A Clinical Evaluation of Implants in Irradiated Oral Cancer Patients
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What is This?
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-resection surgery in the jaw where the implant was installed.
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 intraoral 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

**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**

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

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**REFERENCES**


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