

Systematic Review

Effect of post-implantation radiation therapy on dental implant osseointegration in oral cancer patients: a systematic review of literature

Sundar Ramalingam^{1*}, Lama Dhafer Al Bahis², Rahaf Ali Bin Salamah²,
Rihan Bader Almutairi², Heyam Humood AlKhalaf²

¹Department of Oral and Maxillofacial Surgery, Dental University Hospital, King Saud University Medical City, Riyadh, Saudi Arabia

²Dental Internship Training Program, College of Dentistry, King Saud University, Riyadh, Saudi Arabia

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*Correspondence:

Dr. Sundar Ramalingam,

E-mail: smunusamy@ksu.edu.sa

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ABSTRACT

Dental implant placement for functional rehabilitation after oral cancer surgery could be done either before or after radiation therapy (RT). In both of the above scenarios, radiation exposure could affect implant osseointegration and survival. The present review aimed to evaluate the effect of post-implantation RT on osseointegration of dental implants placed in patients treated for oral cancer. A literature search was conducted to identify studies published in English between 2001 and November 2023. Articles reporting about the success of dental implant osseointegration after post-implantation radiotherapy were selected. Data about overall success of osseointegration and with respect to the anatomic site (maxilla, mandible or grafted bone), radiation dose and time-interval between implant placement and radiation exposure were collected and analyzed. Out of 189 articles identified through literature search, 12 studies fulfilling the inclusion criteria were systematically reviewed. In 403 patients, 1333 dental implants were placed prior to RT, out of which 1223 successfully osseointegrated (91.75%). The implant osseointegration rates in maxilla, mandible and grafted bone were 92.06% (255/277), 95.14% (313/329) and 80% (60/75), respectively. There was no relationship between radiation dose or time-interval and success of implant osseointegration. Based on the present review, it may be concluded that dental implants placed at least 1.5-3 months prior to RT, would successfully osseointegrate without major complications. The native maxilla and mandible are a favored choice for implant placement before radiotherapy, than grafted bone.

Keywords: Dental implant, Osseointegration, Post-implantation RT, Radiotherapy, Oral cancer

INTRODUCTION

Ablative surgery for oral cancer often involves resection of the oral and perioral soft and hard tissues. Resection of the maxilla and mandible not only compromises the structural integrity of the oral cavity, but also hampers masticatory function due to loss of teeth.¹ From a historical perspective, oral reconstructive strategies following ablative tumor surgery have ranged from

simple reconstruction plates to non-vascularized bone blocks and vascularized composite grafts, including bone and soft tissue.² In fact, the future holds promise for tissue regeneration after oral cancer surgery, with the possibility of tissue engineered constructs, for both hard and soft tissue.³⁻⁵ In spite of the multiple reconstruction options available to reconstruct the resected maxilla and mandible, the only choice of restoring masticatory function has been through prosthodontic rehabilitation.²

Similar to the reconstructive surgical options, prosthetic rehabilitation after ablative tumor surgery has also progressed from the conventional removable dentures, to tooth supported partial dentures and more recently implant supported restorations and over dentures.⁶

Dental implant based oral rehabilitation is supported by the ability of implants to osseointegrate with bone, which occurs by way of bone ingrowth into the microscopic implant surface irregularities.¹ In addition to osseointegration, healthy peri-implant hard and soft tissue, and optimally functioning prosthetic superstructure are essential for overall implant success.⁷ In most oral cancer patients, treatment is multimodal involving RT and chemotherapy, in addition to surgical removal.⁸ The predominant modality of treatment though is ablative surgery followed by adjuvant RT, usually planned 6 to 8 weeks after surgery. In addition to the anatomic and functional oral deformity left behind by oncologic surgery, RT poses further challenges in terms of xerostomia, soft-tissue fibrosis and progressive hypovascularity of bones.⁸ The risk of developing osteoradionecrosis, because of reduced vascularity, hypoxia and concomitant bone hypocellularity, is a major deterrent to perform oral surgical procedures in the irradiated maxilla and mandible.⁹ Nevertheless, dental extractions, periodontal surgeries and implant supported prosthetic rehabilitation procedures are inevitable, and are being performed routinely in patients irradiated for oral cancer.⁹

With respect to the timing of dental implant placement after oncologic surgery, it could either be placed immediately at the time of tumor resection or in a delayed manner after following up for a considerable recurrence free period.¹⁰ Accordingly, exposure of dental implants to the radiation effects on bone could be either pre-implantation or post-implantation. While most reports in the literature are about the survival of implants placed after radiotherapy (pre-implantation), very few studies provide information about the osseointegration of dental implants, which are exposed to radiation (post-implantation).¹ In most clinical scenarios of post-implantation radiotherapy, the reason for immediate dental implant placement at the time of tumor surgery is for early functional rehabilitation and placing implants in bone grafts used for reconstruction.⁹

Owing to the diverse range of complications associated with radiotherapy on bone, and the increasing prevalence of dental implants in oral cancer patients who need irradiation, the success of implant osseointegration and maintenance are under question. While sufficient clinical data is available about implant osseointegration in previously irradiated bone, little information is present as to how an implant may osseointegrate on the long term when subjected to RT. Moreover, incorporation of modern technologies in radiotherapy helps deliver different doses of radiation to target tissue when compared to non-target areas, thereby altering implant

site-specific dose.⁹ Based on the aforementioned statements, it is imperative to know more about how successfully dental implants could osseointegrate when exposed to radiation.

Therefore, the aim of the present systematic review was to evaluate the effect of post-implantation RT on osseointegration of dental implants placed in the maxilla, mandible or grafted bone, specifically among patients treated for oral cancer.

LITERATURE SEARCH

The present systematic review was conducted with the focused question, “What is the rate of osseointegration and survival of dental implants placed in the maxilla, mandible or grafted bone, prior to RT in oral cancer patients?” In order to answer the focused question, a literature search was conducted in the PubMed (MEDLINE) database, for clinical studies published in English language, between January 2001 and November 2023. The keywords used for search included, but were not limited to, “dental implant”, “implant”, “osseointegration”, “implant survival”, “oral cancer”, “head and neck cancer”, “RT”, “irradiation”, “radiotherapy” and “post-implantation radiotherapy”. The keywords were used in differing combinations to identify articles within the database, which were all collectively exported to EndNote reference management software package (Clarivate Plc, Philadelphia, USA). The collected articles were subjected to a title search to remove duplicates and subsequently following inclusion criteria were applied for selection of articles to be included in the review.

Clinical studies published in English language within the designated period, reporting about post-implantation RT for oral cancer. Availability of clinical data including size of study population, number of implants placed and number of implants osseointegrated or survived at follow up. A minimum follow up period of at least one-year post implant placement and RT.

The number of dental implants placed before radiation and not the number of patients treated, was considered as the statistical unit for assessing success of osseointegration during the systematic review. Accordingly, any study reporting data about less than 10 dental implants was excluded. Although studies reporting about dental implant placement after (pre-implantation) RT were excluded, whenever comparison data was available in these articles about post-implantation radiotherapy that data alone was included for the review. The flow-chart for sequence of literature search, screening titles for duplicates, as well as evaluating abstracts and full-texts for inclusion is described in the Figure 1.

The selected full text articles were reviewed by all the authors and any disagreement over study selection and

inclusion or exclusion of particular datasets was resolved through discussion. Individual data about study sample size, implant osseointegration and survival, site of implant placement (maxilla, mandible or grafted bone), radiation dose and time interval from implant placement to radiation exposure was extracted from each of the included studies and tabulated using MS-Excel Spreadsheet Software (Microsoft Corporation, Redmond, WA, USA). Summary data from the included articles were obtained for overall success of dental implant osseointegration and with respect to the anatomic site of implant placement (Table 1).

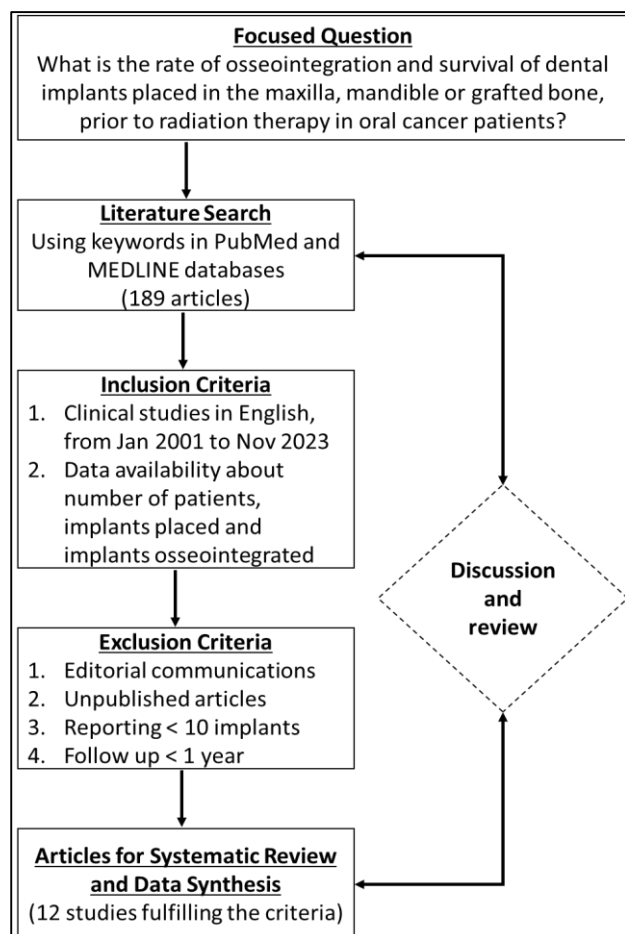


Figure 1: Flow-chart describing the sequence of study selection for review.

OBSERVATIONS

Based on the literature search 189 articles were identified, out of which 12 studies fulfilling the inclusion criteria were selected for systematic review and quantitative data synthesis.^{7,11-21} Overall, 403 patients underwent implant placement prior to RT for oral cancer. In these patients, 1333 dental implants were placed, with a 91.75% success rate (1223 dental implants) for osseointegration. While the median dosage of RT in these studies ranged from 40-66 Gray, the median time interval from implant placement to commencement of RT ranged from 1.5-9

months. Table 1 shows the detailed data analysis from each of the included studies.

Only few studies reported data pertaining to the anatomic site of dental implant placement or the nature of bone in which the implant was inserted. Two studies reported placement of 277 dental implants in the native maxillary bone, with an osseointegration success rate of 92.06% (255 dental implants).^{13,21} With respect to dental implants placed in the native mandible, five studies reported placement of 329 implants, out of which 313 implants successfully osseointegrated (95.14%).^{1,7,12,16,21} Only 60 out of the 75 dental implants placed in grafted bone were osseointegrated (80%), as reported by three studies.^{11,15,20}

Information pertaining to the dose of RT, administered to the head and neck region, was available in only 10 of the 12 included studies.^{7,11-13,15-17,19-21} Comparing the overall success rate of osseointegration in the individual studies to their respective median dose of radiation, there was no statistical relationship observed (Figure 2 A). Similarly, data about the time interval between implant placement and commencement of radiation therapy was available only in six of the included studies.^{7,13,14,16,18,20} Within these studies, there was no statistical correlation between the overall success of osseointegration and the time interval between implantation and radiotherapy (Figure 2 B).

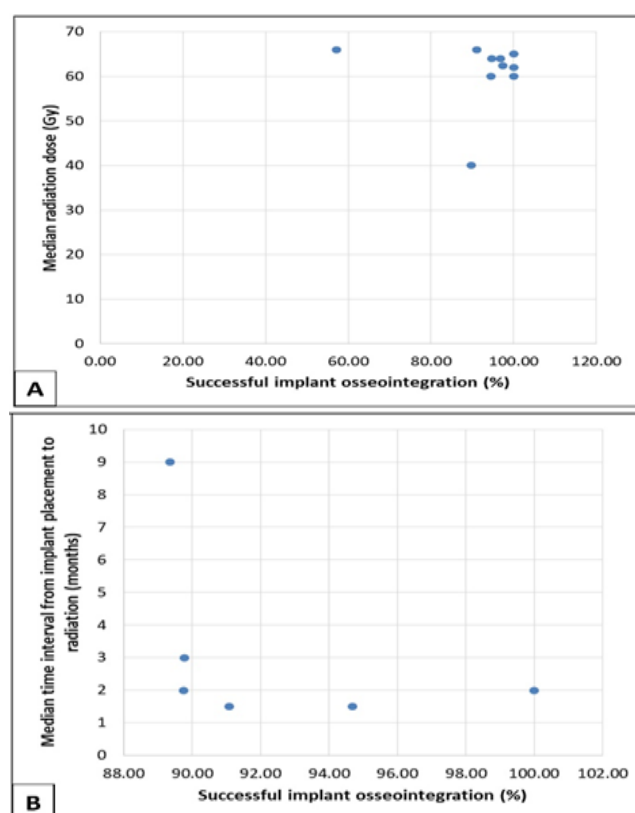


Figure 2 (A and B): Based on the reviewed studies, the relationship between successful implant osseointegration and median dose of RT; time interval from implant placement to commencement of RT.

Table 1: Effect of post-implantation RT on dental implant osseointegration and survival.

Author (s)	Overall			Anatomic site and nature of bone						Median dose of RT (Gray)	Median time from RT to implant placement (Months)
	N	Osseintegrated implants (Survived/ placed)	Implant survival (%)	Maxilla		Mandible		Grafted bone			
				Osseintegrated implants (Survived/ placed)	Implant survival (%)	Osseintegrated implants (Survived/ placed)	Implant survival (%)	Osseintegrated implants (Survived/ placed)	Implant survival (%)		
Schoen et al, 2003	5	20/20	100			20/20	100			62	
Iizuka et al, 2005	7	13/13	100					13/13	100	65	
Schepers et al, 2006	21	59/61	96.72			59/61	96.72			64	
Cuesta-Gil et al, 2009	45	184/205	89.76	184/205	89.76						2
Korfage et al, 2010	31	114/127	89.76							40	3
Fenlon et al, 2012	12	20/35	57.14					20/35	57.14	66	
Mizbah et al, 2013	47	107/113	94.69			107/113	94.69			64	1.5
Korfage et al, 2014	100	260/291	89.35								9
Ettl et al, 2020	39	221/234	94.44							60	
Sandoval et al, 2020	10	27/27	100					27/27	100	60	2
Li et al, 2022	58	147/151	97.35	71/72	98.61	76/79	96.20			62.4	
Alberga et al, 2023	28	51/56	91.07			51/56	91.07			66	1.5
Summary	403	1223/1333	91.75	255/277	92.06	313/329	95.14	60/75	80	40-66	1.5-9

DISCUSSION

The overall success of dental implant osseointegration in response to radiation exposure, as a part of oral cancer therapy, was 91.75% with 1223 out of 1333 implants surviving in 403 patients. These results are in line with a similar review reported by Nooh, who reported 92.2% dental implant survival rate after post-implantation radiotherapy.¹ Based on a comparative review between pre-implant and post-implant radiotherapy, Atanásio Pitorro et al reported better overall survival for implants placed prior to RT (89.4-97%) than implants placed after radiation (80-100%).¹⁰ These results could possibly be attributed to the significant benefit of osseointegration in healthy bone afforded by post-implantation radiotherapy, in comparison to irradiated bone, which is less conducive for bone healing after implant placement.²¹ In addition, the present review considered implant osseointegration as the criteria for success and not implant survival after prosthetic rehabilitation. This was because the primary outcome analyzed was the bone healing response after implant placement and subsequent exposure to radiation. On the contrary, dental implant survival after rehabilitation might be affected by associated factors such as functional loading and peri-implant soft tissue response.¹⁹

Dental implants placed before radiation in the mandible had greater success of osseointegration (95.14%) in comparison to maxillary implants (92.06%) and implants placed in grafted bone (80%). In general, the native bone seemed to favor better osseointegration of dental implants in response to radiation exposure (568/606) than bone grafts (60/75). This again is similar to what has been reported in previously published reviews.^{1,9,10,22} Reviewing the literature over a 22-year period from 1990 to 2012, Nooh reported only 320 dental implants placed prior to RT.¹ In contrast, we were able to identify data about 1333 dental implants from 2001 until November 2023. This indicates a shift in choice towards immediate implant placement after ablative surgery for oral cancer, both in native maxilla and mandible, and grafted bone. Furthermore, with advanced three-dimensional surgical planning better oral anatomic and functional rehabilitation is achieved through guided implant placement and restorations.^{9,21} Similarly, dental implant placement in vascularized and non-vascularized bone grafts used for maxilla-mandibular reconstruction has also seen a paradigm shift towards immediate implant rehabilitation and administering radiotherapy thereafter.^{2,12,16,20,21} Interestingly, out of the three studies reporting implant placement before RT in the present review, Iizuka et al and Sandoval et al reported 100% implant osseointegration even after exposure to RT.^{12,16,20} The study by Fenlon et al alone reported more than 45% failure of osseointegration.¹⁶

Although, the authors mentioned no specific reason, one attributable cause could be the greater radiation received at the implant site.²¹

The effects of radiation on bone are well documented. Evidence from the literature suggests greater risk of osteoradionecrosis and failure of all kinds of implants after exposure to radiation doses greater than 70 gray.²³ A higher rate of failure has been reported with dental implants placed after radiation exposure greater than 55 Gray.^{1,23} In the present review, out of the 10 studies reporting about the median radiation dose administered at tumor site, nine studies reported radiotherapy more than 60 Gray. In the study by Korfage et al the median dose of radiotherapy was 40 Gray, and the success rate of osseointegration was 89.76%.¹⁵ Based on currently reviewed data, there was no correlation between the radiotherapy dose and success rate of implant osseointegration. Nevertheless, there was no data collected about the degree of peri-implant bone loss, which might be an indicator of long-term implant function after RT.⁸ Yet another important determinant of dental implant osseointegration after radiotherapy, is the implant site-specific dose of radiation, wherein doses greater the 50 Gray specifically at the implant site could reportedly lead to bone loss around the implant and subsequent failure.⁷ In the present review, we could not obtain data about site-specific radiation dosage.

Out of the six studies reporting about the time interval from implant placement to commencement of RT, all but one study¹⁸ followed a median time period ranging from 1.5-3 months, to allow unhindered osseointegration.^{7,14,15,17,18,20} However, Korfage et al reportedly allowed a nine-month gap between implant surgery and radiation.¹⁸ Yet there was no observable correlation between the time interval and success of implant osseointegration, based on the reviewed data. This is similar to what was reported in the systematic review of literature by Nooh.¹ One of the major limitations of the present review was the heterogeneity of reported data in terms of prosthetic rehabilitation, which ensued after implant osseointegration. The collected data included both single and multiple implants supported fixed tooth restorations, as well as overdentures retained by implant-based attachments. Therefore, functional loading of the implant could not be considered as a criterion for selection of studies, and in a few studies, osseointegrated implants submerged without prosthetic rehabilitation were also considered for data analysis. In addition, adjuvant modalities to enhance implant osseointegration and peri-implant tissue health after radiation exposure were not considered as part of the review. Bazie et al reported an antibiotic protocol for preventing deleterious after effects of RT on bone tissue healing, after oral surgical procedures.²⁴

The criteria for selection of studies in this review mandated a minimum follow up period of one year after implant placement and RT. Although a longer follow up period might yield different outcomes in terms of implant success, the present findings act as a baseline data to judge the positive clinical results associated with post-implantation radiotherapy. Moreover, there seems to be a

consensus towards early oral rehabilitation of oral cancer patients undergoing ablative surgery, wherein dental implants do not affect radiation dosing of the tumor site, but rather help patients acquire early positive quality of life.²⁰

CONCLUSION

Within the limitations of the present study and based on the reviewed data it may be concluded that dental implants placed at least 1.5-3 months prior to RT, would successfully osseointegrate without major complications. Although there is no relationship between median dose of radiation reported in the present review and rate of implant osseointegration, site-specific radiation dosage at the implant site needs to be considered for evaluation in future clinical studies. In terms of the anatomic site of implant placement, native bone (mandible more than maxilla) seems to be a favored choice for implant placement before radiotherapy, than in grafted bone used for reconstruction.

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Ethical approval: Not required

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