).

Emphasizing modalities aimed at preventing or reducing oral complications associated with radiotherapy, Rocha et al. [37] recommends the use of individualized intraoral stents with metal alloys for shielding and protection of tissues. Similarly, to other authors who contributed to this review, suggesting the adoption of devices with the same objective (Khan 2014,Butson 2015; Hawari 2022; Singh 2022). Studies like that of Herpel et al. [17], suggest reducing doses to healthy tissues and secondary reduction of side effects through tissue separation with stents without any interfering dosimetric material (Verrone 2014; Doi 2017; Rocha 2017; Appendino 2019; Bruno 2020; Brandão 2021; Herpel 2021; Hawari 2022; Singh 2022; Srivastava 2022). Rosen et al. [39] indicates the use of a specific IPD for radiation delivery in brachytherapy, with radioactive materials that provide greater precision in dose range in the tumor bed, and like him, other authors have also made recommendations regarding this device (Hawari 2022; Singh 2022).

Before evaluating existing protective devices and their effectiveness, it is important to describe the main effects of radiation on oral tissues for an understanding of the applicability of protection.

Mucositis is one of the most common radio induced toxicities, as noted by Appendino et al. [2], a finding supported by Rocha et al. [37], who reported that 80% of patients undergoing HNC irradiation may experience this condition. This information aligns with data from included studies, where mucositis was described as a side effect of radiotherapy in twelve out of the thirteen articles (Khan 2014; Verrone 2014; Rosen 2015; Doi 2017; Rocha 2017; Appendino 2019; Bruno 2020; Brandão 2021; Herpel 2021; Hawari 2022; Singh 2022; Srivastava 2022). Mucositis was noted as the most prevalent adverse effect, with the only exception being Butson et al. [6], who referred to general tissue damage without specifying the condition. Xerostomia was also highly prevalent in the studies (Khan 2014,Verrone 2014; Rosen 2015; Rocha 2017; Appendino 2019; Bruno 2020; Brandão 2021; Herpel 2021; Singh 2022). Herpel et al. [17] indicated that xerostomia contributes to radiation-induced caries, tooth loss, and reduced chewing and speech abilities, ultimately affecting quality of life. Xerostomia results from impaired salivary gland function, with prevalence rates ranging from 30 to 60%. Additionally, taste alterations (Khan 2014,Rosen 2015; Rocha 2017; Appendino 2019; Herpel 2021; Brandão 2021; Singh 2022; Srivastava 2022), osteoradionecrosis (Appendino 2019; Bruno 2020; Singh 2022; Srivastava 2022), fibrosis Herpel 2021), trismus (Khan 2014; Sroussi 2018; Appendino 2019; Brandão 2021; Singh 2022),, loss of insertion (Singh 2022),. Bruno et al. (2020) found that severe mucositis occurs in 22% to 66% of cases, leading to pain and odynophagia, with higher radiation doses to salivary glands correlating with worsening xerostomia and hyposalivation.

Helmers et al. [16] suggested that these side effects may be explained by the late-stage disruption of oral microcirculation, observing capillary rarefaction, altered angiomorphology, and reduced vessel diameters in irradiated tissue compared to healthy mucosa.

Evaluation of the effectiveness of intraoral device usage

The studies analyzed in this review emphasize, as a central aspect, the effectiveness of IPDs application in reducing toxic doses to healthy oral tissues and minimizing side effects. This focus was predominant in eight of the included studies (Verrone 2014; Doi 2017; Rocha 2017; Appendino 2019; Bruno 2020; Brandão 2021; Herpel 2021; Srivastava 2022). Among these, five studies (Verrone 2014; Doi 2017; Rocha 2017; Bruno 2020; Brandão 2021) provided quantitative data, allowing the assessment of the positive impact of these devices in reducing toxic doses and side effects in healthy tissues adjacent to the tumor region.

None of the studies opposed the use of IPDs regarding their ability to reduce radiation dose and side effects during RT. However, none of the studies presented a low risk of bias, which suggests the need for caution in interpreting the results, as they may be more prone to systematic errors that could affect the validity of the conclusions (Bruno 2020; Brandão 2021). Nonetheless, the results were promising, supporting the hypothesis that IPDs are effective in reducing radiation doses to healthy tissues and can serve as adjuncts in HNC radiotherapy.

Such a statement is strongly supported by Doi et al. (2017), who assessed 18 patients undergoing head and neck radiotherapy, including 12 without intraoral devices and 6 with individually fitted intraoral devices. The study revealed significant differences in dosimetric outcomes between the groups. While the total prescribed dose and fractionation schemes were identical across most patients (66 Gy delivered in 33 fractions), those in the intraoral stent group demonstrated improved dose distribution and reduced random errors in the 3D-direction, measuring 0.904 ± 0.181 mm compared to 1.172 ± 0.370 mm in the group without intraoral stents ($P = 0.081$). These findings underscore the dosimetric advantage of intraoral devices in reducing radiation exposure to surrounding tissues while maintaining treatment precision.

Brandão et al. (2021), through a systematic literature review, also identified a significant difference in the use of IPDs of the stent type, without associated metal alloys, in conjunction with IMRT using photon beams for the prevention of oral mucositis ($P < 0.001$, $I2 = 95\%$). The authors reported favorable effects in terms of reduction of salivary flux, a lower incidence of trismus, improvement in pain levels, food intake capacity, and a reduction in the need for feeding tubes and weight loss. This approach was also associated with reduced rates of prolonged hospitalizations, contributing to savings in hospital supply costs and overall expenses. Consequently, the study supports the recommendation for manufacturing intraoral stents due to their positive effects on minimizing side effects and improving patient outcomes.

In line with the same theory, Rocha et al. [37] demonstrate the effectiveness of IPDs, this time using dense materials, in superficial two-dimensional treatment to minimize potential radiation side effects in the oral tissues of the patient. In their experiment, they employed IPDs with a metallic alloy in 6 patients with early lip cancers. The effectiveness was highlighted by the identification of cases of oral mucositis only in areas unprotected by the IPD around the tumor. None of the patients exhibited dysgeusia or dysphagia, and only one case reported mild oral dryness, which occurred after 13 days of radiation therapy without interference in habits. However, dosimetric differences in radiation were not pointed out due to the absence of a control group.

Herpel et al. [17] brought another assessment perspective on IPDs, seeing that the devices are more accurate in patients without major tooth loss, due to the greater stability of the apparatus during therapy. A relevant feature of Herpel's study is that the developed devices contained three size patterns (S, M, and L), and they were well adaptable to all 10 patients in the research. Furthermore, another relevant result obtained by this study is the hypothesis that a greater lingual displacement to the posterior would further reduce tissue dosage.

Similarly, Appendino et al. [2] suggests, based on the experience of using IPD in combination with Volumetric Modulated Arc Therapy (VMAT) in three patients, that these devices are effective in reducing side effects and allow for greater tolerance to treatment without the need for interruptions. However, he emphasizes the importance of daily evaluation of the patient's position and proper alignment with the treatment plan, highlighting the relevance of these practices, especially when using IPDs.

In the study conducted by Bruno et al. (2020), the application of an IPD made by additive manufacturing with material used for occlusal splints, in a carcinoma located on the right lateral border of the tongue, whose type of radiation used is not described, but with a dosage of 30 fractions of 2 Gy, totaling 60 Gy, demonstrated a more effective radiation distribution and preservation of healthy tissues. The results showed a significant reduction in side effects, as the radiation dose delivered to the hard palate, right parotid gland, and left parotid gland was reduced by 42%, 21%, and 8.5%, respectively, compared to the initial planned dose.

Manufacturing technologies and predominant materials

IPDs are instruments that can be used as adjuncts in head and neck radiotherapy to prevent unnecessary radiation exposure through shielding and/or physical displacement of normal tissues away from the radiation field, aiming to prevent and reduce oral complications associated with therapy (Rocha 2017; Srivastava 2022). Strategically designed to cover tissues and/or teeth for protection, they can also be used to transport drugs and/or radioactive materials to displace adjacent tissues or protect against radiation scatter. Maxillofacial prosthodontics specialists collaborate with radiation oncologists to project these devices. Different types can be classified depending on the tumor type and location, radiotherapy protocol, and method, and guidance from the radiation therapist is provided to the prosthetist for device design according to each clinical case. Examples of such devices include stents with or without metal alloys, brachytherapy prostheses, and mouthguards (Hawari 2022). However, despite clinical evidence supporting the minimization of radiation-induced toxicities and improved quality of life scores, the application of these devices in clinical practice is reported as limited to high-volume comprehensive cancer centers (Singh 2022).

However, with the analysis of different IPDs, it is demonstrated that they can be made of dense alloys for shielding or not. Among the experiments, 8 authors used acrylic resin (Polymethyl methacrylate (Verrone 2014; Khan 2014; Rosen 2015; Doi 2017; Rocha 2017; Appendino 2019; Hawari 2022; Singh 2022; Srivastava 2022).

Rocha et al. [37] opted for acrylic resin as an intraoral material due to non-toxic, non-irritating nature, cost-effectiveness, ease of handling, durability, hygienic properties, and because it does not interfere with radiation. However, Doi et al. (2017) observed that acrylic resin absorbed X-rays, prompting them to switch the device material to Polyethylene Terephthalate. In contrast, Herpel et al. [17] took a different approach, using 3D printing technology to manufacture a device with dental splint resin (Freeprint splint 2.0, Detax). The 3D printing was performed after CAD file alignment at a 45° build angle, with layers of 100 µm, and the fixation part was filled with a dental silicone impression material (Flexitime Putty, Kulzer). In some cases, wax is used as a material layer to filter and protect against radiation dispersion, especially in devices that incorporate dense shielding materials (Khan 2014; Butson 2015).

To date, no study has systematically evaluated and compared commonly used multifunctional stent materials. Additionally, the toxicity and leakage of IPD materials, such as plastics and dental alloys, into saliva have not been thoroughly investigated. Components of acrylic materials, including formaldehyde, methyl methacrylate, methacrylic acid, and benzoic acid, have been shown to leach and diffuse into saliva, potentially impacting oral tissues and the oral microbiota. These toxic components can be absorbed by the oral mucosa, gastrointestinal tract, skin, and respiratory system, leading to adverse side effects (Kazemian 2022).

Devices configured with materials that interact dosimetrically for shielding purposes often used lead, in the majority (Khan 2014; Rosen 2015; Bruno 2020; Hawari 2022), or Cerrobend or Lipowitz alloys (Hawari 2022; Singh 2022), for intraoral shielding of electron beams. Rosen et al. used a lead shield to create a prosthesis for brachytherapy, explaining its use due to the material's ability to protect intraoral structures from additional damage and unnecessary radiation exposure.

Another device in this regard is described by Butson et al. [6], made with lead shielding positioned with a thickness of copper tape and aluminum foil, coated with wax for filtration. The objective of the analysis was to minimize the thickness of this device's filtration, optimizing comfort and effectiveness while dispersing radiation. This is crucial since, as observed by Brandão et al. (2021), metallic material can cause radiation scattering due to their respective densities, consequently increasing the severity of mucositis. Another IPD described in the review by Singh et al. (2022) uses low-temperature melting alloys (158°Fahrenheit). Cerrobend or Lipowitz alloys, composed of bismuth (50%), lead (26.7%), tin (13.3%), and cadmium (10%), were used as protective materials and are incorporated with acrylic to form the shielding. In addition to Singh et al. (2022), Rocha et al. [37], in their device, used Cerrobend or lead as shielding with a thickness of 5 mm, adapted to the metal plate and wrapped in polyvinyl chloride film and wax to avoid contact with metal and reduce backscatter. Brandão et al. (2021) highlighted that metallic materials used in IPDs and their respective densities can affect the delineation of areas of radiation interest (the tumor), especially when associated with IMRT. Another observation is that, like lead, the constituents of the aforementioned metallic alloys are potentially toxic materials (Kazemian 2022).

Doi et al. (2017) provided information that IPDs are usually manufactured with thin, hard materials made to fit the upper gums, but at the same time, they stated that the ideal material and shape for these devices are not yet clear. Regarding this, there is a significant variability indicating a lack of standardization for IPDs, whether based on tumor location, device function, therapeutic radiation method, or ideal materials, making it challenging to understand their indications. On the other hand, one certainty, following what Singh et al. (2022) states, is that the use of additive manufacturing for stent production is demonstrated as a viable technology. This information aligns with the observations made in the devices by Bruno et al. (2020) and Herpel et al. [17] who used such a manufacturing strategy in their devices.

Discussion

This review highlights the main side effects caused by head and neck cancer radiotherapy in the oral cavity. Additionally, it investigates the use of IPDs to minimize these effects, providing a mapping of the characteristics of these devices, including indications, manufacturing techniques, and materials used. Furthermore, the effectiveness of these devices is analyzed based on the trials discussed here.

Regarding the highlighted side effects, mucositis stands out due to its high incidence in irradiated patients, with 80% of patients, as reported by Rocha et al. [37], describing it as a causative factor for pain, with a direct functional impact and consequent deterioration in the quality of life. In addition to the impact on the mucosa evidenced by mucositis, radiation affects the salivary glands, leading to recurrent xerostomia. Alterations in taste buds, represented by ageusias, dysgeusias, and hypogeusias, are also prevalent in the evaluated studies. Moreover, there are repercussions on bone tissue, both secondary to vascular changes (Helmers 2018) and directly impacting hard tissue, leading to the risk of osteoradionecrosis (Sroussi 2018; Wang 2021). Structural damage to dental tissues and loss of dental insertion is also described, which may be multifactorial due to increased risks of infections and alterations in oral bacterial colonies. Radiation caries represent another effect in the same vein, which can be explained by various functional changes resulting from radiation. Furthermore, fibrosis, trismus, and other tissue necroses are present when it comes to adverse effects caused by radiation intoxication (Sroussi 2018). These effects, whether temporary or permanent, can emerge months after the completion of radiotherapy, leading to dramatic effects on the ability to perform daily functions such as speaking, chewing, tasting, and swallowing. Their aggravation can result in the interruption of cancer treatment, consequently negatively impacting the prognosis and well-being of these patients (Colloc 2020; Brandão 2021).

Sroussi et al. [46] highlighted the complex oral health needs of head and neck cancer patients, stressing the importance of multidisciplinary collaboration between oncologists and dental professionals with specialized expertise in the oral care of cancer patients. This collaboration is essential for providing comprehensive care that includes assessment, treatment, and supportive care before, during, and after therapy. Preventive approaches aimed at reducing side effects had been linked to lower rates of prolonged hospitalization and contribute to cost savings in hospital supplies and overall healthcare costs.

According to the studies obtained in the review, unanimously, the devices are effective in reducing radiation dose to healthy oral tissues, resulting in a subsequent reduction in the occurrence of side effects. Following the beliefs of Rocha et al. [37] and Srivastava et al. [45], these instruments in their different classifications can and should be used, even in conjunction with modern and sophisticated radiotherapy treatments, to avoid unnecessary radiation through shielding or physical displacement of normal tissues away from the radiation field, thereby preventing and reducing oral complications accompanying therapy. However, Singh et al. (2022) provides information that, even though the minimization of toxicities and better scores in quality-of-life tests have been scientifically proven, the application of these devices is limited to major cancer centers.

IPDs are strategically designed to cover relevant oral tissues, promoting shielding protection, transporting radiotherapy materials, and displacing adjacent tissues or protecting against radiation scatter. In clinical practice, these intraoral devices are commonly made of thin and hard materials and are designed to fit the upper gums. However, Doi et al. (2017) clarify that the ideal material and ideal form factors are not yet clear, explaining why the material used for the devices evaluated in this study is not described in all studies.

Despite this, it is observed that the majority of studies presented in this research opted for the use of polymethylmethacrylate in the manufacture of devices. The choice is supported by the characteristics highlighted by Rocha et al. [37], who present polymethylmethacrylate as an excellent option due to its non-toxicity, absence of irritation in oral tissues, affordable cost, ease of handling, durability, hygiene, and no interference with radiation. However, it is important to mention that this perspective is contradicted by the study of Doi et al. (2017), which argues that devices made of acrylic resin absorb X-rays and suggesting that Polyethylene Terephthalate would be a superior material option. It is worth noting that, to date, there has been no systematic and comparative analysis of materials commonly used in multifunctional stents. Additionally, studies on the toxicity and leakage of materials from IPDs (i.e., plastics and dental alloys) into saliva lack detailed investigation. Specific components of acrylic materials, such as formaldehyde, methyl methacrylate, methacrylic acid, and benzoic acid, have the ability to leach and diffuse into saliva, impacting oral tissues and the oral microbiota. These toxic components released can also be absorbed into the oral mucosa, gastrointestinal tract, skin, and respiratory system, potentially triggering adverse effects (Kazemian 2022). For devices whose analysis objective was to obtain direct interference with radiation through shielding or transport, metallic materials such as lead, metallic alloys like Cerrobend and Lipowitz, were highlighted as effective for the function. Rosen et al. [39] advocate for the use of lead in their device due to its ability to protect intraoral structures from additional damage and unnecessary radiation exposure. However, the use of these materials requires the application of layers of other materials to filter radiation, prevent dispersion, and reduce dose escalation in undesired tissues, increasing the complexity and cost of the devices.

The use of devices with radiological interference is feasible only in treatments where radiation delivery occurs in reduced dimensions. On the other hand, technologies such as IMRT and other more advanced RT techniques, where radiation beams are propagated in multiple beams around the 360° of the tumor bed, become highly specific and require individualized planning and fabrication of devices, whose density does not interfere with the delineation of the tumor for the delivery of the planned dose. Based on this, one can mention the concern of Brandão et al. (2021) regarding the use of metallic materials in IPDs, as their densities can affect the delineation of areas of radiation interest when associated with IMRT. Given this statement, for treatments with photon beams, the use of low-density materials, similar to water, should be chosen to fabricate devices. On the other hand, in treatments with electron beams, the preference is for high-density materials, as their use usually covers more external regions where radiation scattering is not relevant.

From the understanding of the great variability in formats and materials of these devices, the lack of a well-defined standard for the choice of design, material, manufacturing technique, and indication regarding associated treatment is emphasized. This signals a gap in comprehensive studies and technological advances in this area, emphasizing the need for new research addressing this issue.

However, given the complexity of this topic and the uncertainties observed when comparing studies regarding device characteristics, there is an evident consensus regarding the use of 3D printing technology in the manufacture of stents, as demonstrated by Bruno et al. (2020), Herpel et al. [17], and Singh et al. (2022).

Conclusion

Based on the data obtained from the studies evaluated in this work, it was possible to conclude that patients diagnosed with head and neck cancer have specific dental needs due to the damage caused to epithelial tissues, mucosa, salivary glands, dental enamel, dentin, amelocemental junction, bone tissue, and taste buds. These damages result in symptoms such as mucositis, xerostomia, osteoradionecrosis, radiation caries, ageusia, and other side effects.

Researchers have proposed various approaches to using protective devices during radiotherapy for head and neck cancer treatment. Most authors opt for the use of customized stents made from acrylic resin (polymethyl methacrylate) or polyester, primarily aiming to reduce treatment configuration errors, minimize toxicity, and control the radiation dose delivered to healthy oral structures. 3D printing technology has emerged as a viable alternative for manufacturing these stents. While conventional radiotherapy and intensity-modulated radiotherapy (IMRT) are the most frequently discussed techniques, it is crucial to explore the applicability of these devices in conjunction with other radiation modalities and determine the most suitable indications for each clinical case.

However, the studies presented in the literature have several limitations, many of which stem from the scarcity of research on this topic. In addition to these aspects, we have identified some of the main limitations found in the literature, all of which have been included in the conclusion of the article.

One of the observed limitations is the lack of standardization in materials and techniques. There is no systematic comparative analysis of the materials used in intraoral devices, making it difficult to conduct meta-analyses and determine the ideal material for protection during radiotherapy. Furthermore, there is a scarcity of studies on toxicity, as the release of components from intraoral device materials, such as plastics and metal alloys, into saliva has not yet been thoroughly investigated. However, it is already known that certain components, such as formaldehyde and methyl methacrylate, can be absorbed by mucous membranes and cause adverse effects.

Another significant limitation is the absence of a detailed technical rationale, as many studies do not provide robust technical justifications for the choice of materials and device design. This makes it difficult to replicate results in different clinical settings. Additionally, there is a bias in the included studies, as none of the analyzed studies demonstrated a low risk of bias, highlighting the need for caution when interpreting results and potentially compromising the validity of the conclusions drawn.

Finally, there is a need for more clinical research. Despite promising evidence, the clinical applicability of intraoral devices remains limited to major oncology centers, making their adoption in broader clinical settings challenging. Moreover, there is a lack of controlled clinical studies to confirm their efficacy and establish standardized protocols for protection against the adverse effects of radiotherapy.

These limitations emphasize the need for further research to enhance the safety and effectiveness of intraoral devices in protecting against the effects of radiotherapy.

Supplementary Information

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Supplementary Material 1.

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Authors' contributions
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Data availability
All data generated or analyzed during this study are included in this published article and its supplementary files.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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