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Osseointegrated Implants in Irradiated Bone: A Case-Controlled Study Using Adjunctive Hyperbaric Oxygen Therapy

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Purpose: The current investigation was undertaken to study whether osseointegration of implants in irradiated tissues is subject to a higher failure rate than in nonirradiated tissues. It further aimed to study whether hyperbaric oxygen treatment (HBO) can be used to reduce implant failure.

Patients and Methods: Seventy-eight cancer patients who were rehabilitated using osseointegrated implants between 1981 and 1997 were investigated. Three groups of patients were compared: irradiated (A), nonirradiated (B), and irradiated and HBO-treated (C). In addition, 10 irradiated patients who had lost most of their implants received new ones after HBO treatment. These were compared as a case-control group.

Results: Implant failures were highest in group A (53.7%). Implant failure was 13.5% in group B and 8.1% in group C. The difference between group A and the other two groups was statistically significant ($P = .001$ to .0023, Mantell's test). HBO significantly improved implant survival in the case-control group from 34 of 43 implants lost to 5 of 42 lost ($P = .0078$).

Conclusions: Implant insertion in irradiated bone is associated with a higher failure rate. Adjuvant HBO treatment can reduce the failures.

Modern cancer therapy has improved the survival rate of patients with tumors of the head and neck region. Such treatment is based on a combination of chemotherapy, radiation therapy, and surgical removal of the tumor. Generally, an individual treatment program is advocated for each patient based on an agreement between the oncologist and the cancer surgeon. With this treatment protocol, in large series, more than 50% of patients are cured of their malignancies and survive.[1] However, of the surviving patients, an increasing number are left with large soft and hard tissue defects, fistulas, skin dehiscencies, chronic pain, tissue fibrosis, and reduced sensory function, chewing capacity, and deglutition. This means a reduced quality of life.[2]

The osseointegrated implant concept has dramatically improved the rehabilitation of cancer patients with defects in the craniomaxillofacial region.[3] Using osseointegrated implants, dental bridges and tissue prostheses can be anchored on retention elements attached directly in the craniofacial skeleton. Dental bridges are accepted by the patient as "their own teeth." Modern materials, used to make extraoral craniofacial prostheses, can mimic the original tissue in a very natural-looking way.[4]

Because most patients with cancer-induced defects of the maxillofacial region have been irradiated before implant surgery, a major concern among clinicians using endosseous implants is whether the treatment outcome is affected by the preoperative radiation therapy. In a recent debate in this publication,[5,6] two major opinions were identified: 1) there is/is not an increased complication rate after implant surgery in

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irradiated bone and 2) adjunctive hyperbaric oxygen treatment (HBO) can be used/is useless to prevent/ does not prevent these complications. To add further data to this discussion, the authors present their experience in regard to these questions.

Patients and Methods

All patients who were rehabilitated after devastating cancer surgery using the osseointegrated implant concept in the Department of Otolaryngology, Head and Neck Surgery, Sahlgrenska University Hospital were studied. The first patient was included December 1, 1981, and the end of the study was October 1, 1997. The patients' charts were investigated with respect to tumor type, tumor stage, presence of local nodes, type of tumor treatment, and the timing and region of installation of the endosseous implants. Irradiation therapy was given in the Department of Oncology at Sahlgrenska University Hospital using Cobalt-60 radiation. Dosage, fractionation, radiation fields, and timing from irradiation to surgery were calculated from the patients' charts.

All patients were followed-up postoperatively, initially at 3-month intervals and, after 1 year, at 6-month intervals. Implant stability was checked by clinical inspection and radiographic investigation. Implant losses were registered, as were adverse soft tissue reactions.

The patients were divided into three groups. Group A consisted of patients who had been irradiated before implant surgery. Group B was composed of patients who were nonirradiated. Group C included irradiated patients who had undergone hyperbaric oxygen treatment (HBO) before implant surgery. In these patients, HBO had been given 20 times before surgery and 10 times postoperatively. Pure oxygen was delivered at 250 kPa, for 90 minutes via BIBS-masks (type Scott, Gothenburg Diving Technique, Gothenburg, Sweden) in a multiplace chamber (Magpie Ltd, Fraserburgh, Scotland).

Ten previously irradiated patients who had implants installed and later lost most of them were treated with HBO using the previous protocol, after which new endosseous implants were installed. These patients were specifically studied as a case-control group D.

Statistical comparisons were performed using Mantel's test[7] and Fisher's test for paired comparisons.[8]

Results

There were 78 patients, 47 men and 31 women, in the study. Mean age was 64.9 years (range, 23 to 94). Fourteen patients died during the study, resulting in a mortality rate of 17.9%. Forty-seven patients had orbit defects, 16 had temporal defects, nine had nose defects, eight had maxillary defects, and three had mandibular defects in which endosseous implants had been installed. All implants were inserted in the host bone without bone grafting or covering with expanded polytetrafluoroethylene membranes. Implants designated as irradiated were inserted in the tumor cavity and thus in the radiation field. Only implants that were exposed and loaded were included in the study. They were followed from the time of surgery until the last clinical follow-up. Altogether 335 endosseous implants of the Brånemark system® type (Nobel Biocare, Gothenburg, Sweden) were inserted, of which 99 were lost during follow-up, for a total loss rate of 29.5%.

In group A (irradiated), which consisted of 32 patients, 18 men and 14 women, with a mean age of 67.4 years (range, 24 to 94), 147 endosseous implants were installed, of which 79 were lost (53.7%). A mean of 4.6 implants were inserted, and 2.5 were lost per patient. The radiation field covered the implant area in all patients. The mean radiation dose was 57.7 Gy (range, 25 to 145). Mean observation time in this group was 5.8 years (range, 0.1 to 15.1 yrs). Seven patients died in this group (mortality rate, 21.8%). Only four patients had not lost a single implant during the follow-up.

In group B (nonirradiated), which consisted of 26 patients, 18 men and 8 women, with a mean age of 66.4 years (range, 23 to 89), 89 endosseous implants were installed, of which 12 were lost (13.5%). Mean observation time in this group was 7.4 years (range, 0.3 to 14.7 yrs). Four patients died in this group (mortality rate, 15.4%). Nineteen patients had not lost a single implant during the follow-up.

In group C (irradiation + HBO), which consisted of 20 patients, 11 men and nine women, with a mean age of 61.0 years, (range, 24 to 81), 99 endosseous implant were installed, of which eight were lost (8.1%). The mean radiation dose was 65.4 Gy (range, 30 to 145). Mean observation time in this group was 3.4 years (range, 0.9 to 8,2 years). Three patients died in this group (mortality rate, 15%). Fourteen patients had not lost a single implant during the follow-up.

In group D (retreated after HBO), which consisted of 10 patients, five men and five women with a mean age of 61.1 years (range, 24 to 81), 43 endosseous implants were inserted in the first treatment period, of which 34 were lost (79.0%). Mean implant survival time was 2.4 years in a mean follow-up period of 4.7 years (range, 1.7 to 14.9). In the second treatment period (after preoperative HBO), 42 endosseous implants were inserted, of which five were lost (11.9%). Mean implant survival time was 3.1 years in a mean follow-up period of 3.5 years. One patient died in this group (mortality rate, 10%).

Table 1. SURVIVAL STATISTICS OF IMPLANTS OF GROUP A (IRRADIATED)

INT	OT	NI	RF	SF	95% CI	
0.0-0.5	68	17	0.250925	0.882	0.831	0.936
0.5-1.0	55	13	0.237769	0.783	0.717	0.855
1.0-1.5	47	11	0.234852	0.696	0.623	0.779
1.5-2.0	41	7	0.170923	0.639	0.562	0.727
2.0-2.5	36	8	0.223395	0.572	0.492	0.664
2.5-3.0	26	6	0.231410	0.509	0.427	0.608
3.0-3.5	22	4	0.178364	0.466	0.383	0.567
3.5-4.0	21	2	0.095616	0.444	0.361	0.547
4.0-4.5	18	2	0.113740	0.420	0.336	0.524
4.5-5.0	17	0	0.000000	0.420	0.336	0.524
5.0-5.5	17	0	0.000000	0.420	0.336	0.524
5.5-6.0	15	2	0.129651	0.393	0.309	0.500
6.0-6.5	13	2	0.157778	0.363	0.279	0.473
6.5-7.0	12	0	0.000000	0.363	0.279	0.473
7.0-7.5	10	3	0.296150	0.313	0.229	0.428
7.5-8.0	10	0	0.000000	0.313	0.229	0.428
8.0-8.5	9	0	0.000000	0.313	0.229	0.428
8.5-9.0	8	0	0.000000	0.313	0.229	0.428
9.0-9.5	7	2	0.285103	0.272	0.188	0.393
9.5-10.0	7	0	0.000000	0.272	0.188	0.393
10.0-10.5	7	0	0.000000	0.272	0.188	0.393
10.5-11.0	6	1	0.154679	0.252	0.169	0.375
11.0-11.5	6	0	0.000000	0.252	0.169	0.375
11.5-12.0	4	0	0.000000	0.252	0.169	0.375
12.0-12.5	4	0	0.000000	0.252	0.169	0.375
12.5-13.0	3	1	0.365497	0.210	0.123	0.358
13.0-13.5	3	0	0.000000	0.210	0.123	0.358
13.5-14.0	2	0	0.000000	0.210	0.123	0.358
14.0-14.5	2	0	0.000000	0.210	0.123	0.358
14.5-15.0	1	0	0.000000	0.210	0.123	0.358

Abbreviations: INT, time in months; OT, observation time (mo); NI, number of implants lost in interval; RF, risk function; SF, survival function; 95% CI, 95% confidence interval.

Table 2. SURVIVAL STATISTICS OF IMPLANTS OF GROUP B (NONIRRADIATED)

INT	OT	NI	RF	SF	95% CI	
0.0-0.5	44	3	0.068666	0.966	0.929	1.005
0.5-1.0	42	2	0.047327	0.944	0.897	0.993
1.0-1.5	42	0	0.000000	0.944	0.897	0.993
1.5-2.0	42	1	0.024061	0.932	0.882	0.986
2.0-2.5	41	1	0.024138	0.921	0.867	0.979
2.5-3.0	40	0	0.000000	0.921	0.867	0.979
3.0-3.5	39	0	0.000000	0.921	0.867	0.979
3.5-4.0	37	1	0.026812	0.909	0.851	0.971
4.0-4.5	34	0	0.000000	0.909	0.851	0.971
4.5-5.0	33	0	0.000000	0.909	0.851	0.971
5.0-5.5	32	1	0.031548	0.895	0.832	0.963
5.5-6.0	29	0	0.000000	0.895	0.832	0.963
6.0-6.5	26	0	0.000000	0.895	0.832	0.963
6.5-7.0	25	0	0.000000	0.895	0.832	0.963
7.0-7.5	21	2	0.095361	0.853	0.773	0.941
7.5-8.0	20	0	0.000000	0.853	0.773	0.941
8.0-8.5	18	0	0.000000	0.853	0.773	0.941
8.5-9.0	17	0	0.000000	0.853	0.773	0.941
9.0-9.5	17	0	0.000000	0.853	0.773	0.941
9.5-10.0	15	1	0.066573	0.825	0.733	0.929
10.0-10.5	12	0	0.000000	0.825	0.733	0.929
10.5-11.0	11	0	0.000000	0.825	0.733	0.929
11.0-11.5	8	0	0.000000	0.825	0.733	0.929
11.5-12.0	7	0	0.000000	0.825	0.733	0.929
12.0-12.5	5	0	0.000000	0.825	0.733	0.929
12.5-13.0	4	0	0.000000	0.825	0.733	0.929
13.0-13.5	4	0	0.000000	0.825	0.733	0.929
13.5-14.0	4	0	0.000000	0.825	0.733	0.929
14.0-14.5	4	0	0.000000	0.825	0.733	0.929
14.5-15.0	0	0	0.000000	0.825	0.733	0.929

Abbreviations: INT, time in months; OT, observation time; NI, number of implants lost in interval; RF, risk function; SF, survival function; 95% CI, 95% confidence interval.

Implant survival statistics for each treatment group (A through C) are presented in Tables 1 through 3. A statistical comparison between group A (irradiated) and B (nonirradiated) using Mantel's test showed the difference to be significant ($P = .0023$). A statistical comparison between groups A (irradiated) and C (irradiated + HBO-treated) showed the difference to be significant ($P = .0010$). A statistical comparison between groups B (nonirradiated) and C (irradiated, HBO-treated) was not significant ($P > .30$). A statistical comparison of the implants of group D using Fisher's test for paired comparisons shows a better implant survival after HBO treatment; $P = .0078$. The correlation of implant survival with time in the different groups is graphically presented in Figure 1.

Discussion

To improve the outcome for cancer patients who require endosseous implants, it is important not only to report on the development of new techniques and successful outcome, but also to report on problems

Table 3. SURVIVAL STATISTICS OF IMPLANTS OF GROUP C (IRRADIATED AND HBO-TREATED)

INT	OT	NI	RF	SF	95% CI	
0.0-0.5	49	2	0.040501	0.980	0.953	1.008
0.5-1.0	45	1	0.022287	0.969	0.935	1.004
1.0-1.5	38	0	0.000000	0.969	0.935	1.004
1.5-2.0	30	0	0.000000	0.969	0.935	1.004
2.0-2.5	24	0	0.000000	0.969	0.935	1.004
2.5-3.0	22	1	0.044486	0.948	0.896	1.003
3.0-3.5	18	2	0.113675	0.895	0.813	0.986
3.5-4.0	15	0	0.000000	0.895	0.813	0.986
4.0-4.5	13	2	0.156900	0.828	0.716	0.958
4.5-5.0	10	0	0.000000	0.828	0.716	0.958
5.0-5.5	8	0	0.000000	0.828	0.716	0.958
5.5-6.0	8	0	0.000000	0.828	0.716	0.958
6.0-6.5	8	0	0.000000	0.828	0.716	0.958
6.5-7.0	8	0	0.000000	0.828	0.716	0.958
7.0-7.5	8	0	0.000000	0.828	0.716	0.958
7.5-8.0	7	0	0.000000	0.828	0.716	0.958
8.0-8.5	1	0	0.000000	0.828	0.716	0.958
8.5-9.0	0	0	—	—		

Abbreviations: INT, time in months; OT, observation time; NI, number of implants lost in interval; RF, risk function; SF, survival function; 95% CI, 95% confidence interval.

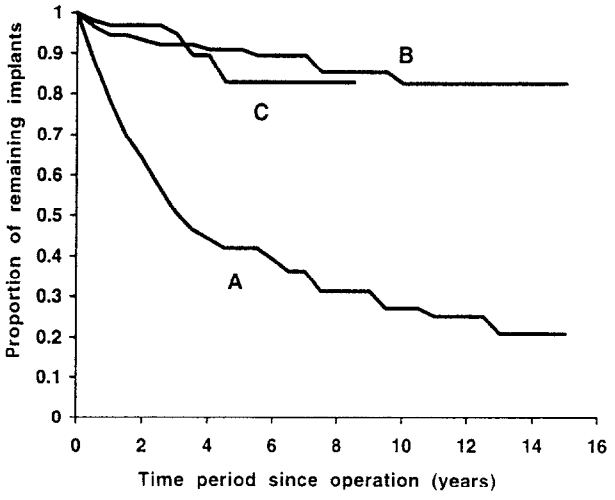

FIGURE 1. Implant loss as a function of time. A = irradiated group; B = nonirradiated group, C = irradiated and HBO-treated group. With increasing time, more implants are lost in group A. The difference between group A and the other two groups is statistically significant (P = .001 to .0023) using Mantel's test.

whenever they arise and to seek solutions for these complications. From the previous discussions by Larsen[5] and Keller,[6] we have identified several aspects in relation to the question of whether osseointegrated implants in irradiated bone are subject to more complications. Because our experience in treating irradiated patients is that there are more complications in this group, we have sought solutions to improve the outcome, of which HBO is one. Nevertheless, we are aware that there might be additional solutions that could be recommended in the future, and this will form a continuing part of the discussion.

Is osseointegration surgery in irradiated bone a clinical problem? The information necessary to answer this question can be obtained in four ways: 1) ask clinicians, 2) read the clinical literature, 3) perform animal studies, and 4) perform clinical studies.

OPINIONS OF CLINICIANS

In response to the first method, a questionnaire was sent to 189 major osseointegration centers all over the world.[9] Sixty-seven percent of those clinicians who responded considered preoperative radiation therapy a contraindication to osseointegration surgery, and hence such surgery was not performed at these clinics. Nevertheless, there is general agreement among clinicians that cancer patients with large tissue defects in the maxillofacial region might benefit from osseointegrated implants and hence need such treatment despite earlier radiation therapy. In selecting patients carefully, it is possible to avoid some complications and to improve the outcome of surgery.[5,6] However, it is our strongest recommendation that implant surgery in irradiated patients be performed only at the major craniofacial rehabilitation centers, with the facilities and experience necessary to perform the treatment and to handle possible complications.

CLINICAL STUDIES

With respect to obtaining information from the clinical literature, the first clinical report relating to the question regarding possible failure of osseointegration in irradiated bone was published in 1988.[10] In this study, nine patients were followed-up for 44 months, during which time 14% of the implants lost osseointegration. At that time, this number was not regarded as an exceedingly high implant failure rate, but later studies showed that with increasing follow-up time, more implants lost integration.[11-14] In our earlier studies, we noticed that the different facial bones showed different rates of implant loss after irradiation.[11] Thus, the frontal bone showed the highest failure rate, followed by the zygoma, maxilla, mandible, and temporal bone.[15] Most of the discussion between Larsen and Keller is related to the fate of endosseous implants in the mandible. Keller's point of view is that even the irradiated mandible has an outstanding capacity to integrate endosseous implants. This theory is supported by a number of clinical reports.[16-20]

However, whereas it is stated that the mandible has a unique possibility to integrate endosseous implants, the mandible is the most susceptible bone in the body to osteoradionecrosis.[21-23] It is known that even a minor surgical trauma such as a tooth extraction could start the osteoradionecrotic process.[24] Even well-accomplished osseointegration surgery can be the initiating factor for such a process. That osteoradionecrosis can occur after implant surgery has been reported.[5,6] The reason for the mandible's sensitivity to osteoradionecrosis is related to its compact construction, where irradiation against intraoral tumors can cause backscatter effects because of the high mineral content of this bone. The restricted arterial supply of the mandible by end-arteries, in combination with tumor surgery and node dissection, also might endanger the regional blood supply. In a randomized, controlled study, we noticed the highest risk of developing osteoradionecrosis was among irradiated patients with intraoral resections near the mandible in combination with extraoral node dissection.[25]

Whenever reporting on the clinical outcome of osseointegrated implants, it is necessary to state the circumstances involving the studies performed. Thus, one must report type and specifications of the implant used, whether the implants were loaded or not, whether the implants were inserted in the host bone or in grafted bone, whether all implants have been followed-up, and whether the patient left the study, is

deceased, and so forth.[26] Furthermore, in relation to endosseous implants in irradiated bone, one must report whether all implants had been inserted in the field of irradiation. It is well known, for example, that external beam radiation therapy for oral malignancies does not always include the whole mandible and, hence, implants inserted anterior to the mental foramina might be inserted in a field of lower radiation dose. This will naturally affect the outcome for the implants. It is also of great importance that the patients are followed-up long enough before reporting implant success in irradiated bone. As can be seen from Figure 1, evaluation of success in irradiated patients is made on a continuously sloping curve; the longer one follows the patients, the higher the failure rate will be.

Other aspects of osseointegration in irradiated bone are also of great importance. We have shown, for example, that the time from radiation therapy to implant surgery affects implant survival. The longer the period that has elapsed since radiation therapy, the higher the failure rate.[27] This is considered to be related to the gradual progressive endarteritis in the bone bed. Keller's[6] statement that the improved bone formation after HBO is merely a factor of increased observation time is contradicted by this finding. Other factors of importance that have been shown to affect implant survival in irradiated bone are related to technical aspects. This includes type of implant used, implant length, and type of retention used. Also, aspects such as open or closed tumor cavities and the surgeon's experience can affect the results.[27]

ANIMAL STUDIES

To study irradiation effects in conjunction with osseointegrated implants, a number of experimental investigations have been performed.[28-35] Different implant systems were used to study tissue reactions inside and outside of titanium elements. The most commonly used implant systems were the Vital Microscopic Chamber (VMC), the Bone Harvest Chamber (BHC), and different kinds of titanium screws. The VMC was developed to enable tissue reactions in a 100-μm-thick slit in the implant to be followed by light microscopy. The tissue reactions that followed radiation therapy established in the VMC were decreased bone formation capacity (decreased number of osteoblasts and osteocytes), increased resorption of bone (increased number of osteoclasts), and reduced number of capillaries inside irradiated tissue.[29] By using the BHC, quantitative parameters could be used to follow tissue reactions after irradiation. Irradiation was delivered by ^{60}Co-gamma rays in single doses varying from 0 to 40 Gy. A single dose of 15 Gy reduced the bone formation capacity by 72%. Increasing the radiation dose to 25 Gy did not further affect the bone formation capacity, and hence the 15-Gy single-dose radiation protocol was used in the studies to elaborate effects of HBO on osseointegration in irradiated tissues.

The BHC was used to study effects of HBO on bone formation capacity in an experiment in which the animals served as their own controls. Three weeks of HBO (280 kPa, 2 hours daily) was compared with 3 weeks of normobaric air. It could be shown that HBO significantly stimulated bone formation capacity during this time.[31]

Using histomorphometry, it was shown that periosteal bone formation and remodeling of bone in the implant threads was decreased earlier after 15 Gy ^{60}Co irradiation, than in the nonirradiated controls. There was also a reduced bone-to-metal contact in the irradiated group. After 20 HBO treatments at 280 kPa, 2 hours daily, more mature bone developed in the threads of the irradiated group than in an irradiated group receiving normobaric air.[32]

In an experimental study by Larsen et al,[33] using other types of implant systems for osseointegration, late effects of radiation therapy in conjunction to implants were studied. It could be shown that despite clinical and radiographic evidence of success of all implants, there was a significant decrease in the amount of histologic integration of the implants placed in bone that had received 45 Gy of ^{137}Cesium radiation. Adjunctive HBO (240 kPa, 90 minutes daily, 20 + 10 treatments) significantly increased the amount of bone surrounding the implants. Use of HBO was also associated with better soft tissue wound healing in the irradiated surgical site.

Increasing the ^{60}Co radiation dose from 10 to 30 Gy in another experimental system significantly reduced the biomechanical stability of endosseous implants.[34] The highest radiation doses also caused significant soft tissue problems. In studies conducted to investigate the effects of HBO on biomechanical stability, standardized titanium screws were used to measure the removal torque necessary to untighten them.[35] It was shown that the force necessary to unscrew the implants after radiation therapy was significantly decreased (54%). HBO (280 kPa, 2 hours daily for 21 days) increased the force necessary to unscrew the implants in the control group by 22% and in the experimental group (irradiated by 15 Gy ^{60}Co radiation) by 44%.

CLINICAL STUDIES

We were well aware of the higher failure rate of endosseous implants in irradiated bone by the late 1980s. The constantly increasing implant failures necessitated action to improve the treatment outcome. Our first report on the higher failure rate came in 1991.[11] We then also proposed the use of adjunc-

tive HBO to improve osseointegration and our preliminary results supported this idea. The reason for choosing HBO was that the literature at that time gave strong support to the positive effects of intermittent and surplus oxygen delivered to a compromised tissue such as after irradiation.[36-38] Hyperbaric chambers are available in all countries in the world in which implant surgery is performed. Using adequate methods to survey and treat the patients, HBO is a safe and predictable technique. Its cost in the clinic can be defended.[38] Since 1991, we have regularly reported our data on the outcome of irradiated patients,[15,27,39,40] and also added data on patients that have been irradiated after implant surgery,[41] as well as those who have been irradiated both before and after implant surgery.[42] The benefit of HBO to osseointegration is also supported by other clinical studies.[5]

An often-repeated statement is that there are no randomized, controlled, double-blind studies conducted to prove that HBO really has a significant osseointegration stimulating effect in irradiated patients.[6,18] Although there are certain technical difficulties related to designing such a study (blinding a chamber treatment; the design of placebo treatment), we also support a critical analysis of the value of HBO. However, criticizing the use of HBO, demands the recommendation of alternative methods to improve osseointegration and reduce surgical problems in the irradiated patient. As an alternative to a randomized, double-blind, controlled study, a case-control study, as in this report can add further information. The conclusions we thus draw from this study are that: 1) irradiation causes significant changes in the host bone bed that reduce the potential for osseointegration, thus increasing implant loss; and that 2) adjunctive HBO treatment can improve osseointegration.

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Discussion

Osseointegrated Implants in Irradiated Bone: A Case-Controlled Study Using Adjunctive Hyperbaric Oxygen Therapy

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The treatment of head and neck malignancies has become increasingly successful, and with the improved survival rate, there should no longer be any objection to reconstructive surgery. The introduction of osseointegrated implants has further improved the ability to rehabilitate these patients and consequently enhance their quality of life. However, rehabilitation using endosseous implants requires exposure of bone rendered less viable by radiation therapy as part of the tumor treatment and increases the risk of osteoradionecrosis or implant loss. This has been an argument for the use of adjunctive hyperbaric oxygen (HBO) in conjunction with implant surgery. The issue of using HBO is controversial and has recently been discussed in this journal with arguments for[1] and against[2] its use in relation to implant surgery in the mandible—a bone claimed to be very susceptible to implant loss and osteoradionecrosis.[3] A number of case reports have added to our knowledge—most recently a report by Andersson et al[4] on 15 patients who received 90 implants, 78 to the mandible and 12 to the maxilla after radiotherapy of between 44 and 68 Gy. The implant survival rate was 97.9% without the use of adjunctive HBO.

This article is a good example of a report that, although advocating a preferred approach, does not provide enough and detailed information for the reader to reach his/her own conclusions; the needed information is scarce, although the importance of such details is discussed. With an observation time of between 0.1 and 15.1 years, it is reasonable to assume that changes in both radiation therapy and implant surgery techniques might have occurred during the period.

The article does not give any clear information as to the interval between radiation therapy and implant surgery, which is particularly remarkable because the authors in a previous report,[5] as well as this one, have shown that "the time from radiation therapy to implant surgery affects implant survival." However, most importantly, is the fact that the material is heterogeneous, with the patients in each group representing an undisclosed number of implants of different sizes and in different sites ranging from the frontal bone to the mandible. In an earlier article,[6] the authors reported on implant losses ranging between 9% (in the temporal bone) and 50% (in the frontal bone). Thus, although the conclusion that HBO treatment can improve osseointegration and decrease implant loss is valid in mixed groups in general, it does not apply to the individual implant site. Consequently, this article does not bring us any closer to the answer to the key question: ***When is HBO treatment a necessary part of the treatment plan and when is it not?***

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