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J DENT RES 2002 81: 856

DOI: 10.1177/154405910208101212

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J Dent Res 81(12):856-859, 2002

ABSTRACT

In this prospective study, we determined the effects of the time interval between irradiation and implant therapy, implant location, bone-resection surgery, and irradiation dose on implant survival. We analyzed the survival of 446 implants inserted after radiotherapy over a period of up to 14 years in 130 consecutive patients treated for oral cancer. The 10-year overall Kaplan-Meier implant survival percentage is 78%. The difference in survival percentages of implants inserted < 1 year and \geq 1 year after irradiation (76% and 81%, respectively) is not significant. We concluded that implant survival is significantly influenced by the location (maxilla or mandible, 59% and 85%, respectively; $p = 0.001$), by the incidence of bone-resection surgery in the jaw where the implant was installed ($p = 0.04$), and by the irradiation dose at the implant site (< 50 Gray or \geq 50 Gray, $p = 0.05$).

KEY WORDS: dental implants, irradiation, osseointegration, prosthetic reconstruction, oral cancer.

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INTRODUCTION

Cancer in the head and neck region is commonly treated with a combination of surgery and radiotherapy. Both modalities have adverse effects on the healthy soft and hard tissues in the oral cavity. Surgery may cause anatomical deformations, and radiotherapy may result in progressive fibrosis of blood vessels and soft tissues, in xerostomia, and in reduction of bone-healing capacity. Implants are especially important in patients treated for oral cancer, since dryness and anatomical changes may hamper a proper retention of removable prostheses, and overloading of vulnerable soft-tissues must be reduced (Granström *et al.*, 1993; Marx and Morales, 1998). Although the side-effects of radiotherapy have a negative influence on the results of implant therapy (Jacobsson, 1985; Marx and Johnson, 1987), implants have been increasingly used in oral cancer patients over the past decade (Keller *et al.*, 1997; Marker *et al.*, 1997; August *et al.*, 1998; Wagner *et al.*, 1998; Granström *et al.*, 1999; Kovacs, 2000).

Time has two antagonistic effects on the recovery of irradiated tissues: a short-term positive cellular effect, resulting in the improvement of reduced bone-healing capacity (Jacobsson, 1985); and a long-term negative effect, resulting in increased vascular damage (Marx and Johnson, 1987). We surmise that the effects of cellular recovery and vascular fibrosis influence the survival of implants, but recommendations for an optimal time interval between radiotherapy and implant surgery are inconsistent and range from < 6 months to > 24 months (Chiapasco, 1999).

In this study, we analyzed the long-term survival of implants inserted into the jaws of irradiated oral cancer patients in relation to: (1) the time-span between irradiation and implant surgery, (2) the irradiation dose at the implant location, and (3) the incidence of bone surgery in the jaw where the implants were inserted.

MATERIALS & METHODS

During a follow-up period up to a maximum of 14 years (1987-2001), 130 consecutive patients, 78 males (60%) and 52 females (40%), who had been irradiated for head and neck cancer, received 446 oral implants at various intervals after radiotherapy, to improve the outcome of prosthetic treatment. The mean age of the patients at the time of surgery was 62 years (range, 34-87 years). This prospective study was approved by the Medical Ethical Commission of the University Hospital Rotterdam-Daniel. Patients participated in this study after providing informed consent to the protocol.

For all patients, tumor therapy consisted of radiotherapy (2-6 MV) delivered with external beams in daily fractions of 2 Gray. Five fractions were delivered in a week.

The surgical and prosthetic treatments were carried out in the University Hospital Rotterdam-Daniel. The prosthodontist and the oral surgeon made the decision for implant treatment after consultation with the radiation-oncologist and extensive discussion with the patient. Implant surgery was not carried out when

Received June 22, 2001; Last revision September 6, 2002;
Accepted September 23, 2002

periodontal infection was present. Hydroxyapatite-coated titanium implants, type Dyna (390 implants) or Screw-Vent (56 implants), were applied in a two-stage surgical procedure. Implant sockets were prepared under local anesthesia with internal cooling. Implants were placed at bone level and were completely covered with soft tissues. Preventive hyperbaric oxygen treatment was not applied. Prophylactic antibiotic therapy and mouthrinses were prescribed.

The healing period, starting at implant insertion and ending with abutment surgery, lasted at least six months.

Patients were instructed to maintain optimal oral hygiene and were recalled at least every 12 months. Annual standardized intra-oral radiographs were examined for peri-implant pathology. As long as there was no pain, mobility, recurrent peri-implant infection, or peri-implant radiolucency, the implant was considered successful (van Steenberghe, 1997). The survival time was measured from initial implantation to removal or last control of the implant (Weyant and Burt, 1993).

Statistical Methods

Implant survival was analyzed with the Kaplan-Meier method for overall estimation of results and with an adapted proportional hazards model for assessing the influence of one or more factors on this survival. Observations on implants can be assumed to be sampled with clusters. Each patient is a cluster (or primary sample unit), and, within that cluster, implants are obtained as an approximate random sample. This clustering design does not affect the overall estimation of survival results, but it does affect standard errors and p-values: Using a method assuming independence will result in too-small values for both standard errors and p-values. Therefore, when studying potential prognostic factors in a proportional hazards model, instead of using the conventional estimation of the variance of regression coefficients, we used a robust method (Lin and Wei, 1989). These analyses are performed with release 5.0 of the statistical program STATA for Windows 95 and documented in the manual (Stata Corp., 1997).

RESULTS

Fifty patients (38%) died during the study. For all 446 implants (11 of which were in the healing phase), the 10-year Kaplan-Meier survival percentage was 78%. Sixty-four implants failed (14%), 27 during the healing phase and 37 during the loading phase (Table 1). In the mandible, 338 implants were inserted, 296 implants in the anterior part and 42 implants in the posterior part. In the maxilla, 108 implants were inserted, 51 implants anteriorly and 57 implants posteriorly.

The 10-year survival percentages in the maxilla (33 failures) and in the mandible (31 failures) are 60% and 85%, respectively (p = 0.001, Fig. 1). The survival rate of implants in the anterior and posterior mandible is 85% (26 failures) and 83% (5 failures), respectively. In the anterior and posterior maxilla, the survival rate is 55% (17 failures) and 62% (16 failures), respectively. The difference in survival percentages between anterior and posterior locations in the mandible or maxilla is not significant. The implant brand, length, or diameter does not significantly correlate with implant survival.

Radiotherapy was combined with surgery (tumor surgery, reconstructive surgery, or neck

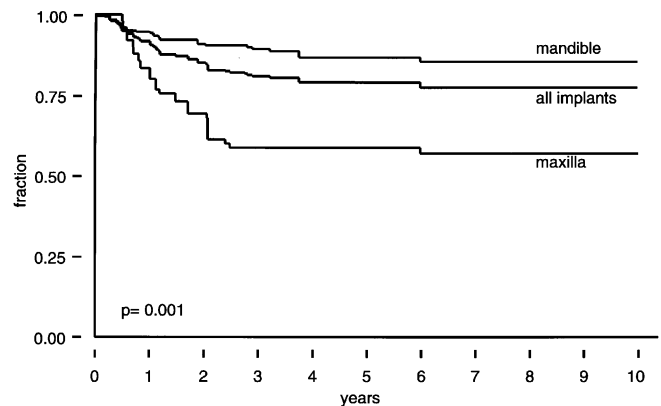


Figure 1. Kaplan-Meier survival curves of all implants located in both the maxilla and the mandible.

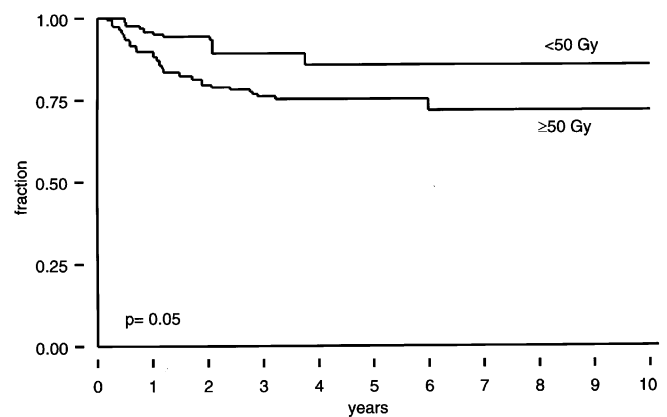


Figure 2. Kaplan-Meier survival curves of implants inserted into sites that received < 50 Gray and those that received ≥ 50 Gray.

Table 1. Number of Patients Treated with Implant Therapy, Number of Deceased Patients, Number of Implants Inserted, and Number of Implant Failures at the End of Each Year

Year	No. of New Patients	No. of Deceased Patients	Cumulative No. of Patients	No. of New Implants	No. of Implant Failures	Cumulative No. of Implants
1987	2	0	2	7	0	7
1988	2	0	4	4	0	11
1989	10	0	14	24	5	30
1990	20	4	30	73	14	89
1991	18	2	46	66	4	151
1992	8	6	48	36	10	177
1993	4	5	47	13	10	180
1994	12	8	51	39	5	214
1995	11	5	57	38	7	245
1996	16	9	64	62	2	305
1997	12	5	71	40	6	339
1998	5	1	75	13	0	352
1999	4	3	76	12	0	364
2000	6	2	80	19	1	382
Total	130	50		446	64	

Table 2. Irradiation Doses Delivered to Patients (n = 130) and to Implant Sites (n = 446)

No. of Patients (% of total)	Dose (Gray)	No. of Implant Sites (% of total)
0 (0)	0	95 (21)
30 (23)	> 0-50	112 (25)
9 (7)	51-60	59 (13)
84 (65)	61-72	166 (37)
7 (5)	> 72	4 (3)
130 patients		446 implants

surgery) for 119 patients. Six patients received a second irradiation therapy, and 15 patients also underwent interstitial irradiation. The interval between implant surgery and radiotherapy ranged from six months to 22 years. We calculated both the local dose at the implant site and the dose at the tumor site by analyzing the radiotherapy reports and the planning-radiographs (Table 2). Implants in sites that received < 50 Gray (207 implants, 19 failures) show a 10-year survival percentage of 84%. Ninety-five of these implants, positioned outside the irradiation field, showed 8 failures and a survival rate of 86%. Implants in sites that received \geq 50 Gray (239 implants, 45 failures) show a survival rate of 71% ($p = 0.05$, Fig. 2).

The survival of implants inserted < 12 months (175 implants, 29 failures) or \geq 12 months (271 implants, 35 failures) after the end of radiotherapy was 76% and 81%, respectively. This difference was not significant.

Thirty-five implants (8%) were inserted into jaws treated with bone resections (partial maxillectomy and partial or segmental mandibulectomy). The survival of these implants was significantly ($p = 0.04$) worse compared with that of implants in jaws without these surgical treatments (61% and 83%, respectively).

DISCUSSION

The only patient drop-out was caused by 50 patients who died during the study. Since this event had no relation to the implant treatment, these patients were not excluded from the study. The lifetime of implants from deceased patients, as that of all implants in this study, was measured from implant installation until the last implant examination.

In this study, implants inserted into the maxilla and mandible showed a significant ($p = 0.001$) survival difference (59% and 85%, respectively). Similar differences are described in studies with various implants in non-irradiated tissues and are caused by differences in bone quality, bone volume, and vascularization (Jemt *et al.*, 1996; Nishimura *et al.*, 1998).

Preventive hyperbaric oxygen treatment was not applied in this study, since there is no consensus about its indications (Franzen *et al.*, 1995; Chiapasco, 1999). This treatment results in an increased oxygen tension in the irradiated ischemic bone and provokes capillary angiogenesis and bone formation (Taylor and Worthington, 1993), and is therefore suggested by some authors when implant therapy in irradiated bone is planned (Marx and Johnson, 1987; Granström *et al.*, 1992). The

rather disappointing survival percentage (59%) in the irradiated maxilla in this study is an argument for preventive HBO treatments at this location.

Implants inserted into locations irradiated with \geq 50 Gray (239 implants) have a significantly ($p = 0.05$) lower survival rate (73%) than implants in locations that are irradiated with < 50 Gray (207 implants, survival rate 84%). Also, other authors have observed that the majority of complications occur with doses > 50 Gray (Jisander *et al.*, 1997). Among the implants irradiated with < 50 Gray are 95 implants that were inserted into locations outside the irradiation field. These implants show a survival rate of 86% that does not differ significantly from the survival rate in locations irradiated with < 50 Gray. The comparable survival rates of both groups might be caused by the effects of reduced vascularization that compromises both irradiated and non-irradiated locations (Marx and Johnson, 1987).

Bone resections may result in unfavorable prosthetic circumstances by producing bulky and soft areas. In these situations, (removable) prosthetic appliances are often complicated and may cause overloading of the implants (Nishimura *et al.*, 1998). This negative influence may be responsible for the significantly ($p = 0.04$) low survival rate of 61% for implants inserted into jaws treated with bone resections, compared with that of implants inserted into jaws that did not undergo bone surgery (survival rate, 83%).

It is concluded from this study that:

- after a post-irradiation interval of six months, the influence of time on implant survival is not significant;
- the survival of implants in previously irradiated tissues is 71% if irradiated with \geq 50 Gray and 84% if irradiated with < 50 Gray (significant at $p = 0.05$);
- the incidence of bone-resection surgery in the jaw where the implant is placed has a significantly ($p = 0.04$) negative influence on implant survival; and
- the most dominant variable ($p = 0.001$) influencing implant survival in irradiated bone is the implant's location in the maxilla or mandible.

ACKNOWLEDGMENTS

This study was financially supported by the Daniel den Hoed Cancer Hospital, Rotterdam, and by the Foundation for Head and Neck Tumors, Rotterdam.

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