Advances of 3D printing in oral oncology: personalized technologies for patients – a narrative review

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Abstract. This study presents a narrative review of the literature that focuses on the substantial relevance and practical application of additive manufacturing and 3D printing in the context of oncology patients in the dental field. To address innovative technologies for diagnosis and treatment, this review underscores the progressive role of 3D printing in the creation of customized models for rehabilitation, surgical planning, prosthetics, examinations, and even tissue engineering. We analyzed five articles focused on the following categories: applications, benefits, and challenges associated with additive manufacturing; 3D printing; head and neck cancer; as well as assistive technology in the context of improving the effectiveness of treatments for people with this type of neoplasm. Oropharyngeal squamous cell carcinoma stood out as the most cited neoplasm for the use of 3D printing. 3D printing has played a significant role in transforming oral cancer treatment by providing customized solutions and enhancing outcomes: custom implants and prosthetics, patient-specific radiotherapy accessories, dose modulation devices, and improved preoperative planning. Additionally, 3D printing enables the production of complex medical devices in a single process, reducing steps and potentially costs. This also opens doors to creating more affordable solutions and extends the reach of personalized treatment to a greater number of patients. Continuous advancements in research and development of additive manufacturing and 3D printing technologies demonstrate significant potential for optimizing treatments and improving outcomes for patients with head and neck cancer.

Keywords: 3D printing, additive manufacturing, oral cancer, oral oncology, oral neoplasm, digital dentistry.

1. Introduction

Cancer has significant implications for both patients' physical health and self-esteem. Head and neck cancer (HNC) is the eighth most prevalent type globally, registering more than 830,000 new cases and 408,000 deaths annually [1]. Its influence on oral health affects vital aspects such as nutrition, communication, social interaction and self-esteem, playing a determining role in the general well-being of the individual [2]. In India, neoplasms of the oral cavity account for between 30 % and 40 % of all cancer cases [3]. These numbers highlight the relevance of early detection of oral cancer, which is directly associated with improved patient survival rates. Therefore, the use of advanced technologies in early diagnosis and minimizing the harm of therapies plays a crucial role in this process.

Cancer in the dentistry area comprises the head and neck (HN) region, and can affect the tongue, pharynx, mucous membranes and bones. The main etiological factors include tobacco, alcohol, and genetic predisposition [4]. Treatment commonly involves surgical intervention, often complemented by radiotherapy and/or chemotherapy, resulting in side effects such as mucositis,

xerostomia, irradiation caries, opportunistic infections, loss of taste, and bone deterioration [4]. In addition to the physical alterations, it is relevant to highlight the emotional impacts, such as depression and low self-esteem, with challenges in accepting the new image after the removal of the tumors [5]. In this context, the use of additive manufacturing and 3D printing technologies emerge as essential allies. These technologies not only allow anatomical rehabilitation, but also improve the efficacy of cancer treatments by enabling the use of lower doses of radiation, due to the high precision and delimitation of the area to be irradiated.

Additive manufacturing is a manufacturing process that builds objects layer by layer from a three-dimensional digital model [6]. This innovation has found application in several industries, including medical and dental oncology [7]. 3D printing, a technique within additive manufacturing, consists of the controlled deposition of materials, usually plastics or resins, to create precise three-dimensional objects. Its main advantages include the ability for customization, reduction of material waste, and efficient production of complex parts for facial reconstruction structures [6, 8].

In this scenario, innovation and the application of technology-assisted dentistry emerge as fundamental elements to overcome these limitations, ensuring humanized, inclusive, and effective care [9]. Additionally, adapted devices and innovative approaches using 3D technology can improve the effectiveness of devices employed in the diagnosis and treatment of HNC [10].

The additive manufacturing and 3D printing revolution in advanced dentistry, as highlighted by Liwei, et al. [11], offers unprecedented possibilities in the creation of customized devices. These technologies not only promise to improve the quality of life of patients, but also democratize access to more technological solutions available in engineering to face the challenges of diagnosis and treatment of neoplasms in the HN region.

In addition to treating head and neck tumors, dentistry contributes to proper speech ability, nutrition and, crucially, self-esteem [12]. In cases where physical or cognitive limitations occur due to mouth cancer, assistive technology plays a crucial role. This includes adapted devices such as dental splints to guide radiotherapy and reduce the toxicity associated with oncological radiation, the use of radioprotective masks, and the 3D fabrication of prostheses for the nose, jaw, and other structures that can restore the patient's function and self-image [10, 13, 14].

Given the relevance of the topic, this narrative review aims to analyze the use of additive manufacturing and 3D printing in cancer patients within the dentistry area, exploring their impact on treatment effectiveness, patient outcomes, and the future prospects for integrating these technologies into standard dental oncology practices.

2. Methods

This study constitutes a qualitative narrative review examining the significance of additive manufacturing and 3D printing in cancer patients within the dental field. Data collection occurred between October and November 2023, utilizing the PubMed, Scopus, and Web of Science databases. The search employed the key search: "((((3D printing*) OR (additive manufacturing)) OR (digital dentistry)) AND (oral cancer)) AND (oral oncology)) AND (oral neoplasia)". Selected articles were required to be either original or reviewed. Initially, 193 articles were identified upon indexing, considering their titles and abstracts. After abstract analysis, 20 articles were chosen. Subsequently, three independent researchers conducted duplicate checks, resulting in the selection of five articles for inclusion in this study. It's important to note that this topic is recent, with publications mainly from 2017 onwards, which limited the number of articles available for analysis.

After the careful selection of the articles, we proceeded with a series of steps: an exploratory reading, selection of material aligned with the study's objectives, text analysis, and finally, an interpretative reading preceding the writing process. Data analysis and synthesis were undertaken to identify pertinent information regarding the applications, benefits, and challenges of additive manufacturing, 3D printing, HNC, and assistive technology. The objective was to verify the use

of 3D printing in the treatment of patients with HNC. The results were organized in the corresponding section, with relevant citations throughout the text to substantiate the presented arguments.

3. Results

In the selection based on the search criteria, five articles (see Table 1) related to 3D printing, additive manufacturing, digital dentistry, oral cancer, oral oncology, and oral neoplasms were chosen. Among the five papers, four consisted of clinical trials, with one being a pilot study for a clinical trial. Only one out of the four clinical trials was randomized. The studies encompassed various scopes: one was conducted on rats, another on clinical samples collected from biopsies, while the remaining three involved patients aged between 18 and 75 years. These studies originated from two in the United States, one in Canada, one in Germany, and one in England. Squamous cell carcinoma in the oropharynx and at the base of the tongue emerged as the most frequent type of neoplasm in the five selected articles.

Table 1. Articles related to 3D printing, additive manufacturing, digital dentistry, oral cancer, oral oncology, and oral neoplasms

Ranking	Article (Table A1)	No. of citations
1	Zaid, Mohamed et al. “Creating customized oral stents for head and neck radiotherapy using 3D scanning and printing.” Radiation oncology (London, England) vol. 14,1 148. 19 Aug. 2019 [14]	21
2	Hughesman, Curtis B et al. “Detection of clinically relevant copy number alterations in oral cancer progression using multiplexed droplet digital PCR.” Scientific reports vol. 7,1 11855. 19 Sep. 2017 [15]	7
3	Held, Thomas et al. “3D-printed individualized tooth-borne tissue retraction devices compared to conventional dental splints for head and neck cancer radiotherapy: a randomized controlled trial.” Radiation oncology (London, England) vol. 16,1 75. 17 Apr. 2021 [16]	5
4	Byrne, James D et al. “Personalized Radiation Attenuating Materials for Gastrointestinal Mucosal Protection.” Advanced science (Weinheim, Baden-Wurttemberg, Germany) vol. 8,12 2100510. 27 Apr. 2021 [13]	2
5	Zaid, Mohamed et al. “A prospective parallel design study testing non-inferiority of customized oral stents made using 3D printing or manually fabricated methods.” Oral oncology vol. 106, 2020 [10]	1

Table 1 displays the five selected articles covering 3D printing, additive manufacturing, digital dentistry, oral cancer, oral oncology, and oral neoplasms, along with their respective number of citations in descending order. Table A1 (Appendix) exhibits the institutions, departments, and countries involved in the studies presented.

The case studies presented in Table 1 demonstrate the successful application of additive manufacturing in HNC. These cases highlight the remarkable benefits achieved through the personalization of assistive devices and oncological dentistry treatments. The following are detailed specific examples illustrating how additive manufacturing was employed, highlighting the methods and technologies used to create these devices and treatments.

3.1. Creating custom oral stents for head and neck radiation therapy using 3D scanning and printing

The use of digital workflow in radiation oncology has proven to be fast and efficient. This study published in England in 2019 [14], with 21 restrictions, evidenced the efficacy of personalized oral stents in minimizing toxicity in patients undergoing HNC radiotherapy. In addition, another study in the United States in 2020 compared personalized 3D printed oral stents with manually manufactured ones, demonstrating the superiority of 3D stents in reducing toxicity

during radiotherapy [10].

3.2. Radiation attenuation system for protection of the gastrointestinal mucosa

In Germany, customized radioprotective devices, manufactured by 3D printing, have been used to reduce gastrointestinal/oropharyngeal tissue injuries in cancer patients undergoing therapeutic radiation [13].

3.3. Detection of clinically relevant copy number changes in oral cancer progression using multiplexed digital droplet polymerase chain reaction (PCR)

In this study, conducted in Canada, digital PCR was employed as a highly accurate approach to detect and quantify sensitive nucleic acids, using multiplexed droplets. This technique was able to identify elements associated with the formation of oral squamous cell carcinoma, being applied both in DNA from oral cell lines and in clinical samples from different stages of the disease. It has been shown to be effective in identifying specific oncogenic events in the genome, in addition to its capabilities to assess human papillomavirus status and viral load. This precision and versatility may have significant clinical value in differentiating between benign oral lesions and those with the potential to progress to oral cancer [15].

3.4. 3D printed individualized metal tissue retraction devices compared to dental splints for head and neck cancer radiation therapy: a randomized clinical trial

This study conducted in England in 2021 investigated the effectiveness of 3D-printed dental tissue retraction devices (TRDs), compared to conventional dental splints, for patients undergoing HNC radiation therapy. The preliminary clinical application of TRD has demonstrated significant potential in reducing both acute and delayed radiotherapy toxicity in cancer patients in this region [16].

3.5. Accurate anatomical models and tactile scales in dental practice

In addition to treatments, additive manufacturing is widely used in the creation of accurate anatomical models for educational and surgical planning purposes in dentistry. For example, a tactile scale to measure dental anxiety [17], illustrating the effort to humanize care in order to improve the patient experience.

These examples highlight how additive manufacturing is revolutionizing dentistry by enabling unprecedented customization of assistive devices and dental treatments. These approaches not only improve the quality of life of patients, but also increase the efficacy and accuracy of therapeutic procedures for the detection and treatment of neoplasms in the HNC region.

4. Discussion

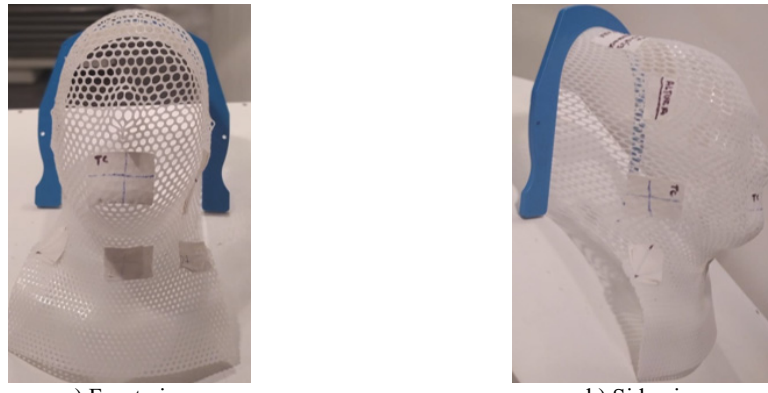
The analysis of these innovations in this study was directed to evaluate their correspondence to the objectives of the study, with an emphasis on the positive impact on the quality of life of cancer patients. Additionally, the implications and benefits of additive manufacturing and assistive technology were explored, both in oncology and oral and maxillofacial surgery, biomedicine, and related fields, particularly in terms of diagnosis and treatment. Throughout the discussion, opportunities and limitations for future research are identified. The five examined articles demonstrate the predominance of squamous cell carcinoma in the oropharynx, especially at the base of the tongue, prompting reflections on the predominant etiological factors in this type of neoplasia, including smoking [4].

4.1. Analysis of the results in the light of the study objectives

The results of this study clearly demonstrated how additive manufacturing has been successfully applied in the treatment of HNC, with a focus on the personalization of assistive devices and oncology treatments. The original proposal was to explore the applications and benefits of these interdisciplinary technologies and their contribution to improving the quality of life of patients with neoplasms. The case studies and examples presented in this study illustrate how additive manufacturing enables unprecedented personalization in oncology, meeting the specific needs of each patient and, consequently, promoting greater effectiveness of chemotherapy/radiotherapy treatments.

4.2. Implications and benefits of integrating additive manufacturing into head and neck cancer and assistive technology

The integration of additive manufacturing into dentistry brings with it a number of significant implications and benefits, especially as it relates to assistive technology. Customizing devices to target specific irradiation areas in radiotherapy (see Fig. 1), using 3D printing technology, results in better fit and increased comfort for cancer patients. This not only improves the efficiency of treatment, but also positively impacts the overall quality of life by facilitating functions such as feeding, speaking, and maintenance of the masticatory system [16]. Innovations in additive manufacturing and 3D printing have revolutionized healthcare by personalizing prosthetics and treatments, resulting in improvements in quality of life, reduced discomfort, and increased access to cancer care [7, 12, 18]. Fig. 2 shows an example of virtual modeling and application of 3D printing: A customized facial prosthesis for a patient with a squamous cell carcinoma lesion.



a) Front view b) Side view

Fig. 1. Photograph of a radiotherapy mask manufactured by additive manufacturing. This mask is used to immobilize the patient during radiotherapy sessions in the head and neck region.
Photo credits: Author RFN, 2023

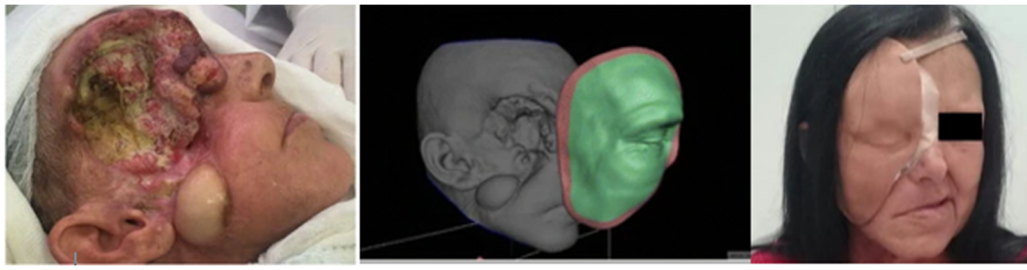


Fig. 2. Example of virtual modeling and application of 3D printing in a customized facial prosthesis for a patient with squamous cell carcinoma lesion [19]

In addition, 3D printing of accurate anatomical models plays a key role in surgical planning and the training of professionals in the field of HNC. This not only improves the training of future professionals, but also facilitates effective communication with patients, helping them to better understand the proposed procedures [11].

4.3. Study limitations and opportunities for future research

Some limitations of this study are acknowledged. Firstly, this research was based on a narrative literature review, which means that the examples and case studies presented are representative of the research available up to the date of the analysis, without assessing the quality of the studies analyzed. It is also noteworthy that gray literature was not included in the databases consulted. Therefore, it is possible that there are more recent advancements and applications not covered in this article. In addition, while the benefits of additive manufacturing have been highlighted, it is relevant to consider the challenges associated with this technology and how they can affect the accessibility of these personalized treatments [6, 18].

Opportunities for future research include further investigations into the long-term efficacy of these personalized devices, as well as studies evaluating the impact on survival and improved comfort during examinations in patients with HNC. It is noteworthy that no work in Latin America was found in the databases consulted and this work should be encouraged on all continents. Furthermore, collaboration between healthcare professionals, engineers, assistive technology specialists, and other fields can result in even more innovative and affordable solutions.

5. Conclusions

This study highlighted the positive impact of additive manufacturing on HNC as well as assistive technology, highlighting its ability to enhance treatments for people with cancer. The personalization of prostheses and treatments through 3D printing and additive manufacturing has revolutionized healthcare services, resulting in significant improvements in quality of life, reduced discomfort, and access to cancer care. Despite these advances, challenges remain, such as cost-related issues, that need to be overcome. Future research should focus on evaluating long-term efficacy and the impact on patient survival. The relevance of interdisciplinary collaboration between professionals for the creation of accessible solutions is highlighted. The continuous transformation of additive manufacturing in oncology and assistive technology promises a promising future, providing opportunities in constant research and development to benefit patients with head and neck cancer by optimizing their treatments in a humanized way.

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Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author contributions

Mirian Castro-Braga, Wellingtânia Domingos Dias, and Junia Maria Serra-Negra worked on

the concept and design of the study; Mirian Castro-Braga, Wellingtânia Domingos Dias and Junia Maria Serra-Negra also contributed to the management and coordination of the planning and execution of research activities. Additionally, Mirian Castro-Braga, Wellingtânia Domingos Dias, Junia Maria Serra-Negra, Raquel Fabiane Nogueira, Lucas Guimarães Abreu, and Rudolf Huebner contributed to the intellectual content of the manuscript, actively participating in the writing of the article and providing critical review and final approval.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethics statement

This article does not contain any studies with human participants performed by any of the authors.

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Appendix

Table A1. Departments and institutions involved in the production of the five selected articles with a survey of all authors involved in the publication

Institutions and departments	Countries
Oral & Maxillofacial Surgery, Faculty of Dentistry, The University of Hong Kong	China
Bioinformatics Core, University of Michigan, Ann Arbor, Michigan	EUA
Biostatistics, University of Michigan School of Public Health, Ann Arbor, Michigan 7	
Center For Immuno-Oncology, Dana-Farber Cancer Institute, Boston, Massachusetts	
Department Of Biostatistics, The University of Texas Md Anderson Cancer Center, 1515 Holcombe Blvd, Houston	
Department Of Head and Neck Surgery, Division of Surgery, The University of Texas Md Anderson Cancer Center, 1515 Holcombe Blvd, Houston, Tx	
Department Of Medical Oncology, Dana-Farber Cancer Institute, Boston	
Department Of Pathology, Brigham & Women's Hospital, Boston	
Department Of Radiation Oncology, Division of Radiation Oncology, The University of Texas Md Anderson Cancer Center, 1515 Holcombe Blvd, Unit 0097, Houston, Tx	
Department Of Radiation Oncology, University of Minnesota Medical School, 516 Delaware St Se, Minneapolis	
Division Of Oral Medicine and Dentistry, Harvard School of Dental Medicine, Boston, Massachusetts	
Division Of Otolaryngology-Head and Neck Surgery, Department of Surgery, Brigham & Women's Hospital, Boston, Massachusetts	
Environmental Health Sciences, University of Michigan School of Public Health, Ann Arbor, Michigan	
Immunopurified, Brigham & Women's Hospital and Dana-Farber Cancer Institute, Boston, Massachusetts	
Oral Medicine Clinic, University of California San Francisco School of Dentistry, San Francisco, California	
Otolaryngology, University of Michigan Medical School, Ann Arbor, Michigan	
Pathology, University of Michigan Medical School, Ann Arbor, Michigan	
Periodontics And Oral Medicine, University of Michigan School of Dentistry, Ann Arbor, Michigan	
Radiation Oncology, University of Michigan Medical School, Ann Arbor, Michigan	
Rogel Cancer Center, University of Michigan, Ann Arbor, Michigan	
Department Of Industrial Digitalization, School of Technology and Innovations, University of Vaasa, Vaasa	Finland
Department Of Mathematics and Statistics, University of Helsinki	
Department Of Otorhinolaryngology - Head and Neck Surgery, University of Helsinki and Helsinki University Hospital, Helsinki	

Department Of Pathology, University of Helsinki	
Department Of Pathology, University of Helsinki	
Department Of Public Health, University of Helsinki, Helsinki	
Department Of Public Health, University of Helsinki, Helsinki	
Institute For Molecular Medicine Finland (Film), University of Helsinki, Helsinki	
Institute Of Biomedicine, University of Turku, Pathology, 20500 Turku	
Research Program in Systems Oncology, Faculty of Medicine, University of Helsinki, 00100 Helsinki	
University Of Turku, Institute of Biomedicine, Pathology, Turku	
Advanced Clinical Pharmacist in Oncology, The Mid Yorkshire Hospitals Trust, Wakefield	
Clinical Lecturer in Restorative Dentistry, Department of Restorative Dentistry, School of Dentistry, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool	England
Department Of Molecular and Clinical Cancer Medicine, Institute of Systems, Molecular and Integrative Biology, The University of Liverpool Cancer Research Centre, Liverpool	
Department Of Oral Medicine, Liverpool University Dental Hospital, Liverpool	
Honorary Clinical Research Fellow, School of Health Sciences, The University of Liverpool	
Honorary Consultant in Oral & Maxillofacial /Head & Neck Surgery Liverpool University Hospitals NIHs Foundation Trust, Aintree Hospital, Fazakerley, Liverpool	
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School Of Dentistry, University of Liverpool	
Faculty Of Dentistry, Misurata University, Misurata	
Advanced Clinical Pharmacist in Oncology, The Mid Yorkshire Hospitals Trust, Wakefield	
Clinical Lecturer in Restorative Dentistry, Department of Restorative Dentistry, School of Dentistry, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool	
Department Of Clinical Sciences, Intervention and Technology, Division of Ear, Nose and Throat Diseases, Karolinska Institute, Karolinska University Hospital, 17177 Stockholm	Libya
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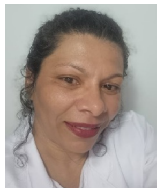

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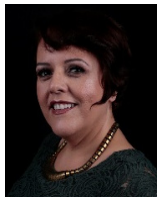

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