J Oral Med Oral Sug 2018;24:103-106
https://www.jomos.org
JOMOS
Journal of Oral Medicine and Oral Surgery
https://doi.org/10.1051/mbcb/2017041

Original Article

Long-term implant failure in patients treated for oral cancer by external radiotherapy: a retrospective monocentric study

Aline Desoutter[1], Sophie Deneuve[1], Sophie-Charlotte Condamin[2], Anne-Gaëlle Chaux-Bodard[1,2,*]

[1] Head and Neck Unit, Surgical Oncology Department, Léon Bérard Regional Center for the Fight Against Cancer, 28 rue Laennec, 69008 Lyon, France
[2] Oral Surgery, Faculty of Odontology, Claude Bernard University, 11 rue Guillaume Paradin, 69008 Lyon, France

(Received: 26 September 2017, accepted: 26 December 2017)

Keywords: dental implants / failure / radiotherapy

Abstract – Introduction: The placement of dental implants in irradiated bone has allowed functional rehabilitation for many oral cancer patients. Nonetheless, there is only few data about implant failure in irradiated tissues and their consequences. This retrospective study aims to highlight the rate and circumstances of implant failure. **Material and method:** Patients treated with external radiotherapy for oral carcinoma and who received dental implants were included. Patients reconstructed with free bone flaps were excluded. **Results:** Eighteen patients were included. Forty implants were placed between 2004 and 2007, 8 failed, of whom one osteoradionecrosis was observed. Time interval between radiotherapy and implantation was 44.6 (6–182) months. Mean dose was 51.8 (50–66) Gy. **Discussion:** In the series, the implant failure rate is 20%, which corroborates the literature's data. Failures occur more often for doses over 50 Gy. The placement of dental implant in irradiated bone leads to soft tissue complications but also increases the risk of osteoradionecrosis. The recent reimbursement of dental implants in oral cancer patients by the National Social Health system will probably increase the indications. Multidisciplinary staffs should be aware of benefit/risk ratio for each patient.

Introduction

Dental implants in patients treated for upper aerodigestive tract (UADT) cancers have facilitated the functional and aesthetic rehabilitation of patients whose postoperative anatomy did not allow for the placement of conventional prostheses. Several studies have been conducted and the success rates have varied from 62.5% to over 90% [1]. These success rates would be similar to those found in a healthy patient's mandible, which is reported to be 92.6% [2]. However, there is little information regarding the types of failures that occur with these implants, as well as the consequences and circumstances surrounding their occurrence, especially when the radiation dose at the implant site is >40 Gy. Indeed, most of the published studies are case studies in which there is great heterogeneity in the initial tumor sites and in the radiation doses received at the implant site. It is therefore difficult to precisely determine the failure risk in patients who have received large radiation doses in the oral area. The expected complications are mainly peri-implantitis, loss of implants, and even osteoradionecrosis (ORN) [3]. The aim of this study was to highlight long-term implant failures in patients who were treated with radiotherapy for oral cancer and to observe the circumstances and consequences of these failures.

Material and methods

The clinical records of oral cancer patients treated between 2004 and 2007 by radiotherapy (exclusively or not) and who received implants were reviewed. In the interest of maintaining the homogeneity of the study sample, patients treated with a microanastomosis fibula flap were excluded.

The following information was extracted from the case records: tumor location, tumor stage, and type of treatment received, the duration between radiotherapy and implantation, the type of implants placed, the surgical and operative protocol, the patient's medical history (excluding oncology) as well as any implant or peri-implant clinical events and their time of occurrence. Failure was defined as loss of implant osseointegration resulting in implant loss or removal. Surgical and implant loading failures were considered. Statistical analysis was performed using XLSTAT® software (Microsoft).

* Correspondence: anne-gaelle.bodard@lyon.unicancer.fr

Q4 **Table I.** Population studied: sites, tumor stages, and treatments received.

Location of tumor			Initial tumor stage			Treatment received		
Mandibular Gingiva	Floor	IMC and trigona	T1	T2	T3	Surgery + radiotherapy	Surgery + radio chemotherapy	Radiotherapy + chemotherapy
3	10	5	1	14	3	14	3	1

Table II. Implant failures as a function of the radiation dose received, initial tumor site, and failure onset delay.

Patient	Type of failure	Localization and initial TNM	Treatment	Radiation dose on tumor(Gray)	Delay RTE/ implant placement (months)	Delay implant placement/ failure (months)
1	Bone fracture due to fatigue	Anterior floor of mouth T2NX	Chir + RTE (T + N)	60	25	15
2	Peri-implantitis	Side of tongue T2N1	Chir + RTE (T + N)	58	16	25
3	Peri-implantitis	Anterior floor of mouth T1N1	Chir + RTE (T + N)	64	35	19
4	Peri-implantitis	Anterior floor of mouth T2NX	Chir + RTE (T + N)	54	13	36
5	Peri-implantitis	Anterior floor of mouth T2N0	Chir + RTE	60	13	34
6	Peri-implantitis	Left inf. Gingival T2NX	Chir + RTE (T + N)	60	23	22

Results

Eighteen patients, consisting of 14 males (77%) and four females (13%) were eventually included. The mean age at the time of implant placement was 57.5 years (range: 42–78 years). The initial tumor locations, the initial tumor stage, and the treatments received are presented in Table I.

The average radiation dosage administered to the tumor was 51.8 Gy (range: 50–66 Gy).

Forty implants were placed. These were bone-level (Brånemark system MK III — Nobel Biocare ® type) implants with a two-stage surgical protocol and deferred loading (2–4-month care period). The mean duration between the end of radiation and implant placement was 44.6 (6–183) months.

At the last follow-up visit, there were eight implant failures (seven patients or a rate of 20%) with an average clinical decline of 89 months (range: 58–119 months) (See Tab. II). All the implants had been placed in the symphyseal or para-symphyseal region. There was one case of ORN caused by an implant. All failures occurred >1 year after radiotherapy, with a mean duration of 20.8 months, a standard deviation (SD) of 7.8, and a range of 13–35 months. All implant failures occurred >1 year after placement with a mean of 5.2 months, a SD of 7.6, and a range of 15–36 months. Failures were observed in those patients who received a radiation dose >55 Gy, with a mean radiation dose of 59.33 Gy an, SD of 2.9 and a 54–60 month range. Two patients had past medical history with noncancerous conditions; one was on antithrombotic therapy and one patient had type-2 diabetes mellitus that was under control. For six patients, the root cause of implant failure was a loss of osseointegration, which caused ORN in one patient. For one patient, the implant failed because of mandibular fracture caused by fatigue after >6 months of activity In three patients, there was fracture of prosthetic screws, which needed to be replaced; however, the implants were left intact.

Discussion

Cervicofacial radiation is one of the primary causes of implant loss [1,4] regardless of whether it is administered early or late [5]. Several failure factors specific to implant placement in irradiated areas have been identified; these include the duration after radiotherapy and the radiation dose received.

For successful implantation, the minimum time after radiotherapy before implantation should be 6–12 months [6]. A delay of >12 months would improve implant success rates [7]. In the current study, a minimum period of 6 months was selected after the multidisciplinary consultation with the surgical oncologists and radiotherapists. After excluding the two patients who were treated several years ago, missed their follow-up, and then reappeared for prosthetic rehabilitation, the average implantation time after radiotherapy in our study was 20.37 months (range: 6–49 months). One study [8] showed that the failures are less severe in patients receiving implants a later stage of oncological treatment (17.1% failure rate for intraoperative implants *versus* 4.6% for those placed postoperatively). Of course, the idea of early rehabilitation encourages the surgical team to perform implantation along with tumor removal, before additional treatments are administered. Although this technique has the advantage of decreasing treatment duration, it is not always feasible because of the constraints of tumor management.

The radiation dose received at the implant site is also a major cause of implant failure, with doses <50 Gy being more favorable [9,10]. Animal studies and literature reviews show that the implant failure rate is directly correlated with the radiation dose received [9,10]. In the study, implant sites that received estimated doses >55 Gy had failure (mean: 59.33 Gy). In fact, all implant failures occurred in patients who received treatment for cancer involving the anterior aspect of the floor of the mouth. The therapeutic target was therefore very close to the implant site, and the dose administered at the implant site was close to the therapeutic dose delivered.

The biggest challenge consists in evaluating the radiation dose received at the implantation site. In most studies, the initial tumor sites involved all the UADTs, including the oropharynx, with low radiation doses of about 30 Gy at the symphyseal and parasymphyseal level. It therefore seems more appropriate to limit the evaluation of failure rates to patients treated for cancer of the oral cavity, as the radiation doses at the implant site are therefore more homogeneous. In published studies, only a few authors [11] highlight the antecedents or lack thereof of radiation, with irradiated tissue implants having osseointegration rates of 83% at 5 years.

Long-term implant survival rates reported by the previous clinical studies are nonhomogeneous, with values of 72.8% at 10 years [9], 24% at 5 years [10], or 72% at 8 years [11]; however, these values support the results of our present study. Thus, Wagner [12] reports a 5-year osseointegration rate of 97.5% and at 10 years of 72.8%, whereas other authors report success rates of 48.3% [3]. Another study reports complications in 41.5% patients [13].

Seven out of eight failures encountered in the series began with peri-implantitis. Werkmeister [14] observed a soft-tissue complication rate of 28.6% in irradiated areas *versus* 8.3% in nonirradiated areas. These complications can be explained in part by the small amount of keratinized gingiva, along with the predisposing factors of radiotherapy-related sensitization and dry mouth. The occurrence of peri-implantitis should be carefully monitored to avoid ORN [15].

An increased loss of marginal bone was reported by many authors, with 2–9 mm variations for a period of 3 years after implant surgery [16]. According to Tanaka [17], early failures are more frequent. In the studies, all failures occurred >1 year after implant placement.

In the present series, a case of loss of osseointegration resulted in extensive ORN at a rate of 2.5%. Treatment of ORN required a subsequent free vascularized bone transfer reconstruction. This patient had been treated for a mouth floor lesion in the past and had received a postoperative radiation dose of 64 Gy (see Patient 3, Tab. I). This implant failed 1 year previously, and a reimplantation was proposed because of the impossibility of prosthetic rehabilitation without bone anchorage. Thus, there were two interventions on adjacent parasymphyseal mandibular bone sites. The patient had reverted to smoking regularly despite tobacco counseling. The risk of triggering ORN following implant placement was estimated to be 1.6%–5% [9,16,18,19]. Some authors advocate the use of hyperbaric oxygen therapy before and after implantation to stimulate or optimize healing and decrease ORN risk [20,21]. Others believe that the risk/benefit/cost ratio is not sufficiently favorable. More recently, the use of low-intensity pulsed ultrasound to increase healing capacity has been advocated [22]. Animal studies are currently underway [23].

Conclusion

It is widely accepted that the use of implant techniques in cancer patients is sometimes essential to ensure functional prosthetic rehabilitation. This retrospective study, which was conducted on patients who had specifically received oral radiotherapy, confirmed that it was a reliable therapeutic treatment for radiation doses of 45–50 Gy. However, the small number of patients in this study prevents the extrapolation of results to larger populations, considering the significant morbidity and lower success rate than patients who were not irradiated. Thus, the inherent risk of a past history of radiotherapy must be taken into account. The use of software like Dentalmaps® [24] allows a better evaluation of the doses received at potential implantation sites. This software is based on the automatic segmentation and delineation of the dental zones, making it possible to estimate the dose received at different points of the dental arch to the nearest 2-Gy fraction. However, the software is expensive, the work is laborious, and this device cannot be routinely used. Considering that health organizations are responsible for the cost management of implants in patients with cancer of UADT, there will be a definite increase in the indications for implantation [25]. It is up to the members present at the multidisciplinary consultation meetings to evaluate the benefit/risk ratio on a case-by-case basis.

Conflicts of interests: The authors declare that they have no conflicts of interest in relation to this article.

References

1. Bodard AG, Gourmet R, Lucas R, Bonnet E, Breton P. Dental implants in irradiated areas: a series of 33 patients. Rev Stomatol Chir Maxillofac 2006;107:137–142; discussion 143-144.
2. Balshi TJ, Wolfinger GJ, Stein BE, Balshi SF. A long term retrospective analysis of survival rates of implants in the mandible. Int J Oral maxillofac Implants 2015;30:1348–1354.
3. Mancha de la Plata M, Gias LN, Diez PM, Munoz-Guerra M, Gonzalez-Garcia R, Lee GY, Castrejon-Castrejon S, Rodriguez-Campo FJ. Osseointegrated implant rehabilitation of irradiated oral cancer patients. J Oral maxillofac Surg 2012;70:1052–1063.
4. Chen H, Liu N, Xu X, Qu X, Lu E. Smoking, radiotherapy, diabetes and osteoporosis as risk factors for dental implant failure: a meta-analysis. PLoS One 2013;8:e711955.
5. Linsen SS, Martini M, Stark H. Long-term results of endosteal implants following radical oral cancer surgery with and without adjuvant radiation therapy. Clin Implant Dent Relat Res 2012;14:250–258.

6. Granström G. Osseointegration in irradiated cancer patients: an analysis with respect to implant failures. J Oral Maxillofac Surg 2005;63:579–585.
7. Claudy MP, Miguens SA Jr, Celeste RK, Camara Parente R, Hernandez PA, Da Silva AN Jr. Time interval after radiotherapy and dental implant failure: systematic review of observational studies and meta-analysis. Clin Implant Dent Relat Res 2015;17:402–411.
8. Mizbah K, Dings JP, Kaanders JH, Van den Hoogen FJ, Koole R, Meijer GJ, Merkx MA. Interforaminal implant placement in oral cancer patients: during ablative surgery or delayed? a 5-year retrospective study. Int J Oral Maxillofac Surg 2013;42:651–655.
9. Aisikainen P, Klemetti E, Kotilainen R, Vuillemin T, *et al*. Osseointegration of dental implants in bone irradiated with 40, 50 or 60 Gy doses. An experimental study with beagle dogs. Clin Oral Implant Res 1998;9:20–25.
10. Idhe S, Kopp S, Gundlach K, Konstantinovic VS. Effects of radiation therapy on craniofacial and dental implants: a review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;107:56–65.
11. Dholam KP, Pusalkar HA, Yadav PS, Quazi GA, Somani PP. Implant-retained dental rehabilitation in head and neck cancer patients: an assessment of success and failure. Implant Dent 2013;22:604–609.
12. Yerit KC, Posch M, Seemann M, Hainich S, Dörtbudak O, Turhani D, Ozyuvaci H, Watzinger F, Ewers R. Implant survival in mandibles of irradiated oral cancer patients. Clin Oral Implants Res 2013;17:337–344.
13. Smolka K, Kraehenbuehl M, Eggensperger N, Hallermann W, Thoren H, Iizuka T, Smolka W. Fibula free flap reconstruction of the mandible in cancer patients: evaluation of a combined surgical and prosthodontic treatment concept. Oral Oncol 2008;44:571–581.
14. Werkmeister R, Szulczewski D, Walteros-Benz P, Joos U. Rehabilitation with dental implants of oral cancer patients. J Craniomaxillofac Surg 1999;27:38–41.
15. Ben Slama L, Hasni W, De Labrouhe C, Bado F, Bertrand JC. Osteoradionecrosis and dental implants. Rev Stomatol Chir Maxillofac 2008;109:387–391.
16. Watzinger F, Ewers R, Henninger A, Sudash G, Babka A, Woelfl G. Endosteal implants in the irradiated lower jaw. J Craniomaxillofac Surg 1996;24:237–277.
17. Tanaka TI, Chan HL, Tindle DI, Maceachem M, Oh TJ. Updated clinical considerations for dental implant therapy in irradiated head and neck cancer patients. J Prosthodont 2013;22:432–438.
18. Esser E, Wagner W. Dental implants following radical oral cancer surgery and adjuvant radiotherapy. Int J Oral Maxillofac Implants 1997;12:552–557.
19. Wagner W, Esser E, Ostkamp K. Osseointegration of dental implants in patients with and without radiotherapy. Acta Oncol 1998;37:693–696.
20. Granström G, Tjellström A, Brånemark PI. Osseointegrated implants in irradiated bone: a case-controlled study using adjunctive hyperbaric oxygen therapy. J Oral Maxillofac Surg. 1999;57:493–499.
21. Esposito M, Worthington HV. Interventions for replacing missing teeth: hyperbaric oxygen therapy for irradiated patients who require dental implants. Cochrane Database Syst Rev 2013;30: CD003603.
22. Wu G, Chen L, Zhu G, Wang Y. Low-intensity ultrasound accelerates mandibular implant bone integration in dogs with mandibular osteoradionecrosis. J Surg Res 2013;182:55–61.
23. Bodard AG, Debbache S, Langonnet S, Lafay F, Fleury B. A model of mandibular irradiation in the rabbit: preliminary results. Bull Group Int Rech Sci Stomatol Odontol 2013;52: 12–17.
24. Thariat J, Ramus L, Maingon P, Odin G, Grégoire V, Darcourt V. Dentalmaps: automatic dental delineation of radiotherapy planning in head and neck cancer. Int J Radiat Oncol Biol Phys 2012;82:1858–1865.
25. NGAP- Title III chapter IV: Implanto-prosthetic treatment of the sequelae of a tumor in the oral cavity of the maxillary. cnamts.fr/ameli/cons/CIRCC/2013/CIR-18-2013.