research article

Implant-prosthetic rehabilitation after radiation treatment in head and neck cancer patients: a case-series report of outcome

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Background. Slovenia has a high burden of head and neck cancer. Patients are mostly treated with surgery followed by radiation therapy. Advanced surgical and prosthodontic techniques have expanded the rehabilitation options. The aim of the study was to review the outcome of implant-prosthetic treatment after radiation therapy.

Patients and methods. Twenty irradiated head and neck cancer patients who received a removable implant-supported denture at the University Medical Centre Ljubljana were included in the study. Kaplan-Meier survival analysis, Cox proportional hazard models and logistic regression were used to assess the implant survival and success rate.

Results. Twenty patients had 100 implants inserted. The estimated implant survival rate was 96% after 1 year and 87% after 5 years. Failures were mostly observed before loading (91.2%). Implants inserted in the transplanted bone were significantly more likely to fail. Out of 89 implants supporting the dentures, 79 implants (88.7%) were successful, meaning that they were functionally loaded and exhibited no pain, radiolucency or progressive bone loss. Prosthetic treatment was significantly less successful in older patients. The attachment system and the number of implants did not have a statistically significant influence on the success rate.

Conclusions. Implant-supported dentures have been shown to be a reliable treatment modality after head and neck cancer surgery and radiation therapy. Possible early failures should be communicated with the patients.

Key words: head and neck cancer; radiation therapy; dental implants; implant-supported dentures

Introduction

Slovenia is among the countries with the highest incidence of oral and oropharyngeal cancer.[1,2] In a population of 2 million people, approximately 450 cases are diagnosed per year.[3] Most tumours are regionally advanced and the patients are treated with radical resection and reconstruction followed by radiation therapy.[3] Afterwards, patients experience profound changes in the oral anatomy, function and facial appearance. Radiation therapy causes irreversible damage to both hard and soft tissues by creating a hypoxic, hypocellular and hypovascular environment which impedes wound healing and creates a risk for osteoradionecrosis.[4] A protocol involving hyperbaric oxygen treatment (HBO) has been proposed to enhance wound healing by increasing the tissue oxygenation.[5]

Following the radical procedures to eradicate cancer, the greatest problems perceived by irradiated patients are swallowing, mouth opening, xerostomia and compromised aeshetics.[6] Prosthodontic treatment is advocated to regain lost oral functions, enhance the physical appearance and enable the patient to take part in normal daily activities with greater confidence. However, comprehensive prosthetic treatment after head and neck cancer is challenging, time-consuming and costly. Therefore, only 40% of such patients are treated following the postsurgical prosthetic protocol. Among them, 70% receive dentures supported by the residual teeth and bone and 30% receive implant-supported dentures.[7] Edentulous patients with head and neck cancer after radiation therapy are an especially vulnerable subgroup. Radiation treatment sequelae persist throughout the patient's lifetime and in the past, radiation therapy used to be an absolute contraindication to placing of dental implants.[8] Treatment options have therefore been limited to conventional complete dentures or no prosthetic rehabilitation at all.

Advanced surgical and prosthodontic techniques, such as 3D planning and guided implant surgery, have expanded the treatment options.[9] In addition to conventional ball- and bar-retained dentures, new attachments have been introduced to clinical practice. Locator attachment is commonly used in removable implant prosthodontics. It is a self-aligning system with relatively simple maintenance requirements.[10] Locator is, however, a non-rigid type of attachment and does not completely relieve the stress from the underlying mucosa. The nylon matrices and male parts are subjected to wear, which diminishes retention. Their replacement is one of the most frequent reasons for maintenance visits.[11-13]

To address these issues, a technically more advanced system of prefabricated double crowns on implants has been introduced.[14] The SynCone system (Dentsply, Germany) is indicated in unfavourable resection areas, where completely rigid constructions are necessary due to the anatomical constraints. Among the possible complications, debonding of the secondary crowns and the abutment screw loosening are reported.[15]

Both Locator and Syncone systems are commonly used at the University Medical Centre Ljubljana, Slovenia. These attachment systems have expanded the treatment possibilities for the rehabilitation of head and neck cancer patients, which is always a collaborative work between oral surgeons and prosthodontists. The aim of the study was to review the outcome of the implant-prosthetic rehabilitation of irradiated patients performed at the University Medical Centre Ljubljana.

Patients and methods

A retrospective chart review was performed for the patients who were treated jointly by the Department of oral and maxillofacial surgery and the Department of prosthodontics at the University Medical Centre Ljubljana in the time period from 2008 to 2014. Only patients who underwent resection of malignant tumours with a subsequent radiation treatment and received removable implant-supported dentures were included in the study. The recorded data included patient gender and date of birth, smoking status at the time of prosthetic rehabilitation, cancer type, surgical management, date and dose of radiation treatment, administration of hyperbaric oxygen treatment (HBO), timing to implant surgery and to functional loading, treated jaw, type of implant bed, number of implants supporting the dentures, implant system and the denture attachment system used. At University Medical Centre Ljubljana, HBO is provided according to the protocol suggested by Marx and Larsen.[4,5] Patients are scheduled for 20 sessions before and 10 sessions after the implant insertion, respectively. Each 90-minute session consists of exposure to 100% oxygen on 2.5 ATA (1.5 bar) with three breaks during which patients breathe normal air. The study was conducted according to the Helsinki Declaration. Each patient's informed consent was obtained and Institutional Review board approval was granted.

The implants were assessed for survival and success using the guidelines proposed by van Steenberghe *et al*.[16] The survival criteria included osseointegration and presence in the mouth. To be considered successful, the implant had to be functionally loaded, immobile, without persistent pain or inflammation of the periimplant tissue and without progressive bone loss evident from radiographs and probing depth at the recall.

The survival time was measured from the date of the implant insertion to the date of the implant failure or the last control of the implant.

The present series consisted of 20 patients (11 men and 9 women) with a median age of 57.6 years (range 46.7 to 77.2 years) at the time of the implant insertion. Seventeen patients (85%) had a history of squamous cell carcinoma. Mucoepidermoid, adenoid cystic and *origo ignota* metastatic cancer were diagnosed in 1 patient each. The most common sites of primary cancer were the tongue and the floor of the mouth (6 patients each), followed by pharynx and maxilla (2 patients each). Mandible, tonsilla, larynx and *origo ignota* metastases in lymph nodes

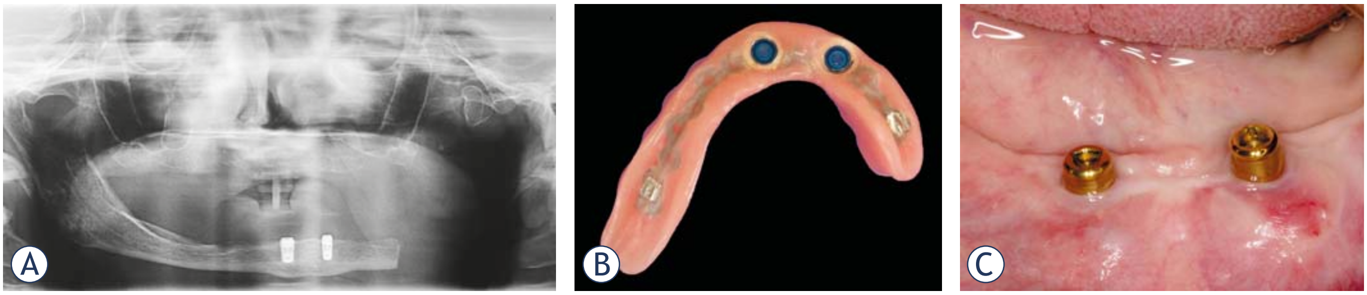

FIGURE 1. A patient after segmental resection of the left mandible body due to cancer, with two implants as seen on the radiograph **(A)**. The patient received an implant-supported lower denture **(B)**, where the retention was based on the Locator attachments **(C)**.

TABLE 1. Summary of the implant survival according to the factors of interest

Parameter	All implants (n = 100)	Survived implants (n = 88)	Failed implants (n = 12)
Patient's median age at implant insertion in years (range)	58.3 (46.7–77.2)	61.5 (46.7–77.2)	57.9 (46.7–77.2)
Median time interval between radiation therapy and implant insertion in years (range)	3.8 (1.1–38.1)	3.2 (1.1–38.1)	5.2 (2.4–12.8)
Patient's gender			
Female, n (%)	40 (40%)	32 (36%)	8 (67%)
Male, n (%)	60 (60%)	56 (64%)	4 (33%)
Smoking			
No, n (%)	66 (66%)	57 (65%)	9 (75%)
Yes, n (%)	34 (34%)	31 (35%)	3 (25%)
Implant system			
Astra, n (%)	18 (18%)	18 (20%)	0 (0%)
Straumann, n (%)	22 (22%)	17 (20%)	5 (42%)
Ankylos, n (%)	60 (60%)	53 (60%)	7 (58%)
Jaw			
Lower, n (%)	72 (72%)	63 (72%)	9 (75%)
Upper, n (%)	28 (28%)	25 (28%)	3 (25%)
Bone			
Native, n (%)	92 (92%)	85 (97%)	7 (58%)
Transplanted, n (%)	8 (8%)	3 (3%)	5 (42%)
HBO administered			
No, n (%)	19 (19%)	14 (16%)	5 (42%)
Yes, n (%)	81 (81%)	74 (84%)	7 (58%)

were encountered in one patient each. A segmental resection of the mandible was performed in 8 patients. In one patient, the tumour resection in the maxilla resulted in an oronasal communication. After surgery, all patients were subjected to the radiation therapy, with reported doses ranging from 54 to 66 Gy.

Reconstruction with bone and soft tissue grafts was accomplished in 3 patients. In two cases the fibular graft was used to reconstruct the mandible. In one patient the maxilla was reconstructed with the iliac crest bone graft.

The Kaplan-Meier method was utilized to estimate the implant survival rate. The association between the survival and the potential prognostic factors was analysed by fitting univariate Cox proportional hazards models. The association between the potential prognostic factors and implant success was analysed with univariate logistic regression models. The Holm-Bonferroni method was used to account for multiple comparisons and the level of significance was set to $\alpha = 0.05$. Statistical analyses were conducted with the statistical software package R.[17]

Results

As presented in Table 1, 100 implants of 3 different implant systems were included in the study: 18 Astra Tech implants (Dentsply, Mannheim, Germany), 22 Straumann implants (Institut Straumann AG, Basel, Switzerland) and 60 Ankylos implants (Dentsply, Mannheim, Germany). 28 implants were inserted in the maxilla and 72 in the mandible. 92 implants were inserted in native bone and 8 in transplanted bone. The median time between the end of the radiation therapy and the implant surgery was 3.8 years (range 1.1 to 38.1 years).

Prophylactic antibiotic therapy was prescribed to all patients and HBO was administered to 16 patients. Osteoradionecrosis was not observed in this study. All implants were inserted in edentulous jaws, with 5 patients receiving implants in both jaws, 14 only in the mandible and 1 only in the maxilla. Twelve patients were non-smokers and 8 patients were smokers at the time of the prosthetic rehabilitation. A two-stage implant insertion protocol was used in all cases. The median healing period between the implant insertion and functional loading was 15.1 months (range 4.3 to 54.3 months). Three different attachment systems for implant-supported dentures were used: 39 Locator attachments (Zest Anchors, Escondido, USA) (Figure 1), 40 prefabricated conical crowns (SynCone, Dentsply Friadent, Mannheim,

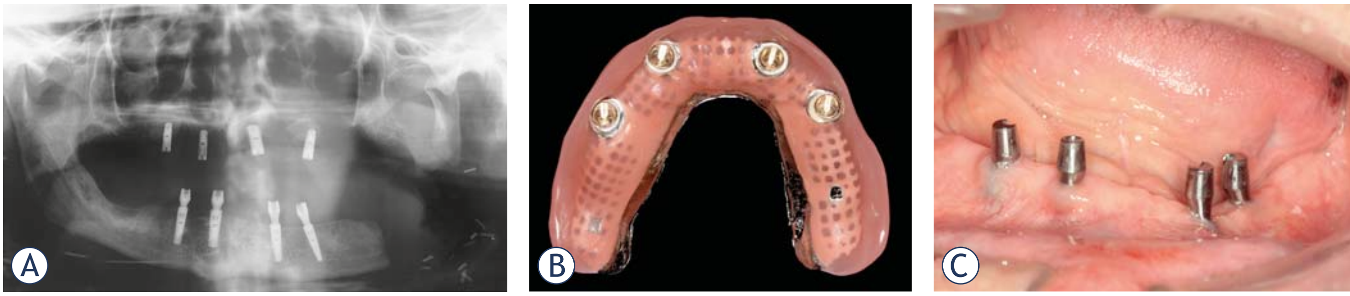

FIGURE 2. A patient after surgical treatment of oropharyngeal carcinoma. Segmental resection of the left mandible body is visible on the radiograph **(A)**. Patient received implant-supported lower and upper dentures **(B)** with retention based on the SynCone double crowns **(C)**.

TABLE 2. Predictors of the implant failure

Parameter	Hazard ratio (95% confidence interval)	*p*
Patient's age at implant insertion in years	1.05 (0.99–1.12)	1.0000
Time interval between the radiation therapy and the implant insertion in years	0.99 (0.92–1.07)	1.0000
Female gender	2.74 (0.82–9.10)	1.0000
Smoker	0.72 (0.19–2.66)	1.0000
Lower jaw	0.84 (0.23–3.09)	1.0000
Transplanted bone	12.37 (3.87–39.56)	**0.0003**
HBO administered	0.31 (0.10–0.98)	0.4753

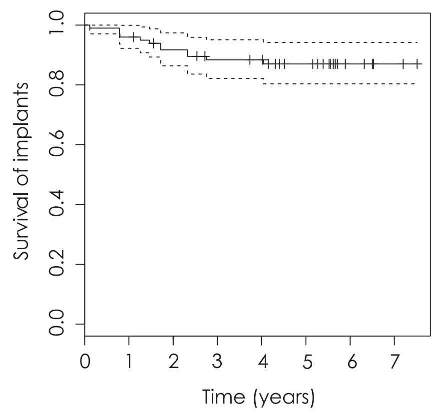

FIGURE 3. The Kaplan-Meier curve for the survival of the implants. 95% confidence intervals and censored data are included on the plot.

Germany) (Figure 2), and 10 custom designed bar-clip systems. Median follow up after implant insertion was 61.9 months (range 1.4 to 90.2 months).

The Kaplan-Meier estimated 1- and 5-year cumulative implant survival rates were 96% (95% confidence interval: 92.2%–99.9%) and 87.0% (95% confidence interval: 80.4–94.2%). The survival curve is shown on Figure 3. During the examination period, three patients died. Time of these 14 implants' service in the mouth was, as with other implants, registered from the date of the implant insertion to the date of the last follow-up examination. The median time of failure was 19.1 months (range 1.4 to 48.5 months) after implantation.

The crude survival rate in our sample was 88%, as 12 implants in 5 patients failed. Data for all the implants and for the subgroups of survived and failed implants are described in Table 1. Primary implant failure during the healing period before functional loading was recorded in 11 implants (91.2%). The causes of implant removal in our sample were incomplete osseointegration (4), persistent pain (4), and periimplantitis with recurrent soft tissue hyperplasia (3). The only implant that was lost after functional loading (secondary implant failure) was included in a bar-supported denture and had to be removed because of periimplantitis. Results of the analysis with the Cox regression models is presented in Table 2.

The survived and failed implants were comparable considering the patient's gender, age and smoking status, the time elapsed between the radiation therapy and the implant surgery, the jaw of the implant insertion and the administration of HBO. The results for the bone type indicated that the implants inserted in the transplanted bone were statistically significantly more likely to fail than those inserted in the native bone. The influence of the implant system on the survival could not be analysed because of the insufficient number of failure events among the three groups. As presented in Table 3, 89 implants were observed after functional loading.

Seventy-nine of those implants (88.7%) were successful, meaning that they were functionally loaded and exhibited no pain, radiolucency or progressive

TABLE 3. Summary of the loaded implants' success according to the factors of interest

Parameter	All loaded implants (n = 89)	Successful loaded implants (n = 79)	Unsuccessful loaded implants (n = 10)
Median patient's age at prosthetic rehabilitation in years (range)	59.1 (49.3–79.2)	58.9 (49.3–67.9)	71.7 (59.1–79.2)
Median healing time after the implant insertion in months (range)	15.1 (4.3–54.4)	15.2 (4.3–54.4)	13.0 (4.3–24.6)
Patient's gender			
Female, n (%)	33 (37%)	25 (32%)	8 (80%)
Male, n (%)	56 (63%)	54 (68%)	2 (20%)
Smoking			
No, n (%)	57 (64%)	49 (62%)	8 (80%)
Yes, n (%)	32 (36%)	30 (38%)	2 (20%)
Median number of the implants supporting the denture (range)	4 (2–5)	4 (2–5)	4
Implant denture system			
Bar, n (%)	10 (11%)	6 (8%)	4 (40%)
Locator, n (%)	39 (44%)	37 (47%)	2 (20%)
SynCone, n (%)	40 (45%)	36 (45%)	4 (40%)
Jaw			
Upper, n (%)	25 (28%)	21 (27%)	4 (40%)
Lower, n (%)	64 (72%)	58 (73%)	6 (60%)
Bone			
Native, n (%)	86 (97%)	76 (96%)	10 (100%)
Transplanted, n (%)	3 (3%)	3 (4%)	0 (0%)
HBO administered			
Yes	75 (84%)	65 (82%)	10 (100%)
No	14 (16%)	14 (18%)	0 (0%)

TABLE 4. Predictors of the loaded implants' success

Parameter	Odds ratio for the loaded implants' success (95% confidence interval)	p
Patient's age at prosthetic rehabilitation	0.66 (0.49–0.80)	**0.0075**
Healing time after the implant insertion	1.09 (0.53–2.73)	1.0000
Male gender	8.64 (1.99–60.09)	0.1456
Smoker	2.44 (0.57–16.95)	1.0000
Number of the implants supporting the denture	0.78 (0.24–1.94)	1.0000
Denture attachment system		
Locator vs bar	12.33 (1.98–104.98)	0.1456
SynCone vs bar	6.00 (1.15–32.68)	0.4416
SynCone vs Locator	0.48 (0.06–2.65)	1.0000
Upper jaw	0.54 (0.14–2.30)	1.0000

bone loss evident from radiographs and probing depth at yearly recall. Regardless of the appropriate osseointegration, prosthetic rehabilitation of 10 implants (11.2%) in four patients (20%) did not have a favourable outcome. Two patients with 4 implants experienced difficulties in adapting to dentures and did not wear them on regular basis. In addition, two further implants were considered unsuccessful because of persistent soft tissue discomfort reported by the patients. As shown in Table 4, patient age was a statistically significant predictor for the success. Gender, smoking status, healing time after implant insertion, the number of implants supporting the denture, the prosthetic system, jaw, bone type and administered HBO did not have a statistically significant effect on the success rate of loaded implants in this sample of irradiated patients.

Discussion

It has been shown in this study that the implant-supported denture is a reliable treatment modality for the head and neck cancer patients that undergo radiation therapy. When surgical and prosthodontic protocols are conducted appropriately, dental implants greatly enhance the stability of the dentures and improve the facial contours. According to the current guidelines, very few absolute contraindications exist for using dental implants in medically compromised patients.[18] Radiation therapy in the head and neck region is no longer a contraindication, as there is a growing number of reports that a high osseointegration rate and a predictable treatment outcome can be expected.[19,20] When considering prosthetic treatment options, the socio-economic status of patients should carefully be evaluated. Head and neck cancer is commonly associated with smoking and alcohol abuse. Both tobacco and alcohol are known as strong risk factors and when combined, their carcinogenic potential has been shown to be even more pronounced.[21,22] Many patients do not give up smoking and drinking after the initial cancer treatment, which puts them at risk for cancer recurrence and might also jeopardize the implant-prosthetic rehabilitation outcome.

In this case series of irradiated patients, the implant failures were rare and mostly confined to the healing period. The predominantly early implant loss is in accordance with the findings of Linsen *et al.*[23] Extended healing time should therefore be allowed after implantation and immediate loading protocols are not advised.[18]

The Kaplan-Meier estimated 1- and 5-year cumulative implant survival rates were 96% and 87%. This is in accordance with Buddula *et al.*[24] reporting implant survival rates of 98.9% and 89.9% after 1 and 5 years and Yerit *et al.*[25] reporting a 95% and 91% survival after 2 and 5 years, respectively. Due to the small number of failed implants, detailed statistical analysis of prognostic factors for implant failure is often not possible or lacks power. It is therefore difficult to draw meaningful conclusions from the results of single studies alone. In this study, some limited insight could be obtained regarding the survival of implants. There was a statistically significant higher failure rate in the transplanted bone. The reduced survival of implants in the transplanted bone may be explained by differences in bone quality, bone volume, and revascularization compared to the native bone.[9] Our findings are in agreement with Yerit *et al.*[25], where lower survival was also reported for the transplanted bone. In contrast, Buddula *et al.*[24] reported no difference between implant survival in the native and transplanted bone. They also reported no difference in survival between genders and considering the time span between radiation treatment and implant insertion, which is in accordance with this study. Their finding of the statistically significant higher hazard ratio for implants in the upper jaw could not be confirmed in this study.

The risk for implant failure is generally higher in smoking patients, as shown in the systematic review papers by Chambrone *et al*. and Moraschini and Barboza.[26,27] The smoking status was not a statistically significant predictor for the implant survival in this study, but the effect might have been detected with a larger sample size and more precise smoking classification. It is also notable that the risk for implant failure in smokers was suggested to be significantly elevated only for a limited time after surgery, presumably when tobacco smoke components impede bone healing.[27]

HBO, which is commonly used at the University Medical Centre Ljubljana for the head and neck cancer patients requiring surgery, was also not a statistically significant predictor for the implant survival in this study. Generally, there is no agreement on the HBO efficacy and value.[28]

Implant osseointegration and survival data provide valuable information about the success of the implant therapy. Nevertheless, the final judgement of the implant-prosthetic therapy should be made according the denture performance in the oral cavity. Successful implants enable patients to use the dentures and do not cause any persistent discomfort. To achieve a favourable clinical outcome, it is crucial to design a viable prosthetic plan early in the rehabilitation process. Head and neck cancer patients present severely altered and unfavourable tissue conditions, making it challenging to model rehabilitation using the optimal top-down approach. The fragile mucosa, xerostomia, limited mouth opening and jaw deviations are additional factors to consider. The possible locations, angulations and implant dimensions might not be ideal and should be discussed thoroughly between the oral surgeon and the prosthodontist.

The optimal number of implants should be carefully planned. There is a tendency to insert as few implants as possible in oncological patients, to facilitate bone healing. On the other hand increased number is often required to design rigid, implant-borne prosthetic constructions.[18] More implants also allow more flexibility in prosthetic treatment planning. Moreover, if some implants are lost, implant dentures can be successfully repaired and worn by the patients. It is currently thought that the number of implants is not critical for the success of the prosthetic treatment[29], but long-term clinical studies are lacking. In the present study the number of implants supporting the dentures was not a detectable factor in the success rate of the prosthodontic rehabilitation. Similarly, neither was the treated jaw or the healing time, which exceeded 4 months in all implants.

The loaded implants also exhibited similar success rates regardless of the denture attachment system used. While the bar-supporting implants experienced less success, the differences in comparison to the Locator attachments and SynCone systems were not significant.

Additional systemic and patient-related factors might play an important role in implant prosthetic rehabilitation. In this case series of irradiated patients, advanced age showed a negative prognostic value for the rehabilitation success, but not for implant survival. One of the possible limitations of this study was that the data on systemic diseases and alcohol consumption which might negatively affect implant performance were not included. After the implant-prosthetic rehabilitation, it is of utmost importance to enrol the patient in an appropriate supportive program, with regular recalls, cancer screening and maintenance of the peri-implant conditions. The recall program should meet the individual needs of the patients according to the overall risk profile. Some patients should be recalled every 3 months, while others may need to be checked once per year.[30]

This study has shown that favourable rehabilitation results can be obtained with implant-prosthetic treatment in irradiated patients. With proper collaboration between experienced surgeons and prosthodontists, this treatment modality can be regarded a viable option for oral rehabilitation after head and neck cancer.

References

1. De Camargo Cancela M, Voti L, Guerra-Yi M, Chapuis F, Mazuir M, Curado MP. Oral cavity cancer in developed and in developing countries: population-based incidence. *Head Neck* 2010; **32:** 357-67.
2. De Camargo Cancela M, de Souza DL, Curado MP. International incidence of oropharyngeal cancer: a population-based study. *Oral Oncol* 2012; **48:** 484-90.
3. Cancer in Slovenia 2011. Ljubljana: Institute of Oncology Ljubljana, Epidemiology and Cancer Registry, Cancer Registry of Republic of Slovenia; 2015.
4. Marx RE. Osteoradionecrosis: a new concept of its pathophysiology. *J Oral Maxillofac Surg* 1983; **41:** 283-8.
5. Larsen PE. Placement of dental implants in the irradiated mandible: a protocol involving adjunctive hyperbaric oxygen. *J Oral Maxillofac Surg* 1997; **55:** 967-71.
6. Fierz J, Bürgin W, Mericske-Stern R. Patients with oral tumors. Part 2: Quality of life after treatment with resection prostheses. Resection prosthetics: evaluation of quality of life. *Schweiz Monatsschr Zahnmed* 2013; **123:** 180-91.
7. Brauner E, Cassoni A, Battisti A, Bartoli D, Valentini V. Prosthetic rehabilitation of post-oncological patients: Report of two cases. *Ann Stomatol* 2010; **1:** 19-25.
8. Carini F, Pisapia V, Monai D, Barbano L, Porcaro G. Implant rehabilitation in patients irradiated for head and neck cancer: role of Intensity-Moduled Radiotherapy (IMRT) in planning the insertion site. *Ann Stomatol* 2012; **3:** 8-20.
9. Schiegnitz E, Al-Nawas B, Kämmerer PW, Grötz KA. Oral rehabilitation with dental implants in irradiated patients: a meta-analysis on implant survival. *Clin Oral Investig* 2014; **18:** 687-98.
10. Andreiotelli M, Att W, Strub JR. Prosthodontic complications with implant overdentures: a systematic literature review. *Int J Prosthodont* 2010; **23:** 195-203.
11. Kleis WK, Kämmerer PW, Hartmann S, Al-Nawas B, Wagner W. A comparison of three different attachment systems for mandibular two-implant overdentures: one-year report. *Clin Implant Dent Relat Res* 2009; **13:** 209-218.
12. Mackie A, Lyons K, Thomson WM, Payne AG. Mandibular two-implant overdentures: three-year prosthodontic maintenance using the locator attachment system. *Int J Prosthodont* 2011; **24:** 328-31.
13. Troeltzsch M, Troeltzsch V, Brodine AH, Frankenberger R, Messlinger K, Troeltzsch M. Clinical performance and peri-implant parameters of 132 implants supporting locator-retained overdentures: a case series of 33 patients. *Int J Oral Maxillofac Implants* 2013; **28:** 1132-9.
14. May D, Romanos GE. Immediate implant-supported mandibular overdentures retained by conical crowns: A new treatment concept. *Quintessence Int* 2002; **33:** 5-12.
15. Bernhart G, Koob A, Schmitter M, Gabbert O, Stober T, Rammelsberg P. Clinical success of implant-supported and tooth-implant-supported double crown-retained dentures. *Clin Oral Investig* 2012; **16:** 1031-7.
16. Van Steenberghe D. Outcomes and their measurement in clinical trials of endosseous oral implants. *Ann Periodontol* 1997; **2:** 291-8.
17. R Development Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2014. [Citated 15 Nov 2015]. Available at http://www.gbif.org/resource/81287
18. Diz P, Scully C, Sanz M. Dental implants in the medically compromised patient. *J Dent* 2013; **41:** 195-206.
19. Ihde S, Kopp S, Gundlach K, Konstantinović 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.
20. Tanaka TI, Chan HL, Tindle DI, Maceachern M, Oh TJ. Updated clinical considerations for dental implant therapy in irradiated head and neck cancer patients. *J Prosthodont* 2013; **22:** 432-8.
21. Tobias JS. Cancer of the head and neck. *BMJ* 1994; **308:** 961-6.
22. Cognetti DM, Weber RS, Lai SY. Head and neck cancer: an evolving treatment paradigm. *Cancer* 2008; **113:** 1911-32.
23. 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:** 250-8.
24. Buddula A, Assad DA, Salinas TJ, Garces YI, Volz JE, Weaver AL. Survival of dental implants in irradiated head and neck cancer patients: a retrospective analysis. *Clin Implant Dent Relat Res* 2012; **14:** 716-22.
25. Yerit KC, Posch M, Seemann M, Hainich S, Dörtbudak O, Turhani D, et al. Implant survival in mandibles of irradiated oral cancer patients. *Clin Oral Implants Res* 2006; **17:** 337-44.
26. Chambrone L, Preshaw PM, Ferreira JD, Rodrigues JA, Cassoni A, Shibli JA. Effects of tobacco smoking on the survival rates of dental implants placed in areas of maxillary sinus floor augmentation: a systematic review. *Clin Oral Implants Res* 2014; **25:** 408-16.
27. Moraschini V, Barboza ED. Success of dental implants in smokers and non-smokers: a systematic review and meta-analysis. *Int J Oral Maxillofac Surg* 2015; doi: 10.1016/j.ijom.2015.08.996
28. Spiegelberg L, Djasim UM, van Neck HW, Wolvius EB, van der Wal KG. Hyperbaric oxygen therapy in the management of radiation-induced injury in the head and neck region: a review of the literature. *J Oral Maxillofac Surg* 2010; **68:** 1732-9.
29. Roccuzzo M, Bonino F, Gaudioso L, Zwahlen M, Meijer HJ. What is the optimal number of implants for removable constructions? A systematic review on implant-supported overdentures. *Clin Oral Implants Res* 2012; **23:** 229-37.
30. Lang NP, Lindhe J. Clinical Periodontology and Implant Dentistry. Chichester: John Wiley & Sons; 2015.