
Oral Implant Rehabilitation in Irradiated Patients Without Adjunctive Hyperbaric Oxygen

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In 15 patients treated for malignant tumors in the maxillofacial region, 90 Brånemark implants have been placed in irradiated alveolar bone without adjunctive hyperbaric oxygen therapy. Seventy-eight implants were placed in the mandible and 12 in the maxilla. After a follow-up period of 1 to 8 years, 88 implants are still stable, 27 after 6 to 8 years, 44 after 3 to 4 years, and 17 after 1 to 2 years. Two patients lost 1 implant each, both at an early stage. The success rate is 97.8% according to remaining implants, and prosthesis stability is 100%. Implant treatment for oral rehabilitation can be carried out as a safe and successful procedure in the irradiated patient without adjunctive hyperbaric oxygen therapy.

(INT J ORAL MAXILLOFAC IMPLANTS 1998;13:647-654)

Key words: intraoral implant, irradiation, oral malignancy

In Scandinavia, malignant tumors in the maxillofacial region are commonly treated with radiotherapy combined with surgery. The oral rehabilitation of these patients to restore function and improve cosmetic appearance is very important. However, radiotherapy in the head and neck region almost invariably leads to a vulnerable mucosa and persistent xerostomia, which makes oral rehabilitation with denture prostheses difficult and even impossible in many patients. Furthermore, surgical treatment can result in changed anatomy, rendering conventional prosthetic treatment difficult. The use of osseointegrated implants is therefore of great value to restore the masticatory function in these patients. However, in previously irradiated patients, such treatment has sometimes been complicated by osteoradionecrosis and loss of implants.^{1,2} Since hyperbaric oxygen (HBO) therapy has been successfully used in the treatment of osteoradionecrosis,³⁻⁵ it has been advocated as an

adjunct in implant therapy to decrease an anticipated loss of implants.⁶ Further, HBO therapy has been considered a preventive measure in patients who have received more than 50 Gy to the implant site.¹ However, studies from Scandinavia^{7,8} and Japan⁹ have reported successful implant treatment in patients with irradiated bone tissue without adjunctive HBO therapy. This is further elucidated in a recent publication,¹⁰ where it was shown that the success rate for endosseous implants in irradiated patients is similar to the results in nonirradiated patients.

The aim of this study was to evaluate the outcome of oral rehabilitation using implants without HBO therapy in a series of patients treated for oral malignant tumors with radiotherapy and surgery.

Materials and Methods

This study comprises 15 patients, 11 males with a mean age of 68 years (range 62 to 74 years) and 4 females with a mean age of 68 years (range 67 to 70 years) at the time of implant treatment. All patients had been treated for malignant tumors in the head and neck region at the University Hospital MAS in Malmö, Sweden. Ten patients had squamous cell carcinomas, 3 had malignant lymphomas, and 2 had malignant salivary gland tumors. Detailed patient data are presented in Table 1.

All patients received radiotherapy: 3 patients received a dose of 44 Gy, 7 received 50 Gy, 1

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Table 1 Patient Data

	Patient 1	Patient 2	Patient 3	Patient 4
Year of birth	1924	1921	1927	1915
Sex	Male	Female	Male	Male
Tobacco habits	> 20 cig/day	10–20 cig/day	40 cig/day	None (stopped–1972)
Dental status	Edentulous	Edentulous	Edentulous	Partially edentulous
Original tumor*	SCC, floor of the mouth, 9/85	SCC, floor of the mouth, 3/87	Lymphoma malignant non-Hodgkin	SCC, epipharynx, regional lymph nodes, 3/87
TNM classification	T3 N0 M0	T3 N0 M0	Stad II A	T1 N1 M0
Surgical treatment	Soft tissue resection; resection of left mandible to first premolar; neck dissection; myocutaneous pectoral flap, 10/85	Soft tissue resection; platysma flap, 6/87	None	None
Radiotherapy	50 Gy preop, 9/85–10/85	50 Gy preop, 4/87–5/87	44 Gy, 9/85–10/85	68 Gy, 6/87–9/87
Implant surgery	Implant operation 11/87, abutment connection 4/88, both under local anesthesia	Implant operation 7/88, abutment connection 11/88, both under local anesthesia	Implant operation 4/89, abutment connection 9/89, both under local anesthesia	Implant operation 9/89, abutment connection 4/90, both under local anesthesia
No. of implants	5	5	6	6
Implant length	10 mm (3), 13 mm (2)	13 mm (3), 15 mm (2)	10 mm (2), 15 mm (4)	10 mm (4), 13 mm (2)
Implant site†	33, 31, 41, 43, 45	34, 33, 31, 41, 44	35, 33, 31, 41, 43, 45	47, 46, 45, 35, 36, 37
Estimated dose (Gy) to each implant site	50, 50, 50, 50, 50	50, 50, 50, 50, 32	44, 44, 22, 22, 44, 44	68, 58, 34, 34, 58, 68
Implants lost	0	0	0	0
Follow-up time (y)	4	7	8	7.5
Recurrence or second primary	Second primary hypopharynx 1991; radiotherapy 30 Gy posterior of the implants	Local recurrence 1995; surgical treatment, resection of mandible including 4 implants	None	None
Present status	Deceased 1991 second primary	Deceased 1997 local recurrence	Alive without disease	Alive without disease
Other disease	Hypertonia	Esophagus hernia	None	Myocardial infarction 1994

received 60 Gy, and 4 received 68 Gy (Table 1). In addition, one of the patients who received a dose of 68 Gy also received chemotherapy. The radiotherapy was given with external beam therapy using megavoltage radiation. The dose specifications were mean dose to target in 5 patients and specified in a dose specification point according to ICRU in the remaining 10 patients.¹¹ This did not make any difference, since the dose was homogenous within the target volume. To evaluate the radiation dose for each implant site, the calculated dose plan, simulation radiographs, and field photographs were used. After careful evaluation, the radiation dose to each implant site in Gy was calculated from the dose plan. The data are presented in detail in Table 1.

Ten patients were also treated surgically with soft tissue resection, and 6 of these patients were treated with block resection of the mandible as well. Primary closure was possible in 3 patients. Immediate soft tissue reconstruction was obtained by platysma flap in 1 patient, by myocutaneous pectoral flap in 3 patients, and by microvascular radial forearm flap in 3 patients (Table 1). All patients have been followed regularly according to a specific posttreatment protocol, initially at 3-month intervals, then at 4-month intervals, and later at 6-month intervals, for a total period of 5 years.

Implant surgery was carried out using the Brånemark system¹² (Nobel Biocare AB, Göteborg, Sweden) 8 to 65 months (mean 22.1 ± 8.1 months) after radiotherapy (Table 1). In all but 2 patients, the

Table 1 Patient Data (continued)

	Patient 5	Patient 6	Patient 7	Patient 8
Year of birth	1920	1920	1926	1929
Sex	Female	Male	Male	Male
Tobacco habits	10–20 cig/day	> 20 cig/day	> 20 cig/day	> 20 cig/day
Dental status	Edentulous	Edentulous	Partially edentulous	Partially edentulous
Original tumor*	SCC, floor of the mouth, 7/87	SCC, tongue, 7/87	Lymphoma malignant, non-Hodgkin, 6/85	SCC, floor of the mouth, 3/92
TNM classification	T3 N0 M0	T2 N0 M0	Stad I A	T3 N0 M0
Surgical treatment	Soft tissue resection, block resection of mandible between mental foramina, myocutaneous pectoral flap, 1/88	None	None	Superior neck dissection, soft tissue resection, block resection of anterior mandible between first molars, radial microvascular flap, 6/92
Radiotherapy	68 Gy, 7/87–10/87	68 Gy, 8/87–10/87	44 Gy, 6/85–7/85	50 Gy preop, 4/92–5/92
Implant surgery	Implant operation 3/90, abutment connection 9/90, former under general anesthesia, latter under local anesthesia	Implant operation 4/90, under local anesthesia	Implant operation 12/90, abutment connection 6/90, both under local anesthesia	Implant operation 1/93, abutment connection 4/93, both under local anesthesia
No. of implants	6	5	4	6
Implant length	10 mm	18 mm (1), 20 mm (4)	10 mm (2), 13 mm (2)	15 mm (conical)
Implant site†	34, 33, 31, 41, 43, 44	34, 32, 41, 43, 44	47, 46, 36, 37	34, 33, 31, 41, 43, 44
Estimated dose (Gy) to each implant site	69, 68, 68, 68, 67, 67	66, 34, 34, 68, 68	44, 44, 44, 44	50, 50, 51, 51, 50, 50
Implants lost	0	0	0	0
Follow-up time (y)	7	1	6.5	4
Recurrence or second primary	None	Lung metastasis 10/90	None	Right mandible 12/94, soft tissue resection and block resection of right mandible region second molar to second premolar
Present status	Alive without disease	Deceased 1991, lung metastasis	Alive without disease	Alive without disease
Other disease	Cerebral transient ischemic attacks, asthma	None	None	Cerebral transient ischemic attacks, diverticulitis

Table continued on next page

implant operations were carried out by one of the authors (GA). The procedure followed the routine protocol with prescription of 2 g phenoxymethyl penicillin twice daily for 10 days, commencing 1 hour before surgery. The surgical procedure was carried out under local anesthesia (lidocaine with 2% adrenaline as a vasoconstrictor) combined with diazepam orally about 1 hour preoperatively in 14 patients. One patient received general anesthesia. An incision was made in the depth of the buccal sulcus and a mucoperiosteal flap was reflected lingually

to expose the jaw bone. Under profuse irrigation of saline solution, implants of optimal length were placed (Table 1).

After a healing period of 3 to 6 months in the mandible and 6 months in the maxilla, the implants were exposed and the abutments connected. The patients were followed annually for at least 3 years. The follow-up visits included clinical examination and radiographs without removal of the prosthesis. During March 1997, all 12 patients still alive had been followed both clinically and with radiographs.

Table 1 Patient Data (continued)

	Patient 9	Patient 10	Patient 11	Patient 12
Year of birth	1923	1920	1921	1928
Sex	Female	Male	Male	Male
Tobacco habits	10 cig/day (stopped 1990)	> 20 cig/day	None	> 20 cig/day
Dental status	Edentulous	Edentulous	Edentulous	Edentulous
Original tumor*	Mucoepidermoid cancer columella 6/90, metastasis submandibular regional lymph nodes, 10/91	SCC, floor of the mouth, 7/92	Lymphoma malignant, non-Hodgkin, 3/92	Adenoid cystic cancer right submandibular gland, 7/92
TNM classification	None	T2 N0 M0	Stad I A	T1 N0 M0
Surgical treatment	Soft tissue resection nose, 1/91, suprahyoidal neck dissection, 10/91	Soft tissue resection, neck dissection, block resection of left anterior mandible from angle to right canine, myocutaneous pectoral flap, 10/92	Tonsillectomy, 1992	Soft tissue resection, 6/92, neck dissection, 9/92
Radiotherapy	60 Gy postop 1/92–3/92	50 Gy preop 8/92–9/92	44 Gy postop 4/92–6/92	50 Gy preop 7/92–8/92
Implant surgery	Implant operation 3/93, abutment connection 8/93, both under local anesthesia	Implant operation 9/93, abutment connection 1/94, both under local anesthesia	Implant operation 7/93 and 10/93, abutment connections 2/94, all under local anesthesia	Implant operation 11/93 and 4/95, abutment connections 5/94 and 9/95, all under local anesthesia
No. of implants	6	6	12	6
Implant length	10 mm	10 mm (5), 18 mm (1)	Maxilla: 10 mm (3), 13 mm (2), 15 mm (1); mandible: 15 mm (1), 15 mm (3), 18 mm (4)	13 mm (3), 15 mm (1), 18 mm (2)
Implant site [†]	34, 33, 31, 41, 43, 44	34, 32, 41, 42, 43, 44	15, 13, 11, 21, 23, 25, 34, 33, 31, 41, 43, 44	22, 23, 24 (11/93) 14, 13, 11 (4/95)
Estimated dose (Gy) to each implant site	65, 65, 60, 30, 25, 20	53, 53, 53, 53, 53, 52	20, 10, 4, 4, 10, 20, 43, 40, 30, 30, 40, 43	15, 15, 15, 50, 40, 25
Implants lost	0	0	0	0
Follow-up time (y)	4	3.5	4	3.5 and 2
Recurrence or second primary	None	None	None	None
Present status	Alive without disease	Alive without disease	Alive without disease	Alive without disease
Other disease	Non-Hodgkin gastric lymphoma, 1989	Hypertonia	None	Pulmonary embolism

Results

Of the 15 patients who received implants, 12 are still alive, while three have died: one after 1 year (patient 6), one after 4 years (patient 1), and one after 9 years (patient 2). In patient 2, who died in 1997, 4 of the 5 implants were removed in 1995 during a block-dissection of the mandible because of recurrence of the tumor.

Ninety Brånemark implants were placed in irradiated bone without adjunctive HBO therapy. Twelve

implants (10 to 18 mm) were placed in edentulous maxillae, 62 (10 to 20 mm) in edentulous mandibles, and 16 (10 to 15 mm) in partially edentulous mandibles. The abutment operation was carried out 3 to 6 months later. Detailed information about each patient is given in Table 1. At a follow-up visit in the ENT department 1 week after the abutment connection, patient 13 showed an ipsilateral lymph node metastasis and was reoperated and hospitalized for almost 2 months because of postoperative complications. This patient also received radiotherapy postop-

Table 1 Patient Data (continued)

	Patient 13	Patient 14	Patient 15
Year of birth	1926	1921	1926
Sex	Male	Male	Female
Tobacco habits	> 20 cig/day	> 20 cig/day	20 cig/day
Dental status	Edentulous mandible	Edentulous	Edentulous
Original tumor*	SCC, floor of the mouth, 3/93	SCC, right retromolar area, 2/94	SCC, right mandible, retromolar and molar area, 6/93
TNM classification	T4 N0 M0	T4 N0 M0	T4 N0 M0
Surgical treatment	Soft tissue resection, block resection of left and anterior mandible from angle to first premolar, neck dissection, myocutaneous pectoral flap, 6/93	Soft tissue resection block resection of mandible from angle to canine region, neck dissection, free microvascular radial flap, 6/94	None, but additional chemotherapy, Cisplatin, low-dose during radiotherapy
Radiotherapy	50 Gy preop, 4/93–5/93	50 Gy preop, 3/94–5/94	68 Gy, 7/93–9/93
Implant surgery	Implant operation 3/94, abutment connection 8/94, both under local anesthesia	Implant operation 9/95, abutment connection, 6/95, both under local anesthesia	Implant operation 10/95, abutment connection 1/96, both under local anesthesia
No. of implants	7	5	6
Implant length	10 mm (6), 18 mm (1)	18 mm	15 mm (1), 18 mm (4), diameter 4 mm region 2
Implant site†	34, 33, 31, 41, 42, 43, 45	34, 32, 41, 43, 44; soft tissue dehiscence 43, 42	34, 32, 41, 42, 44; soft tissue dehiscence 42
Estimated dose (Gy) to each implant site	54, 50, 50, 50, 50, 50, 50	25, 50, 53, 53, 53	54, 56, 60, 68, 68
Implants lost	1 implant (45, traumatic occlusion)	0	1 (42)
Follow-up time (y)	3	2	1.5
Recurrence or second primary	Regional lymph node metastasis right side; surgical treatment, 10/94, radiotherapy postop	None	None
Present status	Alive without disease	Alive without disease	Alive without disease
Other disease	None	Cerebral transient ischemic attacks	None

*SCC = squamous cell carcinoma.

†Implant sites: 11 = maxillary left central incisor; 13 = max left canine; 14 = max left first premolar; 15 = max left second premolar; 21 = max right central incisor; 22 = max right lateral incisor; 23 = max right canine; 24 = max right first premolar; 25 = max right second premolar; 31 = mandibular right central incisor; 32 = mand right lateral incisor; 33 = mand right canine; 34 = mand right first premolar; 35 = mand right second premolar; 36 = mand right first molar; 37 = mand right second molar; 41 = mand left central incisor; 42 = mand left lateral incisor; 43 = mand left canine; 44 = mand left first premolar; 45 = mand left second premolar; 46 = mand left first molar; 47 = mand left second molar.

eratively, but the dose to the implant area was very low, 4 Gy maximum. In this patient, prosthetic treatment was delayed, but in the remaining 14 patients prosthetic treatment started 10 to 14 days after the abutment operation.

The total radiation dose varied between 44 and 68 Gy, with a mean of 54.3 ± 8.1 Gy. The estimated radiation dose to the implant areas varied between 4 and 68 Gy, with a mean of 45.6 ± 16.4 Gy.

After a follow-up of 1 to 8 years, 88 implants, or 97.8%, were still stable; 6 implants had been stable for 8 years, 17 for 7 years, 4 for 6 years, 29 for 4 years, 15 for 3 years, 8 for 2 years, and 9 for 1 year (Table 1).

Two implants were lost, although they seemed to be osseointegrated at the time of abutment connection. One implant placed in the mandible in the right second premolar region was lost in the patient having

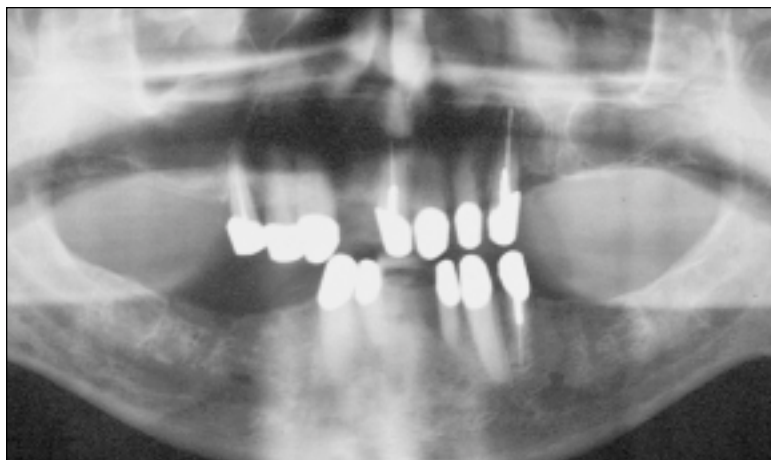


Fig 1 Panoramic radiograph before treatment (patient 13).

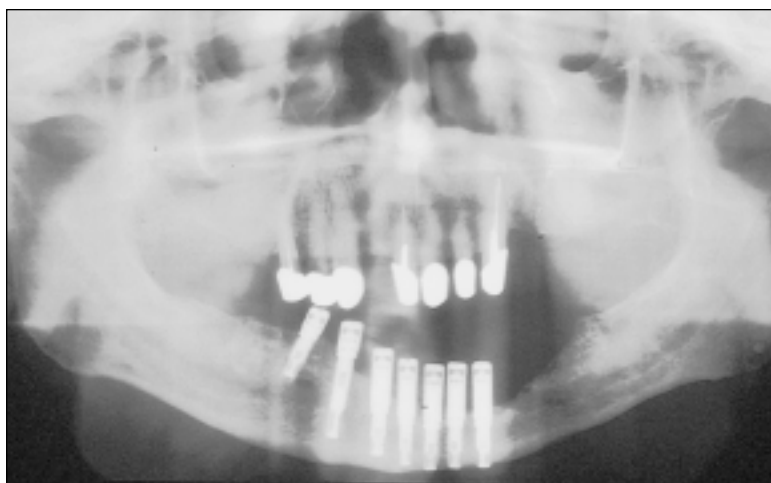


Fig 2 Panoramic radiograph after abutment connection (patient 13).

the delayed prosthetic treatment (patient 13). The most posterior implant in the right mandible, which received a dose of 50 Gy (the same as 5 of the 6 remaining implants and less than the most posterior implant in the left mandible, which received a dose of 54 Gy) was partially loose when the prosthetic treatment started. The lost implant was the only one placed in the remaining mandible and in contact with a fixed prosthesis in the maxilla during the 2-month period before the prosthetic treatment could start (Figs 1 and 2). In patient 15, the only patient receiving chemotherapy, one implant placed in the right incisor region of the mandible, which received a radiation dose of 68 Gy, was lost. The remaining 4 implants were in sites that received 54 to 68 Gy. The healing period after the implant operation was delayed because of soft tissue dehiscence in the region where the implant was lost. This was treated with resuturing, and the mucosa healed properly after 10 days. However, during prosthetic treatment, the patient devel-

oped symptoms from this implant site that resulted in implant removal. This patient also developed osteoradionecrosis in the left auditory canal.

All patients received fixed prostheses, including patients 13 and 15, in whom the remaining implants were sufficient to support these restorations. Prosthesis stability is 100%.

Discussion

Complications following implant placement into irradiated alveolar bone are the result of disturbances of the microvascular and connective tissues.¹³ Stimulated vascular growth and increased partial pressure of oxygen, which in turn promote collagen synthesis and fibroblast proliferation,^{5,14} have been attributed to HBO therapy. In an experimental study in adult rabbits, adjunctive HBO therapy significantly improved the amount of bone in direct contact with the implants.¹⁵ Whether these findings are

of relevance in clinical situations is, however, doubtful. Moreover, as long as the direct bone-implant interface is sufficiently large to support the superstructure, it can be argued that additional support to the implant surface is unnecessary, particularly in light of patient inconvenience and the cost of HBO treatment.

Granström⁶ has suggested that patients who have received radiotherapy in the head and neck region should receive HBO therapy prior to implant surgery to decrease an anticipated loss of implants. This might be true for facial implants, which he and his colleagues² further elucidate in a study that reported a success rate for facial implants of 100% with HBO and 61.6% without HBO. In a limited trial¹ on four patients receiving 21 implants in previously irradiated mandibles, it was the authors' impression that when implants were placed in conjunction with HBO, the healing was slow but more reliable. Although this trial did not demonstrate a clear benefit in the use of HBO therapy, the authors concluded by recommending that HBO therapy should be considered a preventive measure for patients who have received more than 50 Gy to the implant site.

The present study demonstrated a high survival rate (97.8%) for the implants placed in mandibles and maxillae in previously irradiated patients without the use of adjunctive HBO therapy. Of the two failures, one implant received 50 Gy only. This implant was stable at the time of abutment connection, but there was a delay of 2 months in the prosthetic treatment because of treatment for a neck metastasis. During this period, the failed implant was the only one in occlusion with the fixed maxillary prosthesis. Thus, traumatic occlusion might have been an alternative reason or a contributory cause to the loosening. This possibility is further supported by the fact that the remaining six implants were placed in an area that received the same or a higher dose. This patient had additional radiotherapy to the right side of the mandible after the abutment operation, but the radiation dose was so low that it does not seem justifiable to presume that it caused the failure.

The other lost implant was in the only patient who received chemotherapy during radiotherapy. This patient also had osteoradionecrosis of the left auditory canal and an intraoral soft tissue dehiscence. The combination of XRT and chemotherapy could have increased biologic effect of the radiotherapy, possibly contributing to the implant failure.

Both patients in whom implants were lost were heavy smokers. Like all other smokers in this group, they were carefully informed about the risk of recurrence of the cancer associated with a continuation of smoking and strongly advised to stop. All patients

were also offered the opportunity to take part in a smoking cessation program. Four patients managed to stop smoking, while the remaining 8 were able to reduce their consumption. It has been suggested that smoking should be regarded as a contraindication for implant treatment.⁸ The results from this study do not lend support to such a statement, although there is evidence that tobacco smoking negatively affects tissue healing.

The present results strongly support previous reports^{8,9} that show good results of implant treatment in patients with irradiated bone tissue without adjunctive HBO therapy. In the study from Umeå University,⁸ five patients treated for oral malignancies with surgery and radiotherapy (25 to 64 Gy) received implant treatment without adjunctive HBO therapy. A total of 20 implants were placed in mandibles, and 19 still remained after a follow-up period of 3 to 6 years. The authors concluded that adjunctive HBO therapy is not always necessary in oral implant rehabilitation after radiotherapy. In a multicenter study from Japan⁹ carried out in nine centers, 39 maxillary and 71 mandibular implants were placed, all in irradiated tissues. For the maxilla, the survival rate was 62.5% without and 80% with adjunctive HBO therapy. For the mandible, the corresponding figures were 96.4% without and 92.9% with HBO. These findings indicate that HBO might improve the survival rate of implants in the maxilla, and there was no dose dependency of implant failure. The present study does not allow any such conclusion because of the small number of implants placed in the maxilla.

Recently, a German group¹⁰ reported successful results of oral rehabilitation with implants without adjunctive HBO therapy in patients with oral cancer. In 13 irradiated patients, 53 of 57 implants survived during a follow-up period of 26 months. The investigators concluded that irradiated jaws present no contraindication for the placement of endosseous implants, and further, that while HBO therapy might promote implant integration, osseointegration has been reported without HBO.

The follow-up period in the present study was 6 to 8 years for 27 implants, 3 to 4 years for 44 implants, and 1 to 2 years for 17 implants. The two implants that failed were both lost early. This contrasts with the findings of Granström et al,² who found that loss of implants increases with time. While this might be true for facial implants, it does not seem to be the case for intraoral implants, since the follow-up period in this study for at least one third of the implants was comparatively long.

An improvement in bone healing 1 year after irradiation has been reported by Jacobsson.¹⁶ Based on histomorphometric studies, Wächter and Stoll¹⁷ have

stated that implantation can be performed after a minimum of 12 to 18 months following the conclusion of irradiation. The initial patients in this study were first treated at least 2 years after radiotherapy. However, follow-up visits showed promising results, and therefore rehabilitation was started at an increasingly early date. Implant surgery is now performed about 12 months after cancer therapy. Furthermore, in the first patients treated, abutments were connected after a prolonged healing time; today they are connected after 3 months in the mandible and after 6 months in the maxilla as in other patients. This means that patients can have their oral rehabilitation completed within 1.5 years after treatment for the malignant tumor, providing the opportunity for a good quality of life.

Conclusion

Osseointegration of implants in irradiated jawbone seems to be uncomplicated, providing careful surgical technique is used in combination with antibiotics. This conclusion is based on the results of this study and the promising results of other studies. Implant treatment for oral rehabilitation can be carried out as a safe procedure in patients irradiated for cancer in the head and neck region without adjunctive HBO.

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