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Survival of Chemically Modified Titanium Surfaced Implants in Irradiated Jaws of Oral Cancer Patients

Mehmet Yaltirik[1], Bilge Gökçen Röhlig[2], Meltem Özdemir Karataş[2], Melike Ordulu Sübay[1*], Rüştü Cem Tanyel[1], Meltem Koray[1]

[1]Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Istanbul University, Istanbul, Turkey
[2]Department of Prosthodontics, Faculty of Dentistry, Istanbul University, Istanbul, Turkey
Email: [*]melikeordulu@yahoo.com

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Abstract

Objective: To investigate the clinical performance of implants with chemically modified surfaces in irradiated bone in a period of five-years. Patients & Methods: 15 (6 females, 9 males, 50.2 years with a range of 38 - 60 years) patients who had been operated for oral tumors and had undergone radiotherapy were enrolled and 40 SLActive surface implants were placed (24 in the maxilla, 16 in the mandible). Implants were allowed to integrate for a period of 90 days and the stability of the implants was measured with Resonance Frequency Analyzer/Osstell™ Mentor (Integration Diagnostics, Savedalen, Sweden) at implant placement, 30 days later and at the end of the 90th day. Patients follow up periods after the implant placement varied from 20 months to 60 months (mean: 45 months). Results: Two implants were lost in maxilla in healing period as a result of osseointegration failure. The survival rate was 95%. During the observation period, totally 4 implants were lost. The overall success rate was 90%. 3 of the lost implants were in maxilla and one was in mandible. The initial ISQ values of the implants differed from 20 - 71; the second values were between 24 - 71 and the last values were between 30 - 89. The implants which were lost could not show a value greater than 35. Conclusion: There was no any complication on the SLActive surface implant placed bones due to irradiation. Within the limitations of this study, it may be concluded that osseointegrated implants can be placed in irradiated bones, unless a careful patient selection and treatment planning is performed.

Keywords

Irradiation, Resonance Frequency Analysis, SLActive, Success Criteria

[*]Corresponding author.

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1. Introduction

Rehabilitation of patients with head and neck cancer usually involves ablative surgery, chemotherapy, radiotherapy or a combination of these modalities. The surgical treatment often results in clinical situations where prosthetic treatment is mandatory and conventional rehabiliation does not produce satisfactory results. In such cases, use of osseointegrated implants can improve the final outcome of the restorations.

Irradiation leads to progressive fibrosis of blood vessels, alteration in vascular supply of structures and decrease in osteoblastic and osteoclastic activity in surrounding bone [1]. Osteonecrosis and soft tissue dehiscences are further complications encountered in irradiated patients undergoing oral surgical procedures. Although success of osseointegration of implants depends on the bone density, surgical technique and the microscopic and macroscopic morphology of the implants, the survival and the success rates are markedly reduced in irradiated fields. Such a result is explained with reduced bone vitality [2] [3]. Most studies demonstrated that reduction of implant stability in alveolar bone at 8 weeks after implant placement was due to impaired integration that arose from lack of remodeling and reduced bone vascularity [4] [5]. In these cases, there is considerable interest in enhancing the quality and rate of bone formation around dental implants. This formation of new bone can be actively influenced by implant surface properties.

Since the beginning of 1980s, many efforts have been made to improve osseointegration and the amount of bone to implant contact [6]-[10]. Additions of a layer of hydroxyapatite on to the titanium, and plasma-spray coating of the implant body are the common methods for surface modifications and they have been proven to have successful long-term rates. Recently a new chemically modified, sandblasted large grit and acid-etched (SLActive) active and hydrophilic implant surface has been introduced to enhance bone apposition (SLActive, Straumann, AG, Basel, Switzerland). With the use of a specific surface production process (after the titanium surfaces were processed with etch, they were rinsed with N2 protection and stored in an isotonic NaCl solution) standard SLA surfaces were converted into a chemically active surface containing hydrocarbons and carbonates. This active hydroxylated/hydrated surface was shown to have an initial advancing water contact angle of 0˚ and this resulted in an ultra hydrophilic character. Histological studies have also shown that SLActive implants exhibited a significantly greater bone-to-implant contact than conventional SLA surfaces at 2 and 4 weeks of healing [9] [11] [12]. These preliminary studies suggest that SLActive surfaces might also help to improve the stability of implants placed in irradiated bone. If this newly developed surface could produce predictable results, then the prosthetic rehabilitation of head and neck cancer patients may be improved.

Therefore, the aim of the present pilot study was to investigate clinically the osseointegration course of the chemically modified titanium surfaces (SLActive) in irradiated bone.

2. Patients and Methods

This study was approved by the Ethical Committee of the Istanbul University, Medical School of Istanbul (nr. 2007/1032). All participating individuals signed an informed consent.

The patients were selected consecutively among the patients referred to the Department of Maxillofacial Prosthodontics, Faculty of Dentistry, Istanbul University for prosthetic restoration. Fourty implants placed in 15 patients with maxillofacial defects caused by tumor resections of oral cancers at a university clinic between 1989 and 2005 were included in the study. They had been operated because of oral cancer and received radiation for tumors. Chemically modified surfaced implants (SLActive Straumann®, AG, Waldenburg, Switzerland) were placed by the same oral surgeon in irradiated bones.

The inclusion criteria for enrollment in this study were: 1) patients who had been operated for oral tumors and fallowed at least 5 years for metastasis 2) patients who had undergone radiotherapy in areas including future implant sides, 3) a period of minimum 12 months following radiotherapy. The exclusion criteria of study were patients who had been subject to bone-grafting procedures were excluded.

A comprehensive treatment plan was presented to each of the patients based on clinical and radiographic findings, specialty consultations with head and neck surgeon, oncologist and oral surgeon. After consultations, placement of osseointegrated SLActive surface implants was planned.

All patients received an antibiotic therapy using clindamycin 300 mg three times daily pre and postoperatively (1 day preoperatively and 3 days postoperatively). The surgical procedure was conducted in 2 stage with general guidelines defined by Brånemark *et al.* and the specific indications that were recommended by Buser *et al.* for Straumann Dental Implants. Totally 40 SLActive implants (24 maxilla, 16 mandible) (Straumann AG, Walden-

burg, Switzerland) were placed. The demographic and treatment data of the patients are listed in **Table 1**.

Implants were allowed to integrate for a period of 90 days and the stability of the implants was measured with Resonance Frequency Analyzer (RFA)/Osstell™ Mentor (Integration Diagnostics, Savedalen, Sweden) at implant placement, 30 days later and at the end of the 90th day and if the measurements were not high enough for an abutment connection, measurements were performed monthly until satisfactory results were gained. RFA values are recorded in Implant Stability Quotient (ISQ) ranging from 1 to 100. ISQ values are derived from the stiffness (N/μm) of the implant/bone system and the calibration parameters of the transducer. High ISQ value indicates high stability, whereas low value indicates a low implant stability. All of the implants' measurements were high enough for an abutment connection at the end of the 3rd month.

Prosthetic treatment of the patients was performed by the same prosthodontist. Locater abutments (Zest Anchors, Inc., California, USA, Distributor; Institut Straumann AG Basel, Switzerland) were used to assist with retention of the obturators, dolder bar was used to retain mandibular resection prosthesis.

All participants received digital (Morita Veraview IC5®, J Morita MFG Corp, Kyoto, Japan) or analog panoramic radiographs (Planmeca®, Proline XC, Helsinki, Finland) using the imaging equipment preoperatively, immediately after surgery, immediately after loading and at scheluded appointments for the evaluation of marginal bone levels of the implants.

3. Results

The study population consisted of 15 patients (6 female 9 male). 11 patients had been operated because of squamous cell carcinoma while the others had been treated because of epidermoid carcinoma.

Of the forty implants, 24 implants were placed in the maxilla, 16 were placed in the mandible. All implants had a diameter of 4.1 mm and the lengths are 8 mm (n = 1) to 10 mm (n = 23) and 12 mm (n = 16). The mean age at the implant placement was 50.2 years with a range of 38 - 60 years.

All implants were placed in radiated bone. The radiation doses varied from 30 Gy (n = 3) to 40 Gy (n = 11) and 120 Gy (n = 1). Time from the last radiotherapy session to implant placement differs from 12 months to 28 months. None of the patients had recurrences of their tumors at the end of the follow up periods.

The initial ISQ values of the implants differs from 20 - 71 at the time of the operation. The second measurement was made at the 30th day and the values were measured between 24 - 71. At 90th day after the operation the

Table 1. The demographic and treatment data of the patients.

	Gender	Age	Tumor type	Time of cancer diagnosis and medical history	Surgical treatment	Radiation dose	N. of implants inserted	Location of implants	Implant dimensions	N. of imp. lost	Time from end of RT to imp. placement	Follow-up
1	Male	58	Squamous cell carsinoma	Diagnosed in 1972, operated in 1972, 1976 and 1989	Partial right maxillectomy (in 1989)	40 Gy (postoperative)	3	Premaxilla and premolar region	1(3.3 × 10); 2(4.1 × 12)	None	18 months	60 months
2	Male	50	Squamous cell carsinoma	Diagnosed and operated in 2001, till then no metastases or recurrence	Partial left maxillectomy	120 Gy and received chemotherapy (postoperative).	3	Premaxilla and premolar region	2(4.1 × 10); 1(4.1 × 8)	1 (in premolar region)	21 months	48 months
3	Female	49	Squamous cell carsinoma	Diagnosed and operated in 2000 and till then no metastases or recurrence	Palatectomy	30 Gy (postoperative)	3	Premaxilla on defect side	1(4.1 × 10); 2(4.1 × 12)	None	20 months	60 months
4	Female	60	Squamous cell carsinoma	Diagnosed and operated in 2002 till then no metastases or recurrence	Partial left maxillectomy	40 Gy (postoperative)	2	Premaxilla and tuber region	1(4.1 × 10); 1(4.1 × 12)	None	18 months	60 months

Continued

5	Male	38	Epidermoid carcinoma	Diagnosed and operated in 2002 till then no metastases or recurrence	Segmental resection of mandible	30 Gy (postoperative)	2	Intra-foraminal region	2(4.1 × 12)	None	18 months	40 months
6	Male	45	Squamous cell carsinoma	Diagnosed and operated in 2002, till then no metastases or recurrence	Partial right maxillectomy	40 Gy (postoperative)	2	Premaxilla and premolar region	1(4.1 × 10); 1(4.1 × 12)	None	20 months	60 months
7	Female	50	Squamous cell carsinoma	Diagnosed and operated in 2001, till then no metastases or recurrence	Partial left maxillectomy	40 Gy (postoperative)	3	Premaxilla and premolar region	2(4.1 × 10); 1(4.1 × 12)	None	26 months	60 months
8	Male	42	Epidermoid carcinoma	Diagnosed and operated in 2000 and till then no metastases or recurrence	Segmental resection of mandible (resection of left posterior)	40 Gy (postoperative)	2	Premaxilla on defect side	1(4.1 × 10); 1(4.1 × 12)	None	18 months	60 months
9	Male	56	Squamous cell carsinoma	Diagnosed and operated in 2002 till then no metastases or recurrence	Partial right maxillectomy	40 Gy (postoperative)	2	Premaxilla and tuber region	1(4.1 × 10); 1(4.1 × 12)	1 (in canine region)	28 months	60 months
10	Female	44	Squamous cell carsinoma	Diagnosed and operated in 2002 till then no metastases or recurrence	Partial right maxillectomy	40 Gy (postoperative)	2	Intra-foraminal region	2(4.1 × 12)	None	12 months	60 months
11	Female	52	Squamous cell carsinoma	Diagnosed and operated in 2004, till then no metastases or recurrence	Partial right maxillectomy	40 Gy (postoperative)	4	Premaxilla and premolar region	2(4.1 × 10); 2(4.1 × 12)	1 (in canine region)	18 months	24 months
12	Male	46	Squamous cell carsinoma	Diagnosed and operated in 2004, till then no metastases or recurrence	Segmental resection of mandible (resection of left posterior)	40 Gy (postoperative)	3	Intra-foraminal region	2(4.1 × 10); 1(4.1 × 12)	None	20 months	24 months
13	Male	48	Epidermoid carcinoma	Diagnosed and operated in 2000 and till then no metastases or recurrence	Mandible Alveolar resection	40 Gy (postoperative)	3	Intra-foraminal region	3(4.1 × 10)	None	18 months	20 months
14	Female	56	Epidermoid carcinoma	Diagnosed and operated in 2005 and till then no metastases or recurrence	Segmental resection of mandible (resection of right posterior)	40 Gy (postoperative)	2	Intra-foraminal region	2(4.1 × 10)	None	18 months	20 months
15	Male	60	Squamous cell carsinoma	Diagnosed and operated in 2005 and till then no metastases or recurrence	Mandible Alveolar resection	30 Gy (postoperative)	4	Premolar and intraforaminal region	4(4.1 × 10)	1 (in premolar region)	20 months	20 months

measurements were renewed and the minimum score was 30 while the highest score was measured 89. The implants which were lost could not showed a value greater than 35.

Patients follow up periods after the implant placement varied from 20 months to 60 months (mean 45 months).

3.1. Implant Success, Survival Rate

Two implants were lost in maxilla in healing period as a result of osseointegration failure. The survival rate was 95%. During the observation period, totally 4 implants (3 in maxilla, 1 in mandible) were lost. 37 implants were regarded as successful according to the criteria proposed by Misch *et al.* [9] and overall success rate was 90%.

3.2. The Marginal Bone Loss

The mean marginal bone loss (MBL) was 1.2 mm on the mesial side and 1.4 mm on the distal side of the implants. The MBL on the distal and mesial aspects of the implants up to 48 mo to 60 mo following loading did not exceed 2 mm.

No patient reported low satisfaction and oral health related quality of life scores (score lower than 50) [13].

4. Discussion

Patients with oral cancer need multidisciplinary approach from the beginning of their therapies. Surgeons, radiation and medical oncologists and dental specialists involving this process. Oral cancer therapy contains three main stages such as surgery, radiotherapy and chemotherapy. Of the three modalities surgery is most commonly used. Resection of the tumoral tissue is the main aim of the cancer therapy. The formed defect size after surgical intervention can range from a small soft tissue deformity to a large defect where significant amounts of maxilla or mandible are lost. In these kinds of patients, achieving the prosthetic stability is the main goal of the dental treatment and dental implants are playing an important role in achieving this aim [14]. The use of dental implants in oral cancer patients is being increased day to day [15] [16].

Most of the oral cancer patients take radiation therapy in the course of their rehabilitation. It is known that can have a negative effect on implant survival [17] [18]. During treatment, irradiated bone change properties, with loss of bone quality and vasculature. Additionally, the quantity of doses has been shown to be very important for bone recovery after treatment [19]. Some researchers analyzed the comparison between the radiation dose and the implant success and its stated that the amount of the dose directly effect on the implant stability [13] [17] [20]. Visch *et al.* [20] had shown that lower radiation dose (<50 Gy) is associated with significantly improved implant survival than in patients after irradiation with a higher dose (>50 Gy). In this study we could not confirm these statements because most of the patients received radiotherapy less than 50 Gy. Only one patient received a radiation dose of 120 Gy and lost one of the three implants which was in peremolar region in maxilla.

Histological studies have also shown that SLActive implants exhibited a significantly greater bone-to-implant contact than conventional SLA surfaces at 2 and 4 weeks of healing [9] [11] [12]. In the present study there was no any complication on the SLActive surface implant placed bones due to irradiation and the overall success rate was 90% regarding implant success.

The time of the implant placement after the last radiotherapy session may contribute to the success or failure of osseointegration. In literature different studies have investigated the required time interval between radiotherapy and implant installation that may influence osseointegration [21]-[24]. Marx and Johnson [25] reported that the probability of implant failure is higher in cases where dental implants are inserted between one and six months following radiotherapy. Cao *et al.* [21] shared the same findings where the dental implants installed 6 months following radiation showed significantly lower implant survival rate. In Visch's [20] study, they stated that there is no significant difference in survival of implants inserted less than 12 months (76%) or at least one year (81%) after radiotherapy. Werkmeister *et al.* [26] found osteointegration is negatively influenced in dental implants that installed 2 years following end of radiotherapy. But in mentioned study the implant survival rate of the implants which were in non-irradiated bone was also low (68%). In our study the implant placement time differs from 12 months to 28 months. Remarkably, one of the 4 implants that we have lost installed in 28th month after radiation in the maxilla in canine region.

Resonance frequency analysis is a reliable and reproducible standardized method measuring implant stability.

Differences in implant stability can be recorded in vivo at insertion of an implant and during the course of osseointegration [27] [28]. ISQ values may range from 0 to 100. Successfully integrated implants have ISQ values above 40 [27] [29]-[34]. Verdonk *et al.* [27] reported that in 2008, immediately after placement, ISQ values were not statistically significant different in irradiated and non-irradiated alveolar bone. But at 8 weeks after implant placement, they found a statistically significant difference in ISQ value. ISQ values of 16 and 24 weeks after implant placement showed a stabilization or even slight increase when compared with the values of 8 weeks after implant placement. They also report that primary stability depends on bone density. But after the implant placement, the stability depends on osteointegration. In our study we prefer to measure implant stability at the time of implant placement, 30th day and 90th day after the operation. Our results are most likely the Verdonk and his friends results but most of the implants that include our study showed slight continuous rate of increase ISQ values during the 90 days.

The success of osseointegrated implants depends on the bone density, surgical technique and on the microscopic and macroscopic morphology of the implants used. Studies in animals shown that the chemically modified SLActive surface furnished the adhesion and stabilization of the blood clot in early hours following implant placement. In early days osteoblast differentiation and vascular structures can be observed in the connective tissue that formed around the implant [17] [35]. Compared with the SLA implant surface, SLActive implant surface has shown significant higher levels in ALP (alkaline phosphatase) expression as well as early osteocalsin synthesis [17] [36]. In addition to these findings Schwarz *et al.* [12] and Buser *et al.* [9] reported that the bone implant contact rate was significantly higher in SLActive implants after 7 and 14 days. If its taken in consideration that most implant failures seen in irradited patients occurred shortly after implant placement in the early period between primary and secondary stability in bone as reported by the researchers, using SLActive surface implants could be useful in these kind of individuals [13] [18] [37] [38]. There are many investigations in the literature aiming to evaluate the survival of dental implants in patients with oral cancers. If we take a look at previous studies about this topic we can encounter different outcomes. Some authors stated that, dental implant supported prosthesis have significantly lower survival rates in irradiated patients compared to non-irradiated patients. Visch *et al.* [20] reported after a 14 years follow up period implant survival (78%) is significantly influenced by location, extent of surgery and by the irradiation dose at the implant site. Cao and Weicher's [21] and Werkmeister's [26] findings supports this conclusion and they found the implant survival rates in irradiated bones in turn (88%) and (68.8%). On the other hand, most of the researchers conclude their investigations by the statement that dental implants can osseointegrate and can remain functionally stable in patients having undergone radiotherapy [16] [17] [22] [23]. After 60 months period our cumulative survival rate is 90%. 36 of 40 implants that we include in the study were functionally stable.

5. Conclusion

Although the survival and success rates of implants were slightly lower than standard conditions, from the results of this pilot study, it may be concluded that SLActive surface implants can be placed in irradiated bones, unless a careful patient selection and treatment planning is performed. Studying with larger case numbers will help gather more information about the success of SLActive surface implants as a treatment of modality in maxillofacial defects patients, with irradiated bones.

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