

## A Review of the Success Rate of Dental Implants in Patients Undergoing Radiotherapy and Chemotherapy

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### Abstract

**Introduction:** According to the World Health Organization, the incidence of head and neck cancers, both primary and secondary (metastatic), is increasing. Currently, the main treatments for this complication are radiotherapy and chemotherapy. On the other hand, the success of implant treatment in these patients due to the cellular changes is a very significant point that should be considered.

**Objective:** The aim of this study was to review the success rate of dental implants in patients undergoing radiotherapy and chemotherapy.

**Materials and Methods:** This study was a narrative review. In this study, research published in PubMed, Google Scholar, and Scopus databases has been reviewed by a review method and with a keyword search strategy.

**Results:** 4320 articles were found from the mentioned databases that after deleting unrelated research (3101 cases) and duplicate research (1050 cases), 105 articles remained for final review. Then, those that were presented in the scientific conference and were in the form of abstracts or did not have a correct statistical population were excluded from the study (90 cases). Finally, 15 articles in this study were reviewed.

**Conclusion:** The survival rate of dental implants may be negatively affected by radiotherapy; however, implants can remain osteointegrated and remain functionally stable and, therefore, can be a good treatment option for rehabilitation and improving the quality of life of cancer patients. The use of bone grafts and higher doses of radiation in the jaw area can be negative prognostic factors.

**Keywords:** Dental Implants; Radiotherapy; Drug Therapy; Head and Neck Neoplasms; Radiation; Mouth Neoplasms

### Introduction

According to World Health Organization (WHO), cancer is the first or second main reason for death in the world [1]. Drugs abuse

is the most important and controllable factor for the danger. The danger of suffering from oral cancer among smoking patients is 5-20 times more than the number of non-smoking patients

[2]. Metastatic Tumors (MT) are unusual in the oral area, and they include only 1% to 3% of all the oral malignant neoplasms. Metastatic lesions might be created in the mouth's soft tissue, jaw bone, and both bone and soft tissues. The lower jaw is the most popular place for metastases, and the area of the molars is the most popular place for engagement [3]. The oral metastases can grow fast, cause pain, create a chewing problem, cause dysphagia, change form and make alternative bleeding. These problems result in low quality of life [4]. Radiotherapy and chemotherapy are the most effective treatment methods for cancer. Along with surgery and chemotherapy, radiotherapy is an important treatment method for cancer. X-ray is a physical factor to eradicate cancer cells [5,6]. The used radiation is called ionizing radiation because ion (electrically charged particles) forms this radiation and transfers energy to the cells of the tissues that pass through them. This saved energy can eradicate the cancer cells or cause genetic changes leading to the cancer cells' death. As a consequence of radiotherapy, most patients suffer from soft and hard tissues faults resulting in dysfunction and beauty deformity. Dental rehabilitation using the usual prosthesis might be endangered by inappropriate changes in oral anatomy or prevent it, and radiotherapy can create mucositis, dry mouth, and disorder in bone improvement [7]. Chemotherapy causes a change in the cancer cells to stop them from growing or killing them. Therefore, the chemotherapy medicines are two branches of Cytostatic (biological drugs) and Cytotoxic, respectively [8]. The patients suffer from immune deficiency as a consequence of intense chemotherapy, and this leads to complex infections and, death. The chemotherapy medicines have been designed to target the tumor cells, particularly so that they eradicate these cells via genotoxic effect (producing Reactive Oxygen Species (Ros)). However, these medicines almost influence the body's natural cells [9]. Implant placement in reconstructed jaws provides dental prostheses with better stability and durability. This operation facilitates to support of soft tissues and provides a stable condition for chewing and talking. Reconstructing the dental function and the beauty is accessible by using bone flaps and placing implants [10]. Atrophic mucosa, erythematous, and jawbones condition challenge the removable prosthesis placement. Thus, the absence of satisfactory returning of chewing ability usually increases the general complications of cancer treatment and decreases the life quality among the patients who suffer from head and neck cancer. Using dental implants for rehabilitation has more advantages

than conventional tissue prostheses. These advantages include improvements in retention, chewing, and patient satisfaction; however, dental implants rehabilitation is a complex operation and previously has been forbidden for the patients undergoing radiotherapy [11]. Dental implants as a treatment method are successful and have a high survival rate [12]. Promoting the success criteria of dental implants indicates the evolution of the implants' knowledge of performance and biological reaction to them. The suggested recourses by Albrektsson., *et al.* include motionless, radiolucent absence around the implant, not feeling pain, infection absence, and less than 0.2 mm bone resorption per year (except the first year). Some authors have defined alternative criteria for success that include pocket probing depth and bleeding. The criteria for these indexes are bone resorption up to 0.2 mm at most [13]. According to the mentioned contents, this study aims at investigating the degree of dental implants success among the patients under radiotherapy and chemotherapy treatment. This study has been conducted in the form of a review. Finally, the selected research findings have been investigated and reported regarding implant success among these patients.

## Materials and Methods

### The type of the study and its methodology

This study is a review, and searching on scientific websites has been the main method of collecting the data.

### The method of finding articles

The required data for this research have been collected via searching in the databases. These databases include Web of Science, PubMed, Scopus, and Google Scholar from 2010 to September 2021.

### Keywords

- The following electronic databases were searched.
- MEDLINE (via Ovid and PubMed, Appendix, from 2000 up to 2021), Embase (via Ovid), the Cochrane Oral Health Group's Trials Register, and CENTRAL.
- The following phrases were searched as keywords. All the keywords were inserted in quotation marks for searching in the databases. Further, the Boolean Operators of <AND> and <OR> were used.

## Keywords

Cancer, Head and neck cancer, radiotherapy, chemotherapy, dental implants, Implant success, and Implant survival.

## The research procedure

The studies related to the success degree of the dental implants among the patients under radiotherapy and chemotherapy were searched and selected electronically.

## The inclusion and exclusion criteria

### The inclusion criteria

The inclusion criteria included the studies in English that investigated the survival of the implants' placement in vascularized and in-vascularized bone grafts.

### The exclusion criteria

The review research and low-quality studies in the hierarchy of scientific evidence (doctoral dissertations, experts' opinions, letters, editorial, and histological studies) did not enter the current study. Animal studies, technical reports, the studies related to the patients suffering from the systematic condition, and the studies that had not reported investigated consequences were removed.

## Introducing the population and statistical sample of the research

All the confirmed articles have been collected based on inclusion and exclusion criteria in this study. They are related to the considered keywords from 2010 up to 2021. These articles are the statistic population of the current study (article). After checking and removing the contradictory cases, the remaining articles were investigated, including 15 studies.

## The ethical consideration

Because the current investigation is reviewing and checking the present published studies, there was no ethical limitation to conducting this research. Ethical considerations are restricted to keeping the correct writing.

- Respecting honesty and trustworthiness in reviewing the references
- Not using suspicious and invalid references
- Respecting honesty in collecting the data.

## Results

Searching was done in the mentioned databases about the survival rate of the implants. Further, the search was performed on the patients' studies under radiotherapy and chemotherapy treatment from 2010 to 2021.

Figure 1 shows a plan of research selection in this review study. According to this chart, 4320 articles were found in the mentioned databases. The irrelevant research and those less related to implant survival among the patients undergoing radiotherapy and chemotherapy treatment were removed. Three thousand one hundred one repetitive studies were removed, and finally, 1219 articles remained. After that, the titles and abstracts were checked, and the irrelevant or less relevant researches were removed (1050 cases). There were 105 remaining articles for the final investigation. Then, those studies that were not accessible, or were not investigated based on the inclusion and exclusion criteria, were removed (90 cases) among the last number. Finally, 15 cases were finalized and studied (Figure 1).

**Figure 1:** The stages of research selection (Figure of the study process).

The result of the dental implant survival and success among the patients under radiotherapy and chemotherapy treatment has been reported in table 2. The results of the studies investigation have been presented based on cancer type, radiotherapy, chemotherapy, implant survival, and implant success. According to the findings from the nine studies (out of 15 articles), it means 60% of the whole studies reported the survival rate or success of implant had been more than 90% (Table 1, Table 2).

Row	Researchers	Study type
1.	Barrowman, <i>et al.</i> (2011), 20 [14]	Retrospective
2.	Heberer, <i>et al.</i> (2011), [15]	Clinical trial
3.	Buddula, <i>et al.</i> (2012), [16]	Retrospective
4.	Mancha de la Plata, <i>et al.</i> (2012), [17]	Comparative study
5.	Linsen, <i>et al.</i> (2012), [18]	Retrospective
6.	Dholam, <i>et al.</i> (2013), [19]	Interventional study
7.	Hessling, <i>et al.</i> (2015) [20]	Cohort study
8.	Doll, <i>et al.</i> (2015), [21]	Retrospective
9.	Aeran, <i>et al.</i> (2015), [22]	Case report
10.	Al-Mahalawy (2016) [23]	Interventional study
11.	Wu, <i>et al.</i> (2016), [24]	Retrospective
12.	Rana, <i>et al.</i> (2016), [25]	Retrospective
13.	Laverty, <i>et al.</i> (2019), [26]	Cohort
14.	Patel, <i>et al.</i> (2020), [27]	Cohort
15.	Silva, <i>et al.</i> (2020), [1]	Retrospective

**Table 1:** The characteristics of the evaluated studies.

## Discussion

### The dental implants survival in the bone under radiotherapy

There is conflict in the evidence that supports dental implant survival among patients suffering from head and neck cancer. Chambrone, *et al.* [28] recently found that radiotherapy is related to the higher implant failure rate among most individual studies. Another meta-analysis has been conducted by Sheignitz, *et al.* [29] from the present studies in 2007-2013 and the articles in 1990-2006. Their analysis revealed no statistical difference in implant survival between the natural bone without X-ray and natural bone under X-ray in the current studies (2007-2013). However, the articles in 1990-2006 showed a significant difference in the implant. These findings and the current research findings claim that the fundamental changes in implant survival can be made among patients under X-ray treatment. These changes can be associated with the recent progress in implant treatment, including

Article no	Cancer type	radiotherapy	Chemotherapy	Implant survival	Implant success	Radiology evaluation
1.	Oral cancer	Yes	No	89.5% for bone, 33.3% for bone without flap	-	-
2.	Oral cancer	Yes	Yes	-	Sandblasted acid-etched surface (SLA) equals 96%, Mod-SLA equals 100%	SLA mesial (.4mm) and distal (04mm) resorption, mod-SLA mesial (.3mm) and distal (.3mm) resorption
3.	Head and neck cancer	Yes	No	72.3%	-	-
4.	Oral cancer	Yes	Yes	92.6%	-	-
5.	Oral cancer	Yes	No	86.9%	-	-
6.	Head and neck cancer	Yes	No	-	71%	-
7.	Oral cancer	Yes	No	96.3%	-	-
8.	Oral cancer	Yes	Yes	90.8%	-	-
9.	Head and neck cancer	Yes	Yes	-	100%	-

10.	-	No	Yes	-	-	Significant decrease of the ratio of bone size to total ratio, intense reduction of the bone-implant contact
11.	Oral cancer	Yes	No	-	93.6%	-
12.	Oral cancer	Yes	No	-	67.9%	-
13.	Head and neck cancer	Yes	Yes	95.5%	-	-
14.	Head and neck cancer	Yes	Yes	97%	-	-
15.	Oral cancer	Yes	Yes	-	93.02%	-

**Table 2:** The results of the implant survival in vascularized and in-vascularized grafts in the two jaws.

guided implants surgery and the technical progress in the features of implant level. Consequently, nowadays, dental implants seem to be suitable treatment options for dental rehabilitation among patients suffering from head and neck cancer experiencing radiotherapy. Nevertheless, the patients should be already aware of the complications related to implant placement [11].

There is no agreement in the previous studies about the radiation threshold dose that might influence dental implants survival. Osteonecrosis and implant survival might depend on radiation dose. Some studies have reported that the danger of osteonecrosis increases by doses more than Gy 50, Gy 60, Gy 65, and Gy 70. Soft tissue necrosis can happen with less than Gy 50 doses, and damaging salivary glands might happen with less than Gy 20 doses as well [30]. Danger and severity of osteonecrosis are related to radiation dose, the tissue size under radiation, and the patients' dental health [31]. It has been suggested that consulting the oncologist before placing the implants is important to achieve the radiation dose distribution that might help plan the best place for the implant placement [32]. Several authors have reported a better survival rate with less dose of radiation. However, fewer studies of radiotherapy with less dose make confirming these findings difficult [33]. The time of implants replacement, either before or after the radiotherapy, is really important that might influence the success or failure of Osteointegration. This subject is debatable broadly, and so far, no scientific evidence has been presented for optimal time of implant placement. Quick implant placement before the radiotherapy and during the tumor surgery is called primary replacement. In

contrast, placing after radiotherapy without considering time intervals is called secondary placement. The primary placement to accessing osteointegration before the destructive effects of radiotherapy and preventing extra surgery have been supported for dental rehabilitation in many studies [34,35]. However, the primary placement might lead to intervention or delay in oncology treatment such as radiotherapy and is not always accessible for the patients in hospitals. The secondary placement provides the possibility for evaluating the patients' conditions after their surgery and prognosis of cancer. When the secondary placement is considered, the patient is aware of the physical and physiological conditions caused by oncology treatment so far. They accept the shortcomings and are more psychologically ready for long-term treatment and rehabilitation. Nooh [36]. has reported the dental implant survival rate before the radiotherapy (92.2%) and after the radiotherapy (88.9%). Nevertheless, statistical confirmation is not possible due to considerable differences in studies number for each group. There is no sufficient information about the time interval of implant placement after radiotherapy. Usually, the dental implants are placed after a delay of six months after radiotherapy [37]; however, it is not clear if a longer delay is beneficial or not. It has been reported that there is no significant difference between implant survival rates that have been placed 12<months and <12 months after radiotherapy. The recent systematic review study of observational studies determined that a higher risk of failure might be due to placing dental implants less than 12 months after the radiotherapy. In contrast, there is no evidence of clinical trial to confirm this risk. Granstorm [38] has reported that implant

placement after radiotherapy is more harmful than early placement because there is a reduction in improvement potential that can be explained with progressive under-treat that increases over time.

### Dental implant survival in the bone under chemotherapy treatment

The implant survival after jaw radiotherapy has been mostly studied. In one of these studies, losing implant in a group of patients under adjuvant chemotherapy treatment with Cisplatin (20 mg per square meter for five days) was investigated for radiation sensitivity. There was no difference between losing an implant caused by radiotherapy or chemotherapy. A problem was reported in a case in another study on the endosteal implants among the patients after their oncology surgery. Three reports investigated the effects of anti-neoplastic chemotherapy over the placed dental implants before the treatment. These reports described the acute side effects on the soft tissues that could affect the implants. Mucositis around the implant might lead to implant loosening. The Bone-Lock implants should be covered during three months of improvement. Even if the chemotherapy has late effects on mucus (that has not been considered), this method protects the implants [39-42]. Experiments have investigated the chemotherapy with Cisplatin among dogs. Cisplatin chemotherapy was applied for bone formation around the femoral prosthesis before or after the surgery. The chemotherapy resulted in less bone formation; however, it had not restrained forming the extracortical capsule. In contrast, the chemotherapy before the surgery had not changed the new bone formation. Linking an animal experiment to a clinical environment is difficult. Nevertheless, the connective formation around the implant is harmful to the bone unity of the dental implants. In this study, chemotherapy was done before the implant placement. However, the investigated research findings support this hypothesis that chemotherapy does not prevent bone fusion of the implants. Achieving a definite result about the time interval effect on the implants' survival among the patients under chemotherapy treatment is complex. Therefore, the researchers did not observe any compatibility in the follow-up time period after placing implants among these patients. For example, the follow-up was performed one decade after implant placement in the studies of Taira, *et al.* [43] and Keller, *et al.* [30]. These follow-up times seem to be reliable considering the stability and function of the implants after oral cancer treatment. On the other hand, Oechslin, *et al.* [44] and August, *et al.* [45] reported the survival rate (100%)

after oral cancer treatment. However, it should be mentioned that in these studies, the follow-up examinations were performed after relatively shorter time periods (6 and 16.4 months, respectively). The point that expecting the same survival rate in these studies as is observed during a longer time (such as after ten years) is debatable. More prospective studies with long-term follow-up are required to elucidate the chemotherapy effect on the implants' survival and stability. The implant can be osteointegrated successfully among the two studies [45-47]. in which the patients were under chemotherapy treatment. Moreover, when the implant is placed at least six months after treatment, it will be constant in terms of function. Further, the following examinations were performed at least five years after implant placement. Therefore, it is suggested that the implant might be stable functionally after radiotherapy and chemotherapy treatment. Since few studies have investigated the radiotherapy and chemotherapy effect on the survival, success and stability of dental implants among patients who have oral cancer in long term, more studies are required in this field [45-47].

### Conclusion

The dental implant survival rate might be negatively influenced by radiotherapy. However, the implants can be osteointegrated and stable functionally. Therefore, they are appropriate options for rehabilitation and improving the patients' life quality who suffer from head and neck cancer. Using bone graft and higher doses of radiation in the jaw area can be the negative prognostic factors. The prospective, randomization and controlled paths of Cohort studies are still required for more conclusions based on evidence about the survival of the dental implant among the patients suffering from head and neck cancer. Thus, it can be generally concluded that the dental implants among the patients under oral cancer treatment, radiotherapy, or chemotherapy can be osteointegrated and be stable functionally. Nevertheless, these patients should have already been informed about implant treatment and radiation or chemotherapy complications. Further, their satisfaction should be received.

### Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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