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Case report

Digital fabrication of customized intraoral appliances for head and neck radiotherapy

Anussara Prayongrat [a,1], Sarin Kitpanit [a,1], Chawalit Lertbutsayanukul [a,1], Pipop Saikaew [b], Thirayu Boonrueng [c], Trakol Mekayarajjananonth [d], Anjalee Vacharaksa [d,e,2,*]

[a] Division of Radiation Oncology, Department of Radiology, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Bangkok, Thailand
[b] Department of Operative Dentistry and Endodontics, Faculty of Dentistry, Mahidol University, Bangkok, Thailand
[c] Department of Dentistry, King Chulalongkorn Memorial Hospital, Bangkok, Thailand
[d] Geriatric and Special Patients (International) Program, Bangkok, Thailand
[e] Research Unit on Microbiology and Immunology, Faculty of Dentistry, Chulalongkorn University, Bangkok, Thailand

A B S T R A C T

Introduction: The radiotherapy received by head and neck cancer patients commonly has adverse effects on oral tissue and the muscles of mastication. This short communication describes the digital fabrication of intraoral appliances for radiotherapy and muscle exercises.
Methods: Three patients diagnosed with tongue squamous carcinoma were treatment-planned for radiotherapy using different radiation techniques. The patients were referred for oral scanning and digital bite records, and the appliance was collaboratively designed by a radiation oncologist, dentist, and laboratory technician. The appliance covered the occlusal surface of the remaining teeth with a 1-mm engagement. The lingual plate was 2-mm below the occlusal plane, and extended 4-mm distally, and the jaws were opened by 20-mm. The appliances were printed overnight using a rigid and biocompatible 3D printing material.
Results: Requiring minimal chair-time, the appliance was easily inserted and adjusted to comfortably fit in the mouth. The patients were trained to insert it themselves. The tongue was at a pre-determined position during daily radiotherapy, and the healthy tissues were separated from the radiation field. The patients had mild adverse effects on their oral mucosa. Additionally, the appliances were used for muscle exercises after the radiation courses to prevent trismus.
Conclusions: The interprofessional collaboration to fabricate customized intraoral appliances using digital workflow to maximize patients' benefits is feasible.
Clinical significance: The use of intraoral appliances is potentially increased when the fabrication process is facilitated. Using an intraoral appliance precisely targets the tumor are for better treatment outcomes, and the healthy adjacent tissues will be preserved to maintain the patient's quality of life.

1. Introduction

Radiotherapy is a common treatment for head and neck cancer (HNC). Radiotherapy can be given as an adjuvant treatment following surgical removal of the tumor, or as a definitive treatment for unresectable tumors, inoperable patients, and organ-

* Corresponding author. Microbiology Department, Faculty of Dentistry, Chulalongkorn University, Bangkok, Thailand. ,
E-mail address: anjalee.v@chula.ac.th (A. Vacharaksa).
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preserving purposes. The common radiation-related toxicities in HNC patients, including tissue damage of the oral mucosa, salivary glands, and alveolar bone, subsequently affect the treatment outcomes and quality of life in patients post-treatment [1].

The acute adverse effect is radiation-induced oral mucositis (RIOM), characterized by erythema and oral mucosa ulcers leading to irritation, pain, and difficulty in swallowing and speech. A cumulative radiation dose of 20 Gy at the oral mucosa reduces epithelial proliferation, and mucosal injury can be clinically observed when the cumulative dose is above 30 Gy. A dose ≥50 Gy can irreversibly damage the salivary glands and surrounding bone, leading to a risk of osteoradionecrosis. The damage to the salivary gland results in hyposalivation, decreased oral immunoglobulin A levels, and impaired antimicrobial mechanisms. These changes make the oral cavity more susceptible to infections, dental caries, and periodontal diseases [2]. Therefore, preserving the normal oral tissues is a prime consideration when treatment planning for radiotherapy.

An intraoral positioning stent effectively preserves the healthy tissue in HNC patients undergoing radiotherapy [3]. By limiting the radiation field, the intraoral stent reduces the radiation dose to the normal tissue, which substantially decreases the radiation-induced toxicity [4–9]. However, positioning stent use remains limited because the process of stent fabrication requires an interprofessional team of a radiologist, dentist, and dental laboratory. When using conventional techniques, the patient is referred to a dentist for an oral impression and bite registration to fabricate dental models. The laboratory technician sets up a wax template of the positioning stent for the desired mouth opening and tongue position and processes it using an acrylic resin material. The analog design and workflow requires many days, or weeks, for communication and processing.

Fabricating a positioning stent for radiotherapy patients requires several dental appointments, an experienced team, and effective communication between the clinic and dental laboratory [10,11]. For some laboratory technicians, several cases are necessary to gain the knowledge and skills needed for stent fabrication. Therefore, the availability, reliability, and reproducibility of the positioning stent from dental laboratories using an analog process may not occur in a timely manner, especially in cases where radiotherapy is urgently needed to prevent cancer progression.

Using computer-aided design (CAD) and computer-aided manufacturing, dental impressions can be digitally obtained and transferred for prosthesis processing. The digital fabrication of dental restorations and prostheses demonstrated similar accuracy with those made using conventional techniques [12,13]. Furthermore, the digital process reduces patient discomfort, chair time, and clinic-to-laboratory transportation. Some laboratory steps, such as production of the stone model, become unnecessary. However, the clinical evaluation of the digital workflow is still lacking. In this report, we demonstrated the feasibility of using digital workflow, including an intraoral scan with CAD and 3D-printing, to aid the design, fabrication, and insertion of intraoral appliances for three HNC patients.

2. Methods

2.1. Tumor characteristics and treatment

Three patients who presented at the Division of Radiation Oncology were diagnosed with squamous carcinoma of the tongue. The tumor location, cancer stage, definitive surgery, and radiotherapy of each patient were planned as described below and summarized in Table 1.

Patient 1: A 62-year-old male presented with the complaint of an ulcer on the tongue. The patient's symptoms started 5 months ago when he noticed an ulcer the left side of the tongue. The patient had a history of smoking for 20 pack years and alcohol consumption. On examination, an ulcerative mass was found on the left ventral tongue. The 4 × 2 cm mass was positioned across the midline and involved the base of the tongue. One-cm cervical lymph nodes were palpable at left level IA. A computed tomography (CT) scan of the neck revealed a 3.7 × 2.1 × 3.7 cm heterogeneous enhanced ulcerative mass at the ventral tongue, and the biopsy report confirmed the well-differentiated squamous cell carcinoma (SCCA) with no sign of metastasis. The patient was referred for a wide excision of the tongue with a left modified radical neck dissection. The right sentinel node dissection at level I-III was performed with left PMMF reconstruction and tracheostomy. The final diagnosis was a 5.5 cm and 1 cm invasive moderately differentiated SCCA. The pathological analysis revealed the presence of lymphovascular and perineural invasion of the right lymph node at level IB, and found a 1.3 cm metastatic SCCA, with extranodal extension. The bilateral lymph nodes at level II–V were not involved. The tumor stage was estimated to be T4aN3bM0. The surgery was followed by postoperative radiation of 66 Gy in 33 fractions using the 3-dimension conformal radiotherapy (3D-CRT) technique.

Table 1
Patient demographics, diagnosis, and treatment planning.

Case	Age	Sex	Tumor	Stage	Surgery	Radiotherapy
1	62	Male	Oral tongue cancer	T4aN0M0	Wide excision with left modified radical neck dissection.	Adjuvant radiotherapy using 3D-CRT; 66 Gy in 33 fractions
2	66	Male	Oral tongue cancer	T4aN0M0	Hemiglossectomy with selective lymph node dissection level I-III	Adjuvant chemoradiotherapy using IMRT; 66 Gy in 33 fractions
3	64	Male	Second primary oral tongue cancer after definitive CCRT for nasopharyngeal carcinoma	T1N0M0	Wide excision after induction chemotherapy	Re-irradiation using IMPT; 70 GyE in 35 fractions

3D-CRT, three-dimensional conformal radiotherapy; IMRT, intensity modulated radiotherapy; IMPT, intensity modulated proton therapy; CCRT, concurrent chemoradiation.

Patient 2: A 66-year-old male presented with the complaint of an ulcer at the left oral tongue and odynophagia for 2 months. The patient had a history of smoking 40 pack-years but quit for 1 year, and social alcohol drinking. On examination, a 3 cm ulcerative mass was found at the left lateral tongue with contact bleeding. No palpable lymph nodes were detected. A computed tomography scan of the neck revealed a 2.7-cm irregular heterogeneous enhancing mass at the left ventral tongue without lymphadenopathy. The tongue mass biopsy confirmed the moderately differentiated SCCA. The patient underwent left hemiglossectomy with selective lymph node dissection at level I–III. The final diagnosis was a 4.5 cm and 10 mm invasive moderately differentiated SCCA and the presence of lymphovascular and perineural invasion. There was no evidence of malignancy in the 24 resected lymph nodes. The tumor stage was estimated to be T4aN0M0. The surgery was followed by postoperative chemoradiation of 66 Gy in 33 fractions using the intensity modulated radiotherapy (IMRT) technique.

Patient 3: A 64-year-old male with a history of nasopharyngeal carcinoma, which had been treated with chemoradiation 9 years ago, presented with a second primary tongue cancer. The MRI scan revealed a new 2.6 × 3.2 × 2.9 cm lesion at the ventral tongue. He underwent palliative chemo-immunotherapy with cisplatin, 5-fluorouracil, and pembrolizumab, followed by surgery. The pathological report confirmed a 1.5 cm moderately differentiated SCCA, with involved surgical margins. The tumor stage was estimated to be recurrent T1N0M0. The re-irradiation with proton therapy was administered at 70 Gy in 35 fractions.

2.2. Customized intraoral appliance design, fabrication, and insertion

The patients were referred to the dental clinic for pre-radiotherapy mouth preparation. On the first visit, a thorough oral examination was performed, intraoral photographs were taken (Fig. 1a–c), and the oral scan was completed within 5–10 min using a Trios 3 intraoral scanner (3Shape, Denmark). A jaw-opening position jig made with self-cured acrylic was used to separate the maxilla and mandible during the bite scan. The digital models demonstrating jaw relationship were submitted to the laboratory (Fig. 2a–f). The design and fabrication of the intraoral appliance was modified from Wilke et al. [14]. Briefly, the intraoral appliance was designed using 3Shape Dental Software (3Shape, Denmark). The appliance covered the total occlusal surfaces of the remaining teeth and engaged the lingual and buccal tooth surfaces for 1-mm (Fig. 3a–b). An open window from the left to right premolar area was designed to facilitate breathing and patient comfort during radiation. The lingual plate was 2 mm below the occlusal plane and extended 4 mm distally from the second mandibular molar area for tongue positioning. The radiologist, dentist, and laboratory technician conveniently communicated online, and the digital design was promptly approved. The oral appliance was printed with a biocompatible, clear, acrylic compound (Stratasys, Germany). The total printing time was 5 h, followed by curing in 405 nm UV light (Formlabs Form Cure, Germany) at 80 °C for 60 min.

The second dental visit was on the next day for an intraoral fitting. The oral appliance was inserted and adjusted intraorally by the dentist (Fig. 4a–c). The patients practiced inserting the intraoral appliance by themselves for their daily radiation treatment. The patients were then sent to undergo the CT simulation for radiotherapy planning on the same day.

2.3. The use of appliances for radiotherapy and muscle exercises

In the simulation session, the intraoral appliance guided the mandible and tongue to the desired positions before the thermoplastic head-shoulder mask was applied. The patients then underwent CT and magnetic resonance (MR) simulation scans. The acquired CT and MR images were used for radiotherapy planning. The treatment plan was calculated for the individual patients using the Eclipse™ treatment planning system (version 15.0, Varian Medical System, Palo Alto, CA). Three-dimensional conformal radiotherapy (3D-CRT), intensity modulated radiotherapy (IMRT), and intensity modulated proton therapy (IMPT) were given to the patients as summarized in Table 1. The intraoral appliance was used to position the mandible and tongue while receiving the daily radiation fraction. In addition, the patients were instructed to use their appliance at home for muscle stretching exercises to prevent trismus. The patients were assessed weekly to identify any adverse events, including RIOM, xerostomia, and weight loss, according to the Common Toxicity Criteria of Adverse Events (CTCAE) version 4.03.

Fig. 1. A representative patient's intraoral examination and photography prior to digital fabrication. The patients were referred to the dental clinic for intraoral appliance fabrication after surgical removal of their tumor. A thorough dental and oral examination was performed, the results were recorded, and intraoral photographs were obtained. The intraoral photographs of one patient demonstrates (A) the occlusal view of the maxillary arch, (B) the occlusal view of the arch illustrating the hemiglossectomy, and (C) the front view of the centric occlusion position.

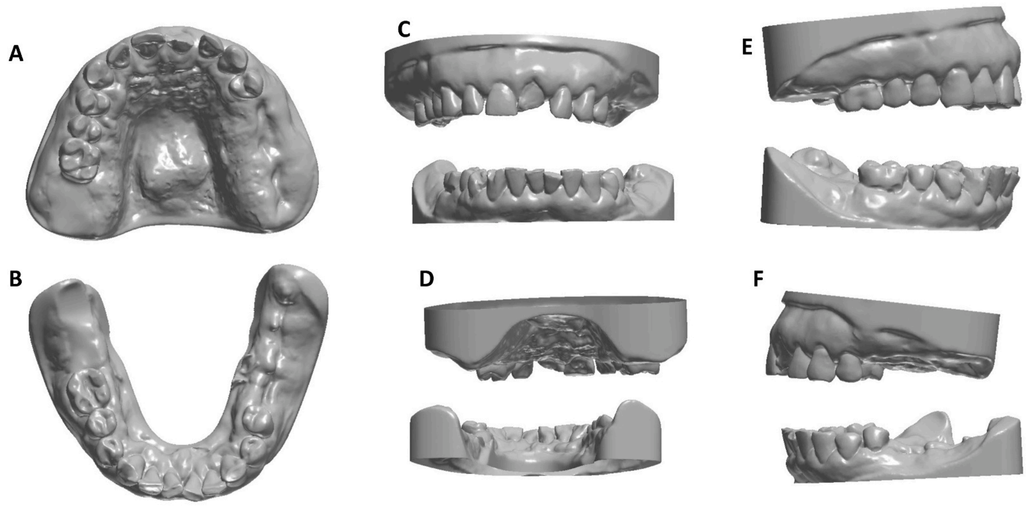

Fig. 2. A representative digital model. The patients were intraorally scanned and had their bite recorded. The digital models were submitted to the dental laboratory for intraoral appliance design and fabrication. The digital model of one patient demonstrates (A) the occlusal view of the maxillary arch, (B) the occlusal view of the mandibular arch, and (C) the front view, and (D) the back view of the 2-mm jaw opening position. (E) The right and, (F) the left view of the jaw opening position.

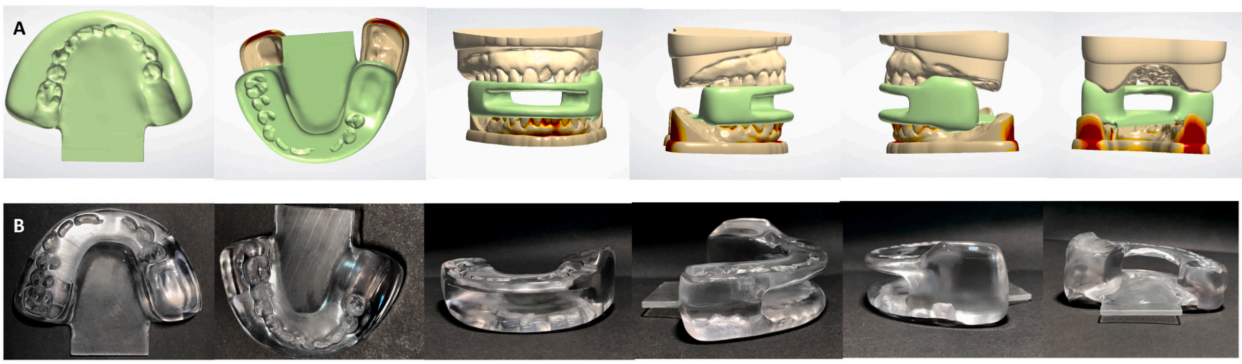

Fig. 3. A representative digital design and fabrication. The digital design (A) was generated by the dental technician and shared between the dentist and radiologist. After the design was approved, the appliance (B) was printed using 3D printing technology as described in the materials and methods. The appliance was polished, cleaned and delivered to the dental clinic.

3. Results

The workflow efficacy was assessed based on three parameters comprising the fitting the appliance, bite accuracy, and chair time for appliance insertion. We found that when the appliance was seated on the occlusal surfaces and clinically evaluated, the fit was as accurate as planned in the digital model. Next, the accuracy of the digital recording of the jaw relation when opening for 2 mm was determined. The digital bite scan using a customized anterior jig successfully replicated the jaw relationship including the case of a severe Angle Class III malocclusion (case no. 3). Therefore, the appliances were easily inserted into the planned position with the desired opened vertical dimension. The chair time for appliance insertion was less than 15 min, including minor adjustments by the dentist. The patients wore the appliance comfortably and could self-insert the appliance within a few minutes after being instructed how to do so. The total chair time during the insertion visit for each case was less than 30 min.

The radiation dose distribution for Case 1, 2, and 3 are demonstrated in Fig. 5a, b, and 5c, respectively. The tongue was depressed when the positioning appliance was inserted. The 20-mm opened bite displaced the hard palate, soft palate, and maxillary alveolar bone away from the radiation field. IMRT and IMPT delivered a lower radiation dose to the bilateral parotid glands and posterior mandibular bone compared with 3D-CRT.

The patients used their intraoral appliance while receiving? The radiation and for muscle exercises at home, throughout the treatment course. Mild adverse effects from the radiation were observed at the weekly assessments. The patients had grade 0–1 xerostomia and weight loss. Patient 1 demonstrated grade 3 RIOM at week 4, whereas patient 2 and 3 experienced grade 1 and 2 RIOM, respectively. No patients developed palatal mucositis.

Fig. 4. A representative intraoral appliance insertion. The front view of the appliance (A) demonstrates the 2-mm jaw opening position. (B) and (C) A large window opening from the premolars to premolars allows patient comfort and breathing.

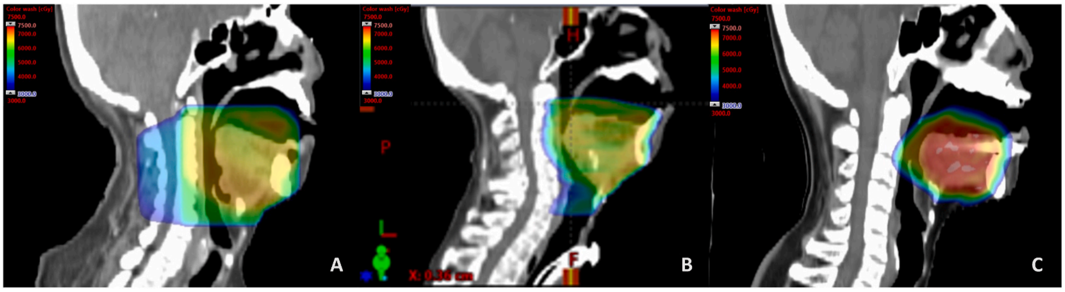

Fig. 5. Dose distribution in patients with the customized intraoral appliance. Three patients were diagnosed with tongue cancer and received radiotherapy. Using the customized intraoral appliances, the radiation dose distribution for each case is demonstrated. The tongue was depressed while the positioning appliance was inserted. With the 20-mm opened bite, hard palate, soft palate, and maxillary alveolar bone were displaced from the radiation field. The radiotherapy techniques were (A) three-dimensional conformal radiotherapy (3D-CRT) in case 1; 66 Gy in 33 fractions, (B) intensity modulated radiotherapy (IMRT) in case 2; 66 Gy in 33 fractions, and (C) intensity modulated proton therapy (IMPT) in case 3; 70 GyE in 35 fractions. The customized intraoral appliances totally separated the maxillary healthy tissue from the radiation field.

4. Discussion

The common adverse events of head and neck cancer radiotherapy patients are mucosal injury, including RIOM, xerostomia, trismus, and dermatitis. RIOM is a dose-limiting toxicity that is enhanced by the concomitant chemotherapy in locally advanced disease and postoperative high-risk patients. Over the course of radiotherapy, the occurrence and severity of RIOM and xerostomia is associated with poor treatment compliance, interrupted planned treatment, extended hospitalization, becoming dependent on nutritional and analgesic support, and increased risk of local and systemic infections. These consequences lead to suboptimal disease control and a lower quality of life [1,2].

Trismus is a late radiation effect that is influenced by the tumor's location and the radiation field involving the muscles of mastication [15]. This effect results in many oral and dental problems, such as poor oral hygiene, difficulty in oral examination and dental procedures, and inadequate oral intake. Multidisciplinary management is crucial for these adverse events and includes oncologists, dentists, rehabilitation therapists, and nurses. There are several approaches to prevent and treat these adverse effects, such as the use of improved radiotherapy techniques to protect the normal structures [16,17], the intraoral appliance to protect healthy oral tissues [3], and muscle exercise intervention [18].

A retrospective study demonstrated that the intraoral appliance significantly reduced the radiation dose and decreased the incidence of RIOM from 81% to 33% [4]. Although radiation-induced toxicity were not within the scope of this case report, the three patients reported only mild adverse events. The patient who received the 3D-CRT technique developed grade 3 RIOM in week 4, which was approximately one week later than those without a stent [5]. In addition, the customized oral appliance can be used after the course of radiotherapy as a device for muscle exercise and trismus prevention [19]. This appliance is therefore multipurpose and is likely cost effective compared with commercial appliances.

This report described the fabrication process for a customized intraoral appliance using CAD and a 3D-printing method for three patients diagnosed with SCCA of the tongue. The process was feasible in a timely manner for the patients who were planned for radiotherapy. An intraoral digital impression reduces the time required for fabricating custom-made appliances, simplifying the procedure for the dentist, and facilitates the communication between dentists, radiologists, and technicians. The process encourages interprofessional collaboration in the appliance design to achieve the best patient benefits. Using the digital workflow presented in this study, only two short dental visits were required. Subsequently, the intraoral stent insertion and adjustment were performed on the same visit and the patient then underwent the CT simulation the same day. The 3D-printing material is affordable, rigid, biocompatible, and can be easily adjusted for insertion. The appliance design provides patient comfort, which increases patient compliance during the radiotherapy sessions, and post-treatment for muscle stretching. Although different radiation techniques were used in the three cases, the intraoral appliances were easily used without any interruption during treatment.

The design of intraoral appliances is customized based on the tumor location. For tongue cancer, we designed a lingual plate to depress the tongue while displacing the hard palate, soft palate, and maxillary alveolar bone from the radiation field that resulted in a minimal radiation dose and toxicity to the normal tissue [6]. Additionally, the minimal occlusal engagement design allowed the appliance to be easily inserted while precisely maintaining the appliance in position during radiotherapy. Compared with a commercial oral positioning stent, such as GrayDuck stent™, that uses an Ethylene-vinyl acetate (EVA) mold for semi-customized fitting, the appliances used in this report provided a fully customized design of stable occlusal engagement with a rigid material that allowed a comfortable fit at the same position through the daily radiation course, and post-treatment for muscle exercise. However, the advantages of commercial appliances are their flexible use. The mouth opening distance can be self-adjustable by patients without a dental visit.

Other digital workflows fabricate the appliances directly from the diagnostic CT images [14]. The drawback of this technique is the quality of the CT images, especially when there are some artifacts from the tooth surfaces. Moreover, the lack of jaw relation records may lead to a discrepancy in the appliance's fit and increase chair time for insertion. In addition to using CT-derived images, Zaid et al. added the step of 3D-scanning of the dental model to improve the procedural time efficiency, fit, accuracy, and dimensional change [20]. However, the proposed processes still required an extra dental visit to acquire the dental impressions, which might delay the start of the radiotherapy sessions.

Although this case report described only three cases that were treated by different radiotherapy techniques, it is well accepted that intraoral stents are beneficial for healthy tissue preservation. However, fabricating a customized intraoral stent using the conventional approach requires dental skills and time, which could delay beginning radiotherapy. The digital workflow used in this case report reduced the fabrication steps and chair time for insertion. Fabricating the appliance overnight is possible for the patient to undergo the CT simulation on the next day. The intraoral adjustment is a one-time procedure, and the material can be easily adjusted using standard dental procedures by general dentists. Therefore, the use of appliances and the collaboration of dentists, radiologists, and dental technicians can be encouraged by digital workflow. Its use by radiologists and dentists in non-academic centers may be broadened by submitting the results of the intraoral scanning to a central institution, consulting about the appliance design, and receiving the appliance back for radiotherapy.

5. Conclusion

The digital workflow of designing and fabricating a customized intraoral appliance is feasible and efficient using CAD and 3D-printing techniques. The use of intraoral appliances during and after radiotherapy effectively preserves healthy adjacent tissues regardless of radiation technique, and potentially reduces the adverse events from radiotherapy.

Author contribution statement

All authors listed have significantly contributed to the investigation, development and writing of this article.

Data availability statement

Data will be made available on request.

Additional information

Supplementary content related to this article has been published online at [URL].

Declaration of competing interest

The authors declare that they have no competing interests, or other interests that might be perceived to influence the results and/or discussion reported in this paper. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e15374.

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