Histologic Evaluation of Clinically Successful Osseointegrated Implants Retrieved from Irradiated Bone: A Report of 2 Patients

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The present study described the histologic findings of 2 implants and surrounding tissues retrieved from human irradiated bone. For the treatment of a malignant tumor, 50 Gy of irradiation after implant placement and 60 Gy of irradiation before implant placement were provided for patients 1 and 2, respectively. In patient 1, the implant and surrounding tissues were removed from the frontal bone 24 months after implant placement because of the patient's death from a tumor recurrence. In patient 2, the implant and surrounding tissues were removed from a maxillectomy site 26 months after implant placement because of tumor recurrence. In each patient, new bone formation surrounding the implants was observed. The ratio of direct bone-implant contact along the threaded implant surface was 61.3% in patient 1 and 69.0% in patient 2. The ratio of the area occupied by mineralized bone in each thread was 75.8% in patient 1 and 81.2% in patient 2. These results indicate the potential of irradiated bone to achieve osseointegration of titanium implants.
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Key words: histologic study, irradiation, osseointegrated implant

Many papers have reported on histologic examinations of osseointegrated implants. Some of these reports have been concerned with failed implants in an effort to determine the cause of the failure.[1,2]

Many investigators have examined the relationship between irradiation and osseointegration. The prognoses of extraoral implants[3–5] and intraoral implants[6–9] placed in irradiated tissues have been reported. These reports suggest that clinical results of osseointegrated implants are not as good in situations in which irradiation had been previously administered, compared to nonirradiated sites, especially in the extraoral region and maxillae. These reports also suggest that the adjunctive use of hyperbaric oxygen (HBO) therapy could reduce implant loss.

However, to the authors' knowledge, there has been no histologic study of successfully osseointegrated implants retrieved from human irradiated tissue. This article reports the histologic results of 2 patients involving clinically successful implants removed from human irradiated bone.

Materials and Methods

Patients. In case 1, the patient was a 57-year-old male. Because of adenocarcinoma of the lacrimal glands, tumor resection was performed. Simultaneously, 4 implants (3.75 × 4 mm) were placed in the manner described by Tjellström.[10] Implants from the Brånemark Craniofacial System were used (Nobel Biocare AB, Göteborg, Sweden). One implant was placed in the medial part of the orbit, and the other 3 were placed in the superior, lateral, and inferior parts of the orbit (Fig 1a). However, for the 1 implant located medially, initial implant mobility was found. One month after tumor resec-

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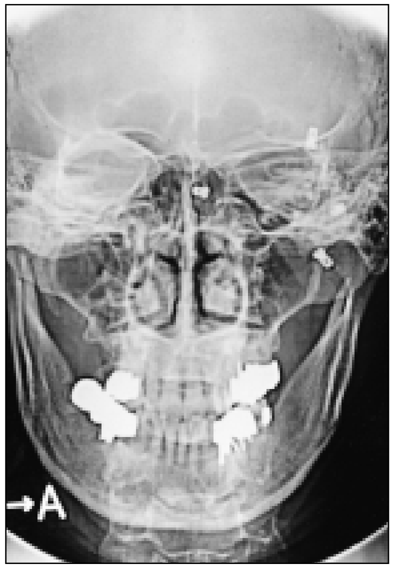


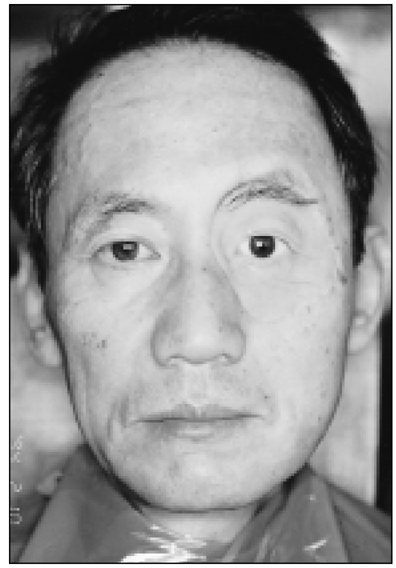


Fig 1a *(Left)* Radiograph after implant placement in patient 1.

Fig 1b *(Right)* Frontal view of patient 1 with completed orbital epithesis.

tion and implant placement, the patient received 50 Gy of irradiation (^{60}Co) at a dose rate of 2 Gy per day, because it was suspected that some cancerous material remained. All implants were included in the field of irradiation. The abutments were connected to the implants 8 months after placement. Because of extensive mobility, the medial implant was removed. The other 3 implants were exposed, and 10-mm-long abutments were connected. Then, approximately 12 months after implant placement, an orbital epithesis supported by the implants was fabricated (Fig 1b). However, 12 months after prosthesis delivery, the patient died of tumor recurrence. With the consent of the patient's family, the implant placed in the superior part of the orbit was removed, along with the surrounding tissue, for histologic study. No tumor was observed involving the implant.

In case 2, the patient was a 77-year-old female. Because of squamous cell carcinoma in the cheek region, tumor resection and postoperative 60 Gy irradiation (^{60}Co) was administered at a dose rate of 2 Gy per day. Eleven months after tumor resection, a hemimaxillectomy was performed because of tumor recurrence in the hard palate. Twenty-five months after irradiation, 5 implants were placed in the maxilla and zygomatic bone, and 5 implants were placed in the mandible. Two Brånemark System implants (Nobel Biocare AB) were placed in the residual alveolar bone (3.75 × 15 mm and 3.75 × 10 mm). The other 3 implants were placed in the frontal process, the base of the zygomatic bone, and the maxillary tuberosity (3.75 × 18 mm, 15 mm, and 15 mm) (Fig 2). All implants were included in the field of irradiation. Hyperbaric oxygen therapy was administered at 2 or 3 atm 20 times before and 10 times after implant placement. Eleven months after implant placement, abutments were connected to the implants (residual alveolar bone: 5.5 mm in length × 2; frontal process: 7 mm; zygomatic bone: 10 mm; maxillary tuberosity: 8.5 mm), and an obturator prosthesis was fabricated. Twenty-six months after implant placement, a maxillectomy, including the implant placed in the alveolar bone, was performed because of tumor recurrence. In the resected tissue, the implant and surrounding tissue were used for histologic study with the patient's consent. No tumor was observed involving the implants.

Histologic Observation. The titanium implant and surrounding tissues removed from both patients were fixed in 70% ethanol. Then the specimens were embedded in methylmethacrylate resin. The blocks were cut and ground at 10 µm using the Exakt Cutting-Grinding System (Exakt-Apparatebau, Norderstedt Hamburg, Germany) following the method described by Donath.[11] The ground sections were stained with toluidine blue. The prepared sections were analyzed using light microscopy and computer-based image analysis software (NIH Image 1.55, National Institutes of Health, Bethesda, MD). The ratio of direct bone-to-implant contact along the threaded implant surface and the ratio of the area occupied by mineralized bone in each thread were calculated.

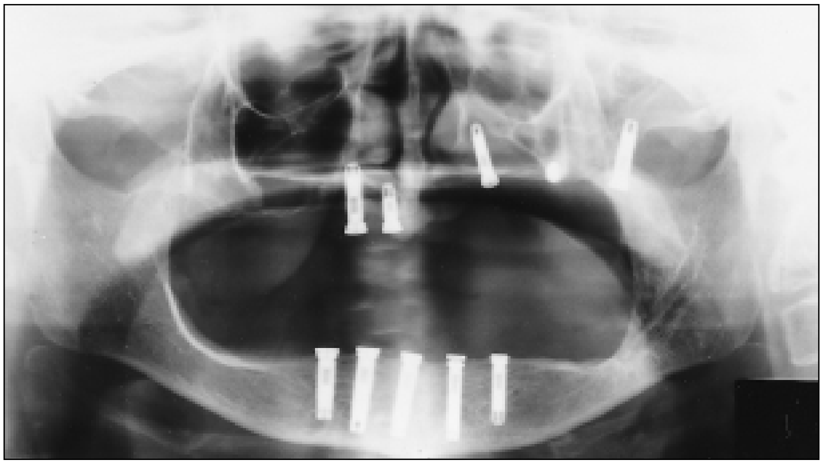


Fig 2 Panoramic radiograph after implant placement in patient 2.

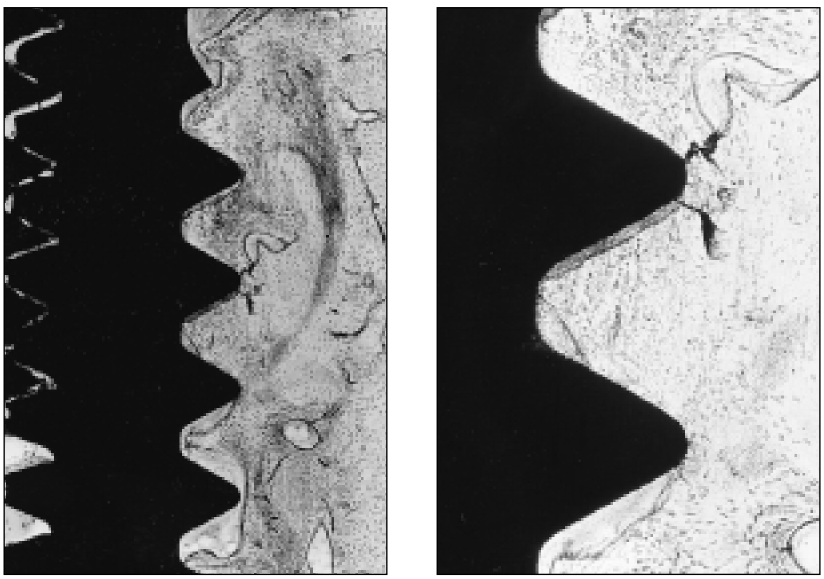


Fig 3a *(Left)* Microscopic view of the bone-implant interface in patient 1. Direct bone contact with the implant surface can be seen (original magnification ×10).

Fig 3b *(Right)* Some fibrous connective tissue can be observed between the bone and the implant (original magnification ×50).

Results

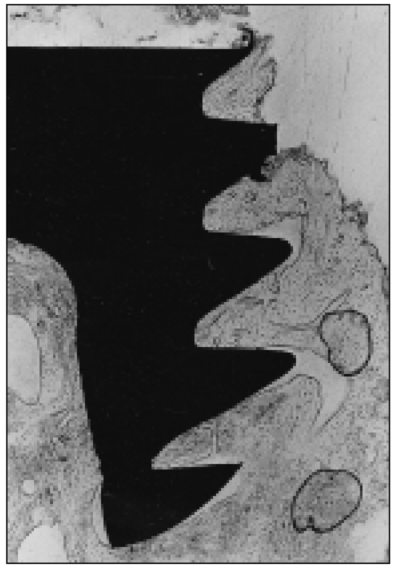
Histologic analysis showed newly formed bone surrounding the implants. The surrounding bone was arranged in a normal manner. Haversian systems were regularly found in the spaces of screw threads. In each specimen, there was some evidence of the formation of occasional patches of soft tissue between the bone and implant. In patient 1, the intervening soft tissue was found at irregular intervals at various parts of the surface of the threads (Fig 3). In patient 2, the intervening soft tissue layer was found mainly at the top of the threads (Fig 4). The ratio of direct bone-implant contact was 61.3% in patient 1 and 69.0% in patient 2. The ratio of the area occupied by mineralized bone in each thread was 75.8% in patient 1 and 81.2% in patient 2.

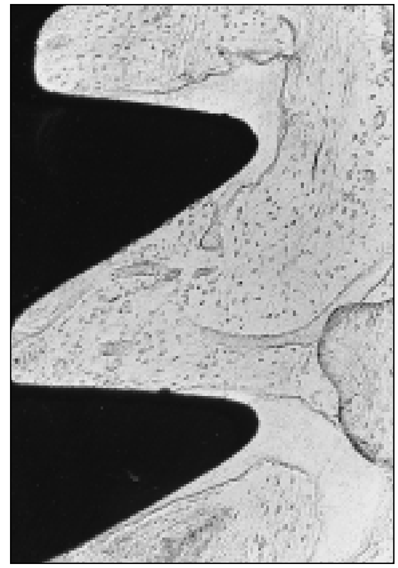
Discussion

Histologic findings of clinically successful osseointegrated implants in human beings are not plentiful in the literature.[12–16] Sutter et al[12] described the histologic investigation of an ITI hollow-cylinder implant that had been removed after a period of 3 years. Gratz et al[13] also studied a histologic section of an ITI hollow-cylinder implant removed after 4 years of functional loading. In these 2 reports, histologic sections revealed newly formed bone through the perforations in the hollow cylinder, and close adaptation of bone with the implant surface was observed. Sennerby et al[14] reported on 7 clinically stable osseointegrated implants retrieved from human jaws. The ratio of the area occupied by mineralized bone in

Fig 4a *(Left)* Microscopic view of the bone-implant interface in patient 2. Direct bone contact with the implant surface can be seen (original magnification ×10).

Fig 4b *(Right)* Fibrous connective tissue was found mainly in the top of the threads of the implant (original magnification ×50).





each thread was 79% to 95%, and the ratio of direct bone-implant contact along the threaded implant surface was 56% to 85%. However, documented histologic studies of implants placed in irradiated bone are few in number.

A combination of surgery and irradiation is a common treatment for a malignant tumor. The relationship between irradiation and the osseointegration of implants has been investigated. Amsell and Dell reported that irradiation reduces neovascularization and impairs cell reproduction.[17] The time interval from irradiation to implant surgery is an important factor in implant placement. Granström et al[5] demonstrated in a clinical study that a longer resting period following irradiation compensates for a reduction in bone healing capacity. Jacobsson et al[18] reported improvement in bone healing capacity by a factor of almost 2.5 over a 12-month period following irradiation. King et al[19] reported an initial decrease in the size of the microvasculature directly after irradiation, and partial recovery took place between 3 and 6 months later. However, Marx and Johnson[20] reported that the incidence of trauma-induced osteoradionecrosis was lowest 1 to 2 years after irradiation. The relationship between the time interval from irradiation to implant placement and the histologic findings of the surrounding tissue need further investigation.

Adjunctive use of HBO has also been recommended to improve implant survival and to counteract osteonecrosis.[20] Animal studies indicated that HBO increases the biomechanical force needed to unscrew osseointegrated implants.[21,22] Moreover, it was reported that the fibroplasia and angiogenesis induced by HBO impart a recovery and repair capacity to irradiated tissue.[20]

In this study, the intervening soft tissue was found in patient 1 at irregular intervals at various parts of the surface of the threads, and in patient 2 the intervening soft tissue layer was found mainly at the top of the threads. These findings may be the result of a higher degree of load applied to the implants in patient 2 than in patient 1. In patient 2, the stress might have been concentrated at the top of the implant threads.

Summary

The results of a histologic survey of clinically successful osseointegrated implants placed in irradiated bone have been reported. In the present study, each implant functioned satisfactorily, and histologic examination revealed that newly formed bone was found surrounding the implant. The ratios of direct bone-implant contact were not much lower than those in nonirradiated tissue as reported in the literature,[14] indicating that osseointegrated implants could be useful in treating cranio-maxillofacial defects after cancer surgery and irradiation.

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